European Food Safety Authority

Peer Review Report on Glyphosate

- Comments on the assessment report and addendum 1
- Reporting tables and commenting table on addendum 1
- Pesticides peer review meeting reports
- Evaluation tables
- Comments on the additional information assessment
- Comments on the draft EFSA conclusion and updated EFSA conclusion

October 2015

PEER REVIEW REPORT ON **GLYPHOSATE** OCTOBER 2015

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Comments on the Renewal Assessment Report on Glyphosate (AIR II)

RMS DE, CO-RMS SK

End of commenting period:
24.03.2014 (MS, EFSA), 27.03.2014 (Applicants), 11.05.2014 (Public)

Date	**Supplier**	**File**
18.03.2014	The United Kingdom	01 Glyphosate comments RAR_UK_2014-03-18.doc
21.03.2014	Spain	02 Glyphosate comments RAR_ES_2014-03-21.doc
23.03.2014	Denmark	03 Glyphosate comments RAR_DK_2014-03-23.doc
24.03.2014	Belgium	04 Glyphosate comments RAR_BE_2014-03-24.doc
24.03.2014	France	05 Glyphosate comments RAR_FR_2014-03-24.doc
24.03.2014	Latvia	06 Glyphosate comments RAR_LV_2014-03-24.doc
24.03.2014	The Netherlands	07 Glyphosate comments RAR_NL_2014-03-24.doc
24.03.2014	Norway	08 Glyphosate comments RAR_NO_2014-03-24.doc
24.03.2014	Sweden	09 Glyphosate comments RAR_SE_2014-03-24.doc
24.03.2014	Greece	10 Glyphosate comments RAR_tox_EL_2014-03-24.doc
24.03.2014	EFSA	11 Glyphosate comments RAR_EFSA_2014-03-24.doc
21.03.2014	Task Force	12 Glyphosate comments RAR_Vol 1 to 3_Task Force_2014-03-21.doc

Date	Supplier	File
27.03.2014	Task Force	13 Glyphosate comments RAR_Vol 4_Task Force_2014-03-27.doc
27.03.2014	Afrasa	14 Glyphosate comments RAR_Vol 4_AFRASA - INA_2014-03-27.doc
27.03.2014	Agria	15 Glyphosate comments RAR_Vol 4_AGRIA - AGR_2014-03-27.doc
27.03.2014	Agrichem	16 Glyphosate comments RAR_Vol 4_Agrichem - AGI_2014-03-27.doc
27.03.2014	Agro Trade	17 Glyphosate comments RAR_Vol 4_Agro Trade - AGT_2014-03-27.doc
27.03.2014	Albaugh UK	18 Glyphosate comments RAR_Vol 4_Albaugh UK - ALB_2014-03-27.doc
27.03.2014	Arysta	19 Glyphosate comments RAR_Vol 4_Arysta - AAP_2014-03-27.doc
27.03.2014	Barclay	20 Glyphosate comments RAR_Vol 4_BARCLAY - BCL_2014-03-27.doc
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27.03.2014	Cheminova	23 Glyphosate comments RAR_Vol 4_Cheminova - CHE_2014-03-27.doc
27.03.2014	DOW	24 Glyphosate comments RAR_Vol 4_DOW AgroSciences-DOW_2014-03-27.doc
27.03.2014	Excel	25 Glyphosate comments RAR_Vol 4_Excel _ XLE_2014-03-27.doc
27.03.2014	Feinchemie	26 Glyphosate comments RAR_Vol 4_Feinchemie - FCS_2014-03-27.doc
27.03.2014	Helm	27 Glyphosate comments RAR_Vol 4_Helm AG - HEL_2014-03-27.doc
27.03.2014	Monsanto	28 Glyphosate comments RAR_Vol 4_Monsanto - MOD_2014-03-27.doc
27.03.2014	Nufarm	29 Glyphosate comments RAR_Vol 4_Nufarm - NUF_2014-03-27.doc
27.03.2014	Rotam	30 Glyphosate comments RAR_Vol 4_Rotam - RTA_2014-03-27.doc
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27.03.2014	Sapec	32 Glyphosate comments RAR_Vol 4_SAPEC - SAP_2014-03-27.doc
27.03.2014	SFP	33 Glyphosate comments RAR_Vol 4_SFP - SFP_2014-03-27.doc
27.03.2014	Sinon	34 Glyphosate comments RAR_Vol 4_Sinon - SNN_2014-03-27.doc

Date	Supplier	File
27.03.2014	Syngenta	35 Glyphosate comments RAR_Vol 4_Syngenta - SYD final_2014-03-27.doc
27.03.2014	United phosphorous	36 Glyphosate comments RAR_Vol 4_United phosphorous - UPL_2014-03-27.doc
27.03.2014	Wynca	37 Glyphosate comments RAR_Vol 4_Wynca - ZXC_2014-03-27.doc
22.04.2014	PAN Europe	38 Glyphosate comments RAR_PAN Europe_2014-04-22.doc
23.04.2014	Gerhart Ryffel	39 Glyphosate comments RAR_Gerhart Ryffel_2014-04-23.doc
29.04.2014	Estonian Green Movement (EGM)	40 Glyphosate comments RAR_Estonian Green Movement_2014-04-29.doc
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07.05.2014	Katja Facius Wald und Garten	43 Glyphosate comments RAR_Katja Facius_Wald und Garten_DE_2014-05-07.doc
07.05.2014	Klara Havlova Friends of the Earth Czech Republic	44 Glyphosate comments RAR_Klara Havlova_Friends of the Earth Czech Rep_CZ_2014-05-07.doc
07.05.2014	Nick Mole PAN UK	45 Glyphosate comments RAR_Nick Mole_PAN UK_UK_2014-05-07.doc
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08.05.2014	Christian Berdot Friends of the Earth France	47 Glyphosate comments RAR_Christian Berdot_Friends of the Earth France_FR_2014-05-08.doc
08.05.2014	Melanie Eben Umweltinstitut München (UIM)	48 Glyphosate comments RAR_Melanie Eben_UIM_DE_2014-05-08.doc

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08.05.2014	Michael Braedt MU Niedersachsen	49 Glyphosate comments RAR_Michael Braedt_MU Niedersachsen_DE_part 1_2014-05-08.doc 49 Glyphosate comments RAR_Michael Braedt_MU Niedersachsen_DE_part 2_2014-05-08.pdf
08.05.2014	Peter Clausing	50 Glyphosate comments RAR_Peter Clausing_DE_2014-05-08.doc
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09.05.2014	Martin Tang Sorensen, Ole Hojberg, Hanne Damgaard Poulsen - Aarhus University (DK)	56 Glyphosate comments RAR_Martin Tang Sorensen_Ole Hojberg_Hanne Damgaard Poulsen_Aarhus University_DK_2014-05-09.pdf
09.05.2014	Mute Schimpf Friends of the Earth Europe	57 Glyphosate comments RAR_Mute Schimpf_Friends of the Earth Europe_BE_2014-05-09.doc
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10.05.2014	Ance Gobina Friends of the Earth Latvia	59 Glyphosate comments RAR_Ance Gobina_Friends of the Earth Latvia_LV_2014-05-10.doc
11.05.2014	Andreas Bauer-Panskus Testbiotech	60 Glyphosate comments RAR_Andreas Bauer-Panskus_Testbiotech_DE_2014-05-11.doc
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11.05.2014	Tony Tweedale RISK Consultancy	63 Glyphosate comments RAR_Tony Tweedale_RISK Consultancy_BE_2014-05-11.doc
12.05.2014	Jeroen Walstra Milieudefensie	64 Glyphosate comments RAR_Jeroen Walstra_Milieudefensie_NL_2014-05-12.doc
12.05.2014	Malcolm Hooper	65 Glyphosate comments RAR_Malcolm Hooper_UK_2014-05-12.doc

Date	Supplier	File
12.05.2014	Nina Holland Corporate Europe Observatory	66 Glyphosate comments RAR_Nina Holland_CEO_BE_2014-05-12.doc

Comments on the addendum of September 2015 on Glyphosate (AIR II)

RMS DE, CO-RMS SK

End of commenting period:
16 Sept 2015 (MS, EFSA)

Date	Supplier	File
16.09.2015	Belgium	67 Glyphosate addendum Sept 2015 comments BE_2015-09-16.doc
16.09.2015	Denmark	68 Glyphosate addendum Sept 2015 comments DK_2015-09-16.doc
16.09.2015	EFSA	69 Glyphosate addendum Sept 2015 comments EFSA_2015-09-16.doc
16.09.2015	Spain	70 Glyphosate addendum Sept 2015 comments ES_2015-09-16.doc
16.09.2015	France	71 Glyphosate addendum Sept 2015 comments FR_2015-09-16.doc
16.09.2015	Norway	72 Glyphosate addendum Sept 2015 comments NO_2015-09-16.doc
16.09.2015	Sweden	73 Glyphosate addendum Sept 2015 comments SE_2015-09-16.doc
16.09.2015	United Kingdom	74 Glyphosate addendum Sept 2015 comments UK_LMC_epi_2015-09-16.doc
16.09.2015	United Kingdom	75 Glyphosate addendum Sept 2015 comments UK_SB_ID_2015-09-16.doc
17.09.2015	Ireland	76 Glyphosate addendum Sept 2015 comments IRL_2015-09-17.doc

1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)

Identity (B.1, Annex C)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Monsanto source, Vol 4 C.1.1.1: Manufacture of the active substance	The UK has considered batch data for these sources and it is apparent that the sources are manufactured as slurries/wet cakes. This is not made that clear in the manufacturing details provided. Furthermore, the batch data have been generated on the wet cake but the results from this analysis and a specification for the material that is actually manufactured has not been given. Only the batch data for the dry material and its specification are given. .	It is important to have a specification of the material that is actually manufactured and hence all subsequent batches must comply with. It would appear that there is no specification for what is actually manufactured. The specification provided would appear to be for a dried material that is never actually produced. It is important to know how the batch analysis data have been generated, and how the specification has been established and if MS agree with this approach. This will have an impact on other actives and also has an impact on the assessment of the tox/ecotox batches and whether they support the TGAI as manufactured. For TK (which would be applicable to a wet cake/slurry) it would be appropriate to have a specification of the material manufactured and then determine a dry weight specification by calculation for the minimum purity in the implementing regulation and for performing technical equivalence. However, for transparency the data should all be outlined clearly giving MS the opportunity to see what was analyzed, the results for this analysis, the conversion of the batch data to a dry weight basis, and how the specification has been derived. Given that it would appear the RAR has not been transparent on how the TGAI is manufactured, what has been analysed and how the specification has been derived then MS have not been given the opportunity to comment on this and hence an agreed approach established. The RAR should be updated to reflect these issues and MS should have the

Identity (B.1, Annex C)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
			opportunity to discuss them.
	Monsanto source, Vol 4 C.1.2.3: Analytical profile of batches	The batches have been manufactured in a short interval of time and no assessment as to whether the batches are representative of the manufacturing process has been made. It is also noted that in some cases the time period from manufacture to analysis appears to be significant. In particular for the [redacted] plant the batches were manufactured from the end of Dec 2007 to the beginning of Jan 2008 with the batch analysis study being completed in 2010.	Depending on how the technical material is manufactured then taking batches in a short period of time/consecutive days may not be representative. If the time period from manufacture to analysis is significant then it raises concerns on the stability of the TGAI in terms of the actives and impurities. While there is clearly no formal data requirement to address the stability of the TGAI, the batches must be representative of the material that will be used in the PPP. If it has degraded then it is clearly not representative.
(2)	Monsanto source, Vol 4 Tables C.1.2-1 – C.1.2.5	There appears to be very little resemblance between the batch data provided and the specification for each source. The levels of the impurities are in most cases significantly below the level stated in the specification.	The specification should be based on the batch analysis data. It is noted for some of the other applicant's the specifications for their sources are more in line with the batch data. Consistency is required.
(3)	Monsanto source, Vol 4 Table C.1.2-5	The level of IDA varies from 6.23 – 8.74 mg/kg with a mean + 3 stdev of 10.56 g/kg. It is therefore unclear why the specification has been set at 8 g/kg and in the reference specification at 7 g/kg.	The batch data show that the level in the specification is exceeded and hence cannot be complied with.
(4)	Monsanto source, Vol 4 C.1.2.4: Comparison of analytical profile of batches	Given that the specification is not equivalent to the reference specification then a tier II assessment should be conducted.	The conclusions reached on the impurities are for the tox assessment to make and not as part of the tier I assessment.

Identity (B.1, Annex C)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		Some of the batch data for [redacted] show the level specified is exceeded. While the batch data for [redacted] show that this impurity is < 1 g/kg and hence does not need to be specified the applicant has specified it at 1 g/kg. It is unclear why the RMS has not accepted the level of 1 g/kg given the very generous limits allowed for the other impurities compared to the batch data.	
	Monsanto source, Vol 4 C.1.3: Analytical methods	UK: Given the batch analysis data (as determined without correction to a dry weight) has not been presented then it is difficult to assess if the validation data support the TGAI. It is not clear if the validation data relate to the material actually analysed and the results obtained or if the validation data have been correct to reflect the dry weight analysis	The RAR should be updated to include the batch analysis results obtained without the correction to a dry weight. It should be made clear what the validation data cover.
	Monsanto source, Vol 4 C.1.3: Analytical methods	As stated above a full assessment of the validation data cannot be made at this time. However, the following points are noted: • For PIA the fortification levels were 5 and 8 g/kg. The levels in some batches were below this and hence are not supported. • It is not stated what concentration the repeatability has been generated at.	Methods of analysis for the technical material are pre-registration methods that must support the results in the study and as accuracy and repeatability are concentration dependent then the data must cover the levels determined in the batches. Usually the specification is based on the batch data and hence validation data for the TGAI can usually be considered to support the batch data and specification. However, in this case the specification bears very little resemblance to the batch analysis results and hence the validation data do not fully support the underlying batch data.
	All vol 4	It is not clear how the confirmation of identity for the	

Identity (B.1, Annex C)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		impurities has been established	

Level 2. Summary of substance hazard and of product risk assessment

Effects on human and animal health (Vol 1. Level 2.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 1, Level 2.6.6 Summary of long-term toxicity and carcinogenicity	ES (MSSSI): An increase in malignant lymphoma incidence is observed in the carcinogenicity studies in mice. We consider the increased incidence of these tumours in Cr1:CD-1 strain mice ([redacted] 2009; [redacted] 1997; [redacted]., 1993) is not relevant because it is within the historical controls published for this strain. Nevertheless, to evaluate the results of the carcinogenicity study with the strain HsdOLA: MF1 (swiss albino) ([redacted] 2001), we deem necessary the historical controls of this strain.	
(2)	Vol. 1, Level 2.6.7 Summary of reproductive toxicity	ES (MSSSI): In the developmental toxicity study in rabbits ([redacted] 1991- TOX9552391), there was an increase in interventricular septal defects (4.2%), at high dose (450 mg/kg b.w./d). At this dose this effect was outside the historical controls range (0.66%) and it occurs without maternal toxicity. Therefore a classification for glyphosate due to developmental toxicity shall be considered.	

Effects on human and animal health (Vol 1. Level 2.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(3)	Vol. 1, Level 2.6.12 Toxicological end point for assessment of risk following long-term dietary exposure - ADI	ES (MSSSI): Erratum: The study code of the development toxicity study in rabbit is [redacted]. 1991, TOX9552391. Therefore, where it says `TOX9552393´ it should say `TOX9552391´.	
(4)	Vol. 1, Level 2.6.14 Toxicological end point for assessment of occupational and bystander risks - AOEL	ES (MSSSI): Erratum: The study code of the development toxicity study in rabbit is [redacted] 1991, TOX9552391. Therefore, where it says `TOX9552393´ it should say `TOX9552391´.	

List of End Points			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	List of Endpoints. Impact on Human and Animal Health). Acute toxicity (Annex IIA, point 5.2) Eye Irritation	ES (MSSSI): In the proposal for classification and labelling according to Regulation (EC) nº 1272/2008, category Eye Dam. should be included.	
(2)	List of Endpoints. Impact on Human and Animal Health). Acute toxicity (Annex IIA, point 5.2)	ES (MSSSI): It should be indicated that the values LD_{50} oral and dermal in rat, LC_{50} inhalation rat, skin irritation and skin sensitisation have been obtained for glyphosate acid and for its salts.	

B.2 - Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)

Physical and chemical properties of the active substance (B.2.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol.3, B.2.1 Physical and chemical properties of the active substance	ES (MSSSI): pH value for the active substance glyphosate and its salts (IPA, K, NH4) it's not included. We consider it should be provided.	

Comments of Denmark on the RAR on Glyphosate

1. General comment

We would like to congratulate Germany and Slovakia on the excellent and comprehensive work done.

* When mentioning page numbers of the DAR in your comments, **the page numbers should refer to the pdf-version** (not the WORD-version) of the DAR to ensure consistency among the Member States.

section 2 - Mammalian toxicology (B.6)

2. Mammalian toxicology (B.6)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca. 10 lines)	Column 3 Further explanations
(1)	B.6.4.8.	DK : Could you please include and evaluate the following study Mesnage R, Defarge N, Spiroux de Vendômois J, Séralini G-E. Major pesticides are more toxic to human cells than their declared active principles. Biomedical Research International, 2014.	
(2)	B.6.7.1	DK: Could you please include and evaluate the reference "Malhotra RC, Ghia DK, Cordato DJ, Beran RG. Glyphosatesurfactant herbicide-induced reversible encephalopathy. *J Clin Neurosci* 2010; **17:** 1472–73."	

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca. 10 lines)	Column 3 Further explanations
(3)	B.6.8.3.3.	DK: Krüger *et al.* (2013, ASB2013-11599). We support the assessment of the aforementioned study. It could be further added that the positive correlation (if indeed there is one – we agree that this has not been properly shown due to unknown origin of the reference-values) between urea and glyphosate lacks plausibility. If urea was indeed above the reference value, indicating some kind of renal dysfunction, a lower clearance of glyphosate would be the consequence and therefore *lower* urine glyphosate. Such a negative correlation was seen in relation to creatinine. In conclusion, two so divergent findings of markers of renal function suggest that these are random.	
(4)	B.6.8.3.3.	DK : Could you please include and evaluate the reference Samsel et Seneff « Glyphosate's Supression of Cytochrome P450 Enzyme and amino acid bosynthesis by the gut microbiome : Pathways to modern diseases » *Entropy* **2013**, *15*, 1416-1463; doi:10.3390/e15041416	

section 3 - Residues (B.7)

3. Residues (B.7)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca. 10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<<MS>>: <<comment>>	

* When mentioning page numbers of the DAR in your comments, **the page numbers should refer to the pdf-version** (not the WORD-version) of the DAR to ensure consistency among the Member States.

4. Environmental fate and behaviour (B.8)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	LoEP, Route of degradation (Annex IIA, point 7.1.1.1.1, mineralization after 100 days. Volume 1, lvel 1 point 2.8.1.1 Aerobic soil degradation (p 105 top).	The rate of mineralization was 16.9 – 79.6 % AR. It was achieved after 60 – 180 days according to Volume 1, level 1. But in the LOEP the period is stated as 210 – 364 days. Please clarify and list corresponding time period.	
(2)	LoEP, Monitoring data, if available (Annex IIA, point 7.4), Groundwater, 6th study (Member states of European Union plus Norway and Switzerland, 2012). Vol. B.8.6.3.1, Groundwater and surface water, page 311 (Horth 2012, BVL no 2310291) and page 329 – 335 (KIIA 7.12/06 Horth, 2012).	The literature study of Horth, 2012 summarises the results of 9908 Danish ground water samples analysed for glyphosate, mainly from the National Danish Groundwater Monitoring Program. The results seem plausible but the conclusion given: « - Denmark: Findings in Denmark appear due to rapid transfer of surface water from nearby surfaces not agricultural use, investigations still ongoing« is not correct. Please delete the above mentioned conclusion in the LoEP and in volume B.8.6.3.1. (The explanation comes from a minor study with few samples from small private digged and/or drilled wells typically in courtyards, which are not representative for the ground water and have nothing to do with the National Ground Water Monitoring Program.	The explanation comes from a minor study with few samples from small private digged and/or drilled wells typically in courtyards, which are not representative for the ground water and have nothing to do with the National Ground Water Monitoring Program. Please delete the explanation in the LoEP and in volume B.8.6.3.1. For your information the annual reports of the Danish National Groundwater Monitoring Program are available at: http://www.geus.dk/DK/publications/groundwater_monitoring/Sider/1989_2012.aspx. Unfortunately the report is in Danish but you can see the results for ground water in appendix 2 (bilag 2). The results of the Danish Pesticide Leaching Assessment Programme (PLAP) can be reached at http://pesticidvarsling.dk/publ_result/2012.html.

* When mentioning page numbers of the DAR in your comments, **the page numbers should refer to the pdf-version** (not the WORD-version) of the DAR to ensure consistency among the Member States.

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		Please delete the explanation in the LoEP and in volume B.8.6.3.1. For your information the annual reports of the Danish National Groundwater Monitoring Program are available at: http://www.geus.dk/DK/publications/groundwater_monitoring/Sider/1989_2012.aspx. Unfortunately the report is in Danish but you can see the results for ground water in appendix 2 (bilag 2). The results of the Danish Pesticide Leaching Assessment Programme (PLAP) can be reached at http://pesticidvarsling.dk/publ_result/2012.html.)	

5. Ecotoxicology (B.9)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca. 10 lines)	Column 3 Further explanations
(1)	Vol. B.9	DK : Could you please include and evaluate the reference Marjo Helander, Irma Saloniemi and Kari Saikkonen 2012. Glyphosate in northern ecosystems. Trends in Plant Science, October 2012, Vol. 17, No. 10.	

Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)

No comments

2. Mammalian toxicology (B.6)

Toxicokinetics (B.6.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
1.		BE agrees with the estimation of the oral absorption, which should be revised downwards from 30% to 20%	

Acute toxicity (B.6.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
2.		No comments	

Short-term toxicity (B.6.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
3.	Vol. 1, level2, 2.6.4.2 Rat 90d studies	BE: RMS proposed an 'overall' NOAEL for the subchronic rat studies, of 300-400 mg/kg b.w./d, but specifies a more precise value which would be 414 mg/kg b.w./d, which compares with the LOAEL of 569 mg/kg b.w./d. BE would propose to choose the NOAEL of the Perry study (1991), i.e. 300 mg/kg b.w./d, which seems more appropriate in order to maintain a sufficient margin of safety. This compares well with	

Short-term toxicity (B.6.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		the overall dog NOAEL at the same dose-level. It is acknowledged that this does not impact on the establishment of a short-term RfD. The LoEP should then be amended accordingly.	
4.	Vol 3, B.6.3, 90d dog (Prakash, 1999)	BE: has some reservations as regards the determination of the study NOAEL at the top-dose, taking into account interim and/or final significant modifications in clotting time, GGT activity, and total bilirubin rise at the top-dose level. The worrying fact is that all these modifications are dose-dependent. It was questioned whether 2000 ppm (52.8 mkd) would not be a more appropriate (conservative) NOAEL. It is recognised that exact the same parameters were unaffected in other dog studies, but on the other hand adverse hepatic effects were observed.	
5.	Vol. 1, level2, 2.6.4.2 Dog 90d-1yr studies	BE: agrees with the proposed overall NOAEL, taking into account all dog studies. The NOAEL of 300 mkd is sufficiently protective, taking into account the 2/8 deaths in the Gaou (2007) study at the top-dose of 1000 mkd.	
6.	LoEP	BE: in the critical short-term effects, the consistent increase of alkaline phosphatase could be explicitly mentioned when reference is made of ‘clinical chemistry findings’.	

Section 2 - Mammalian toxicology (B.6)

Genotoxicity (B.6.4)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
7.	B.6.4.5 Genotoxicity – in-vivo MN (Durward, 2006) p357	BE: the explanation for the equivocally positive response at 24h sampling time is plausible, given the HCD, and also the negative finding at the 48h sampling time. Conclusion of the RMS supported.	
8.	Genotoxicity – in-vivo MN (Zoriki Hosomi, 2007) p359	BE: finds it is surprising that the dose of 30 mg/kg would constitute the highest tolerable one. However, positive effects were observed and the sole criticism of low dose is not sufficient to disregard the study *per se*. More detailed information should be provided with the range-finder. HCD are cited but not represented. Are there batch details from the Helm source possibly explaining a casual pve result?	
9.	Genotoxicity – in-vivo MN (Costa, 2008) p361	BE: again, the low dose of 30 mg/kg is probably not representing the highest tolerable one, but this is on itself an insufficient reason to declare the GLP-study unreliable. Positive effects were observed at the top-dose of Glyphosate. More detailed information should be provided with the range-finder. HCD are not represented. Are there batch details from the HAG source possibly explaining a casual pve result? In addition, contrarily to the text, CPA positive control displays a 0 value in the table B.4-16.	
10.	Genotoxicity- Vol 1	BE: agreement with DE that overall, glyphosate is devoid of genotoxic proprieties.	

Section 2 - Mammalian toxicology (B.6)

Long-term toxicity and carcinogenicity (B.6.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
11.	Rat carcinogenicity studies (Vol 1)	BE: agreement with the approach of the RMS to establish an overall NOAEL of 100 mg/kg b.w./d, for the totality of 9 rat carcinogenesis studies.	
12.	Mouse carcinogenicity studies (Vol 1)	BE: agreement with the approach of the RMS to establish an overall NOAEL of 150 mg/kg b.w./d, for the totality of 7 mouse carcinogenesis studies.	

Reproductive toxicity (B.6.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
13.	Vol 3, B.6.6.1 Two-generation studies (Dhinsa, 2007)	BE: agrees with the RMS to establish the parental, reproductive and offspring toxicity NOAEL at 5000 ppm. The 23% reduction of spermatids and +3d preputial separation delay in F_1 should not be disregarded.	
14.	Vol 3, B.6.6.1 Two-generation studies (Takahashi, 1997)	BE: it is not entirely clear why the 20% decrease of fertility index in the F_1 was considered non-treatment-related (the next-lower dose showed a decrease too, thus there was a trend). The reason to disregard this finding (a re-meeting with untreated males restored a normal fertility index) is not not considered valid (the test methods foresees re-mating with teated males of the same dose-group). BE would take the top-dose effect into account to establish the fertility NOAEL for this study. Agreed	

Reproductive toxicity (B.6.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		that the effect was not observed in the other multigeneration studies. Are there historical control data?	
15.	Vol 1, 2.6.7, LoEP evaluation reproductive toxicity	BE: agrees with the establishment of the overall parental and offspring NOAEL= 197 mkd and the reproductive NOAEL= 351 mkd, taking into account all one- and two-generational studies.	
16.	Vol 1, 2.6.7.2.2, LoEP evaluation developmental toxicity	BE: agreement with the approach of the RMS to establish an overall rabbit maternal and developmental NOAEL of 50 mg/kg b.w./d.	

Neurotoxicity (B.6.7)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
17.		no comments	

Other toxicological studies & Medical data (B.6.8-B.6.9)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
18.	B.6.5.3 Published data on carcinogenicity - Epidemiological studies	BE: The overall lack af association between potential glyphosate exposure and specific cancer incidence is considered sufficiently demonstrated in the open literature. A further recent systematic review	

Other toxicological studies & Medical data (B.6.8-B.6.9)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		on this topic (*Mink et al, Regulat Toxicol Pharmacol, 63, 440-452, 2012*) further supports this evaluation.	
19.	B.6.5.3 Published data on carcinogenicity - animal studies	BE: supports the RMS evaluation on the existing open literature. The Seralini study is pointless, and moreover withdrawn. The skin tumour promoting study of George et al. indicates a certain activity of the product, where it is unknown what the influence is of the coformulant. Given te known toxicity profile of Glyphosate itself, it seems highly unlikely that the latter would have any tumour promoting activity. The study is not entirely conclusive, as no proper negative control is present, is not in favour of the maintenance of the coformulant !	
20.	B.6.6.12 Published data on endocrine perturbation	BE: concurs with the RMS evaluation of all published papers on alleged *in-vivo* or *in-vitro* endocrine effects of glyphosate.	

Summary of mammalian toxicology and setting ADI, AOEL, ARfD (B.6.10)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
21.		RMS agrees with the establishment oft he ADI and the AOEL.	

Section 2 - Mammalian toxicology (B.6)

Toxicity of the product(s) (B.6.11)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
22.	Vol 3, B.6.11- Vol 1, 2.6.15	BE: noted that MON52276 is the representative formulation not containing any ethoxylated tallowamines, which have been proven of higher toxicity than the a.s. itself. However, as the inhalative AOEL of another frequently used surfactant [redacted] is 0.016 mg/kg b.w./d. Has it been demonstrated that a safe use exists for products with this coformulant? Is a restriction necessary?	
23.	Vol 3, B.6.11	BE: it may indeed be expected that the ban of irritant and toxic surfactants like POEA's will reduce the risk of severe health effects and death following intentional or accidental ingestion of glyphosate products containing them. A case should be made at the EU-, and not only at the zonal level to reach such a restriction.	

Dermal absorption (B.6.12)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
24.		no comments	

Section 2 - Mammalian toxicology (B.6)

Toxicity of non-active substances (B.6.13)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
25.	Vol 3, B.6.13	BE: it is obvious that the consumer reference doses from the common POEA coformulant are estimated at a lower level than those of Glyphosate itself. The toxic effects are generally also much more severe. On the basis of this evaluation, a safe use of products containing this coformulant is uncertain. In the estimation of the AOEL, it is assumed that the oral absorption is 100%, which is not supported by facts. The comparison of critical endpoints in table B.6.13-2 for reprotoxicity are not in line (too high) with those listed in the LoEP.	

Exposure data (B.6.14)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
26.		no comments	

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
27.		BE: the clear and transparent evaluation of the vast amount of studies and public literature is highly	

Section 2 - Mammalian toxicology (B.6)

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		appreciated.	

3. Residues (B.7)

No comments

Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)

Identity (B.1, Annex C)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 4 General information	FR: In the general Volume 4, a comparison table with the current proposed specifications of each notifier of the Task Force and reference specification should be presented for better clarity. Moreover a general assessment indicating all the origins considered as acceptable will be very usefull.	
(2)	Vol. 4 General information	FR: This volume is not very clear, FR considers that if no toxicological data are available for all notifiers, this should be mentioned in each vol 4.	
(3)	Vol 4 General comment for all Vol 4	FR: It should be reported the number of concentration levels for each linearity study. Moreover, a LOQ should be reported for each analytical method for the determination of impurity, please RMS adds these data when missing. The reference specifications should be indicated for the peer review they can be deleted in vol.4 provided to the applicants but should be available in the Vol.4 provided to the member states for an easier peer review.	
(4)	Vol 4 General comment for all Vol 4	FR: It should be specify relevant impurities for technical glyphosate. An analytical method for the determination of relevant impurities should be provided.	
(5)	Vol 4 General comment for all Vol 4 – Method for relevant impurities	FR: How do you set the LOQ for relevant impurities? FR considers that the LOQ should be set at the lowest validated concentration.	

Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

Identity (B.1, Annex C)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(6)	Vol. 4 Table C.1.2-1 Excel Crop	FR agrees that a clarification is needed by the applicant concerning the fact that the account of the three batches is lower than 980g/kg. Additionally, based on the 5-batch analysis, the minimum purity should be increased or QC data should be provided to justify this value.	
(7)	Vol.4 C.1.2.4 Excel Crop	FR: If the reference specifications from the initial DAR are not covered by tox and ecotox batches, it cannot be concluded that this origin is equivalent to the reference origin. New evaluation should be performed to set new reference specifications based on toxicological and ecotoxicological studies.	
(8)	Vol. 4 C.1.3.1 Determination of Bis PMA Excel Crop	FR: The identity of Bis PMA should be confirmed.	
(9)	Vol. 4 C.1.3.1 Determination of NNG Excel Crop	FR agrees with the conclusion of RMS concerning the LOQ.	
(10)	Vol. 4 Feinchemie Schweda C.1.1.1	FR: Please RMS clarify the part: “in October 2012, the ..... declared that the licence for manufacturing glyphosate has been transferred to .....”. If the manufacturer is the one reported at the end of this part, the first reported should be removed for better clarity.	
(11)	Vol. 4 C.1.2.2	FR: The identity of impurity 11 ([redacted]) should be reported.	

Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

Identity (B.1, Annex C)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	Feinchemie Schwebda		
(12)	Vol 4 Table C.1.2-1 Feinchemie Schweda	FR: Based on the batch analysis, minimum purity should be increased or QC data should be provided to justify the proposed value.	
(13)	Vol. 4 C.1.3 Determination of formaldehyde Feinchemie Schwebda	FR: The identity of the impurity should be confirmed.	
(14)	Vol.4 Tables C.1.2-2 and C.1.2-3 Dow Agro Sciences	FR: Based on the 5-batch analysis and QC data, the certified values proposed for impurities 14 and 1 should be decreased.	
(15)	Vol. 4 C.1.3.1 table C.1.2-1, C.1.2-2, C.1.2-3, C.1.2-4 Dow agro Sciences	FR: When the content of impurities in the analytical profile of batches is below the LOQ, please RMS indicates <LOQ for better clarity.	
(16)	Vol. 4 C.1.3.1 (Nelson (2008) Dow agro Sciences	FR: The identity of each impurity should be confirmed.	
(17)	Vol. 4 C.1.3.1 Dow agro Sciences	FR: As the content of [redacted] is >0.1% (table C.1.2-2 and table C.1.2-4), an analytical method for the determination of [redacted] in the technical active substance should be provided.	
(18)	Vol.4 Table C.1.2-1	FR: Based on the 5-batch analysis, minimum purity should be increased and specification for all	

Identity (B.1, Annex C)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	Bros Spolka	impurities should be decreased.	
(19)	Vol. 4 C.1.2.2 Albaugh	FR: There is a typo. Impurity 5 is [redacted] not [redacted]	
(20)	Vol.4 C.1.2.4 Albaugh	FR: If the reference specifications from the initial DAR are not covered by tox and ecotox batches, it cannot be concluded that this origin is equivalent to the reference origin. New evaluation should be performed to set new reference specifications based on toxicological and ecotoxicological studies.	
(21)	Vol. 4 C.1.3-1 Albaugh	FR: The identity of formaldehyde should be confirmed.	
(22)	Vol.4 C.1.1.1 Agrichem	FR's point of view is that only the plant location used for the step II of process should be considered. [redacted] should be considered as a starting material.	
(23)	Vol.4 Table C.1.2-1 Industrias Afrasa	FR: Based on the batch analysis, the minimum purity should be increased and the specification proposed for impurity 1 should be decreased to be in accordance with the thumb rule.	
(24)	Vol.4 C.1.2.4 Industrias Afrasa	FR: If the reference specifications from the initial DAR are not covered by tox and ecotox batches, it cannot be concluded that this origin is equivalent to the reference origin. New evaluation should be performed to set new reference specifications based on toxicological and ecotoxicological studies.	
(25)	Vol. 4 C.1.3.1	FR: The identity of each impurity should be confirmed.	

Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

Identity (B.1, Annex C)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	Industrias Afrasa		
(26)	Vol.4 Table C.1.2-1 Agria	FR: Based on the batch analysis, the minimum purity should be increased. Moreover, as impurity 20 [redacted]) is a relevant impurity, a specification should be set even if this impurity is not found in the batches.	
(27)	Vol.4 C.1.2.4 Agria	FR: If the reference specifications from the initial DAR are not covered by tox and eco tox evaluations, it cannot be concluded that this origin is equivalent to the reference specifications. A new evaluation should be performed to set new reference specifications covered by the tox and eco tox evaluation.	
(28)	Vol.4 C.1.2.4 Agro Trade	FR: If the reference specifications from the initial DAR are not covered by tox and eco tox evaluations, it cannot be concluded that this origin is equivalent to the reference specifications. A new evaluation should be performed to set new reference specifications covered by the tox and eco tox evaluation.	
(29)	Vol. 4 C.1.3.1 Agro trade	FR: The identity of impurities [redacted] and formaldehyde should be confirmed.	
(30)	Vol. 4 C.1.1.1 Barclay chemicals	FR: The third source of active substance (manufacturer Monsonto) should be clarified, it should be indicated if Barclay has access to all origins from Monsanto or only one, and in this case clarify which.	
(31)	Vol. 4 C.1.1.2	FR: Data concerning the purity of starting materials should be reported in the table C.1.1-2.	

Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

Identity (B.1, Annex C)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	2.Barclay chemical Manufacturing Barclay chemicals		
(32)	Vol.4 C.1.2.4 Barclay chemicals	FR: If the reference specifications from the initial DAR are not covered by tox and eco tox evaluations, it cannot be concluded that this origin is equivalent to the reference specifications. A new evaluation should be performed to set new reference specifications covered by the tox and eco tox evaluation.	
(33)	Vol. 4 C.1.3.1 Jiangsu source Barclay chemicals	FR: The identity of impurity [redacted] and [redacted] should be confirmed.	
(34)	Vol. 4 C.1.3.1 Barclay source Barclay chemicals	FR: In the table C.1.2-2, content of [redacted] is below <0.2ppm (not 0.1ppm).	
(35)	Vol. 4 C.1.3.1 Barclay source Barclay chemicals	FR: For better clarity, the LOQ of formaldehyde should be indicate in g/kg in order to compare the LOQ with the content of formaldehyde found in tables analytical profile of batches.	
(36)	Vol. 4 C.1.3.1 Barclay source Barclay chemicals	FR: The identity of each impurity should be confirmed.	
(37)	Vol.4 Table C.1.2-1	FR: Based on the 5-batch analysis, the specification for impurity 5 should be decreased.	

Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

Identity (B.1, Annex C)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	Cheminova		
(38)	Vol.4 Table C.1.2-3 Cheminova	FR: The date of manufacture of batches from the three analyses should be indicated.	
(39)	Vol.4 Table C.1.2.4 Cheminova	FR: If the reference specifications from the initial DAR are not covered by tox and eco tox evaluations, it cannot be concluded that this origin is equivalent to the reference specifications. A new evaluation should be performed to set new reference specifications covered by the tox and eco tox evaluation.	
(40)	Vol. 4 C.1.3.1 Table C.1.2-3 Cheminova	FR: The LOQ of [redacted] is 1g/kg. However, in the table C.1.2-3 (batch 0903-0605), the content of [redacted] is 0.83 (< LOQ). Please RMS clarifies.	
(41)	Vol.4 Table C.1.2-1 Arysta	FR: Based on the five batches analysis, the minimum purity should be increased and specifications for impurities 2 and 6 should be removed as these impurities have never been detected at content higher than 0.5 g/kg and they are not relevant.	
(42)	Vol.4 Table C.1.2-2 Arysta life Science	FR: Based on the five batches analysis, the specification for impurity 2 should be removed as this impurity has never been detected at content higher than 0.19 g/kg and it is not relevant.	
(43)	Vol.4 C.1.2.4 Arysta life Science	FR: If the reference specifications from the initial DAR are not covered by tox and eco tox evaluations, it cannot be concluded that this origin is equivalent to the reference specifications. A new evaluation	

Identity (B.1, Annex C)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		should be performed to set new reference specifications covered by the tox and eco tox evaluation.	
(44)	Vol. 4 C.1.3.1 Arysta life Science	FR: Two methods are available for the determination of impurities ([redacted]), specify the method used for the determination of content in table C.1.2-1 and C.1.2-2	
(45)	Vol. 4 C.1.3.1 table C.1.2-2 Arysta life Science	FR: As the LOQ for the determination of [redacted] is 0.5ppm, it is perferable indicate <LOQ (0.5ppm).	
(46)	Vol. 4 C.1.3.1 table C.1.2-2 Arysta life Science	FR: The LOQ of formaldehyde should be expressed in g/kg in order to compare the LOQ with the content of formaldehyde found in tables C.1.2-1 and table C.1.2-2.	
(47)	Vol. 4 C.1.3.1 Arysta life Science	FR: The identity of each impurity should be confirmed.	
(48)	Vol.4 Table C.1.2-1 Wynca	FR: Based on the 5 batches analyzed, the minimum purity should be increased, specification for formaldehyde should be decreased and specification for [redacted] should be removed as its maximum content is lower than 0.5 g/kg Please RMS confirms that no evaluation can be performed for the variants.	

Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

Identity (B.1, Annex C)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(49)	Vol.4 Table C.1.2-1 United phosphorus	FR: Base on the 5-batch analysis, minimum purity should be increased and specification for impurities [redacted] should be decreased or QC data should be provided to justify these values.	
(50)	Vol. 4 C.1.3.1 United Phosphorus	FR: The identity of each impurity should be confirmed.	
(51)	Vol. 4 C.1.1.1 Syngenta	FR: The second source of active substance (manufacturer [redacted] should be clarified, it should be indicated if Syngenta has access to all origins [redacted], and in this case clarify which.	
(52)	Vol. 4 C.1.1.2 Syngenta	FR: Please MS clarify how two different processes are used in the same location. It should be indicated if production is performed simultaneously using [redacted] or not.	
(53)	Vol.4 Table C.1.2-1 Syngenta	FR: Based on the 5-batches and QC data, the minimum purity should be increased. As different specifications were proposed for each process, the minimum purity should not necessary be similar for both processes.	
(54)	Vol. 4 Table C1.2-1 Syngenta	FR: Information on the date of production of the batches should be reported.	
(55)	Vol.4 Table C.1.2-2 Syngenta	FR: Based on the 5 batches, specifications for impurities 21 and 22 should be removed and specifications for impurities 2 and 2 should be decreased or QC data should be provided	

Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

Identity (B.1, Annex C)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(56)	Vol. 4 C.1.2.4 Syngenta	FR: According to the applicant, the impurity 14 is no longer formed at significant levels (<1g/kg). So the profile of batches (table C.1.2-2) is not in accordance with the manufacturing process. A new five batches analysis should be provided.	
(57)	Vol. 4 C.1.3.1 Determination of NNG and formaldehyde Syngenta	FR: Validation data for the determination of [redacted] and formaldehyde in the glyphosate technical should be reported.	
(58)	Vol. 4 C.1.1.2 Table C.1.1-1 Société Financière de Pontarlier	FR: Information concerning the CAS Number of each starting material should be reported.	
(59)	Vol. 4 C.1.3.1 Determination of formaldehyde and NNG Société Financière de Pontarlier	FR: The identity of impurities [redacted] [redacted] and formaldehyde should be confirmed.	
(60)	Vol. 4 C.1.1.1 Manufacturing process Sinon	FR: More details concerning each step of the manufacturing process should be reported.	
(61)	Vol. 4 C.1.1.1 Table C.1.2.3-1	FR: As the profil of batch has more than 10 years, a new profil of batches should be provided.	

Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

Identity (B.1, Annex C)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	Manufacturing process Sinon		
(62)	Vol.4 Table C.1.2.3-1 Sinon	FR: The specifications are not in accordance with the batch analysis, they should be modified to be in accordance with the thumb rule or QC data should be provided. This DRAR is performed for a total re evaluation of the active substance.	
(63)	Vol.4 C.1.1.1 SAPEC	FR: it should be noted that the first plant location has been evaluated according to the article 38 and equivalence report available on CIRCA.	
(64)	Vol.4 Table C.1.2.3-1 SAPEC	FR: Based on the 5-bath analysis, minimum purity should be increased and specification for impurity [redacted] should be decreased or QC data should be provided	
(65)	Vol.4 Table C.1.2.3-2 SAPEC	FR: Based on the 5-bath analysis, specification for impurity [redacted] should be decreased or QC data should be provided	
(66)	Vol. 4 C.1.3.1 Sapec	FR: The identity of each impurity should be confirmed.	
(67)	Vol. 4 Table C.1.2-1 Sabero	FR: Based on the 5-batch analysis, the minimum purity should be increased or QC data should be provided. It should be clarified if some of the impurities are considered as relevant, in the other case, no specification should be proposed below 1 g/kg.	
(68)	Vol.4 C.1.2.4	FR: If the reference specifications from the initial DAR are not covered by tox and eco tox evaluations, it cannot be concluded that this origin is equivalent	

Identity (B.1, Annex C)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	Sabero	to the reference specifications. A new evaluation should be performed to set new reference specifications covered by the tox and eco tox evaluation.	
(69)	Vol. 4 C.1.3.1 Sabero	FR: The identity of each impurity should be confirmed.	
(70)	Vol.4 Table C.1.2-1 Rotam	FR: No specification should be set lower than 1 g/kg for not relevant impurities.	
(71)	Vol.4 C.1.2.3.1 Rotam	FR: If the reference specifications from the initial DAR are not covered by tox and eco tox evaluations, it cannot be concluded that this origin is equivalent to the reference specifications. A new evaluation should be performed to set new reference specifications covered by the tox and eco tox evaluation.	
(72)	Vol. 4 C.1.3.1 Rotam	FR: The identity of impurities 1, 3, 21, 31 and 33 should be confirmed.	
(73)	Vol.4 Tables C.1.2-1, C.1.2-2, C.1.2-3, C.1.2-4 and C.1.2-5 Monsanto	FR: Specifications for impurities are not in accordance with the batch analyses, they should be revised or QC data should be provided.	
(74)	Vol. 4 C.1.2.4 Monsanto	FR: Proposed specification is not covered by Tox profile. Consequently, FR disagrees with the proposed specifications.	

Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

Identity (B.1, Annex C)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(75)	Vol. 4 C.1.3.1 Monsanto	FR: The identity of each impurity should be confirmed.	
(76)	Vol.4 C.1.1.1 Nufarm	FR: The address of the manufacturer should be added.	
(77)	Vol.4 Table C.1.2-1 Nufarm	FR: If the reference specifications from the initial DAR are not covered by tox and eco tox evaluations, it cannot be concluded that this origin is equivalent to the reference specifications. A new evaluation should be performed to set new reference specifications covered by the tox and eco tox evaluation.	
(78)	Vol.4 Table C.1.2.3 Helm	FR: Based on the 5-batch analysis, the specification for impurity 3 should be decreased or QC data should be provided.	
(79)	Vol.4 Table C.1.2.4 Helm	FR: Based on the 5-batch analysis, the specification for impurity 1 should be decreased or QC data should be provided.	
(80)	Vol.4 Table C.1.2.7 Helm	FR: Based on the 5-batch analysis, the specification for impurity 4 should be decreased or QC data should be provided.	
(81)	Vol.4 Table C.1.3-9 Helm source 3	FR: Without recovery data, the analytical method cannot be considered as validated, consequently contents of impurities 1, 3, 5 and 9 found in the 5-batch cannot be considered a new batch analysis is required for this plant location using fully validated analytical methods.	

Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

Identity (B.1, Annex C)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(82)	Vol 1, 1.2.1 Level 1	FR: There are 24 notifiers for the active substance glyphosate. However, in point 1.2.1, an applicant Pinus TKI is reported. Please RMS clarify.	

Physical and chemical properties of the active substance (B.2.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(83)	Vol 3 B.2.1.6 solubility in water	FR: Indicate the method in which the test of solubility in water was performed for K salt.	
(84)	Vol 3 B.2.1.6, B.2.1.7 solubility in water and in organic solvents	FR: It is more appropriate to use column elution method when the solubility is $<10^2$g/l.	
(85)	Vol 3 B.2.1.15 Oxydising properties	FR: A statement has been provided to justify that K salt has no oxidising properties. More details concerning the statement should be reported.	

Physical, chemical and technical properties of the formulation (B.2.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(86)	Vol. 3 B.2.2.5.1 Kinematic viscosity	FR: the method in which the test of kinematic viscosity was performed should be reported.	

Physical, chemical and technical properties of the formulation (B.2.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(87)	Vol. 3 B.2.2.6.1 Relative density	FR: Relative density has no unity. Please RMS indicates relative density of the formulation.	
(88)	Vol 3 B .2.2.7.1 Stability after storage for 14 days at 54°C.	FR: Please RMS indicates methods of the different test reported.	
(89)	Vol 3 B .2.2.7.1 and B.2.2.7.5	FR: Please RMS indicate if the method for the determination of the active substance in the formulation is validated or not.	
(90)	Vol 3 B.2.2.7.5	FR: The method CIPAC 284/SL/(M)/3 (HPLC) is used for the determination of active substance in the formulation . However, according to the section B.5.1.3, the method is validated in the formulation MON 78043, MON 78044 and MON 2139 (not in the representative formulation MON 52276). Please RMS justify.	
(91)	Vol 3 B.2.2.8.2	FR: In the persistent foaming test (CIPAC MT 47), there is 73ml of foam (after 1min) indicating that the formulation is a foaming product. While in the persistent foaming test (CIPAC MT 47.2), there is 0ml of foam (after 1min) indicating that the formulation is not a foaming product. Please RMS clarify.	

Methods of analysis (B.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(92)	Vol. 3 B.5	FR: It should be specify the number of concentration level tested for linearity.	
(93)	Vol.3 B.5.1.2 B.5.1.4	FR: The confirmation of identity of relevant impurities should be reported.	
(94)	Vol.3 B.5.1.2	FR: The LOQ of NNG is 0.125ppm. However, the lowest validated concentration for formaldehyde is 0.50ppm. How do you set the LOQ? Please RMS clarify.	
(95)	Vol.3 B.5.1.2	FR: The LOQ of formaldehyde is 20ppm. However, the lowest validated concentration for formaldehyde is 52.96ppm. How do you set the LOQ? Please RMS clarify.	
(96)	Vol.3 B.5.1.3	FR: The composition of formulations MON 78043, MON 78044 and MON 2139 and MON 52276 should be provided. The specificity of the method CIPAC 284/SL/(M)/3 (HPLC) should be demonstrated in the formulation MON 52276.	
(97)	Vol.3 B.5.1.4	FR: The LOQ of formaldehyde is 20ppm. However, the lowest validated concentration for formaldehyde is 155.508ppm. How do you set the LOQ? Please RMS clarify.	
(98)	Vol.3 B.5.1.4	FR: Determination of [redacted]e As no validation data is reported, the method is not validated.	

Methods of analysis (B.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(99)	Vol. 3 B.5.2 B.5.3	FR: According to Sanco 825/00 rev 8.1, when an analytical method uses a derivitisation step, the efficiency and precision of the derivitisation step should be demonstrated. Please RMS justify.	
(100)	Vol. 3 B.5.2.1.1.1 B.5.2.1.1.2	FR: The method 1 and the ILV used internal standards radio labelled. So, a certificate ensuring that the Notifier can supply internal standard radio labelled in case of control should be provided and mentioned in the text. In the other case, the method 1 is not taking into account for monitoring purposes.	
(101)	Vol. 3 B.5.2.1.1.2	FR: The ILV method is validated on high acid content (grape) and high oil content (soybean seed) commodities. So, the ILV of the method 1 is acceptable only for soybean seed (no data validation in grape in method 1).	
(102)	Vol. 3 B.5.2.1.1.3 B.5.2.1.1.4	FR: The method 2 and its ILV have the same test facility. Please RMS clarify. If they are the same test facility, the method reported in B.5.2.1.1.4 cannot be accepted as ILV of method 2.	
(103)	Vol. 3 B.2.2.1.1	FR: The method 1 and the ILV used internal standards radio labelled. So, a certificate ensuring that the Notifier can supply internal standard radio labelled in case of control should be provided and mentioned in the text. In the other case, the method 1 is not taking into account for monitoring purposes	

Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

Methods of analysis (B.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(104)	Vol. 3 B.2.2.1.4 method 3	FR: The method 3 used internal standards radio labelled. So, a certificate ensuring that the Notifier can supply internal standard radio labelled in case of control should be provided and mentioned in the text. In the other case, the method 3 is not taking into account for monitoring purposes	
(105)	Vol. 3 B.5.3.1.1 method 1	FR: The method 1 used internal standards radio labelled. So, a certificate ensuring that the Notifier can supply internal standard radio labelled in case of control should be provided and mentioned in the text. In the other case, the method 1 is not taking into account for monitoring purposes	
(106)	Vol. 3 B.5.3.2	FR: The method (Knoch E 2010) used internal standards radio labelled. So, a certificate ensuring that the Notifier can supply internal standard radio labelled in case of control should be provided and mentioned in the text. In the other case, the method is not taking into account for monitoring purposes.	
(107)	Vol. 3 B.5.3.2	FR: As validation data has been provided for two transitions for glyphosate and [redacted], the method (Knoch E 2010) and its ILV (Gesscke.S 2011) are considered as highly specific.	

Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

Methods of analysis (B.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(108)	Vol. 3 B.5.3.3	FR: The method (Schneider V (2001)) used an internal standard radio labelled. So, a certificate ensuring that the Notifier can supply internal standard radio labelled in case of control should be provided and mentioned in the text. In the other case, the method is not taking into account for monitoring purposes.	

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	Vol. #, <<data point>>, <<description>>	<<MS/notifier/applicant>>: <<comment>>	

2. Mammalian toxicology (B.6)

Toxicokinetics (B.6.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)		-	

Acute toxicity (B.6.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)		-	

Short-term toxicity (B.6.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)		-	

Genotoxicity (B.6.4)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)		-	

Long-term toxicity and carcinogenicity (B.6.5)

No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)		-	

Reproductive toxicity (B.6.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	B.6.6.11 Teratogenicity test by oral route in the rabbit,	FR: In several developmental studies in rabbit suspected occurrence of heart malformations were observed. Indeed, in the study by [redacted]. (1995) cardiac malformation mainly intraventricular septal defect was observed at 450 mg/kg/d, higher tested dose. This heart finding was slightly outside of the historical background. Moreover, post implantation losses and late embryonic death were also observed in the high-dose group (450 mg/kg/d). In the study by [redacted] (1993), the percentage of fetuses with "dilated heart" was increased in the high dose group despite a low number of fetuses and litters included in the high-dose group. Moreover, in the study by [redacted] (1989), ventricular septal defects as in the study by [redacted]. (1991) were also noted in the high dose group. A higher number of further visceral malformations at the top dose level were due to kidneys defects. The relevance of the heart and kidney findings observed in several studies should be discussed at an expert meeting.	
(2)	B.6.6.11 Teratogenicity	FR: These effects on cardiovascular development	

Reproductive toxicity (B.6.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	test by oral route in the rabbit,	(described above) were discussed in the published review of Kimmel et al. (Crit Rev Toxicol. 2013 Feb;43(2):79-95). The analysis of this review concluded that the observed cardiac malformations were not related to treatment. This article could be more detailed allowing this statement.	

Neurotoxicity (B.6.7)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)		-	

Other toxicological studies & Medical data (B.6.8-B.6.9)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)		-	

Summary of mammalian toxicology and setting ADI, AOEL, ARfD (B.6.10)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 1, level 1, 2.6.13	FR: Based on the study by [redacted]. (1991), the	

Summary of mammalian toxicology and setting ADI, AOEL, ARfD (B.6.10)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	ARfD	developmental NOAEL of 50 mg/kg bw/d due to post implantation losses is considered acceptable. This effect could be considered as a consequence of cardiac malformation observed in fetuses. The observed post implantation losses could be considered as an acute adverse effect occurring within the first days of treatment. As a consequence, an ARfD could be derived based on this effect on the development and the resulting ARfD for glyphosate would be of 0.5 mg/kg bw/d (with a safety factor of 100).	

Toxicity of the product(s) (B.6.11)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)		-	

Dermal absorption (B.6.12)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	B.6.12 Dermal absorption	FR: The preparation MON 52276 is the representation formulation of the Glyphosate Task force. This formulation does not contain any [redacted] For the representation formulation MON 52276,	

Section 2 - Mammalian toxicology (B.6)

Dermal absorption (B.6.12)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		dermal absorption was assessed in vitro on human skin. We agreed with the dermal absorption rates of 0.1, 0.2 and 0.3% for th high, mid and low concentration. However, for the other formulations the new European Guidance document on dermal absorption (EFSA 2012) should be considered to determine dermal absorption values of glyphosate used for exposure calculation and risk assessment.	

Toxicity of non-active substances (B.6.13)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)		-	

Exposure data (B.6.14)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)		-	

Section 2 - Mammalian toxicology (B.6)

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)		-	

3. Residues (B.7)

Storage Stability (B.7.0)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)		FR: agreed	

Metabolism in plants (B.7.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)		FR: agreed	

Metabolism in livestock (B.7.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)		FR: agreed	

Residue definition (B.7.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol.3, B.7.3.1.3 Conclusion for plant matrices; p125 and Table B.7.3-7; p127	FR: it is not clear if the GAT modified crop included oilseed rape and/or lentil.	
2	Vol.3, B.7.3.1.3	FR: France agrees with the new proposed residue	

Section 3 - Residues (B.7)

Residue definition (B.7.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	Conclusion for plant matrices; p126	definition for monitoring for plant commodities that could be tolerant crops (GAT modified).	
3	Vol.3, B.7.3.2 Residue definition for animal commodities; p132	FR: France agrees with the new residue definition for monitoring for animal commodities that could be fed with tolerant crops (GAT modified)	

Use pattern, critical GAP, residues trials (B.7.4 to B.7.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, Table B.7.4-1: List of representative uses (glyphosate); p 138 Table B.7.5-1: Critical GAPs for glyphosate; p 144 Vol 1, Level 1 ; List of representative uses evaluated (Glyphosate); p16	FR: in the column „growth stage &season "should refer to the BBCH GS **of the treated crop** and not **to weeds growth stage**. So „Post emergence of weeds "should be précised with ranges of crops growth stages according to the selected trials to support uses in orchards (BBCH 70-75). If not a PHI should be proposed. For the use in orchard, could you please precise all the commodities concerned. For the use on "all crop **", could you precise to what referred "**"in Vol3 tables.	

Section 3 - Residues (B.7)

Use pattern, critical GAP, residues trials (B.7.4 to B.7.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	Vol 3, B.7.6 Residues resulting from supervised trials	FR: in this section it is mentioned: “The formulation and the active ingredient (salt) are not expected to influence the residue for glyphosate.” Could you please argue and give elements to support this position?	

Processing (B.7.7)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)		FR: agreed	

Livestock feeding (B.7.8)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)		FR: agreed	

Succeeding/Rotational crops (B.7.9)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)		FR: agreed	

Section 3 - Residues (B.7)

MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
1	Vol3, B.7.12.8 Animal commodities ; p296	FR: It is noted that “N-acetyl-glyphosate can also not be taken into account, since no information in residues in imported feed items were evaluated within this document”. However, some residue data on GAT modified crop from USA (maize and soybean) are presented p 306.	
2	Vol3, B.7.12.8 Animal commodities ; p296	FR: It is noted that “N-acetyl-glyphosate can also not be taken into account, since no information in residues in imported feed items were evaluated within this document”. It could be then concluded that the proposed MRL for animal commodities should be revised as soon as new data on GAT modified feed would be available. Awaiting for these data, it could be more accurate to precise that “no feed commodities issued from GAT modified crops should be fed to livestock”.	
3	Vol3, B.7.12.8 Animal commodities ; p298	FR : It is surprising to see that the mean DB for chicken is higher than max DB. This is clearly linked to the addition of AMPA residue level. It could be helpful to precise that Max DB is calculated with regard to enforcement residue definition when mean DB is calculated according to RA residue definition and then avoid any misunderstanding.	
4	Vol3, B.7.12.8 Animal	FR: the MRL proposed for bovine commodities	

Section 3 - Residues (B.7)

MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	commodities ; p302	could be extrapolated to the ruminant group. So MRL on sheep and goat commodities could be proposed in accordance with MRL proposed for bovine commodities.	
5	Vol. 3 B.7.15.1 Long-term dietary intake assessment; p309	FR: the potential presence of GAT modified commodities is not taken into account in risk assessment, although some residue data on GAT modified crop from USA (maize and soybean) are presented p 306. It could be then concluded that the consumer risk assessment should be revised as soon as new data on GAT modified crops(lentils, soya, rapeseed, maize, corn) would be available. Awaiting for these data, it could be more accurate to precise that “no food commodities issued from GAT modified crops should be authorized for human alimentation”.	

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol.3, B.7.17 References	FR why some studies (highlighted in yellow) were	

Section 3 - Residues (B.7)

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	relied on; p 353	not “part of the dossier for the renewal”? Could you please precise the meaning of this sentence?	
2	Vol.3, B.7.18 Appendix – Supervised field trials	FR: 1 trial treated at BBCH 69 is underlined for pome fruits p375 – The selection in field trials is not “fully” clear, could you please give some precisions?	
3	Vol.3, B.7.18 Appendix – Supervised field trials	FR: Even if it could be discussed how LOQ where “managed” FR considers the approach as consistent: - When compound 1 and compound 2 < 0.05* then “total residue” noticed as 0.05* - When compound 1 = 0.05 and compound 2 < 0.05* then “total residue” noticed as 0.10 (if “close” molar mass) This point could be a general point of discussion (other compounds could be concerned)	

4. Environmental fate and behaviour (B.8)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
1	Volume 3 Volume 1	FR: FR acknowledges the huge work performed by RMS in providing a comprehensive AIR dossier with up to date risk-assessment and feedbacks on extensive monitoring programs / databases / experiments on glyphosate occurrence in water resources.	
2	Volume 3 Annex B.8 (Appendix) Volume 1 3.1.6 Critical areas of concern	FR: RMS has provided key messages in its draft-AIR dossier regarding glyphosate occurrence in water resources that may not be addressed at risk assessment level but have to be undoubtedly delivered to the risk manager. FR strongly recommends making this point visible to risk managers, by being reported in vol 1 section: Critical area of concern identified in the RAR and future Efsa conclusions.	Please see detailed points below.
3	Volume 3 B.8.6.3 Monitoring data Annex B.8 (Appendix) Volume 1 3.1.6 Critical areas of concern	FR: FR would strongly support to account for the feedbacks from "control and inspection programs" and national datasets. FR fully agrees with the statement provided by RMS on non-professional uses, desiccant use, non agricultural uses, urban uses and application to time harvest (see column 3) and strongly believes that such a key point has to be delivered to risk managers and reported in Critical area of concern identified in the RAR and future Efsa conclusions. "Member States might consider the appropriateness of additional herbicide uses especially when addressing sustainable use of plant protection products according to Directive 2009/128/EC"	As indicated by RMS, "In addition, control and inspection programs at local authority level in Germany show high rates (35 % in 2009 and 36 % in 2010 during controls that were not event-related) of noncompliance regarding the application of plant protection products on walks and places in housing areas, foot-walks, traffic islands and paved surfaces in private properties (Anonymous, 2011, BVL no 2537364 and Anonymous, 2012, BVL no 2537365). This indicates that misuses of plant protection products on paved surfaces, which often contain glyphosate as active ingredient, by non-professional users occur to a relatively large extent. Therefore, current discussions in Germany are focusing on

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
			whether the findings of glyphosate and its metabolite AMPA in surface waters originate to some extent from these misuses of plant protection products containing glyphosate on paved surfaces by non-professional users. In any event, the other EU Member States should be aware of this problem and, if necessary, take appropriate risk management measures at the national level. Next to the use of glyphosate based products by non-professional users, we point to the environmental risks associated with the intended uses of glyphosate as desiccant. An herbicide application to time harvest poses additional ecological risks for surface waters and for non-target species (please refer also to chapter 2.9.6). Member States might consider the appropriateness of additional herbicide uses especially when addressing sustainable use of plant protection products according to Directive 2009/128/EC".
4	Volume 3 B.8.1.2 Points considered for kinetics	FR: It is not clear whether modeling endpoints for glyphosate were calculated taking points over 120 days into account from the different laboratory studies. Some clarification might be needed.	It seems the notifier chose not to take the points over 120 days into account for estimating the degradation rate of glyphosate in soil, but that the RMS considered some of the points above 120 days could be used.
5	Volume 3 B.8.1.2 Table B.8.1-75 and B.8.1-94 LoEP, p31 (of pdf)	FR: it seems the recommended kinetics for Les Evouettes was DFOP for modeling endpoints in Table B.8.1-75, but then in Table B.8.1-94 and in the LoEP, p31 (of pdf) the FOMC kinetics were reported. Some clarification might be needed.	

Section 4 - Environmental fate and behaviour (B.8)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
6	Volume 3 B.8.1.2 Table B.8.1-76 LoEP p 34	FR: FR questions the approach used for modeling endpoints of AMPA of excluding some soils because of the lack of decline and the absence of acceptable fit. New modeling endpoints (DT50 and ffm) may therefore have to be calculated, LoEP and PEC calculation may need to be updated.	According to FOCUS kinetics guidance (updated 2011), p155, in case of no decline for the metabolite, a DT50 of 1000 days should be considered, along with a formation fraction of 1. FR recommends following the guidance and considering the couple DT50 (=1000 days)/ffm (=1) for the six soils where no decline in the formation of AMPA could be observed.
7	Volume 3 B.8.1.2 laboratory studies B.8.6 PEC calculations in groundwater and surface water LoEP, p 32	FR: Since 17 half-lives are available for glyphosate and according to FOCUS recommendations, the median should be considered instead of the geometric mean for modeling endpoints. LoEP and PEC calculation may need to be updated.	
8	Volume 3 B.8.1.2.2 Field studies	FR: it seems that results from the Oppenhuizen et al. (1993) study are not reported in this part of the RAR when they seem to be used for calculation of PECsoil for glyphosate. Please clarify.	
9	Volume 3 B.8.2.1 Adsorption/desorption B.8.6 PEC calculations in groundwater and surface water LoEP, p 37	FR: similarly to comment (7), the Kfoc of both glyphosate and AMPA recommended for modeling should be a median since 24 data are available for glyphosate and 16 for AMPA. LoEP and PEC calculation may need to be updated.	

Section 4 - Environmental fate and behaviour (B.8)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
10	Volume 3 B.8.6 PEC calculations in groundwater and surface water B.8.6.3 Monitoring data Annex B.8 (Appendix)	FR: When summarizing feedbacks on monitoring programs and glyphosate occurrence in water resources, RMS indicates in most cases that "results are valid for that particular place and time". Referring to PPR opinion, this statement may be acceptable but one has to admit that most if not all monitoring results in EU point out glyphosate occurrence in water resources. Therefore, a factual statement indicating that monitoring in EU indicated occurrence in water resources could be added in the conclusion of PECgw results.	

5. Ecotoxicology (B.9)

Birds and mammals (B.9.1 and B.9.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.9.1.4, Toxicity of the formulation	FR: Two dietary studies conducted with MON 52276 were included in the initial DAR both giving a LC50 > 5620 mg/kg diet (AVS94-116 and 115) corresponding to 1574 mg/kg bw/d in Colinus and 1629 mg/kg bw/d in the mallard. Please clarify the reasons why these studies are not reported. Please clarify whether the endpoints are expressed in product or active substance.	
(2)	Vol.3, B.9.1.7.2, Tier 1 acute risk assessment, Cereals pre harvest / crop maturity	FR: Scenario 35 is assessed but scenarios 21 and 34 were not considered although they are worst-case (EFSA 2009, appendix A). The justification to reconsider the shortcut value of scenario 35 is agreed.	It would be advisable to consider all the relevant scenarios for a total herbicide use in order to harmonise the assessment.
(3)	Vol.3, B.9.1.7.2, Tier 1 acute risk assessment, Oilseed pre harvest / crop maturity	FR: Scenario 122 is assessed but scenarios 120, 134 and 138 were not considered although they are not worst-case (EFSA 2009, appendix A).	It would be advisable to consider all the relevant scenarios for a total herbicide use in order to harmonise the assessment.
(4)	Vol.3, B.9.1.7.2, Tier 1 acute risk assessment, Orchard _ orchard	FR: Scenario 146 is assessed but scenario 142 was not considered (EFSA 2009, appendix A).	It would be advisable to consider all the relevant scenarios for a total herbicide use in order to harmonise the assessment.
(5)	Vol.3, B.9.1.7.2, Tier 1 acute risk assessment, Orchard _ vineyard	FR: Scenario 217 is assessed (EFSA 2009, appendix A). The option “not crop directed all season” is not available. Therefore, for zonal registration, scenarios 219 (granivorous) and 231	It would be advisable to consider all the relevant scenarios for a total herbicide use in order to harmonise the assessment.

<table>
<tr><th colspan="4">Birds and mammals (B.9.1 and B.9.3)</th></tr>
<tr><th>No.</th><th>Column 1
Reference to assessment report</th><th>Column 2
Comment (restricted to 500 characters, ca.10 lines)</th><th>Column 3
Further explanations</th></tr>
<tr><td></td><td></td><td>(omnivorous) have been considered with adaptations to take into account an application to the ground for vineyard herbicide uses:
- For granivorous and omnivorous birds, no interception has been considered.
- Moreover for omnivorous bird, the RUD of “non-grass weeds” was substituted by the RUD of “grass + cereals”.
<table><tr><td>219</td><td>Small granivorous “finch”, Small seeds 100% weed seeds without interception</td></tr><tr><td>231</td><td>Small omnivorous bird “lark” 25% grass, 25% weed seeds without interception, 50% ground arthropods with interception</td></tr></table>A feedback on this proposal will be appreciated.</td><td></td></tr>
<tr><td>(6)</td><td>Vol.3, B.9.3, LD50 for mammals</td><td>FR: The lowest limit LD50 of 2000 mg/kg bw/d was used in the risk assessment however there is evidence that it would be likely over 5000 mg/kg bw/d.</td><td></td></tr>
<tr><td>(7)</td><td>Vol.3, B.9.3, overall NOAEL for mammals</td><td>FR: The overall NOAEL of 50 mg/kg bw/d represents a significant change compared to the previous NOAEL. However, the reasons for this new proposal are well developed.</td><td></td></tr>
<tr><td>(8)</td><td>Vol.3, B.9.3.3, All crops</td><td>FR: It is questioned why the grassland scenarios were not considered as for birds (tier 1 scenarios 72, 73, 74 and 75).</td><td>It would be advisable to consider all the relevant scenarios for a total herbicide use in order to harmonise the assessment.</td></tr>
</table>

Section 5 - Ecotoxicology (B.9)

Birds and mammals (B.9.1 and B.9.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(9)	Vol.3, B.9.3.3.2, Tier 1 risk assessment	FR: The risk assessment is conducted for the small herbivorous mammal (vole). The other mammals that might be considered as generic focal species are not assessed as far as there is a need to refine for the vole.	It would be advisable to consider all the relevant scenarios for a total herbicide use in order to harmonise the assessment. It would be advisable to consider all the relevant scenarios for a total herbicide use in order to harmonise the assessment. Options for refinement depend on the generic focal species.

Aquatic organisms (B.9.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.9.2, glyphosate acid, chronic toxicity endpoint for fish Vol. 1, 2.9.2	FR: As indicated the validity of the ELS study with Danio rerio (7 d instead of 30 days) is questionable. In addition D. rerio is the least sensitive species in acute toxicity studies. Therefore, the chronic endpoint for fish should be reconsidered although it is not the most critical to derive a RAC. Please indicate by a note in the summary tables the NOEC which are found at the highest test concentration.	
(2)	Vol. 3, B.9.2, glyphosate acid, Skeletonema costatum (Hugnes, 1987), study 96-00455	FR: It is agreed to consider this study as not valid as proposed.	
(3)	Vol. 3, B.9.2, NOEC for algae and aquatic plants Vol. 1, 2.10	FR: For classification purposes, it would be nice to get an overview of the relevant NOEC values in the summary tables for algae and aquatic plants.	

Section 5 - Ecotoxicology (B.9)

Aquatic organisms (B.9.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		Please check if reference to 790/2009 (1st ATP) is the correct one (may be replaced by 286/2011 (2nd ATP) for the current classification rules).	
(4)	Vol. 3, B.9.2, Risk assessment Vol. 1, 2.9.2 & 3.2	FR: The risk assessment as proposed in the DAR is agreed. **However, attention should be given at the MS level when evaluating the risk for aquatic organisms when the preparation is more toxic than predicted (increase of toxicity may be higher than a factor 100 on green algae).**	Under point 3.2, there is no indication with regard to aquatic organisms based on the RAR with the representative preparation MON 52276. The possibility that some preparations are more toxic than predicted is not reflected.

Bees and non-target arthropods (B.9.4 and B.9.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.9.4 data and risk assessment for bees Vol. 1, 2.9.3.1	FR: No comment	
(2)	Vol. 3, B.9.5 data and risk assessment for non-target arthropods Vol. 1, 2.9.3.2	FR: It would be useful to have the dose rates as kg ae/ha in Tables B.9.5-1 and 2. The correction of the drift rate for application on mature crop is understood but not sufficiently justified to get further harmonisation of the risk assessment at national/zonal levels. The risk assessment is agreed. However, it is considered more appropriate to replace the term " low" by "acceptable according to ESCORT II" (Vol. 3,	It is proposed to consider the drift scenario "ground crop" x 2 for application in mature crops (i.e. 2.77% x 2 = 5.54%) to consider crop height. Surrogate values for "vegetables, ornementals > 50cm" = "grapes, late stage" = 8.02%". The drift scenario depends also on typical application techniques and not only on crop height, which is not explain in the drift tables.

Bees and non-target arthropods (B.9.4 and B.9.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		B.9.5, page 222).	

Earthworms and other soil non-target organisms (macro and micro) (B.9.6, B.9.7 and B.9.8)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.9.6 data and risk assessment for earthworms Vol. 1, 2.9.4	FR: Please clarify which endpoint for glyphosate acid (technical or pure) should be reported and used in the risk assessment (vol. 3, B.9, pages 226 and 244). No other comment.	
(2)	Vol. 3, B.9.7 data and risk assessment for other soil mesofauna Vol. 1, 2.9.4	FR: No comment	
(3)	Vol. 3, B.9.8 data and risk assessment for soil microorganisms Vol. 1, 2.9.4 & 3.1.4.9	FR: No comment	

Other non-target organisms (flora and fauna), sewage treatment (B.9.9 and B.9.10)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol 3, B.9.9 data and risk assessment for terrestrial	FR: The correction of the drift rate for application on mature crop is understood but not sufficiently	It is proposed to consider the drift scenario “ground crop” x 2 for application in mature crops (i.e. 2.77% x 2 = 5.54%) to consider crop

Other non-target organisms (flora and fauna), sewage treatment (B.9.9 and B.9.10)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	plants Vol. 1, 2.9.6 & 3.1.4.9 & 3.2	justified to get further harmonisation of the risk assessment at national/zonal levels. It is agreed that study MSL-13320 by Chetram & Lucash, 1994 is not considered sufficient to address the risk of a preparation to non-target plants. The data requirement for MON 52276 is agreed as a reference. Although the proposed increased trigger value (15 instead of 5 page 282 of vol. 3) is debetable, it is agreed that the "Final risk assessment should then be performed on the level of product authorisation with reliable data –sets providing the ER50 values of the plant protection product to non-target plants" (B.9.9, page 282). Therefore, it is suggested to clarify under vol.1, point 3.2 "the risk to non-target plants **with appropriate Annex III data**".	height. Surrogate values for "vegetables, ornementals > 50cm" = "grapes, late stage" = 8.02%". The drift scenario depends also on typical application techniques and not only on crop height, which is not explain in the drift tables.

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.9, reference to detailed summaries in the initial DAR and addenda	FR: Detailed summaries in the initial DAR and addenda were not found. However, it is clear that the initial endpoints were all clarified. The details are available in the RAR when necessary (i.e. in	

Section 5 - Ecotoxicology (B.9)

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		support of the chronic endpoints for birds, when the validity of a study is discussed).	
(2)	Vol.3, B.9.12 References relied on	FR: Some data protection claims may not be considered as justified.	
(3)	Vol. 4_Monsanto	FR: The compositions of the preparations MON other than MON 52276 and used as test item have not been reported.	

Comments of Latvia on the renewal assessment report on glyphosate

Section 3 - Residues (B.7)

1. **Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)**

2. **Mammalian toxicology (B.6)**

3. **Residues (B.7)**

Metabolism in livestock (B.7.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol.3, B.7.2., Metabolism, distribution and expression of residues in livestock	LV: Table B.7.2-5 "Identification of radioactive residues in urine, faeces, liver and kidney of lactating goats following administration of 14C-glyphosate to lactating goats at nominal feed levels of 200 mg/kg feed", shows that unknown substances represent as much as 22.34% of TRR. However, according to SANCO 7030/VI/95 Rev.3 all components of the residue which exceed 10% or 0.05 mg/kg of TRR need to be characterised and identified.	-

Livestock feeding (B.7.8)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(2)	Vol.3, B.7.8.1., Livestock feeding studies	LV: Please clarify if any unusual health and behaviour of animals was observed during these studies.	-

4. **Environmental fate and behaviour (B.8)**

5. **Ecotoxicology (B.9)**

Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)

Identity (B.1, Annex C) Volume 4 General Information, version rar 14 and/or 22			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	C, General rar_14_volume_4_general information	NL: Please note that this version seems to be a condensed version of rar_22_volume4_general_information, without a table with reference specification. For some reason we did not receive nr 22. Nr 22 that we received seems to be a specific Volume 4 for a notifier named Brokden. Please clarify.	
(2)	C, General rar_22_volume4_general_information	NL: Please note that this volume 4 was not available for comments, at least not in our system. Was it available for other MS? Compared to the rar_14_volume 4 General Information, this one seems to be the appropriate one, including a very useful summary of all specifications for all sources compared to the reference source.	
(3)	C, General rar_14_volume4_general_information	NL: When Volume 4_22 in our system seems to be Volume_14 (condensed version of 22), doe the RMS have a different version rar_14_volume 4 than the general version?Perhaps for a notifier? Please clarify.	
(4)	C, General rar_22_volume4_general_information	NL: Please note that as rar_14 seems to be a condensed version of the general information, NL comments will be made on the rar_22 version, as it contains information relevant for the evaluation of the various sources.	

Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

Identity (B.1, Annex C) Volume 4 General Information, version rar 14 and/or 22			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(5)	C1 rar_22_volume4_general_information	NL: Agreed with the RMS that as no information was available in the volume 4 of the DAR, it seems rather difficult to check what material has been used in tox and ecotox studies being representative for the reference specification..	
(6)	C1 rar_22_volume4_general_information, reference speicification	NL: It is not clear what specification should be considered as the reference specification in the original DAR/Volume 4. Hence how can the various specifications in the RAR be compared to what if there is no clear reference specification?	
(7)	C1 rar_22_volume4_general_information	NL: The very helpful overview table on page 5 depicts for all the sources their minimum purities and corresponding specifications for all sources during AIR. Thank you.	
(8)	C1 rar_22_volume4_general_information	NL: In the table on page 5, for the Brokden source no impurities at all are indicated. In volume 4 for Brokden (rar_22_volume4_Brokden_2013_12_18 impurities are indicated, also at significant level but somehow not on the specification. NL agrees with the RMS that technical equivalence can not be evaluated this way. However at table 5 it shuld be indicated that the Brokden specification is preliminary since it is not supported by the batches. Should Brokden then be included as one of the notifiers, when the specification is not supported by the batches?	
(9)	C2.1. rar_22_volume4_general_information	NL: It is stated in this section that *There were 24 notifiers for the active substance glyphosate.*	

Identity (B.1, Annex C) Volume 4 General Information, version rar 14 and/or 22			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		All these companies created a Task Force. Plese clarify what is meant here with that all companies created a task force since all notifiers submitted own specifications instead of a joined specification.	
(10)	C2.2. rar_22_volume4_general_information	NL: It is stated in this section that *The Task Force submitted one collective dossier.* One collective dossier to our understanding would mean one active substance dossier/formulation dossier with all the same tox/ecotox studies (tox batches) based on 1 joined specification. As can be seen in table on page 5, all notifiers have their own specifications. Are they considered technical equivalent to the reference source, hence all _ox/ecotox studies seem to cover the batch data of all notifiers? Since some impurities can be found _n higher level than or are not present in the reference specification. Like for instance for Monsanto, Syngenta, Arysta, DOW, Bros, ... Please clarify.	
(11)	C2.2. rar_20_volume4_arysta_2013-12-18	NL: Impurity [redacted] is available in higher amounts than in the reference specification. Please indicate this in the conclusion on page 10.	
(12)	C2.2. rar_25_volume4_dow_2013-12-18	NL: Impurity [redacted] is available in higher amounts than in the reference specification, for sources of DOW. Please indicate this in the conclusion on page 17.	

2. Mammalian toxicology (B.6)

Toxicokinetics (B.6.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.6.1	NL: No comments	

Acute toxicity (B.6.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.6.2.1	NL: Minor comment, typo: under RMS comment (August 2013) “Glyphosate” should be replaced by “glyphosate”.	
(2)	Vol. 3, B.6.2	NL: Minor comment: throughout the document the Magnusson & Kligman test for skin sensitisation is inconsequently referred to as “Magnusson Kligman”, “Magnusson-Kligman”, “Magnusson and Kligman”, or “Magnusson & Kligman”.	

Short-term toxicity (B.6.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.6.3	NL: No comments	

Section 2 - Mammalian toxicology (B.6)

Genotoxicity (B.6.4)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.6.4.	NL: No comments	

Long-term toxicity and carcinogenicity (B.6.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.6.5	NL: No comments	

Reproductive toxicity (B.6.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.6.6.12 (page 662)	NL: The publication by Mesnage et al. (in press, ASB2012-13917) is published in 2013 in its final form (Toxicology 313(2-3): 122-128, 2013). Please also correct in reference list.	
(2)	Vol. 3, B.6.6.12 (page 536)	NL: The paper discussed, by Seralini et al. (ASB2012-15514), has meanwhile been retracted. This could be reason to remove it from the RAR, or it should at least be mentioned. NB there is also a reference to it on page 621.	

Neurotoxicity (B.6.7)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations

Section 2 - Mammalian toxicology (B.6)

Neurotoxicity (B.6.7)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.6.7	NL: No comments	

Other toxicological studies & Medical data (B.6.8-B.6.9)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.6.8-B.6.9	NL: No comments	

Summary of mammalian toxicology and setting ADI, AOEL, ARfD (B.6.10)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.6.10	NL: No comments	

Toxicity of the product(s) (B.6.11)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.6.11	NL: No comments	

Section 2 - Mammalian toxicology (B.6)

Dermal absorption (B.6.12)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.6.12	NL: No comments	

Toxicity of non-active substances (B.6.13)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.6.13.3.1, page 836	NL: Under 'conclusion' is mentioned "(Xi, R43, corresponding to "Skin sens. 1, H302)" – this should be Skin sens. 1, H317	
(2)	Vol. 3, B.6.13.3.1, page 850	NL: Under 'Impact of [redacted] on the toxicity of Roundup formulations is stated that the oral absorption of glyphosate is about 30% only. Should be decreased to 20%, the newly suggested value.	

Exposure data (B.6.14)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.6.14.1.2	NL: Minor comment: first paragraph, please do not abbreviate "according " into "acc.". And one dot too many at the end of the first paragraph.	

Section 2 - Mammalian toxicology (B.6)

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 1, 2.6.3.6 (page 45)	In the conclusion glyphosate acid is classified as H318: “irreversible effects on the eye / serious damage to eyes” - should cat. 1 not just read “causes serious eye damage” ?	
(2)	Vol. 1, 2.6.7.2.2 (page 79)	NL: The publication by Mesnage et al. (in press, ASB2012-13917) is published in 2013 in its final form (Toxicology 313(2-3): 122-128, 2013). Please also correct in reference list.	
(3)	Vol. 1, 2.6.7.2.2 (page 64)	NL: The paper discussed, by Seralini et al. (ASB2012-15514), has meanwhile been retracted. This could be reason to remove it from the RAR, or mention this work in this context.	
(4)	Vol. 3, B.6	NL: The title page of the Toxicology and metabolism section reads “Annex B.6.1”, this should be “Annex B.6”.	
(5)	Vol. 3, B.6.15	The reference Krüger et al. (ASB2013-8527) is not in press anymore; published in Anaerobe 20: 74-78, 2013.	

3. Residues (B.7)

Storage Stability (B.7.0)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.7.0, table B.7.6-13	NL: Storage stability of AMPA in barley straw is really low in month 6 and 12. Please reconsider these data, since in the conclusion of this study storage stability of 18 months is suggested in all matrices studied. In particular for barley straw, this conclusion is questionable.	

Metabolism in plants (B.7.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.7.1.1, Conclusion non-tolerant crops	NL: Since glyphosate is considered to be a systemic herbicide, how is it possible that translocation to untreated parts of the plants is limited?	
(2)	Vol. 3, B.7.1.1, Conclusion non-tolerant crops	NL: Glyphosate is considered to kill the plant, however, the plants in the metabolism studies are not being killed. How is that possible?	

Metabolism in livestock (B.7.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.7.2	NL: No comments	

Section 3 - Residues (B.7)

Residue definition (B.7.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.7.3, Residue definition for plant commodities	NL: The different glyphosate-salts are shortly mentioned. It would be appreciated if the results obtained with different salt can be shortly discussed on their comparability and whether they are exchangeable.	

Use pattern, critical GAP, residues trials (B.7.4 to B.7.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.7.6, table 7.6-1	NL: Since it is presented that levels of AMPA are very minor compared to parent glyphosate, wouldn't calculation number 2 from this table (0.05 mg/kg glyphosate + <0.05 mg/kg AMPA, calculated as 0.13 mg/kg total residues) still be an overestimation? Could you consider to calculate such cases as 0.05 mg/kg total residues (so no addition of AMPA in this case)?	
(2)	Vol. 3, B.7.6.2	NL: Is it acceptable to extrapolate to all other crops, based on the number of trials and the selected crops (e.g. only 2 trials on carrots and 2 trials on potato)?	
(3)	Vol. 3, B.7.6.4	NL: Since the PHI is an important factor in the level of residues concerning the GAPs for desiccation of the crops (see text: longer PHI are also acceptable, since drying of the crops generally results in higher residues), shouldn't trials be	It is known that there is no data requirement to study residues at longer PHIs than the PHI of the critical GAP, however, regarding this particular situation with glyphosate it might be of importance.

Section 3 - Residues (B.7)

Use pattern, critical GAP, residues trials (B.7.4 to B.7.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		conducted with longer PHIs included? If residues still increase after a PHI of 7 days, it is important to monitor the residue level at longer PHIs as well.	

Processing (B.7.7)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.7.7.2.1, Citrus fruit	NL: Since the initial residue level (before processing) in many cases is already low (often <0.05 mg/kg), how relevant is it to use these studies?	

Livestock feeding (B.7.8)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.7.8	NL: No comments	

Succeeding/Rotational crops (B.7.9)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.7.9	NL: No comments	

Section 3 - Residues (B.7)

MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.7.12, Proposed EU MRLs and justification for the acceptability of those residues	NL: It appears that not all residue data (e.g. barley and oats grain) are supported by the current MRL. Will there be any continuation regarding these MRLs?	

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	List of Endpoints	NL: In the LoEP it is stated that the TMDI (consumer risk assessment) is not calculated, while in Volume 1 and Volume 3 part B7 a calculation of the TMDI is provided.	
(2)	Vol 3, B.7, Residue data	NL: In the toxicology section, the surfactant [redacted] is being evaluated. Shouldn't this surfactant be considered in the residue section as well, since it appears to be more toxic that the active substance (in accordance with article 27 of Regulation 1107/2009)?	

4. Environmental fate and behaviour (B.8)

Route and rate of degradation in soil (B.8.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.8.1.1.1 aerobic degradation	NL: RMS states that several studies (Kesterson & Atkins (1991, BVL no 1932061)/ Honegger (1992, BVL no 2325652)) that were deemed unacceptable in the first DAR are now considered acceptable (temperature deviation is no problem anymore). For these studies microbial activity was tested at the beginning of the incubation. However no measurement after the end of the experiment is described. Were the soils viable throughout the experiments (NB study duration 1 year)? See later remark of the RMS itself on page 9: "rate and pathway studies should normally not exceed 120 days, because thereafter a decrease of the soil microbial activity with time would be expected in an artificial laboratory system isolated from natural replenishment. Longer incubation periods should *[be]* accompanied by biomass measurements during and at the end of these periods." In Table B.8.1-33 further on it was acknowledged that the microbial biomass was not known at the end. NL doubts if these studies should now be considered reliable when such data are not available.	
	Vol 3, B.8.1.2.1 page 46	NL: it is not clear why DT50 and fit information is provided here, already before the description of the rate of degradation in soil studies. It is not clear if this refers to the Dorn kinetic results which are only described pages away. It seems that RMS has provided the reader with a certain kind of summary on beforehand. (also for the route studies section in which studies are rejected first and then evaluated – this is a bit confusing).	
	Vol 3, B.8.1.2.1, KIIA	NL: it is stated in Dorn that „The exclusion of sampling intervals	

Route and rate of degradation in soil (B.8.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	7.2.1/03 Dorn study	beyond the typical duration of 120 days is justified when taking into account that viability of soil microbes is known to suffer during prolonged storage of soils under laboratory conditions". However for the earlier commented study of Kesterson/ Honegger (duration 12 months) no data points seem to have been left out. In Table B.8.1-26 the footnote 1) is missing (not tested?). Figures of all kinetic fits are missing. (also in RMS refitting) In Table B.8.1-75 correction factors for normalisation for tem and moisture would be appreciated. (also for later summarizing tables by RMS ie B.8.1-92- B.8.1-94) Page 80: PMG is mentioned (non labelled study Runnals), this means phosphonomethylglycine Anion but this is only mentioned on the next page. The best fit should be used for determination of the P criterion, not a back-calculated value. This only comes in place as a second tier: when the substance is indeed PBT (but not toxic not bioaacumulating), the DT90/3.32 approach can be followed as a second tier for candidates for substitution (CFS) alone. This approach is only intended for active substances as only they can be designated as candidates for substitution. (DG SANCO Working Document on "Evidence Needed to Identify POP, PBT and vPvB Properties for Pesticides" (version 3): The kinetic model that gives the best description of the chemical's behaviour should be selected. Guidance provided in FOCUS Degradation Kinetics Guidance (Sanco/10058/2005, ver 2.0, June 2006) on how to derive best fit DT50 should be	

Route and rate of degradation in soil (B.8.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		applied. As regards the initial establishment of a list of CFS, if a DT50 value based on single first order kinetics is available in the list of endpoints, the cut-off value should be compared to it directly. Otherwise, the cut-off value should be compared to the DT90 value in the list of endpoints divided by 3.32, provided the DT90 value is calculated and not estimated.)	
	Vol 3, B.8.1.2.1, Summary of persistence & modelling endpoints by RMS	Please indicate why the geomean is taken even when n=17 (see e.g. Table B.8.1-94). What is trigger for median used by Germany?	
	Vol 3, B.8.1.2.2, field studies	NL: when no fit could be derived for AMPA due to no decline, a value of 1000 days should be taken for those trials (i.e. in 3 out of 8 field studies) RMS states: *If there was no acceptable pathway fit or a clear decline phase for the metabolite AMPA during the study duration, it seems not appropriate to use a default DT50 value of 1000 days, because it could demonstrated in other field trials, that a slow degradation of AMPA takes place under field conditions and that reliable half lives could provided in more than four cases. In soils without a decline phase it is only shown, that the formation of the metabolite is higher than its degradation during the duration time of the study, but no information can provided on the rate of degradation of AMPA in these soils. Therefore in the opinion of RMS it is more proper to exclude soils without a clear decline phase from further assessment.* This is not agreed.	

Adsorption, desorption and mobility in soil (B.8.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.8.2.1	NL: *The RMS proposes to use 1/n default values of 0.9 in cases where no reliable 1/n value could be derived in the study and 1.0 in cases where no investigations of the relationship between soil solution concentration and adsorption behaviour were conducted in the study.* Reference is made to: ´Clarification note from EFSA concerning data requirements, study guideline, guidance and consensus of member state fate and behaviour experts on soil adsorption measurements and selection of the slope (1/n value) that describe the Freundlich coefficient (2010)´. The meant clarification note states that the use of 0.9 is only allowed when there are experimental difficulties (for example a labile active substance). The clarification note is not specifii on what to do when the data set is mixed i.e. reliable 1/n vaues are available but complemented with default values. NB for example in the case of imazamox the LoEP clearly states different number of KOC and 1/n. hence it could also be an option to only use the measured and valid 1/n endpoints. In this case the use of default 0.9 concerns the data of Table B8.2-5 (old study of Van Noorloos & Slangen) for which in three out of four soils the 1/n was < 0.7. These values are now replaced with 0.9. This does not seem logical. NL considers that either the 1/n values as measured should be used (when considered reliable) or the experiments should be left out due to „unrealistic/unexpected“ (low) 1/n values.	

Adsorption, desorption and mobility in soil (B.8.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		NL considers that if there is a sufficiently robust number of data for which a 1/n was determined, it may be more correct to leave out 1/n values than to introduce a certain bias towards Freundlich behaviour (or linear behaviour, in case of 1/n = 1 in case of KD studies)In this case there is plenty of reliable data and therefore NL suggests to remove the less reliable values (KOC with 1/n 0.9 and KD values with 1/n of 1)	
	Vol. 1 level 2 LoEP sorption	Please indicate in the LoEP the locality of the soil sample as now it is not easy to see which endpoint belongs to which study (only textural class is given) to improve cross-reading of LoEP and Volume 3.	

PEC in soil (B.8.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B8.3	NL: mistake in table B.8.3-12: 2x 2160 does not equal 1x1080. (“indication 2”) AMPA calculation approach is acceptable since only one application is made. If not then please use dose rate correction instead of PEC correction.	

Section 4 - Environmental fate and behaviour (B.8)

Fate and behaviour in water and impact on water treatment procedures (B.8.4 – B.8.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.8.4	NL: no comments	

PEC in surface water and ground water (B.8.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	Vol. 3, B8.6, PECgroundwater/ non-relevance of AMPA	NL: PEARL calculations are not provided by the RMS. (see opinion (2013) to FOCUS 2009 accepted guidance that two models are required) For AMPA a non-relevance assessment was available in the DAR. As the substance is not expected to leach this is no longer present in the current RAR. However on a national level we use the non-relevance assessment also to show non-relevance for drinking water made from surface water. This is sustained by the Guidance Document (GD) on non-relevant metabolites where it is stated in the introduction that: "*This guidance document focuses on groundwater, though the general approach may also be applicable for the **regional management of surface water resources intended for the abstraction of drinking water** in Member States.*" In monitoring programmes AMPA is frequently	

PEC in surface water and ground water (B.8.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		determined above 0.1 µg/L. Therefore it would be welcomed if the non-relevance assessment would still be included in the dossier. (see also remark at page 331 concerning the surface water intake for drinking water in NL)	
	Vol. 3, B8.6.3.2	NL: it seems that not all available information from The Netherlands was used/provided. The VEWIN (Board for the Dutch drinking water companies) maintains a database in which for nine abstraction points substances are monitored (most recent data 2008-2012). Glyphosate exceeds the 0.1 µg/L on the basis of 90th percentile values for two of the eight locations. The 90th percentile concentration for AMPA exceeds the limits at 7 out of 8 drinking water abstraction points. In assessments the NL uses the non-relevance assessment from the DAR to address the risk – see earlier comment.	

Fate and behaviour in air and PEC in air (B.8.7 – B.8.8)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	NL: no comments	

Section 4 - Environmental fate and behaviour (B.8)

Definition of the residues (B.8.9)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	NL: it seems the RMS follows a deviating approach to determine whether a substance should be included in the residue definition for further assessment. To our opinion, major soil metabolite AMPA should be assessed for its risk to groundwater and hence included in the definition. The fact that in the end there is no risk does not mean it should not be in the definition. See (many) earlier EU dossiers. It could be questioned whether it should be in the definition for monitoring. However in view of the many detections in EU countries it seems logical to include it in the definition for monitoring as well.	

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3	NL: no further comments	

5. Ecotoxicology (B.9)

Birds and mammals (B.9.1 and B.9.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3 B.9.7.1	NL: in the acute screening step for birds, the SUV for large herbivorous bird is 50.3 instead of the given 30.5. However, the trigger will still be > 10.	
	Vol. 3 B.9.7.1	NL: in the long-term screening step for birds the SUV for large herbivorous birds should be 26.7 instead of 16.2. This results in an lower TER of 2.2 and 6.3 respectively.	
	Vol. 3 Table B.9.1-12/13	NL: For the spot treatments the actual application rate was assumed to be 50% of the reported rate. However, the NL does not agree with this approach and is of the opinion that the dose that is applied to the spot treatments should be clearly stated. Otherwise the full dose should be taken into account. In addition we would like to refer to the discussion about this topic in Praper 111 on amitrole.	
	Vol. 3 B.9	NL: General comment: For the spot treatments the actual application rate was assumed to be 50% of the reported rate. However, the NL does not agree with this approach and is of the opinion that the dose that is applied to the spot treatments should be clearly stated. Otherwise the full dose should be taken into account. In addition we would like to refer to the discussion about this topic in Praper 111 on amitrole.	

Section 5 - Ecotoxicology (B.9)

Birds and mammals (B.9.1 and B.9.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	Vol.3 B.9.1.7.3	NL: Besides the twa also the MAF is refined. Please mention this.	
	Vol.3 B.9	NL: The methodology used to calculate the TWA is from SANCO/4145/2000, however, risk assessment is done according to EFSA (2009), the TWA should be calculated according to this GD.	
	Vol. 3 B.9.3.3.2	NL: Even with an assumed application rate of 50% the vole is still at risk in the orchard scenario (TER<10). However, this is not mentioned and all acute risk is deemed acceptable. Please explain.	
	Vol. 3		

Aquatic organisms (B.9.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3 B.9.2.4	NL: no comments	

Bees and non-target arthropods (B.9.4 and B.9.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3 B.9	NL: No comments	

Section 5 - Ecotoxicology (B.9)

Earthworms and other soil non-target organisms (macro and micro) (B.9.6, B.9.7 and B.9.8)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3 B.9	NL: No comments	

Other non-target organisms (flora and fauna), sewage treatment (B.9.9 and B.9.10)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3 B.9	NL: no comments	

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3 B.9	NL: Regarding the spot treatment: Praper 111 regarding the type of application: The experts noted that there is a lack of clarity regarding how the application rate should be expressed in the GAP table for products which will be applied only to small areas e.g. band application in vineyards; the experts strongly suggested that this is harmonised (i.e. is the full dose the equivalent dose in the treated area or does it really relate to the amount per hectare). Moreover, further guidance is needed regarding how to express the application rate (to the treated area) for the purposes of the ecotoxicological risk assessments.	NL It suggested that MS experts discuss this issue in their MS and ensure that the GAP table is clear at the completeness check stage (noting this issue is not just related to ecotox, but also relevant for other specialism's).

Comment of Norway
on the Renewal Assessment Report

Glyphosate

Rapporteur Member State: DE

Comments on the Sections

- ☐ Proposed decision
- ☐ Physical/Chemical properties; Details of uses and further information; Methods of analysis
- ☑ Mammalian toxicology
- ☐ Residues
- ☐ Environmental fate and behaviour
- ☐ Ecotoxicology

24 March 2014

Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)

No comments on this section, not reviewed

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2. Mammalian toxicology (B.6)

Reproductive toxicity (B.6.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.6.6.11, IIA, 5.6.11/05 The Effect of Glyphosate on Pregnancy of the Rabbit (Brooker et al., 1991a)	The NOAEL for developmental toxicity in this study should be sett at 50 mg/kg/day based on the increase in the occurrence of the retroesophageal right subclavian artery at 150 mg/kg/day. Based on the increase in the occurrence of the cardiovascular malformations and in the post-implantation loss in this study, glyphosate should be considered for a classification as a developmental toxicant.	The developmental toxicity study in the rabbit ([redacted]., 1991a) shows a treatment-related increase in a variety of malformations of the heart and great vessels (interventricular septal defects, retroesophageal right subclavian artery and other malformations) at 450 mg/kg/day. An increase, above the historical control data, in the retroesophageal right subclavian artery was also seen at 150 mg/kg/day. The increase in the occurrence of this malformation did not follow a clear dose-response. However a possible dose-response relationship for this effect may have been masked by the limited number of fetuses at the highest dose level. A treatment-related increase in the post-implantation loss was seen at 450 mg/kg/day. This parameter was also statistically significant increased at 50 and 150 mg/kg/day, but without a clear dose-response. The developmental toxicity was observed in the presence of maternal toxicity. One death occurred at 450 mg/kg/day. However, the maternal toxicity observed in the remaining dams consisted of a slight reduction in the body weight gain associated with a reduction in food consumption. An increase in the occurrence of soft/liquid faeces was also observed, but gross-examination at necropsy did not identify any treatment-related findings. The NOAEL for developmental toxicity in this study should be sett at 50 mg/kg/day based on the increase in the occurrence of the retroesophageal right subclavian artery at 150 mg/kg/day Based on the increase in the occurrence of the cardiovascular

Reproductive toxicity (B.6.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
			malformations and in the post- implantation loss in this study, glyphosate should be considered for a classification as a developmental toxicant. This is in accordance with the guidance on the application of the CLP criteria (guidance to regulation (EC) No 1272/2008 on classification, labelling and packaging (CLP) of substances and mixtures, version 4, 2013): Annex I: 3.7.2.4.2 `*Based on pragmatic observation, maternal toxicity may, depending on severity, influence development via non-specific secondary mechanisms, producing effects such as depressed foetal weight, retarded ossification, and possibly resorptions and certain malformations in some strains of certain species. However, the limited number of studies which have investigated the relationship between developmental effects and general maternal toxicity have failed to demonstrate a consistent, reproducible relationship across species. Developmental effects which occur even in the presence of maternal toxicity are considered to be evidence of developmental toxicity, unless it can be unequivocally demonstrated on a case-by-case basis that the developmental effects are secondary to maternal toxicity. Moreover, classification shall be considered where there is a significant toxic effect in the offspring, e.g. irreversible effects such as structural malformations, embryo/foetal lethality, significant post-natal functional deficiencies.´*

Section 3 - Residues (B.7)

3. Residues (B.7)

No comments on this section, not reviewed.

4. Environmental fate and behaviour (B.8)

No comments on this section, not reviewed.

5. Ecotoxicology (B.9)

No comments on this section, not reviewed

Comment of Sweden
on the Renewal Assessment Report

Glyphosate

Rapporteur Member State: DE

Comments on the Sections

- ☐ Proposed decision
- ☐ Physical/Chemical properties; Details of uses and further information; Methods of analysis
- ☐ Mammalian toxicology
- ☐ Residues
- ☑ Environmental fate and behaviour
- ☑ Ecotoxicology

24 March 2014

Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)

No comments on this section, not reviewed

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2. Mammalian toxicology (B.6)

No comments on this section, not reviewed.

3. Residues (B.7)

No comments on this section, not reviewed.

4. Environmental fate and behaviour (B.8)

Route and rate of degradation in soil (B.8.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.8.1.1, Rate of degradation (Dorn, 2012)	SE: For transparency, please include visuals fits i.e. graphs of the kinetic fits from study Dorn, 2012 so the visual assessment is clear.	
(2)	Vol. 3, B.8.1.1, Rate of degradation (RMS Comment and recalculation, kinetic analysis)	SE: On page 75 studies that have been data processed and kinetically recalculated by the RMS is discussed. However the Lewis and Turnball study (1992) has not been discussed in the text which also was recalculated by the RMS. Please include this study in the text and clarify why a new kinetic analysis was performed for this study.	
(3)	Vol. 3, B.8.1.1, Rate of degradation (RMS Comment and recalculation, kinetic analysis)	SE: For transparency, please include visuals fits i.e. graphs of the re-evaluated kinetics conducted by the RMS so the fits to the visual assessment is clear.	
(4)	Vol. 3, B.8.1.1, Rate of degradation, Table B.8.1-77, p.76	SE: There seems to be a typo in Table B.8.1-77 in regards to the optimised value of the DFOP fit. The k_2 value in the table indicates that DT_{50} is faster in the k_2 compartment than in the k_1 compartment. Furthermore the DT_{90} seems to have the same value as $DT_{50,\ slow\ phase}$. Is this correct?	
(5)	Vol. 3, B.8.1.1, Rate of degradation, Table B.8.1-	SE: In Table B.8.1-79 the $DT_{50,\ slow\ phase}$ for the DFOP fit seems to have the same value as DT_{90}, is this	

Section 4 - Environmental fate and behaviour (B.8)

Route and rate of degradation in soil (B.8.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	79, p.77	correct?	
(6)	Vol. 3, B.8.1.1, Rate of degradation, Table B.8.1-85, p.80	SE: For transparency, please clarify what PMG stands for.	
(7)	Vol. 3, B.8.1.1, Rate of degradation, last paragraph, p.81	SE: According to the last sentence on page 81 “the residue data of PMG in soils Speyer 2.1 and Beedon Manor can be used without further processing”. However the residue data of the Beedon Manor soil and the kinetic analysis is not provided in the kinetic re-analysis of the RMS. Please include the data and kinetic analysis of the Beedon Manor soil in the RAR.	
(8)	Vol. 3, B.8.1.1, Rate of degradation, Table B.8.1-94, p. 87 (Dean , 1995)	SE: In Table B.8.1-94 for study Dean (1995) the recalculated SFO DT_{50} actual is 300.7 days from DFOP slow phase. However according to table B.8.1-77 on page 76 FOMC fit seems to be a better fit (statistically) and would give a more worst case recalculated DT_{50} actual of 412 days. Please explain why DFOP was chosen as a better fit than FOMC.	
(9)	Vol. 3, B.8.1.1, Rate of degradation, Table B.8.1-94, p. 87 (Galicia & Morgenroth, 1993)	SE: In Table B.8.1-94 for study Galicia & Morgenroth, 1993 the recalculated SFO DT_{50} actual is 48.46 days from DT_{90} FOMC/3.32. However according to Table B.8.1-79 the DT_{90} from the FOMC fit is 347 days which would give a recalculated SFO DT_{50} actual of 104.5 days. Please explain the discrepancy.	

Section 4 - Environmental fate and behaviour (B.8)

Route and rate of degradation in soil (B.8.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(10)	Vol. 3, B.8.1.1, Rate of degradation, Table B.8.1-94, p. 87 (Galicia & Flückiger, 1993/Mamouni, 2002) Speyer 2.2, sand	SE: In Table B.8.1-94 for study Galicia & Flückiger, 1993/Mamouni, 2002 for soil Speyer 2.2 the recalculated SFO DT_{50} actual is 45.4 days from DT_{90} FOMC/3.32. According to the study author of the kinetic analysis (Dorn, 2012) no acceptable fit could be derived for modelling endpoints. SE disagrees with the study author and agrees with the RMS that the Speyer 2.2 soil can be used in the kinetic analysis. However the DT_{90} FOMC/3.32 of 45.4 seems to be an error. According to Table B.8.1-63 the FOMC DT_{90} is >1000 days which would result in a recalculated SFO DT_{50} actual of 301 days. Furthermore the $\chi 2$ error is presented as 1.59 % . However $\chi 2$ error of 1.59% does not correspond with the $\chi 2$-values presented in Table B.8.1-63. Please clarify where $\chi 2$ error of 1.59% comes from.	
(11)	Vol. 3, B.8.1.1, Rate of degradation, Table B.8.1-94, p. 88 (Lewis & Turnball, 1992)	SE: The residue data of the Beedon Manor soil and the kinetic analysis is not provided in the kinetic re-analysis of the RMS. Please include the data and kinetic analysis of the Beedon Manor soil in the RAR so it is clear where the modelling endpoints for this soil come from.	
(12)	Vol. 3, B.8.1.1, Rate of degradation, Table B.8.1-96, p. 90	SE: In Table B.8.1-96 for study McLaughlin &, Schanne, (1996) for soil Speyer 2.3 the presented recalculated SFO DT_{50} actual is 42.14 days from	

Section 4 - Environmental fate and behaviour (B.8)

Route and rate of degradation in soil (B.8.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	(McLaughlin &, Schanne, 1996)	DFOP_SFO and χ2error of 9.41. Firstly there seems to be a typo from which fit 42.14 days is derived from. According to Table B.8.1-72 the fit should be FOMC_SFO and not DFOP_SFO. Secondly, it is not clear where χ2 error of 9.41 comes from as the χ2 error of this study in Table B.8.1-72 is >15% (16.23%, DFOP_SFO and 16.48%, FOMC_SFO). Finally, it is not clear why soil Speyer 2.3 was included and not Speyer 2.1 or Speyer 2.2. According to the footnote under Table 9.1-96 “no statistically fit could be obtained (high chi2 error and/or t-test not passed at 0.05) for parent and metabolite”. This statement is also applicable to soil Speyer 2.3 as the χ2 error is >15%. Please explain why soil Speyer 2.3 was included and not Speyer 2.1 or Speyer 2.2.	

Adsorption, desorption and mobility in soil (B.8.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.8.2, The Freundlich adsorption coefficients	SE: There is an error in the reference to Table B.8.2-5 on page 124. (Fehler! Ungültiger Eigenverweis auf Textmarke.)	

PEC in soil (B.8.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B8.3, PECsoil Table B.8.3-7 p. 168	SE: We agree with the RMS comments regarding the Notifier's derivation of the input parameters for the PECsoil calculations. However there seems to be an error in Table B.8.3-7 on page 168. The degradation parameter used in the ESCAPE 2.0 is k:0.0013 which represents a DT_{50} of 533 days and not 633 days. Please confirm that DT_{50} soil used in the PECsoil calculations is 633 days.	

Fate and behaviour in water and impact on water treatment procedures (B.8.4 – B.8.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.8.4, KIIA 8.3.1/01	SE: The amounts of AMPA in the sediment reported in the text differ from the amounts in the tables. RMS concludes in the study comment (p. 199) that the amounts reported in the table are assumed to be correct. Why are the values in the tables more likely to be correct than the values in the text? Please clarify the comment.	

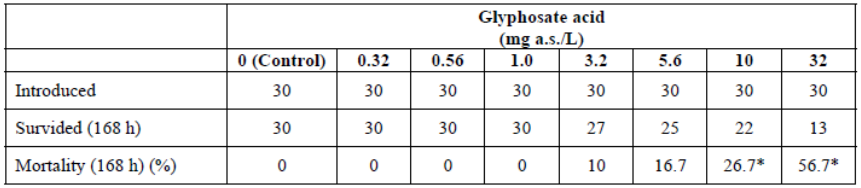
PEC in surface water and ground water (B.8.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.8.6, PECsw and	SE: The max. occurrence in soil used by the RMS	

Section 4 - Environmental fate and behaviour (B.8)

PEC in surface water and ground water (B.8.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	PECsed calculations by the RMS, Table B.8.6-24	for the Step 2 calculations of PECsw and PECsed for AMPA is 50.1%, according to Table B.8.6-24. This is the max. occurrence recommended to be used by the Notifier. The RMS concludes on page 168, 176 and 341 that the max. occurrence that should be used is 53.8 % (Schulz1992, BVL no 1932133, trial Menslage/Germany). Please explain the discrepancy.	

5. Ecotoxicology (B.9)

Birds and mammals (B.9.1 and B.9.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3. Annex B.9. , KIIA 8.1.4/03, long-term avian endpoint.	SE: We agree with the RMS conclusion that egg weight in this case is not likely to be relevant for the long-term risk assessment since at the same treatment level there are no effects on number of surviving hatchlings or body weight of hatchlings. Especially since egg weight is not listed as a recommended endpoint in OECD 206.	

Aquatic organisms (B.9.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, Annex B.9. KIIA 8.2.3/01, Early life stage test.	SE: Although not statistically significant, we would hesitate to set the NOEC to 5.6 mg a.s./L since at this treatment level and the level below the NOEC, a mortality of 16.7% and 10% respectively was observed. Considering these effects would result in a NOEC of 1.0 mg/L. This may need to be discussed further.	

	Glyphosate acid (mg a.s./L)							
	0 (Control)	**0.32**	**0.56**	**1.0**	**3.2**	**5.6**	**10**	**32**
Introduced	30	30	30	30	30	30	30	30
Survided (168 h)	30	30	30	30	27	25	22	13
Mortality (168 h) (%)	0	0	0	0	10	16.7	26.7*	56.7*

*statistically significant different from control

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, Annex B.9.	SE: We welcome the literature reviews on the	

Section 5 - Ecotoxicology (B.9)

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	Sections B.9.9.2.1 and B.9.11.	toxicity of glyphosate and POEA surfactants to amphibians and aquatic organisms.	

2. Mammalian toxicology (B.6)

Toxicokinetics (B.6.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.6.1 Absorption, distribution, excretion and metabolism (toxicokinetics)	EL: The oral absorption value of 20% proposed by the RMS taking into account only the radioactivity detected in urine, cage wash and tissues/carcass, as low biliary excretion has been proven, is considered acceptable. This value has been resulted considering the excretion pattern in female rats as a worst case. The concluded oral absorption value is clearly mentioned only in Vol. 1 in the part for the setting of reference values. For clarity reasons it is proposed to include at the end of this section an overall conclusion for the oral absorption end point giving a detailed rational for this proposal.	

Genotoxicity (B.6.4)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	B.6.4.1 In vitro genotoxicity testing – Bacterial assays for gene mutation, p. 303	EL: In the text it reads: *Some of the studies mentioned in Table B.6.4-1 are considered supplementary because either the plate-incorporation method or the pre-incubation method was performed but not both.* According to the guideline B.13/14 "*Either of them* (pre-incubation or plate incorporation methods) *is acceptable for conducting experiments both with and without metabolic activation.* Therefore, all these studies must be considered as fully	

Genotoxicity (B.6.4)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		acceptable. Please amend.	
	B.6.4.2 In vitro genotoxicity testing – Tests for gene mutation in mammalian cells B.6.4.3 Tests for DNA damage and repair in mammalian cells and bacteria B.6.4.4 *In vitro* genotoxicity testing – Tests for clastogenicity in mammalian cells	EL: Pls provide the results of the following assays in tabulated form to enable their independent evaluation: Clay, 1996, TOX2000-1994; Jensen (1991, TOX9552372) Rossberger (1994, TOX9400697) 2nd new clastogenicity study *in vitro* (Wright, 1996) 3d new clastogenicity study *in vitro* (Fox, 1998)	

Reproductive toxicity (B.6.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	Vol. 1, Level 2, 2.6.7.1 Multi generation studies	EL: Although it was concluded that the 'overall' parental NOAEL is in the magnitude of 300-400 mg/kg b.w./day, based on the overall database for reproductive toxicity, the NOAEL = 197 mg/kg b.w./day was eventually included in the LoEP as relevant parental NOAEL. The reasoning for not using the highest parental NOAEL as most relevant should be presented by the RMS.	
	Vol. 1, Level 2, 2.6.7 Summary of reproductive toxicity	EL: The RMS has presented quite a comprehensive review of the available data on the endocrine disrupting properties of glyphosate and glyphosate based formulations. The available data are suggestive of potential endocrine disrupting properties. The	

Reproductive toxicity (B.6.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		outcome of this review and the endocrine disrupting potential of glyphosate should be discussed in a meeting of experts.	

Dermal absorption (B.6.12)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.6.12.1 Dermal absorption of glyphosate from MON 52276 *in vitro* (Human epidermis)	EL: The dermal absorption values proposed are considered acceptable. The approach that the RMS has followed is in line with the general approach that has been followed even before the EFSA Guidance has come into force. Therefore, the RMS should have no concerns on the validity/applicability of the proposed values.	

Toxicity of non-active substances (B.6.13)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.6.13.2 Available toxicological data for each formulant	EL: Considering the available data it is highly appreciated that a toxicological evaluation for [redacted] has been included in the RAR for glyphosate. The establishment of EU agreed reference values is supported.	
(2)	Vol. 3, B.6.13.3.1 Toxicological evaluation of the [redacted] surfactant (CAS no. 61791-26-2)	EL: An inhalative AOEL of 0.0166 mg/kg b.w./day is proposed by the RMS. Since no toxicokinetic data are available for the examined the [redacted] surfactant, a justification should be provided for the establishment of a higher systemic AOEL (0.1 mg/kg b.w./day) .	

Exposure data (B.6.14)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.6.14 Exposure data Table B.6.14-2	EL: From the summary of supported uses of MON 52276 only the maximum in-use concentration is given. It should be clarified whether a combination of e.g. 0.36 kg a.s./ha application rate and 400 L/ha spray volume is supported. If this is the case the resulted in-use dilution (0.9 g/L) is not covered by the dermal absorption value for the dilution (tested concentration 2.5 g/L).A justification should be given for using the 0.3% value that based on the results of the available *in vitro* study with human skin, dermal absorption is not dose depended and a pro rata approach is not necessary.	

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Volume 1, Level 1; 2.6 Effects on human and animal health B.6 Toxicology and metabolism	EL: In Volume 1, 2.6 Effects on human and animal health, it is stated that «*A huge amount of more than 900 scientific publications (published since 2000 until August 2013) and other relevant information was additionally considered*». Notwithstanding, in B.6 it reads: *With rather few exceptions in the areas of genotoxicity and human data, mainly scientific literature published since 2000 was assessed*. Pls revise/correct Vol.1 to be consistent with B.6.	

1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)

Identity (B.1, Annex C)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 4, RAR, SYN, C.1.1.2 Method of manufacture, [redacted] p.3	EFSA: the description of the manufacturing process is not always clear. Is step 4 an additional 'purification' step, as from the glyphosate obtained in step 3, after this step glyphosate is resulting? Also the naming used is slightly confusing: in step 4 xxx amide is used, however the reaction scheme shows an ammonium salt.	
(2)	Vol. 4, RAR, SYN, C.1.1.2 Method of manufacture, [redacted], impurities, p. 9	EFSA: is [redacted] not a possible impurity?	
(3)	Vol. 4, RAR, SYN, C.1.2.4 Comparison of analytical batches, Conclusion, p. 16	EFSA only partly agrees with the statement that 'It is demonstrated that the compositions of the representative batches comply with the proposed specifications of the technical active substances.' as the purity of the a.s. for example could be higher based on the batch and QC data, or the proposed specifications for Impurity 1 or imp. 4 or imp.27 are not supported by batch data, but possibly by the QC data.	
(4)	Vol. 4, RAR, MON, C.1.2.3 Proposed specification, p. 10	EFSA: small typo in the reference to the proposed specification (C.1.1.2.4)	
(5)	Vol. 4, RAR, MON, C.1.2.3 Batch data, specification, p. 11-21	EFSA: the five batch data from the different sources do not support neither the proposed nor the reference specification in the case of a	

Identity (B.1, Annex C)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		considerable number of impurities.	
(6)	Vol. 4, RAR, MON, C.1.2.3 Batch data, specification, p. 11-21	EFSA: based on the batch data of all sites it is not clear why impurities 6, 7, 8, 10 and 28 should be specified? All the measured values, even with mean values+3xSD added are below 1 g/kg.	
(7)	Vol. 4, RAR, MON, C.1.2.3 Batch data, specification, Conclusion, p. 21	EFSA: inconsistency concerning imp.12: based on batch data RMS doesn't see the need to specify imp.12 (EFSA agrees), however agrees to specify for example impurities 6 and 7 with similar measured values	
(8)	Vol. 4, RAR, MON, C.1.2.3 Batch data, specification, Conclusion, p. 21	EFSA disagrees with the conclusion of the RMS that "It is demonstrated that the composition of the representative batches complies with the proposed specification of the technical active substance"	
(9)	Vol. 4, RAR, MON, C.1.2.2 Impurities, p. 4	EFSA: is [redacted] not a possible impurity?	
(10)	Vol. 4, RAR, MON, C.1.5 Other confidential information, Table C.1.5-1, p. 33	EFSA: are the values for *N*-nitroso glyphosate also expressed as %?	
(11)	Vol. 4, RAR, CHE, C.1.1.2 Method of manufacture, manufacturer 1, p. 2	EFSA: a description of the manufacturing process for the[redacted] would be useful to understand which route is followed in the manufacturing process 1	Our understanding is that basically is following the '[redacted] route'
(12)	Vol. 4, RAR, CHE, C.1.2.4 Specifications, manufacturer 1, p. 16	EFSA: is Cheninova proposing different specifications for each manufacturing site or just a common one covering all saurces?	
(13)	Vol. 4, RAR, FEI, C.1.2.2 Impurities, p. 4	EFSA: impurity 11 is missing from C.1.2.2, while mentioned in 5-batch data	

Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

Identity (B.1, Annex C)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(14)	Vol. 4, RAR, FEI, C.1.5 Other confidential information, tox batches, p. 13	EFSA: it is not clear what is the relationship between the tox batches named 1993 and 1998 and batches used in tox studies named 60, 46 and 01/06/97	
(15)	Vol. 4, RAR, AFR, C.1.2.4 Specification, Conclusion, p. 9	EFSA: not only water, but also impurity 13 is new in comparison to the reference specification	
(16)	Vol. 4, RAR, AFR, C.1.2.4 Toxicological evaluation, p. 9	EFSA did not found impurity 13 as listed in the reference specification (see Vol. 4, Monsanto)	
(17)	Vol. 4, RAR, AGRIA, C.1.1.2 Method of manufacture, manufacturer, p. 1-2	EFSA: there are some inconsistencies in the description of the manufacturing process, de flow diagram and the starting materials.	In the flow diagram [redacted] is a strting material, however looking to the list of starting reagents, it seems that this is also manufactured from them.
(18)	Vol. 4, RAR, AGRICHEM, C.1.3 Methods of analysis, NNG, Table C.1.3-2, p. 11	EFSA: are the concentration units of the linearity range correct? In the 5-batch data NNG is <0.4ppm, how was this quantified if the method has an LOQ of 6 ppm?	
(19)	Vol. 4, RAR, AGRO, C.1.1.2 Method of manufacture, step 2, p. 2	EFSA: small inconsistency in the description of step 2, the addition of a reactant to obtain the respective product is missing	
(20)	Vol. 4, RAR, ALB, C.1.1. Manufacturer, p. 1	EFSA: small typo in the name of the product: [redacted] should be [redacted]	
(21)	Vol. 4, RAR, ALB, C.1.3. Analytical methods, NNG, p. 13	EFSA: the LOQ of the method is 0.3 ppm, however in the 5-batch there are values <0.3 and <0.12 ppm. Is this later value the limit of detection?	
(22)	Vol. 4, RAR, ARY, C.1.1.2 Method of	EFSA: there are some inconsistencies in the description of the manufacturing processes: it is	

Identity (B.1, Annex C)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	manufacture, p. 2	stated that both processes use the same synthesys pathway, however in one of them a starting material containing phosphorus was probably left out by mistake	
(23)	Vol. 4, RAR, ARY, C.1.2.4 Specifcations, Conclusion, p. 10	EFSA: it is unclear why [redacted] was removed from the specification? Does it mean that [redacted] sources have their own specification? Clarification is needed, whether the proposer's intention is to have two different specifications.	EFSA agrees that the specifications were proposed based on mean+3SD values, however they seem to be quite tight taking into account that the batch data reflect a manufacturing period of less than one week
(24)	Vol. 4, RAR, ARY, C.1.3 Analytical methods, p. 13-16 and Table C.1.5-1, p.22	EFSA: it is not clear what is the LOQ for the determination of [redacted] and [redacted]	
(25)	Vol. 4, RAR, ARY, Tox batches, Table C.1.5-1, p.22	EFSA: taking into account the manufacturing route, is there an explanation of the relatively high content of impurity 2 in two of the toxicological batches?	
(26)	Vol. 4, RAR, BAR, C.1.1.2 Method of manufacture, p. 6	EFSA: no information about the purity and commercial availability of the starting materials used	
(27)	Vol. 4, RAR, BAR, C.1.2.4 Specifcations, p. 14	EFSA: Clarification is needed, whether the proposer's intention is to have two different specifications or just one covering all sources?	
(28)	Vol. 4, RAR, BAR, C.1.2.3 Five batch data, p. 12-13	EFSA: are these batch data representative to the production? No manufacturing dates are mentioned.	
(29)	Vol. 4, RAR, BAR, C.1.2.3 Five batch data, Table C.1.2-2, p.13	EFSA: based on batch data, considering the a.s. content and the content of impurities, a higher minimum a.s. content might be specified.	

Identity (B.1, Annex C)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(30)	Vol. 4, RAR, BAR, C.1.3 Analytical methods, C.1.3.1, p. 15	EFSA: small typo in the description of the mobile phase	
(31)	Vol. 4, RAR, BAR, C.1.3 Analytical methods, NNG, p. 16	EFSA: small typo in the description of the mobile phase: 'certyl…'	
(32)	Vol. 4, RAR, BRO, C.1.1.2 Method of manufacture, p. 1	EFSA: no information about the purity and commercial availability of the starting materials used	
(33)	Vol. 4, RAR, BRO, C.1.2.4 Specifcations, p.7	EFSA: the date of the manufactured batches and the specification are missing	
(34)	Vol. 4, RAR, BRO, C.1.3 Analytical methods, NNG, p. 9	EFSA: the LOQ of the NNG method is of 1.4 ppm, while the 5-batch table contains values of <1 ppm	
(35)	Vol. 4, RAR, BRO, C.1.3 Analytical methods, formaldehyde, p. 10	EFSA: the LOQ of the formaldehyde method is of 1.7 g/kg, while the 5-batch table contains values below 1 g/kg	
(36)	Vol. 4, RAR, BRS, C.1.2.3 Five batch data, Table C.1.2-1, p.6	EFSA: based on batch data, considering the a.s. content, a higher minimum a.s. content might be specified.	
(37)	Vol. 4, RAR, BRS, C.1.2.3 Five batch data, Table C.1.2-1, p.6 and C.1.3 Analytical methods, p. 9-12	EFSA: clarification is needed whether the 5-batch data can be relied on considering the conclusion of the RMS that the methods used for the quantification of the significant impurities are not acceptably validated.	
(38)	Vol. 4, RAR, DOW, C.1.2.2 Impurities, p. 10, Table C.1.2-1 p.13	EFSA: small typo in the code of impurity 19	
(39)	Vol. 4, RAR, DOW,	EFSA: are these data representative to the	

Identity (B.1, Annex C)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	C.1.2. Five batches, Table C.1.2-4, p. 16	production, if manufactured in such a short period of time?	
(40)	Vol. 4, RAR, DOW, C.1.2.4 Specifications, p. 17	EFSA: clarification is needed whether the notifier intends to have separate specification for all the different manufacturing sites	
(41)	Vol. 4, RAR, EXC, C.1.1.2 Method of manufacture, p. 2	EFSA: small typo in the formula of glyphosate in the reaction scheme	
(42)	Vol. 4, RAR, EXC, C.1.2.3 five-batch data, p. 6	EFSA agrees with the RMS on the need for clarification on not meeting the minimum account of 980 g/kg for three of the batches out of five	
(43)	Vol. 4, RAR, EXC, C.1.3.1 Analytical methods, p. 11	EFSA agress with the RMS on the need for additional validation data concerning the method for NNG	
(44)	Vol. 4, RAR, HEL, C.1.2.1 Minimum purity, p. 13	EFSA: clarification is needed whether the notifier intends to have 7 different specifications or just one covering all sources? EFSA thinks that it is rather difficult to handle a situation of one notifier having many specifications for the same a.s. Probably maximum two different specifications covering the two main processes would be more appropriate.	
(45)	Vol. 4, RAR, HEL, C.1.3 Analytical methods, NNG, p. 30	EFSA: small typo in the description of the mobile phase: ‘certyl…’	
(46)	Vol. 4, RAR, HEL, C.1.3 Analytical methods, Table C.1.3-12, p. 38	EFSA agrees with RMS on the need for additonal validation data for the determination of [redacted]	
(47)	Vol. 4, RAR, HEL, C.1.5	EFSA:was the NNG content of batch ‘20090506’	

Identity (B.1, Annex C)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	Tox batches, Table C.1.5-1, p. 54	2680 ppm?	
(48)	Vol. 4, RAR, NUF, C.1.5 Tox batches, Table C.1.5-1 and Table C.1.5-2, p. 14	EFSA: clarification is needed on the identity of tox batch identified as 'Mastra' as the two tables contain different values for the a.s content and identical values for the impurities	
(49)	Vol. 4, RAR, ROT, C.1.3 Analytical methods, AMPA, p. 11	EFSA: the method is stated to be LC-MS/MS, however a detector wavelength is given	
(50)	Vol. 4, RAR, SAB, C.1.2.3 Five batch data, Table C.1.2-1, p.7	EFSA: based on batch data, considering the a.s. content, a higher minimum a.s. content might be specified.	
(51)	Vol. 4, RAR, SAB, C.1.2.3 Five batch data, Table C.1.2-1, p.7	EFSA: usually the significant impurities below 1g/kg should not be specified	
(52)	Vol. 4, RAR, SAB, C.1.3 Analytical methods, [redacted] Conclusion, p. 10	EFSA: it is not clear how the method for [redacted] and [redacted] can be acceptably validated and in the same time having considerable interference with other compounds, with recoveries around 100%?	
(53)	Vol. 4, RAR, SAP, C.1.2.3 Five batch data, p.9	EFSA: small typo in the enumeration of the compounds analysed for in the QC, the first Imp 9 should be Imp 3.	
(54)	Vol. 4, RAR, SAP, C.1.2.4 Specifications, p. 12	EFSA: clarification is needed whether the notifier intends to have separate specification for the different manufacturing sites or just covering all?	
(55)	Vol. 4, RAR, SFP, C.1.3 Analytical methods, Table C.1.3-2, p. 11	EFSA agrees with RMS on the need for additonal validation data for the determination of [redacted]	
(56)	Vol. 4, RAR, SIN,	EFSA: manufacturing dates are missing	

Identity (B.1, Annex C)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	C.1.2.3 Five batch data, p.6		
(57)	Vol. 4, RAR, SIN, C.1.2.3 Five batch data, p.6	EFSA: it is not clear what is the additional study supporting the specification of the three impurities whose specifications are not supported by the five-batch data?	
(58)	Vol. 4, RAR, SIN, C.1.3.1 Analytical methods, p. 9-12	EFSA agrees with the RMS on the need for additional clarifications concerning the methods for the determination of the impurities of the technical material	
(59)	Vol. 4, RAR, UPL, C.1.3.1 Analytical methods, p. 12	EFSA agrees with the RMS on the need for additional validation data for the method for the determination of NNG	
(60)	Vol. 4, RAR, WYN, C.1.2.3 Five batch data, Table C.1.2-1, p.7	EFSA: based on batch data, considering the a.s. content, a higher minimum a.s. content might be specified.	
(61)	Vol. 4, RAR, WYN, C.1.2.3 Five batch data, Table C.1.2-1, p.7	EFSA: considering the batch dates, are they representative to the production?	
(62)	Vol. 4, RAR, General information C.1.1, p.1-2	EFSA: based on RMS's evaluation of the confidential volumes it seems that there is no supported reference specification. Clarification is needed whether there would be two proposed reference specifications representing the two main processes and covering all manufacturers or one awerall specification?	"…it cannot be evaluated, whether the material used in toxicological studies is representative for the proposed specification or the reference specification derived during the previous EU evaluation." "In summary, based on the currently available data and information, safe maximum levels for relevant impurities cannot be derived."

Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

Physical and chemical properties of the active substance (B.2.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations

Physical, chemical and technical properties of the formulation (B.2.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, RAR, B.2.2.7.1 Accelerated storage test, persistent foam, p. 28	EFSA: is there any explanation why the initially already high persistent foam value is increasing during storage from 63 to 75 ml?	
(2)	Vol. 3, RAR, B.2.2.7.5 Shelf life, a.s content, p. 30	EFSA: it is not clear what is meant by % recoveries of glyphosate acid? Is the change in the a.s. content after storage acceptable?	

Further information (B.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations

Methods of analysis (B.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, RAR, B.5.2.3.1 Extraction efficiency, p. 72	EFSA agrees with the RMS on the acceptability of the extaction efficiency of plant methods	
(2)	Vol. 3, RAR, B.5.2.3.2 Extraction efficiency, p. 73	EFSA agrees with the RMS on the acceptability of the extaction efficiency of methods for animal matrices	
(3)	Vol. 3, RAR, B.5.3.1.1	EFSA: small typo in the formula of the derivatise d	

Methods of analysis (B.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	Soil methods, Method 2, p. 76 and B.5.3.1.2, p.78	AMPA (F_{17})	
(4)	Vol. 3, RAR, B.5.3.1.1 and B.5.3.1.2 Soil methods, Method 2 (Szuter), p. 76, and method Alferness, p.78	EFSA: RMS considered the method of Alferness as not acceptable because of the number of the validation experiments, however this method validated in 1994 is practically identical with the accepted 'Method 2' validated in 1996.	
(5)	Vol. 3, RAR, B.5.3.2 Water methods, p.81	EFSA: small typo: the unit of electric conductance (siemens) is S (s is second)	
(6)	Vol. 3, RAR, B.5.5.2 Residue methods, p.89	EFSA agrees with the data gaps identified by the RMS conserning the residue monitoring methods	

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 1, RAR, 1.5.1 Deatails of representative uses, p. 16	EFSA: it is not clear to what refers the ** in the first two rows of the GAP table	
(2)	Vol. 1, RAR, 1.5.1 Deatails of representative uses, p. 16	EFSA: probably it would be useful to insert the name/code of the representative formulation, too in the GAP table	
(3)	Vol. 3, RAR, B.5.6 References relied on, p.89-100	EFSA: all the studies that are not part of the dossier for renewal (highlighted in yellow) and were evaluated in the RAR should be submitted to the COM, MSs and EFSA for transparency reasons and to have access to the raw data evaluated. Art. 10(3) of Reg. (EU) No 1141/2010 states that the supplementary complete dossiers shall contain the	.

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		full text of **each** test and study report.	

2. Mammalian toxicology (B.6)

Toxicokinetics (B.6.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3 B.6.1 Oral absorption	EFSA: the proposed oral absorption of 20% is agreed with	

Acute toxicity (B.6.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3 B.6.2 Acute toxicity of the a.s.	EFSA: no comment	

Short-term toxicity (B.6.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3 B.6.3 Short term toxicity of the a.s.	EFSA: no comment	

Genotoxicity (B.6.4)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3 B.6.4 Genotoxicity	EFSA: no comment	

Section 2 - Mammalian toxicology (B.6)

Genotoxicity (B.6.4)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	of the a.s.		

Long-term toxicity and carcinogenicity (B.6.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3 B.6.5 Long term toxicity and carcinogenicity of the a.s.	EFSA: no comment	

Reproductive toxicity (B.6.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3 B.6.6 Reproductive toxicity of the a.s.	EFSA: no comment	

Neurotoxicity (B.6.7)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3 B.7 Neurotoxicity	EFSA: the delayed neurotoxicity study in chicken by Johnson (1996 ASB2013-9828) needs to be submitted.	

Summary of mammalian toxicology and setting ADI, AOEL, ARfD (B.6.10)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Setting Acute reference dose	EFSA: can the RMS please confirm that deaths in rabbits, recorded in different studies, do not occur in the first days of exposure?	

Dermal absorption (B.6.12)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3 B.6.12	EFSA: no comment	

Exposure data (B.6.14)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3 B.6.14	EFSA: no comment	

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Specification and toxicological data	EFSA: considering the comment 62 in the section Identity (based on RMS's evaluation of the confidential volumes it seems that there is no supported reference specification. Clarification is needed whether there would be two proposed	

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		reference specifications representing the two main processes and covering all manufacturers or one overall specification?) it is not possible to confirm whether the batches tested in the mammalian toxicology section adequately represent the reference specification; however, based on the huge amount of available data, including batches likely having lower purity than the most recent ones, it seems quite unlikely that the purer batches would bring additional toxicological burden compared to what has been tested so far and carefully presented in the RAR.	

3. Residues (B.7)

Metabolism in plants (B.7.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.7.1, Metabolism in GAT maize	EFSA: Figure for un-extracted residues in table B.7.1-68 in GAT maize forage (42.9% TRR) is probably wrong and need to be corrected (4.29% ??).	

Residue definition (B.7.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(2)	Vol. 3, B.7.1.3, Plant and animal residue definitions	EFSA agrees the residue definition proposals made by the RMS for plant and animal commodities.	

Use pattern, critical GAP, residues trials (B.7.4 to B.7.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(3)	Vol. 3; B.7.4 Use pattern and LoEP	EFSA: In table B.7.4-1 and LoEP, representative use for olive cannot be defined without PHI as proposed for Orchard. As MRL for olive is based on the residue levels observed in fruits fallen on ground and exposed to the direct spray of the treatment, a minimum PHI has to be defined (length of time between the application and the harvest of the fruits fallen on the ground).	

Section 3 - Residues (B.7)

Use pattern, critical GAP, residues trials (B.7.4 to B.7.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(4)	Vol. 3, 7.6, Table B.7.6-2 residues in orchards	EFSA: Data for apple and pear have to be pooled together, since according to EU guideline, trials on pome fruits may be performed either on apple or pear (LoEP should be corrected accordingly)	
(5)	Vol.3, B.7.6, Table B.7.6-2	EFSA: For olive, contrary to what is reported in the table B.7.6-2, only 4 trials are available to derive MRL from the ground picked fruits. The trials conducted in Spain and reported from page 405 to 408 of the DAR, are **4 reverse decline studies** conducted in 4 locations (Chartaojal, La Carlota, Villa del Rio, Ubeda). It is therefore not appropriate to consider the residues observed in the same location at 3 different time PHIs (7, 14 and 28 days) as separate trials. Therefore, in each location, EFSA proposes to consider only, the highest level observed at 7, 14 or 28 day PHI (0.11, 0.14, 0.53 and 0.93 mg/kg). As olive is a major crop in SEU, additional trials have to be requested (see also comment in 3(3), the selection of the values for MRL calculation is pending the setting of a PHI for olive). Olive trials	
(6)	Vol.3, B.7.6, Table B.7.6-6, Residue trials on barley and oats	EFSA: For Barley grain in NEU, it is difficult to understand how mean values (referenced as [(f)]) have been calculated. Residue levels observed in	

Use pattern, critical GAP, residues trials (B.7.4 to B.7.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		plots conducted in the same location with different application rates seems have been averaged (EFSA is of the opinion that values resulting from plots covered by different application rates have not to be averaged, but the highest value taken into account). In addition, in some locations, 2 residue values (related to 2 different application rates) have been selected for MRL calculations, while only one figure has to be selected in each location (e.g. UK trial, Neston, variety Igri, reported from page 660 to 668), To select the relevant residue trials, EFSA proposes the following approach (see excel file embedded): - When different dose rates are available in one location (within ±25%, 1620 to 2700 g/ha), the closest dose to the supported dose (2160 g/ha) is first considered, - If, higher residue levels are observed in one of the other dose rates (within ±25%), this highest residue value is finally selected for MRL calculation. - If, replicates or several plots are available at the selected dose rate, values are averaged. - Only one value is selected for MRL calculation in each location. Moreover, since residue levels in barley and oats grain and straw (NEU and SEU) are not	

Use pattern, critical GAP, residues trials (B.7.4 to B.7.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		significantly different, it is proposed to pool all data to derive MRL, STMR and HR values. Barley Oats Trials	
(7)	Vol.3, B.7.6, Table B.7.6-7, Residue trials on wheat and rye	EFSA: Similar comments as for barley. In addition, it is difficult to understand why in the German trials reported from pages 832 to 839, values at 14 day PHI have been selected, while data at PHI 7 days are available and higher than at day 14. The same approach as for barley is proposed (see excel file embedded). As residue population for rye is significantly different from NEU + SEU wheat populations (H-test, 5%), it is not appropriate to merged wheat and rye data as done in table B.7.6-7. Separate MRLs have to be derived for wheat and rye. Wheat Rye trials	
(8)	Vol.3, B.7.18, Appendix, Table B.7.18-22, page 742	EFSA: The results reported in table B7.18-22 (Wheat trials NEU) page 754 (DE trial, Bad Segeberd, variety Kraka) are questionable. Residues in grain and straw are listed as: following:	

Use pattern, critical GAP, residues trials (B.7.4 to B.7.6)

No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		PHI 10 14 26 days - grain: 8.8 7.4 **15** - Straw: - 12 **4.9** I should be verified if results for grain and straw at 26 day PHI have not been inverted. Such an inversion would have a significant impact on the MRL proposal for wheat, since the 15 mg/kg value observed in this trial is the highest value observed for wheat grain. As the next highest value for wheat grain is 9.5 mg/kg only, MRL proposal for wheat would be 10 mg/kg, if residues in the Bad Segeberd trial are only 4.9 mg/kg in grain.	
(9)	Vol.3, B.7.6, Residue trials, Conversion Factor for risk assessment (CF)	EFSA: For most of the crops, AMPA residue levels are <LOQ and therefore, as proposed by the RMS, the setting of CFs is not relevant. In contrast, for barley and wheat, significant AMPA residues were measured and CFs have therefore to be proposed. However, these CFs were derived at the intended PHIs only. EFSA is of the opinion that CF proposals should not be based on the values observed at the intended PHI only. CFs may be time dependent and the ratio parent/metabolites subject to significant changes over time. Therefore, the possible variations in the CF values at the different PHI time points should be considered and CF values have to be proposed considering all PHIs investigated in the different	

Plant part	**Crop**		**PHI** (days) 0	1	3~5	6~8	9~12	14~15	20~24	**Total samples**
Grain	Barley & Oats	Nber	67	5	55	139	43	88	25	422
		CF	**1.01**	**1.01**	**1.01**	**1.03**	**1.02**	**1.03**	**1.06**	
	Wheat & Rye	Nber	77	0	8	214	30	54	35	418
		CF	**1.04**		**1.09**	**1.23**	**1.10**	**1 10**	**1.11**	
Straw	Barley & Oats	Nber	32	5	12	118	8	51	24	250
		CF	**1.01**	**1.01**	**1.04**	**1.02**	**1.03**	**1.03**	**1.02**	
	Wheat & Rye	Nber	57	0	4	130	20	51	31	293
		C^2F	**1.01**		**1.02**	**1.02**	**1.02**	**1.04**	**1.05**	

Use pattern, critical GAP, residues trials (B.7.4 to B.7.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		residue trials. According to EFSA assessment (cf. table in Column 3), an overall CF of 1.1 would be appropriate to cover the cereal group (for grain and straw).	
(10)	Vol. 1, LoEP, Conversion factor for plant commodities.	EFSA disagrees RMS statement in the LoEP on the Conversion factor for plant commodities: "*not applicable, CF dependent on point of application (pre-emergence ↔ desiccation) and crop (non-tolerant ↔ tolerant"*. Up to now, GMO cereals are not on the market, and AMPA residues are present in cereals (grain and straw) when glyphosate is applied as desiccant. EFSA is therefore of the opinion that a CF of 1.1 should be proposed on cereals (see comment 3(9)), when positive residues of glyphosate are observed.	
(11)	Vol. 1, LoEP. Table on Summary of the residue trials	EFSA: The Column "*Comments/Recommendations*" is missing in the summary table and would be useful to explain the grouping of the crops and the setting of group MRLs. Residue data according to the residue definition for monitoring (Mo) and for risk assessment (RA) should be reported in the same column.	
(12)	Vol.3, B.7.6.7, Storage stability	EFSA: As mentioned in the current EU guideline 7032/VI/95, "*individual results should not be corrected to 100% yield…"*. This recommendation is indeed taken over in the OECD 506 guideline *"…results not adjusted by recoveries…."*.	

Use pattern, critical GAP, residues trials (B.7.4 to B.7.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		Therefore, columns "*corrected %*" in tables B.7.6-9, B.7.6-11, B.7.6-13, B.7.6-14, B.7.6-15, B.7.6-16, B.7.6-18, B7.6-21 and B.7.6-22 should be deleted and the rational concerning the stability of the residues reconsidered, based on uncorrected recoveries.	

Processing (B.7.7)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(13)	Vol. 3, B.7.7-8, Processing studies on Soya bean	EFSA: In table B.7.7-8, It is unclear how AMPA residues are expressed (as mg AMPA/kg or as mg glyphosate equivalent/kg). This point should be clarified. Moreover, since significant AMPA residues are expected in some processed fractions, conversion factor for risk assessment should be proposed. **Note:** CF for processed fraction calculated as the ration of (*Residue level in processed fraction, expressed according to RD-RA*)/(*Residue level in processed fraction, expressed according to RD-Mo*). It should be highlighted that PFs and CFs for oilseed rape and soybean, as derived in the DAR, should be considered as a best case, since GMO varieties are present on the market and therefore,	

Processing (B.7.7)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		N-acetyl-glyphosate residues are expected to be present in seeds (RAC) and significant levels of AMPA and N-acetyl AMPA expected to be present in the processed fractions.	
(14)	Vol. 3, B.7.7-10, Processing studies on Barley	EFSA: It is unclear in table B.7.7-10, how AMPA residues are expressed (as mg AMPA/kg or as mg glyphosate equivalent/kg). This point should be clarified. As AMPA residues are present in significant levels, Conversion factors for risk assessment have to be proposed.	
(15)	Vol. 3, B.7.7-11, Processing studies on Wheat	EFSA: It is unclear in tables B.7.7-16, B.7.7-18 and B.7.7-19 if AMPA residues are expressed as mg AMPA/kg or as mg glyphosate equivalent/kg,	

Livestock feeding (B.7.8)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(16)	Vol. 3, B.7.8, Livestock feeding studies	EFSA: In table B.7.8-1, it is unclear if the AMPA feeding levels are expressed as "*mg AMPA/kg bw*" or as "*mg glyphosate equivalent/kg bw*". In the same way, in table B.7.8-2, are the AMPA residue levels expressed as "*mg AMPA/kg*" or as "*mg glyphosate equivalent/kg*"? This point should be clarified.	

Section 3 - Residues (B.7)

Livestock feeding (B.7.8)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(17)	Vol. 3, B.7.8, Livestock feeding studies	EFSA: Feeding dose levels in the Graham study (1987) are reported as 0.012, 0.13, 1.44, 7.38 and 19.4 mg eq/kg bw/d on page 243, while reported as 0.012, 0.0053, 0.13, 03.78 and 19.4 mg eq/kg bw/d in tables B.7.8-3 and B.7.8-4. Clarification is requested.	

MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(18)	Vol. 3, B.7.12.3, MRL proposal for olive.	EFSA is of the opinion that an insufficient number of trials has been submitted to derive MRL for olive and that GAP for olive have to be reconsidered (a PHI has to be defined for the treatment on olives fallen to the ground). (see comments in 3(3) and 3(5))	
(19)	Vol. 3, B.7.12.5, MRL proposal for barley and oats	EFSA: As mentioned under comment 3(6), selection of the data for MRL calculation has to be reconsidered. NEU and SEU data sets are not significantly different (U-test, 5%) and therefore, can be merged to propose MRL, HR and STMR.	
(20)	Vol. 3, B.7.12.6, MRL proposal for wheat and rye	EFSA: As mentioned under comment 3(7), selection of the data for MRL calculation has to be reconsidered. Moreover, separate MRL proposals have to be	

MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		done for wheat (NEU+SEU) and rye, since wheat and rye data sets are significantly different (H-test, 5%). Moreover, the highest value in wheat grain is questionable (possible inversion values grain/straw in DE trials on variety Kraka, see comment in 3(8)). If this value has to be disregarded, a MRL of 10 mg/kg for wheat is sufficient. At least, this inconsistent trial should be disregarded. NEU and SEU data sets are not significantly different (U-test, 5%) and can therefore be merged to propose MRL, HR and STMR.	
(21)	Vol. 3, B.7.12.8, MRL proposal for animal products.	EFSA: The changes in the selection of the residue values to be taken into account for MRL, STMR and HR calculations, as proposed by EFSA in comments 3(6) and 3(7), are of no significant impact on the animal burden calculations presented in tables B.7.12-7, B.7.12-8 and B.7.12-9, and EFSA agrees on the MRL values proposed by the RMS for products of animal origin.	
(22)	Vol. 1, LoEP,; Conversion factor for animal commodities.	EFSA: RMS' statement on CF for animal commodities "*not applicable, ratio of metabolites strongly depends on the amount of GMO-feedstuff in the diet*" is right and supported by EFSA. However and since significant levels of AMPA are expected to be present in kidney, EFSA is of the opinion that a CF of 1.2, derived from the Cowell and Graham (1987) feeding studies, has to	

Section 3 - Residues (B.7)

MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		be proposed as a default CF value for kidney, having in mind that additional intakes of AMPA and N-acetyl-AMPA resulting from the consumption of GMO plants may request a higher CF value.	

4. Environmental fate and behaviour (B.8)

Route and rate of degradation in soil (B.8.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.8.1.1.1 Aerobic degradation.	EFSA: RMS indicates that studies Galicia and Morgenroth, 1993, BVL no 1932059 and Matla and Vonk, 1993, BVL no 2151389 in the glyphosate monograph were considered acceptable during the first EU review of glyphosate in 2001 based on evaluation criteria and guidance at that time. As expressed, it is not clear here if the studies are still considered acceptable; however this is clarified later and in the LoEP. If fully valid it would have been helpful to reproduce the summary of the studies in the new RAR in order to have all relevant information in a single document.	
	Vol. 3, B.8.1.1.1 Aerobic degradation.	EFSA: According to the RMS Kesterson &Atkins, 1991 and Honeger, 1992 were not considered valid in the first review for reasons that do no longer apply and that they may be considered valid now (except for sandy loam soil in Kickapoo). New study summary and assessment needs to be produced for these studies to update the assessment to current evaluation criteria.	
	Vol. 3, B.8.1.1.1 Aerobic degradation. Table B.8.1-2.	EFSA: Table B.8.1-2 is a helpful overview of the route of degradation in soil studies considered acceptable by the RMS. An apparent pH	

Route and rate of degradation in soil (B.8.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		dependence of mineralization is noted. This may be the result of differential degradation route or just be caused be the pH dependent solubility of CO_2 in water.	
	Vol. 3, B.8.1.1.1 Aerobic degradation. Goodyear , A 1996.	EFSA: the exclusion of soil A to derive end points for exposure assessment of Europeans agricultural soils is agreed.	
	Vol. 3, B.8.1.1.1 Aerobic degradation. Esser, 1996.	EFSA: The exclusion of study Esser, T. 1996 is agreed.	
	Vol 3. B.8.1.1.2 Anerobic degradation.	EFSA: Only the new study Lowrie et al 2003 is summarized in the RAR. From the LoEP it seems that the RMS has also maintained the results of the old studies Keir & Mackie, 2000 and McBain, 1987. If fully valid, it would have been helpful to reproduce the summary of the studies in the new RAR in order to have all relevant information in a single document. If not fully in accordance with current guidelines a new summary and evaluation would be needed to assess the acceptability of the end points derived from them.	
	Vol 3. B.8.1.1.2 Anaerobic degradation.	EFSA: Why studies McEwen (2004) and Knoch (2003) were not submitted to the RMS in the dossier? Have these studies been submitted to other national authorities? Does any new anaerobic metabolite is identified in these studies? It is stated that the OECD guidance 307 is not exactly followed, what are the deviations?	

Section 4 – Environmental fate and behaviour (B.8)

Route and rate of degradation in soil (B.8.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	Vol 3. B.8.1.1.3. Soil photolysis	EFSA: No results from the dark control are presented for the McGahen 1983 study. An evaluation of available photolysis studies according current guidance would be needed.	
	Vol 3. B.8.1.1.3. Soil photolysis	EFSA: Why soil photolysis study of Esser (1996) has not been submitted to the RMS? If not available in the dossier it cannot be considered additional information.	
	Vol 3. B.8.1.2. Rate of degradation in soil. Laboratory studies.	EFSA: For studies presented in the first review of the substance individual data on measured amounts of parent and metabolite at the different sampling points is neither available in the original monograph not in the new RAR. This data is needed for the peer review. **Note:** the data is already available for Kesterson & Atkins 1991, Honegger, 1992, Runalls 1991 and Lewis & Turnbull 1992 studies for which RMS has done their own kinetic analysis.	
	Vol 3. B.8.1.2. Rate of degradation in soil. Laboratory studies.	EFSA: Graphical representations of the fittings of laboratory study data are not available in the RAR. These may be needed for a proper peer review of the kinetic assessment.	
	Vol 3. B.8.1.2.2 Field studies. Tables B.8.1-98, B.8.1-99	EFSA: Are separated data by horizons available? Are residues above LOQ found in the deeper horizon (3 or 2)?	
	Vol 3. B.8.1.2.2 Field studies.	EFSA: Graphical representations of the fittings of field dissipation data are not available in the	

Section 4 – Environmental fate and behaviour (B.8)

Route and rate of degradation in soil (B.8.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		RAR. These may be needed for a proper peer review of the kinetic assessment	
	Vol 3. B.8.1.2.2 Field studies. Table B.8.1-101 AMPA in Shultz 1992.	EFSA: If visual fitting suggest AMPA to be persistent in this field a default DT50 = 1000 may need to be incorporated to the data set, even if the calculated fitted parameters are not statistically reliable to avoid the bias towards more favourable situations.	
	Vol 3. B.8.1.2.2 Field studies. Shultz 1992 studies	EFSA: Separated references should be given to the Shultz 1992 studies (ie Shultz 1992, Shultz 1992a etc…)	
	Vol 3. B.8.1.2.2 Field studies. Persistence en points of glyphosato and AMPA selected by the RMS	EFSA: By excluding the soils where no degradation of AMPA is observed the overall data set becomes biased towards to the best case soils. To avoid this, a 1000 d half life should be assumed for those soils where it is not possible to derive reliable kinetic parameters due to lack of apparent degradation. If this would result in a too conservative assessment, applicant has the option of obtaining refined degradation parameters with studies in which the metabolites are applied as parent.	

Section 4 – Environmental fate and behaviour (B.8)

Fate and behaviour in water and impact on water treatment procedures (B.8.4 – B.8.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.8.4.4 Water sediment studies. Table B.8.4-2	EFSA: In this table (Table B.8.4-2) the study Heintze, 1996 is listed as pertaining to the 2001 evaluation but it is not summarized neither in the original DAR nor in the Addenda available to EFSA. However it is summarized in new RAR in pg 204. Therefore, it seems the study has been submitted in the updated dossier.	
	Vol. 3, B.8.4.4 Water sediment studies. Feser-Zuegner, W.	EFSA: There has been any attempt to identify metabolite M.3.3 that reaches up to 22.8 % AR in Feser-Zuegner, W AMPA water/sediment study?	
	Vol. 3, B.8.4.4 Water sediment studies. McEwen, A. 2004.	EFSA: There has been any attempt to identify metabolite P1a that reaches up to 53 % AR in McEwen, A. AMPA water/sediment study?	
	Vol. 3, B.8.4.4 Water sediment studies. \\Heintze, A. 1996.	EFSA: Please, clarify what NCR stands for in tables B.8.4-26 to B.8.4-29 of water sediment study Heintze, A. 1996. . Is it a single fraction or is it multi-c omponent? If such, what is the maximum amount found of any single component in it?	
	Vol 3 B.7.4 (1998 monograph). Kesterson, A. and Jackson, S.B., 1990	EFSA: Details of Kesterson, A. and Jackson, S.B., 1990 water sediment study in 1998 monograph do not allow a proper peer review of the study.	
	Vol 3 B.7.4 (1998 monograph). Moellerfeld, J. Roembke, J. 1993.	EFSA: Table with percentage of radioactivity of gyphosate and metabolites states that there is an unknown metabolite but in the text it is stated that the metabolite is actually (hydroxymethyl)-phosphonic acid.	

Fate and behaviour in water and impact on water treatment procedures (B.8.4 – B.8.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	Vol. 3, B.8.4.4 Water sediment studies. Table B.8.4-69	EFSA: It would be very helpful to have an overview table with the properties (pH water and sediment, OC, clay etc) of all the water /sediment systems tested and found acceptable by the RMS.	
	Vol 3. B.8.5.1 Information on drinking water treatment procedures.	EFSA: it is assumed that the applicant has provided this information to address the approval criteria for active substances Art 4.3 (b) of Reg No 1107/2009. Therefore, the information provided should be considered essential and not supplementary. It is noted that main emphasis of the studies presented by the applicant is given to the reduction of glyphosate and AMPA during drinking water treatment procedures. However, also the reaction products would need to be identified (for chemical treatments as oxidation with Cl_2). Taking into account the structure of these substances it is not expected that reaction products will result on an increase of the risk.	

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	Vol 3. B.8.	EFSA: A literature search on peer reviewed scientific literature has been performed and transparently reported and assessed by the RMS in the RAR (B.8 and B.10 appendices). It is	

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		acknowledged that the search of the literature was performed before the EFSA guidance (2011) was released and therefore this guidance has not been followed. For example further details on the search strategy and data bases used would need to be provided and some aspects of the Klimish scheme used to evaluate the reliability of papers submitted scheme are not supported by EFSA guidance. Besides this the search presented seems to comply with the principles of EFSA guidance with respect to exhaustiveness and transparency and can be considered equivalent to asearch that had been performed under the EFSA guidance for literature search.	
(1)	Vol 3. B.8	EFSA: A number of the studies from the previous peer review have been accepted by the RMS to support the annex I renewal. Cross references in the RAR to the monograph of 1998 and subsequent addenda are made. However, information nowadays considered essential for a proper peer review by EFSA and MSs is missing in the summary of some of the reports found in these old documents. An update summary will help for the renewal peer review of these studies.	

5. Ecotoxicology (B.9)

Birds and mammals (B.9.1 and B.9.3)			
No.	**Column 1** **Reference to assessment report**	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.9.1.7.3 higher tier: refined risk assessment to birds Page 29	EFSA: it would be preferable to include in this section the details on the residue data set for validating the approach i.e. the residue decline and the calculation of the refined ftwa.	
	Vol. 3, B.9.3.3.4 refined risk assessment to mammals Page 29	EFSA: the RMS, in accordance to EFSA 2009, has correctly used the for the tier 1 risk assessment the lowest endpoint from mammalian toxicity (i.e. the rabbit developmental NOAEL of 50 mg a.s./kg bw per day). It is noted that this endpoint was then used also for the refined risk assessment, and for some representative uses the TERs resulted still below the trigger. Could the RMS please provide an explanation on why the re-examination of the relevance of the toxicity endpoint was not considered?	

Aquatic organisms (B.9.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.9.2.3 literature Review Page 138	EFSA: a toxicity endpoint of 0.22 mg a.s./l for *Miriophyllum aquaticum* is reported from the literature. This value appears to be 10 fold lower	

Aquatic organisms (B.9.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		than the lowest endpoint used for risk assessment for macrophytes. Could the RMS pleas clarify why this value was not used?	

Bees and non-target arthropods (B.9.4 and B.9.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)		EFSA: no comments	

Earthworms and other soil non-target organisms (macro and micro) (B.9.6, B.9.7 and B.9.8)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)		EFSA: no comments	

Other non-target organisms (flora and fauna), sewage treatment (B.9.9 and B.9.10)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.9.1.5 risk assessment for non-target plants Page 282	EFSA: the available data do not allow concluding the risk assessment for terrestrial non-target plants for the active substance. The potential effect on seedling emergence could not be addressed because no valid studies are available.	

Section 5 - Ecotoxicology (B.9)

Other non-target organisms (flora and fauna), sewage treatment (B.9.9 and B.9.10)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		Furthermore the endpoint for the most sensitivity species could be underestimated due to the shorter duration of the study and an overall decrease of toxicity endpoints in studies with longer duration. Finally, no data are available to EFSA to change the trigger value. Therefore, EFSA thinks that more data would be necessary to conclude a quantitative risk assessment.	

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)		EFSA: no comments	

1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)

No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	List of endpoints, Analytical methods for residues	GTF: Residue definition for monitoring purposes in food of plant origin and food of animal origin should not include N-acetyl-glyphosate as described in Column 3.	In 2009 EFSA issued a reasoned opinion (RO) on the Modification of the residue definition of glyphosate in genetically modified maize grain and soybeans, and in products of animal origin (EFSA Journal 2009; 7(9): 1310). This RO proposed a residue definition for risk assessment in all plant commodities, (including soybean and maize) and all food commodities of animal origin. In addition three (3) possible options were proposed regarding the residue definition in maize and soybeans for enforcement purposes. In the Summary report (SANCO-D(2011) 353285) of the Standing Committee meeting on the Food Chain and animal health; section Pesticide residues + plant protection products-legislation of February 3-4 2011, the committee concluded that the residue definition for enforcement should not change (option 1 in the EFSA reasoned opinion; it is residue = **glyphosate only**) but that for the definition for the purpose of risk assessment the complete residue definition with all metabolites would need to be used. Given the fact that no GM uses are included in the representative GAP of the joint submission and given the argumentation above, no analytical methods for enforcement purposes are needed to cover N-acetyl glyphosate. The primary and confirmatory methods provided in the joint submission (with additional validation data that will be submitted where appropriate) are adequate to cover the residue definition for monitoring and post registration purposes. Also in the context of risk assessment, the uses listed in the representative GAP do not yield N-acetyl Glyphosate as a residue (no GM uses included). The residues (including N-acetyl Glyphosate) related to imported commodities are regulated under EU Regulation 369/2005 and not Regulation 1107/2009 nor regulation 1141/2010. These data have

No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
			recently been submitted by the data owner and considered for risk assessment.
(2)	Vol. 1, Level 1, 3.1.4, List of studies to be generated, still ongoing or available but not evaluated, page 155	GTF: 3.4.1.2. Physical and chemical properties of the active substance and physical, chemical and technical properties of the formulation. Spectra or relevant impurities. Not relevant.	The spectra of relevant impurities have been included, evaluated and found to be acceptable in Volume 3 B.2.1.5.2 (IIA 2.5.2) of the RAR.
(3)	Vol. 3, Annex B.2.1.2, Relative density, page 3	GTF: The result for the relative density of glyphosate technical material with purity 96.9% (Wollerton, Husband, 1997, CHE2001-63) is concluded to be "not acceptable (technical a.s.)". However, the relative density has also been generated using pure glyphosate, the value generated using glyphosate technical may be considered as addition information.	Since this data point has been generated with technical material rather than pure material it may be considered as supplementary information. We suggest that the phrase "not acceptable (technical a.s.)" should be replaced with the phrase "additional information."
(4)	Vol. 3, Annex B.2.1.4.2, Appearance: odour, page 6	GTF: The result for the odour of glyphosate technical material with purity 96.9% (Wollerton, Husband, 1997, CHE2001-63) is concluded to be "not acceptable (technical a.s.)". However, since the odour has also been generated using pure glyphosate, the value generated using glyphosate technical may be considered as addition information.	Since this data point has been generated with technical material rather than pure material it may be considered as supplementary information. We suggest that the phrase "not acceptable (technical a.s.)" should be replaced with the phrase "additional information" or "confirmatory information".
(5)	Vol. 3, Annex B.2.1.4.2, Appearance: odour, page 6	GTF: No data on the odour of the NH_4-salt has been submitted.	

No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(6)	Vol. 3, Annex B.2.1.11.2, Auto-flammability, page 17	GTF: The auto-flammability of the K salt was considered as a missing study. It was confirmed by the applicant in the reporting table that a study will be available by the end of 2013.	A study on the auto-flammability using test method EEC A.10 has been generated. Self-ignition temperature = 348°C Report can be submitted upon EFSA request.
(7)	Vol. 3, Annex B.2.2.2.2, Oxidising properties, page 24	GTF: The oxidising properties of MON 52276 have been extrapolated from the results obtained using the active ingredient which is the major component of the formulation (Krips, 1995, CHE9600635). It was confirmed by the applicant in the reporting that a study (expert judgement) would be available.	It is concluded that MON 52276 has no oxidising properties. Based on the formulation composition it has been established beyond reasonable doubt that the substance is incapable of showing a positive result in the test described in the EEC A.21 (expert statement). Report can be submitted upon EFSA request.
(8)	Vol. 3, Annex B.2.2.8.2, Persistent foaming, page 33	GTF: It should be noted that according to the FAO Manual the test concentration should correspond to the highest rate of use. According to the list of representative uses the highest rate is 8%. It was confirmed by the applicant in the reporting that a study will be conducted if requested.	A study on the persistent foaming at a concentration of 8% v/v has been generated. No foam after 1 minute (CIPAC MT 47.2). Report can be submitted upon EFSA request.
(9)	Vol. 3, Annex B.5.2.1.1.1, Acceptable methods/reports – Method 1, page 28	GTF: At the bottom of page 29 (Findings), it is incorrectly stated that the proposed residue definition for enforcement purpose in lentils is glyphosate and N-acetyl-glyphosate. The recent import tolerance for lentils (EFSA Journal 2012:10(1):2550) is incorrectly included with	The same error was repeated in pages 39, 42, 44, 47, and 87

No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		GAT genetically modified crops (oilseeds rape, soya beans and maize). The import tolerance was for conventional lentils. The GTF refers to 'Comment (1)' and the further explanations under 'Comment (1)'	
(10)	Vol. 3, Annex B.5.2.1.1.3, Acceptable methods/reports – Method 2 (part of Section B.5.2.1 Plant matrices), page 37	GTF: At the top of the page 39 (Conclusion) it is stated that the study of Anderson and Ely (2001, ASB2012-12364) does not allow the determination of the second component N-acetyl-glyphosate (NAG) of the proposed residue definition for enforcement purposes in lentils, oilseeds rape, soya beans and maize. The GTF does not agree and refers to 'Comment (1)' and the further explanations under 'Comment (1)'	The same statement applies to pages 44, 47, 64, 68, 70, 71 and 89
(11)	Vol. 3, Annex B.5.2.1.4, Studies which do not fulfill the requirements (part of Section B.5.2.1 Plant matrices), page 50	GTF: Page 51 - Additional validation data at the limit of quantification level in oranges and sunflower are available and are ready for submission upon request from EFSA.	
(12)	Vol. 3, Annex B.5.2.2.1.3, Method 2, (part of Section B.5.2.2 Animal matrices), page 63	GTF: Report RJ2585B (BVL-2309039, ASB2012-12398 page 63 - GTF has already conducted additional work on the appropriate analytical methods for glyphosate in matrices of animal origin generating additional method validations data and confirming the method of analysis via inter lab validations. The reports are ready for submission upon request from EFSA.	The same statement applies to pages 69 reference to Report TO11644-06, ASB2012-7837 and page 70 reference to Report CEMR-3532, ASB2012-12417

No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(13)	Vol. 3, Annex B.5.5.2, Residue analysis, page 87	GTF: At the bottom of the page 89 it was concluded that the following methods for monitoring are missing: "A confirmatory method for N-acetyl-glyphosate in dry plant materials and those with high water and high fat content. A confirmatory method for N-acetyl-glyphosate in all kinds of animal matrices." The GTF disagrees with this conclusion and refers to 'Comment (1), and the further explanations under 'Comment (1)	

2. Mammalian toxicology (B.6)

No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	List of endpoints, Acute toxicity	GTF: The GTF respectfully restates their position that the rat LD_{50} oral and Rat LD_{50} dermal values are listed as >2000 mg/kg bw, whereas the data presented concludes LD50-values above 5000 mg/kg. This would also be consistent with the values presented in summary Table B.6.2-1 and Table B.6.2-6 in Volume 3 B6. All test materials meeting specifications should be deemed appropriate as representative of the substance undergoing Annex I Renewal.	While > 2000 mg/kg/day is the assigned upper LD 50 limit for EU classification, these acute data are applicable to other sections of the dossier. For example, the acute oral LD50 data submitted reflect a higher value of > 5000 mg/kg/day as appropriate for use in the acute oral wildlife risk assessment. In addition, other world regions which may have adopted the GHS classification scheme look to the EU for guidance in regulatory reviews. Under representation of the EU limit dose as 2000 mg/kg/day rather than 5000 mg/kg/day for GHS, may undermine other regions with less sophisticated regulatory expertise than the EU, possibly resulting in inappropriate classification of glyphosate acute oral/dermal endpoints as GHS category 4 based on LD50 > for 2000 mg/kg/day, rather than the appropriate GHS category 5 (not classified) for > 5000 mg/kg/day.
(2)	List of endpoints, Long term toxicity and carcinogenicity	GTF: Carcinogenicity: the indication “very limited evidence in mice...” may give an erroneous and overly conservative indication of glyphosate’s carcinogenicity potential. The notifier suggests removing this indication. The conclusion should read “Not carcinogenic in rats and mice at relevant doses”.	Please refer to the further explanation under comment (4), below.
(3)	Vol. 1, Level 1, 2.6, *Introductory remarks to the evaluation in Volume 1*, bullet point #3	GTF: The notifiers wish to ensure the statement “Where possible, on the basis of all reliable studies and information, it was tried to establish “overall” NOAELs/LOAELs for a specific toxicological endpoint taking dose spacing into account” is applied consistently for the NOAEL used for ADI	The notifiers believe the NOAEL selected by the Rapporteur for ADI and AOEL calculations, 50 mg/kg bw/day, does not reflect an accurate overall NOAEL/LOAEL for the separate toxicological endpoints of maternal toxicity and offspring effects, as discussed below. An overall NOAEL for maternal toxicity of 75 mg/kg bw/day is reflected in the rabbit maternal data set.

No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		and AOEL calculations".	
(4)	Vol. 1, Level 1, 2.6.1, Overall Summary, page 35	GTF: See paragraph 7 of this section. Further rationale is requested to clarify the basis for the lack of carcinogenicity concern for glyphosate in humans. Propose the additional underlined text.	"At the highest dose level of 1460 mg/kg bw/day (10 000 ppm), in one of five studies there was an increase in the incidence of malignant lymphoma in male mice. This type of tumour is quite common in aging mice and was also found in a high incidence in the control group of this study. There was no significant increase in the incidences of malignant lymphoma in 4 other studies even in the higher dose range up to 40000 ppm (4348 mg/kg bw/day). Considering that the described effect was not reproducible in studies even at higher doses, and that high incidences of malignant lymphoma were found in the untreated control, it is concluded that a true tumorigenic response in the mouse is highly unlikely. Together with the absence of genotoxicity, glyphosate was considered unlikely to be carcinogenic in humans. It is relevant to note that the slight elevation of malignant lymphoma in males at 1460 mg/kg bw/day is well in excess of the current OECD 453 Test Guideline (OECD, 2009) limit dose of 1000 mg/kg bw/day.
(5)	Vol. 1, Level 1, 2.6.1, Overall Summary, page 37	GTF: The assessment of [redacted] is not considered to fall under the review of glyphosate.	[redacted] are not present in the lead formulation of the joint submission and are therefore not relevant in the context of the European re-authorisation of the active substance glyphosate. The evaluation of [redacted] should as such be an issue of ad hoc national re-authorisation post Annex I renewal.
(6)	Vol. 1, Level 1, 2.6.3.1, Acute oral toxicity, page 42	GTF: The GTF respectfully restates their position, that oral LD50 values are noted above 2000 mg/kg/day. The data presented for oral LD50 values are more precisely described as greater than 5000 mg/kg/day.	While > 2000 mg/kg/day is the assigned upper LD 50 limit for EU classification, these acute data are applicable to other sections of the dossier. For example, the acute oral LD50 data submitted reflect a higher value of > 5000 mg/kg/day as appropriate for use in the acute oral wildlife risk assessment. In addition, other world regions which may have adopted the GHS classification scheme look to the EU for guidance regulatory in reviews. Under representation of the EU limit dose as 2000 mg/kg/day rather than 5000 mg/kg/day for GHS, may undermine other regions with less sophisticated regulatory expertise than the EU, possibly resulting in

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			inappropriate classification of glyphosate acute oral/dermal endpoints as GHS category 4 based on LD50 > for 2000 mg/kg/day, rather than the appropriate GHS category 5 (not classified) for > 5000 mg/kg/day.
(7)	Vol. 1, Level 1, 2.6.3.2, Acute dermal toxicity, page 42	GTF: The GTF respectfully restates their position that dermal LD50 values are noted above 2000 mg/kg/day. The data presented for dermal LD50 values are more precisely described as greater than 5000 mg/kg/day.	Other world regions which may have adopted the GHS classification scheme look to the EU for guidance regulatory in reviews. Under representation of the EU limit dose as 2000 mg/kg/day rather than 5000 mg/kg/day for GHS, may undermine other regions with less sophisticated regulatory expertise than the EU, possibly resulting in inappropriate classification of glyphosate acute oral/dermal endpoints as GHS category 4 based on LD50 > for 2000 mg/kg/day, rather than the appropriate GHS category 5 (not classified) for > 5000 mg/kg/day.
(8)	Vol. 1, Level 1, 2.6.4.2, Oral subchronic (90 days and longer) studies, page 48	GTF: It is unlikely that clearly local (irritation) effects have huge interspecies-differences. Addition of the following underlined wording takes this into account.	"All these findings may be assumed to result from physico-chemical properties of glyphosate but this does not necessarily mean that they were not adverse. However, for local effects as a consequence of local irritation, a lower safety factor may be chosen for derivation of a quantitative threshold."
(9)	Vol 1, Level 1, 2.6.6.2, Summary of long-term toxicity and carcinogenicity - Mouse, page 61	GTF: In the table 2.6-8 b we suggest revised wording all three studies under "Targets / Main Effects". Suggested changes in **bold**.	[redacted] (2009): **No evidence of test substance related cancer.** [redacted] (2001): Higher incidence of malignant lymphoma at top dose level (outside **limited** historical control range for males) **at excessively high doses**; cytic glands in stomach in m[ales]↑ (equivocal toxicological relevance) [redacted] (1997): Bw gain, food consumption and efficiency↓, loose stool, caecum distended and organ wt↑, prolapse and ulceration of anus in m[ales]. **No evidence of test substance related cancer.**
(10)	Vol. 1, Level 1, 2.6.7.2.2, Developmental toxicity and teratogenicity – Rabbit, page 73	GTF: The GTF again questions the reliability and utility of this study for establishing a LOAEL for maternal toxicity in rabbits. The GTF respectfully suggests that the additional safety margin for risk assessment (disregarding the 75 mg/kg/day	Given the large dose spacing, reporting deficiencies, and inconsistency of findings at ≥ 100 mg/kg bw/day in other studies of the same design, the notifier believes the [redacted] study is not particularly robust or reliable. Furthermore, preliminary dose-range finding studies by [redacted] noted no mortality up to and including 500 mg/kg bw/day, although only two animals in total were dosed at 500 mg/kg bw/day. The [redacted] data with

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		NOAEL in [redacted], 1980, TOX2552390) as proposed by the RMS, is not necessary.	4/16 mortalities at 100 mg/kg bw/day skews the rabbit mortality data set, with an artificially steep dose response for mortality at 100 mg/kg bw/day. When the data from supplementary studies by [redacted] are not included for mortality, the dose repsone curve for pooled mortality data in rabbit developmental toxicity studies present a rather flat dose-response curve for mortality, demonstrating less than 10% mortality for doses below 175 mg/kg bw/day. This suggests that discarding the NOAEL for maternal toxicity of 75 mg/kg bw/day in [redacted] (1980, TOX2552390) may be considered overly conservative in identifying an appropriate point of departure for establishing the glyphosate ADI. Rejecting 75 mg/kg bw/day and moving to 50 mg/kg/day in essence applies an additional 3X uncertainty factor below the mortality NOEL of 150 mg/kg/day ([redacted], 1991, TOX9552393) to the intraspecies uncertainty factor of 10X, which is effectively a total uncertainty factor of 300X (30X for intraspecies uncertainty and 10X for interspecies uncertainty).
(11)	Vol. 1, Level 1, 2.6.7.2.2, Developmental toxicity and teratogenicity – Rabbit, page 74	GTF: Overall rabbit developmental toxicity study NOAEL for maternal effects is believed to be 75 mg/kg/day, based on [redacted] (1980, TOX2552390) and supported by the maternal NOAEL of 100 mg/kg/day in 2 robust developmental toxicity studies ([redacted] 1995, ASB2012-11498; [redacted] 1996, TOX2000-2001). Further discussion of observations indicating GI effects in rabbits warrant discussion.	The weight of evidence from the many rabbit developmental toxicity studies demonstrate that 75 mg/kg/day as a conservative overall NOAEL for maternal toxicity in rabbits. Studies, by [redacted] (1996, TOX2000-2001) & [redacted] (1995, ASB2012-11498), that were deemed acceptable without restriction, both demonstrated a clear maternal NOAEL of 100 mg/kg/day. The lowest LOAEL of 100 mg/kg/day based on the supplementary study by [redacted], discussed further under comment (16). In addition, the re-evaluation of [redacted] et al. (1980) confirms the validity of the previously assigned NOAEL of 75 mg/kg/day for maternal toxicity. This study is now considered supplementary based on significant maternal toxicity at the high dose group of 350 mg/kg/day, which failed to produce a sufficient number of litters for evaluation. The low maternal survival at 350 mg/kg/day precludes this study for evaluation of

No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
			developmental effects at the high dose, but does not prevent use in evaluating the dose-response for maternal toxicity. The mid dose (175 mg/kg/day) and low dose (75 mg/kg/day) were viable and may be considered appropriate for identifying NOAEL and LOAEL values for use in risk assessment, especially within the context of a weight of evidence evaluation of the vast quantity of data available from other rabbit developmental toxicity studies. Summary graphs of NOAEL/LOAEL values for maternal toxicity and developmental effects follow the toxicology section table of comments, in support of a maternal toxicity NOAEL of 75 mg/kg/day and rabbit developmental effects NOAEL of 175 mg/kg/day (based on the RAR developmental toxicity LOAEL of 200 mg/kg/day, which the GTF believes should be higher for this study, as discussed in comments 12 and 13, below).
(12)	Vol. 1, Level 1, 2.6.7.2.2, Developmental toxicity and teratogenicity – Rabbit, page 75	GTF: The GTF respectfully disagrees with the RMS and restates their opinion that the developmental NOAEL in [redacted] (1996, ASB2012-11499) is 400 mg/kg/day, with no evidence to test substance related dose-response and citing the following published expert review which was included in the RAR literature review; Kimmel et al., 2013, Evaluation of developmental toxicity studies of glyphosate with attention to cardiovascular development, *Crit Rev Toxicol*, 2013; 43(2): 79–95	Restating previous comments, based on expert opinion, the statistically significant increase in post-implantation loss at 200 mg/kg/day with a preponderance of early foetal deaths would be considered relevant if a dose response was noted with early post-implantation loss observed at 400 mg/kg/day. At 200 mg/kg there were early embryonic deaths (slight increase) and at 400 mg/kg there were late embryo/fetal deaths (slight increase). These early and late effects cannot be linked. If there was a true dose response relationship of a single effect one would have seen more early embryonic deaths at 400 mg/kg. Different mechanisms between the two dose levels are attributable to a sudden change in time at which embryos die. Thus a possible mechanism for the early effects at 200 mg/kg/day fails to demonstrate a dose-response, while a possible mechanism for the effect on one animal at the high dose with significant late post implantation loss is not statistically significant, although perhaps biologically relevant in the presence of considerable maternal toxicity at 400 mg/kg/day. The detailed expert review publication, Kimmel et al. (2013) notes;

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			"There was a statistically significant increase in embryo/ fetal death and post-implantation loss at 200 mg/kg/day, and a non-statistically significant increase at 400 mg/kg/day. The standard deviations within these data are considerable and [redacted] (1996) point out that at 200 mg/kg/day, there was a preponderance of ''early fetal deaths'', and at 400 mg/kg/day, the increase could be attributed to one animal with nine late deaths or a post-implantation loss of 69.2%. If the one litter with high implantation loss is excluded, the mean ± standard deviation for post-implantation loss in the remaining litters is 8.0 ± 10.2. With no consistent, statistically significant dose-response pattern, the biological significance of these data is questionable."
(13)	Vol. 1, Level 1, 2.6.7.2.2, Developmental toxicity and teratogenicity – Rabbit, page 76	GTF: Further discussion of observations indicating GI (non-systemic) effects in orally dosed rabbits.	Further evidence that the effects observed in rabbits are not due to systemic toxicity is apparent when the clinical signs and necropsy findings are interrogated. In rabbits, glyphosate exposure via oral gavage led to clinical signs of toxicity in dams consistent with gastro-intestinal disturbances. Rabbits were more sensitive to oral gavage dosing than other species. Clinical signs observed included diarrhoea/soft faeces, reduced faecal output, reduced body weights, reduced food consumption and increased mortality. These effects are consistent with gastro-intestinal stasis (ileus) likely caused by the mucosal membrane irritation potential of glyphosate acid. Rabbits (caecotrophs) are particularly sensitive to disruption of the gastro-intestinal tract. Stress and other environmental factors such as pain can lead to the normal muscular contractions of the stomach and intestines being greatly diminished which in turn leads to disruption of the normal intestinal/ceacum digestion, further exacerbated by caging which may prevent normal coprophagic rabbit behaviour. It is likely that the mucosal membrane of the rabbit gastro-intestinal tract is irritated by bolus administration of glyphosate acid and that the associated stress or pain leads to gastro-intestinal stasis. The gross necropsy signs observed in maternal animals

No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
			in the studies by [redacted] (1995), [redacted] (1996) and [redacted] (1996), such as hair like boluses in the stomach, fluid filled large intestines and gas distension in the lower gastrointestinal tract are indicative of gastro-intestinal stasis. The severity of this finding appears to be relevant to only hindgut fermenters as it is not seen in rats or dogs following administration of an oral bolus dose and likely not relevant to human exposures.
(14)	Vol. 1, Level 1, 2.6.12, Toxicological end point for assessment of risk following long-term dietary exposure – ADI, page 91	GTF: The notifiers agree with the RMS that [redacted] 1980, TOX9552392) is not compliant with current guidelines for establishing developmental toxicity due to insufficient numbers of litters produced. However, this study is acceptable for establishing a maternal toxicity NOAEL, as a maximum tolerated dose was attained with a dose-response and NOAEL demonstrated with sufficient numbers of adult rabbits.	Pooling data for **maternal toxicity** in rabbit developmental toxicity studies clearly demonstrates that 75 mg/kg bw/day is the NOAEL for maternal toxicity. As discussed in comment (10), the supplementary [redacted] study findings at 100 mg/kg bw/day are not in alignment with other studies and may be considered of questionable reliability for risk assessment purposes. However, in an abundance of caution, if the [redacted] dose of 100 mg/kg bw/day is considered the LOAEL for maternal toxicity, additional conservatism by rejecting the [redacted] NOAEL of 75 mg/kg bw/day should be considered overly conservative. **Dose (mg/kg bw/d); <u>Maternal</u> Effects; Study (AIR Ref.)** **10**; **No Adverse Effects**; [redacted] (1995, ASB2012-11498) **20**; **No Adverse Effects**; [redacted] (1993, TOX9551106) **50**; **No Adverse Effects**; [redacted] (1996, ASB2012-11499) **50**; **No Adverse Effects**; [redacted]. (1991, TOX9552393) **75**; **No Adverse Effects**; [redacted] (1980, TOX9552392) **100**; **No Adverse Effects**; [redacted] (1995, ASB2012-11498) **100**; **No Adverse Effects**; [redacted] (1996, TOX2000-2001) **100**; Mortality (4/16); [redacted]h (1993, TOX9551106) **125**; **No Adverse Effects**; [redacted] (1989, TOX9551960) **150**; Reduced feed intake, fecal output and body weight gain. Soft/liquid stools; [redacted]. (1991, TOX9552393) **175**; Reduced feed consumption and bw gain, reduced feces, diarrhoea; [redacted] (1996, TOX2000-2001)

No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
			175; Equivocal increase in mortality (2/16), slight increase in soft stools and diarrhoea; [redacted] (1980, TOX9552392) **200**; Slight reduction in bw gain, not statistically significant; [redacted] 1996, ASB2012-11499) **250**; **No Adverse Effects**; [redacted] (1989, TOX9551960) **300**; GI effects (loose stool); [redacted] (1995, ASB2012-11498) **300**; Reduced feed consumption and bw gain, reduced feces, diarrhoea; [redacted] (1996, TOX2000-2001) **350**; Mortality (10/17), increase in soft stools and diarrhoea; [redacted] (1980, TOX9552392) **400**; Reduced feed consumption and bw gain; [redacted] (1996, ASB2012-11499) **450**; Reduced feed intake, fecal output and body weight gain. Soft/liquid stools; [redacted] (1991, TOX9552393) **500**; Mortality, soft/liquid stool and mucus stool; [redacted] (1993, TOX9551106) **500**; Reduced body weights during study, including Day 0; [redacted] (1989, TOX9551960)
(15)	Vol. 1, Level 1, 2.6.12, Toxicological end point for assessment of risk following long-term dietary exposure - ADI, page 91	GTF: The notifiers suggest that findings of maternal toxicity in rabbits reported by [redacted] (1993, TOX9551106) are not consistent with the six other studies of the same design and therefore the lower NOAEL of 100 mg/kg bw/day should be considered unreliable.	If the Rapporteur is to consider the 100 mg/kg bw/day in [redacted] (1993, TOX9551106) as of sufficient merit to select as the LOAEL for maternal toxicity in rabbits, the notifiers believe that equal merit of the maternal toxicity NOAEL established in [redacted] (1980, TOX9552392) should be of equal merit, resulting in a NOAEL of 75 mg/kg bw/day as the point of departure resulting in an ADI of 0.75 mg/kg bw. If both Suresh (1993, TOX9551106) and [redacted] (1980, TOX9552392) are considered unreliable for establishing the maternal toxicity endpoint, then a NOAEL of 100 mg/kg bw/day as the point of departure resulting in an ADI of 1 mg/kg bw.
(16)	Vol. 1, Level 1, 2.6.12,	GTF:	Pooling data for **developmental effects** in rabbits clearly demonstrates

No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	Toxicological end point for assessment of risk following long-term dietary exposure - ADI, page 91	The appropriate point of departure for developmental effects in rabbits in the overall NOAEL value of 175 mg/kg bw/day. Therefore the endpoint for developmental toxicity is not a driver for risk assessment purposes.	that 175 mg/kg bw/day is the NOAEL for developmental toxicity. **Dose (mg/kg bw/d); Developmental Effects; Study (AIR Ref.)** **10**; **No Adverse Effects**; [redacted] (1995, ASB2012-11498) **20**; **No Adverse Effects**; [redacted] (1993, TOX9551106) **50**; **No Adverse Effects**; [redacted] (1996, ASB2012-11499) **50**; **No Adverse Effects**; [redacted]. (1991, TOX9552393) **75**; **No Adverse Effects**; [redacted]. (1980, TOX9552392) **100**; **No Adverse Effects**; [redacted](1995, ASB2012-11498) **100**; **No Adverse Effects**; [redacted] (1996, TOX2000-2001) **100**; **No Adverse Effects** (insufficient number of adults and litters); [redacted] (1993, TOX9551106) **125**; **No Adverse Effects**; [redacted] (1989, TOX9551960) **150**; **No Adverse Effects**; [redacted]. (1991, TOX9552393) **175**; **No Adverse Effects**; [redacted] (1996, TOX2000-2001) **175**; **No Adverse Effects** (supplementary data due to insufficient number of litters); [redacted] (1980, TOX9552392) **200**; Increased post-implantation loss (early foetal death); [redacted] (1996, ASB2012-11499) **250**; **No Adverse Effects**; [redacted] (1989, TOX9551960) **300**; Abortion/premature delivery; [redacted] (1995, ASB2012-11498) **300**; Reduced foetal body weight and reduced ossification; [redacted] (1996, TOX2000-2001) **350**; **No Adverse Effects** (insufficient number of surviving dams and thus litters); [redacted] (1980, TOX9552392) **400**; Increased post-implantation loss (late foetal death); [redacted](1996, ASB2012-11499) **450**; Reduced feed intake, fecal output and body weight gain. Soft/liquid stools; [redacted]. (1991, TOX9552393) **500**; **No Adverse Effects** (insufficient number adults and litters); [redacted] (1993, TOX9551106)

No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
			500; failed to produce viable litters (aborted or no live fetuses); [redacted] (1989, TOX9551960)
(17)	Vol. 1, Level 1, 2.6.14, Toxicological end point for assessment of risk following long-term dietary exposure - AOEL, page 94	GTF: The notifiers do not believe that the overall NOAEL for maternal toxicity in rabbit developmental toxicity studies reflects systemic toxicity in these rabbits. Rather effects were a consequence of gavage dosing of acidic technical glyphosate and local gastrointestinal effects consequent of this route of dosing. The GTF investigated dermal absorption in rabbit skin to estimate systemic exposures for the highest dose tested in repeat dose dermal toxicity studies rabbits.	All repeat dose dermal toxicity studies in the rabbit failed to elicit any systemic adverse effects in multiple studies. Therefore the GTF sought to determine an appropriate rabbit systemic NOAEL, based on the dermal absorption at the highest dose tested of 5000 mg/kg bw/day. The rationale for this approach was is reflected in the EFSA guidance document *Investigation of the state of the art on identification of appropriate reference points for the derivation of health-based guidance values (ADI, AOEL and AAOEL) for pesticides and on the derivation of uncertainty factors to be used in human risk assessment*, prepared by the Chemicals Regulation Directorate, Health & Safety Executive, UK HSE (EFSA, 2013), which notes in Section *3.6 Consideration of a chronic AOEL*, page 47; "In determining the relevance of a chronic AOEL based on an oral study the primary route of exposure would need to characterised and considered on a case-by-case basis. Refinement might be possible (e.g. if the ADI is based on gastrointestinal effects) but this would need to be justified." The List of Endpoints reports a glyphosate systemic NOAEL for repeat dose dermal toxicity studies in rabbits is 5000 mg/kg/day. The GTF sponsored an *in vitro* dermal absorption study with rabbit skin (Hadfield, 2012, ASB2012-11459) in order to establish the actual systemic glyphosate dose and verify whether the maternal toxicity observed in rabbit developmental toxicity studies were really attributable to systemic toxicity or rather local gastrointestinal effects from high oral doses of acidic technical glyphosate. It is important to note that formulated glyphosate products are not acidic in nature, but are rather more neutral

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<tr><td></td><td></td><td></td><td>pH salt forms. As such, agricultural operators will not be exposed to acidic technical glyphosate and therefore the maternal toxicity observed in rabbit developmental toxicity studied may not be relevant to human health risk assessment if not attributable to systemic doses of glyphosate. This type of pH related irritation is also reflected in eye irritation studies in which technical glyphosate acid is more irritating than formulated glyphosate products which contain glyphosate salts of more neutral pH.

Hadfield (2012, ASB2012-11459) determined that the dermally applied dose of 5000 mg/kg bw/day was equivalent to a systemic dose of 133 mg/kg/day. This systemic NOAEL suggests a significantly higher NOAEL for systemic toxicity than was established in rabbit developmental toxicity studies. In order for an oral dose to achieve a systemic dose of 133 mg/kg bw/day, given oral absorption of 20%, the equivalent repeat dose oral NOAEL would be 665 mg/kg bw/day in the rabbit. This suggests that the maternal toxicity observed in rabbit developmental toxicity studies should not be attributable to systemic toxicity and thus a different endpoint should be used for establishing a relevant AOEL value.

<table>
<tr><td>Study Type</td><td>Rabbit Developmental</td><td>Rabbit Repeat Dose Dermal</td></tr>
<tr><td>Dose Level</td><td>100 mg/kg bw/day</td><td>5000 mg/kg bw/day</td></tr>
<tr><td>% Absorption</td><td>20% (oral)</td><td>2.66% (dermal)</td></tr>
<tr><td>Systemic exposure</td><td>20 mg/kg bw/day</td><td>133 mg/kg bw/day</td></tr>
<tr><td>Toxicological effect</td><td>Increased mortality</td><td>None</td></tr>
</table>

A significantly higher systemic exposure was predicted from the repeat dose dermal study compared the developmental toxicity study at which</td></tr>
</table>

No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
			treatment related effects were proposed to occur. No effects were observed in the repeat dose dermal study. This indicates that the toxicity observed in the developmental toxicity study were due to the route of exposure and the different gastrointestinal system of the rabbit and not due to systemic toxicity.
(18)	Vol. 1, Level 1, 2.6.14, Toxicological end point for assessment of risk following long-term dietary exposure - AOEL, page 94	GTF: Given the questionable relevance of the rabbit model for establishing a point of departure from systemic toxicity, the GTF proposes the overall NOAEL for chronic rat studies of 100 mg/kg bw/day.	Applying the Rapporteur's overall chronic rat oral NOAEL of 100 mg/kg bw/day ([redacted]al., 1993, TOX9750499) as the point of departure and assuming 20% oral availability, a systemic NOAEL of 20 mg/kg bw/day leads to an AOEL of 0.2 mg/kg bw/day. However, the notifier does not agree that the overall chronic NOAEL of 100 mg/kg bw/day, based on increased interim parotid salivary gland weights at one year and interim liver enzyme (ALP) elevation without correlating histopathological findings. Rather, the notifier proposes an overall chronic NOAEL from the same study of 300 mg/kg bw/day, leading to an AOEL value of 0.6 mg/kg bw/day.
(19)	Vol. 3, Annex B.6.5.3, Published data on carcinogenicity, page 518	GTF: Regarding the RMS review of Hardell and Eriksson (1999, ASB2012-11838) and Hardell et al. (ASB2012-11839).	The RMS comes to a similar conclusion as the comments in the notifier's report. "In conclusion, the study by Hardell and Eriksson (1999, ASB2012-11838) found a modest association between NHL and several chemical pesticides - most notably for MCPA and the collective group of fungicides. The reported weak to moderate associations for glyphosate are not statistically significant and could be due to chance or to recall or confounding bias." The same applies for the following Hardell et al. Study (ASB2012-11839). However, the comment "These data fail to demonstrate convincing evidence for an association between glyphosate and NHL or HCL." is justifiable and should be included.
(20)	Vol. 3, Annex B.6.6.11,	GTF:	Restating previous comments, based on expert opinion, the statistically

No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	Teratogenicity test by the oral route in the rabbit, IIA, 5.6.11/02, [redacted] 1996, (ASB2012-11499), page 607	The GTF respectfully disagrees with the RMS and restates their opinion that the developmental NOAEL in [redacted] (1996, ASB2012-11499) is 400 mg/kg/day, with no evidence to test substance related dose-response and citing the following published expert review which was included in the RAR literature review; Kimmel et al., 2013, Evaluation of developmental toxicity studies of glyphosate with attention to cardiovascular development, *Crit Rev Toxicol*, 2013; 43(2): 79–95	significant increase in post-implantation loss at 200 mg/kg/day with a preponderance of early foetal deaths would be considered relevant if a dose response was noted with early post-implantation loss observed at 400 mg/kg/day. At 200 mg/kg there were early embryonic deaths (slight increase) and at 400 mg/kg there were late embryo/fetal deaths (slight increase). These early and late effects cannot be linked. If there was a true dose response relationship of a single effect one would have seen more early embryonic deaths at 400 mg/kg. Different mechanisms between the two dose levels are attributable to a sudden change in time at which embryos die. Thus a possible mechanism for the early effects at 200 mg/kg/day fails to demonstrate a dose-response, while a possible mechanism for the effect on one animal at the high dose with significant late post implantation loss is not statistically significant, although perhaps biologically relevant in the presence of considerable maternal toxicity at 400 mg/kg/day. The detailed expert review publication, Kimmel et al. (2013) notes; "There was a statistically significant increase in embryo/ fetal death and post-implantation loss at 200 mg/kg/day, and a non-statistically significant increase at 400 mg/kg/day. The standard deviations within these data are considerable and [redacted] (1996) point out that at 200 mg/kg/day, there was a preponderance of ''early fetal deaths'', and at 400 mg/kg/day, the increase could be attributed to one animal with nine late deaths or a post-implantation loss of 69.2%. If the one litter with high implantation loss is excluded, the mean ± standard deviation for post-implantation loss in the remaining litters is 8.0 ± 10.2. With no consistent, statistically significant dose-response pattern, the biological significance of these data is questionable."
(21)	Vol. 3, Annex B.6.6.11, Teratogenicity test by the oral route in the rabbit,	GTF response to RMS comment (August 2013): *What is the idea behind this comment? It is only a summary of the conclusion/comment given by the*	The GTF emphasizes the second paragraph previously submitted. It is important to note that this study should be considered acceptable for establishing a maternal toxicity NOAEL of 75 mg/kg bw/day and for the

No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	IIA, 5.6.11/04, [redacted], 1980 (TOX9552392), page 607	*RMS in the Draft RAR.* page 635	point of departure in human health risk assessment. While a dose-response curve up to the high dose cannot be confirmed for adverse developmental endpoints, due to high maternal morality and thus insufficient number of litters at the high dose, a dose-response is evident for maternal mortality and toxicity. Therefore this study may be considered robust for establishing the maternal toxicity NOAEL of 75 mg/kg/day. This NOAEL is an appropriate point of departure for maternal toxicity in rabbit developmental toxicity studies.
(22)	Vol. 3, Annex B.6.6.11, Teratogenicity test by the oral route in the rabbit, IIA, 5.6.11/06, [redacted] 1993 (TOX9551106), page 607	GTF: The GTF again questions the reliability and utility of this study for establishing a LOAEL for maternal toxicity in rabbits. The GTF respectfully suggests that the additional safety margin for risk assessment (disregarding the 75 mg/kg/day NOAEL in [redacted], 1980, TOX2552390) as proposed by the RMS, is not necessary.	Given the large dose spacing, reporting deficiencies, and inconsistency of findings at ≥ 100 mg/kg bw/day in other studies of the same design, the notifier believes the [redacted] study is not particularly robust or reliable. Furthermore, preliminary dose-range finding studies by [redacted] noted no mortality up to and including 500 mg/kg bw/day, although only two animals in total were dosed at 500 mg/kg bw/day. The full [redacted] study data with 4/16 mortalities at 100 mg/kg bw/day skews the rabbit mortality data set across all studies, with an artificially steep dose response for mortality at 100 mg/kg bw/day. When the data from the supplementary by [redacted] study and the unacceptable [redacted] study are not included for mortality, the dose response curve for pooled mortality data in rabbit developmental toxicity studies present a rather flat dose-response curve for mortality, demonstrating less than 10% mortality for doses below 175 mg/kg bw/day (i.e. zero or one animal mortality per study for each dose below 175 mg/kg bw/day). This suggests that discarding the NOAEL for maternal toxicity of 75 mg/kg bw/day in [redacted] (1980, TOX2552390) may be considered overly conservative in identifying an appropriate point of departure for establishing the glyphosate ADI. Rejecting 75 mg/kg bw/day and moving to 50 mg/kg/day in essence applies an additional 3X uncertainty factor below the mortality NOEL of 150 mg/kg/day ([redacted] 1991,

No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
			TOX9552393) to the intraspecies uncertainty factor of 10X, which is effectively a total uncertainty factor of 300X (30X for intraspecies uncertainty and 10X for interspecies uncertainty).
(23)	Vol.3, Annex B.6.6.12, Published data, Page 687, 688	GTF: Aris et Leblanc 20011 "Maternal and fetal exposure to pesticides associated to genetically modified foods in Eastern Townships of Quebec, Canada." Monsanto's letter to the editor which was submitted in the dossier is not referenced.	Goldstein DA, Dubelman S, Grothaus D, Hammond BG. 2012. Comment: Aris and Leblanc, Maternal and fetal exposure to pesticides associated to genetically modified foods in Eastern Townships of Quebec, Canada. *Reproductive Toxicology* 33: 120– 121. Doi:10.1016/j.reprotox.2011.10.007
(24)	Vol. 3, Annex B.6.8.2.1, Studies on mechanisms of salivary gland findings, page 729	GTF: This section repeats the previous DAR position under "*Copy from the previous DAR: Possible explanation for salivary gland alterations",* without consideration of the evaluations by Williams et al. (2000) and the 2004 JMPR review of this endpoint.	From the 2004 JMPR review, please consider the rationale discounting an adrenergic mechanism as being responsible for the salivary gland effects. The hypothesis that glyphosate produced the salivary gland changes via b-adrenergic activity was questioned in a recent review paper (Williams et al., 2000). The authors emphasized that, first, if glyphosate was a β-agonist, its effect would be to stimulate β-receptors in other effector organs and produce a characteristic set of cardiocirculatory effects, such as increased heart rate and cardiac output as well as decreased blood pressure and peripheral resistance. None of these effects were noted in other studies. Similarly, it is known that isoproterenol and other β-agonists cause myocardial necrosis and enlargement of heart ventricles after prolonged treatment. Glyphosate did not produce any effects in heart tissue, even after long-term exposure at very high doses, providing additional support for the argument that glyphosate does not act as a β-agonist. The authors concluded that glyphosate has no significant β-adrenergic activity and therefore could not produce salivary gland changes via β-agonist activity. They proposed a number of other potential mechanisms for salivary gland alteration, including non-chemical modes of action. For example, salivary gland secretion has been shown to be

No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
			affected by the texture and moistness of feed, and salivary gland enlargement has been caused by malnutrition. Glyphosate could be acting by such a non-chemical mechanism. Because glyphosate is a strong organic acid, dietary administration at relatively high concentrations may cause mild oral irritation leading to increased salivary gland size and flow. In the long-term exposure studies with glyphosate there were several salivary gland changes. These changes were: most pronounced in the parotid gland, responsible for secretion of serous fluid in response to such stimuli as acidic materials; absent in the sublingual gland that releases mucous fluid in response to other stimuli; and observed to an intermediate degree in the submandibular gland that contains a mixture of mucous and serous secreting cells. This pattern of observations was considered to be consistent with the hypothesis that the salivary gland changes observed are a biological response to the acidic nature of glyphosate. These salivary gland alterations are not known to represent any pathological condition and were not considered to be either toxicologically significant or adverse by Williams et al. (2000).
(25)	Vol. 3, Annex B.6.8.2.1, Studies on mechanisms of salivary gland findings, Effects of citric acid ([redacted] 2010), page 729	GTF: Regarding RMS comments on [redacted] (2010), "*However, in principle, severe organ weight and histological changes may become adverse even if they are adaptive by nature."*	There is no evidence that the salivary gland alterations noted in shorter term studies had developed into adverse effects in the multiple chronic studies with glyphosate. The reported findings were not severe and failed prove adverse. Data demonstrate that salivary gland alterations are clearly reversible, being attenuated over time. The following results support the position that these are adaptive and reversible responses. [redacted] (1996): 1-year NOEL/LOEL 141/560 mg/kg bw/day (M); 671/1664 mg/kg bw/day (F) [redacted] (2001): No effects noted up to 1214/1498 (M/F) at 2-years [redacted] (1993): At 52 weeks parotid salivary gland weight was increased in males at 100, 300 and 1000 mg/kg bw/day. Combined sublingual and submaxillary gland weight was increased in high-dose

No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
			males and females. However, salivary gland weights were not affected at week 104 at any dose level.
(26)	Vol. 3, Annex B.6.8.2.1, Studies on mechanisms of salivary gland findings, Comparison of sensitivity of different rat strains to salivary gland lesions (Allen, 1996), RMS comments page 740	GTF: The GTF is of the opinion that changes in salivary glands result from constant exposure to a low pH diet.	Allen (1996; ASB2012-11520/11537) demonstrates that changes were observed following dietary administration only – ruling out any possible systemic mechanism. This correlates with observation across all the toxicology studies presented. Therefore, these changes are considered adaptive. In many long term toxicity studies where changes were observed in the parotid salivary gland they were neither severe nor did they have an adverse impact.
(27)	Vol. 3, Annex B.6.8.2.1, Studies on mechanisms of salivary gland findings, Comparison of sensitivity of different rat strains to salivary gland lesions [redacted], 1996), RMS comments page 740	GTF: The incidence of basophilia of parotid acinar cells in F344 rats in the control group was 7/8, 0/8 & 1/8 at different time points throughout this study. This suggests that there is a large variation in the background incidence of this finding in this strain of rat. Basophilia of parotid acinar cells was observed in 6/8 and 5/8 animals after 4 and 13 weeks recovery respectively. This incidence is well within the control incidence of this finding observed in this strain in this study.	This study is further evidence that the salivary gland findings observed following high levels of glyphosate acid exposure in the diet are an adaptive change to compensate for the low pH. This change was clearly reversible in 2/3 strains tested and likely reversed in the F344 strain too. Together with the other weight of evidence presented: • The finding was observed with another organic acid with a similar pH-dilution curve to glyphosate. • The effect has only been observed following dietary administration. • ADME studies indicate that glyphosate does not accumulate in the salivary glands. • The finding has not been consistently observed across, sex, dose, strain. • The cellular alteration did not progress in terms of severity or development to preneoplastic or neoplastic lesion with time. When the control incidence of basophilia of parotid salivary glands is taken into account in F344 rats there is no indication that this strain is more sensitive. Furthermore, group mean bodyweight differences were

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Further explanations</th></tr>
<tr><td></td><td></td><td></td><td>observed in both the AP & CD rat strains whereas no effect was noted in the F344 strain rats. This indicates that the most sensitive strains were used in the toxicology studies.</td></tr>
<tr><td>(28)</td><td>Vol. 3, Annex B.6.12.2, Dermal absorption of glyphosate active substance in vitro (abraded rabbit skin), page 827</td><td>GTF:
This study was originally submitted in Section B.6.3.1.3 to supplement the repeat dose dermal toxicity study, [redacted] (1982, TOX9552366), in order to calculate the systemic NOAEL from the rabbit repeat dose dermal NOAEL of 5000 mg/kg/day by [redacted] The RMS apparently did not address the purpose of this study in linking this with the Johnson study to calculate the systemic dose and NOAEL in rabbits, as stated in the opening paragraph of the study summary.</td><td>The GTF agrees that this study would be considered supplementary for the purpose of understanding human dermal absorption of glyphosate. However, the opening paragraph of the study summary clearly explains this was not the purpose of the study, which is why it was originally submitted in section B.6.3.1.3, to better characterize the systemic dose resulting from the 5000 mg/kg bw/day dermal dose NOAEL in [redacted] (1982, TOX9552366).
The results of Hadfield (2012) with 2.66% biological availability of a 5000 mg/kg/day dermal dose to abraded rabbit skin, was used to determine the systemic rabbit NOAEL in [redacted] (1982, TOX9552366) of 133 mg/kg/day. This systemic NOAEL, which converted to an equivalent repeat oral dose NOAEL (based on 20% oral absorption) equals 665 mg/kg/day, which is 13.3 times greater than the rabbit NOAEL applied to the RMS proposed AOEL calculation. This oral dose is also significantly higher than doses which elicited significant maternal toxicity including mortality, presumably via non-systemic toxicity (i.e. GI irritation). The Hadfield study is critical in demonstrating the RMS proposed endpoint selection is not appropriate for determining a systemic toxicity driven AOEL for glyphosate.
<table>
<tr><td>Study Type</td><td>Rabbit Developmental</td><td>Rabbit Repeat Dose Dermal</td></tr>
<tr><td>Dose Level</td><td>100 mg/kg bw/day</td><td>5000 mg/kg bw/day</td></tr>
<tr><td>% Absorption</td><td>20% (oral)</td><td>2.66% (dermal)</td></tr>
<tr><td>Systemic exposure</td><td>20 mg/kg bw/day</td><td>133 mg/kg bw/day</td></tr>
</table>
</td></tr>
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No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
			Toxicological effect: Increased mortality: None
(29)	Vol. 3, Annex B.6.13.3.1, Toxicological evaluation of the [redacted] surfactant (CAS no. 61791-26-2), page 835	GTF: The assessment of [redacted] is not considered to fall under the review of glyphosate Annex I Renewal.	[redacted] are not present in the lead formulation of the joint submission and are therefore not relevant in the context of the European re-authorisation of the active substance glyphosate. The evaluation of [redacted] should as such be an issue of ad hoc national re-authorisation post Annex I renewal.

3. Metabolism and Residues Data(B.7)

No.	Column 1 Reference to assessment report *	Column 2 Comment * (restricted to 500 characters, ca. 10 lines)	Column 3 Further explanations
(1)	Vol. 1, Level 1, 2.7.9, Proposed MRLs and compliance with existing MRLs, page 103 Also relevant for Vol. 3, Annex B.7.12, Proposed EU MRLs and justification for the acceptability of those residues (Annex IIA 6.7; Annex IIIA 8.7)	GTF: In Vol.1 it is indicated 'In comparison to established MRLs for glyphosate (according to Reg. (EC) 396/2005) the MRLs for barley and oats (20 mg/kg), wheat and rye (10 mg/kg), olives (1 mg/kg) and bovine kidney (2 mg/kg) are lower than the values estimated in this document.' It should be noted that the increase in MRL reflects a change in calculation methodology and does not reflect new data/higher residues.	
(2)	List of endpoints, Residues (Annex Point IIA 6.7) Also relevant for: Vol. 3, Annex B.7.16, Summary and evaluation of residue behaviour, page 312	GTF: Residue definition for monitoring does not include N-acetyl Glyphosate or N-acetyl AMPA but is defined as Glyphosate only for foods of both plant and animal origin.	In 2009 EFSA issued a reasoned opinion (RO) on the Modification of the residue definition of glyphosate in genetically modified maize grain and soybeans, and in products of animal origin (EFSA Journal 2009; 7(9): 1310). This RO proposed a residue definition for risk assessment in all plant commodities, (including soybean and maize) and all food commodities of animal origin. In addition three (3) possible options were proposed regarding the residue definition in maize and soybeans for enforcement purposes. In the Summary report (SANCO-D(2011) 353285) of the Standing Committee meeting on the Food Chain and animal health; section Pesticide residues + plant protection products-legislation of February 3-4 2011, the committee concluded that the residue definition for enforcement should not change (option 1 in the EFSA reasoned opinion; it is residue = **glyphosate only**) but that for the definition for the purpose of risk assessment the complete residue definition with all metabolites would

No.	Column 1 Reference to assessment report *	Column 2 Comment * (restricted to 500 characters, ca. 10 lines)	Column 3 Further explanations
			need to be used. Given the fact that no GM uses are included in the representative GAP of the joint submission and given the argumentation above, no analytical methods for enforcement purposes are needed to cover N-acetyl glyphosate. The primary and confirmatory methods provided in the joint submission (with additional validation data that will be submitted where appropriate) are adequate to cover the residue definition for monitoring and post registration purposes. Also in the context of risk assessment, the uses listed in the representative GAP do not yield N-acetyl Glyphosate as a residue (no GM uses included). The residues (including N-acetyl Glyphosate) related to imported commodities are regulated under EU Regulation 369/2005 and not Regulation 1107/2009 nor regulation 1141/2010. These data have recently been submitted by the data owner and considered for risk assessment.
(3)	Vol. 3, Annex B.7.1.1.3, Pulses and oilseeds. Report No. 304, (RIP9600099), page 20	GTF: This report was not conducted under GLP.	
(4)	Vol. 3, Annex B.7.1.1.3, Pulses and oilseeds, Report RR 91-029B (RIP9500015), page 19	GTF: In Table 7.1-20, several values differ from those presented in the study report: Total extracted from both green and yellow seeds should be 53.1% TRR Total extracted from hay should be 48.5% TRR	
(5)	Vol. 3, Annex B.7.1.1.4, Cereal grains, Report A1	GTF: Report RIP9501209 is provided in the plant	

No.	Column 1 Reference to assessment report *	Column 2 Comment * (restricted to 500 characters, ca. 10 lines)	Column 3 Further explanations
	(RIP95012109), page 31	metabolism section, under B.7.1.1.4 – Cereal grains. It is a residue study, not a metabolism study.	
(6)	Vol. 3, Annex B.7.1.1.5, Miscellaneous crops, Report RD93 (RIP9501198), page 37	GTF: Report RIP9501198 is provided in the plant metabolism section, under B.7.1.15 – Miscellaneous Crops. It is a residue study, not a metabolism study.	
(7)	Vol. 3, Annex B.7.2.1, Lactating goats, Report RR 93-062B (RIP9500022), page 76	GTF: In Table 7.2-14, the following reported value appears to be incorrect: The amount of glyphosate found in milk was 0.005 mg eq/kg, not 0.004.	These difference also affects Table 7.3-8
(8)	Vol. 3, Annex B.7.3.1.2.2, GOX ("glyphosate oxidoreductase") modified crops, page 122	GTF: Table 7.3-5 (Overview of glyphosate residues and its metabolites in CP4-EPSPS and GOX modified crops), Maize values for fodder and grain are reversed in Cols 5-7 and Col 9. In Column 4, fodder and its value are listed first and grain second. In columns 5-7 and 9, the grain value is listed above the fodder value. Grain values are lower than fodder values for all metabolites	
(9)	Vol 3, Annex B.7.3.1.3, Conclusions for plant matrices. Table B.7.3-7, page 127	GTF: In the comment under Current evaluation (proposal), it mentions pending import tolerances for GAT modified lentils. The import tolerance is for conventional lentils, not GAT modified lentils.	
(10)	Vol 3, Annex B.7.3.2 Residue definition for animal commodities, page	GTF: The following value for AMPA in Table 7.3-8 (for hen studies Bodden, 1988, RIP9501205 &	

No.	Column 1 Reference to assessment report *	Column 2 Comment * (restricted to 500 characters, ca. 10 lines)	Column 3 Further explanations
	131	Patanella et al,1988, RIP9501206) is incorrect based on revisions to the summary table on page 86: Hen kidney, Group 4 (49.9 mg glyphosate + 5.3 mg AMPA per kg bw), AMPA should be 4.4% TRR, not 4.2%.	
(11)	Vol. 3, Annex B.7.6.3, Linseed, mustard seed and rape seed, page 151	GTF: Trials involving a PHI of 14 days and an application rate > +25% (2.8 - 2.9 kg as/ha) should be accepted as they represent a worst case scenario. In this case, sufficient data to defend the pre-harvest use in linseed, mustard seed and oilseed rape is available. If the proportionality principle is adopted, then additional trials will also be available to fill the data gap.	
(12)	Vol. 3, Table 7.6.5, Glyphosate and AMPA residues after application to rape and linseed with application rates deviating more than 25 % to the cGAP, page 153	GTF: In Table B.7.6-5, the HR value for Rape Seeds is incorrect and should be reduced from 30.35 to 11.9 mg/kg to reflect the residue data presented.	
(13)	Vol. 3, Annex B.7.6.7, Storage stability, Crop, Report MSL-10843 (RIP9501332), page 163	GTF: For report RIP9501332 it is noted that there is a deviation: 'original guideline not provided'. The study was conducted under the current guideline at the time, which was referenced in the report (and noted in the DAR), and therefore this is not concluded to be a deviation.	The same comment applies to additional studies on the following pages: 177, 220, 222, 223, 243, 253, 264, 267 and 274.
(14)	Vol. 3, Annex B.7.13,	GTF:	

Section 6 – Metabolism and Residues Data (B.7)

No.	Column 1 Reference to assessment report *	Column 2 Comment * (restricted to 500 characters, ca. 10 lines)	Column 3 Further explanations
	Proposed EU Import tolerances and justification for the acceptability of those residues, page 303	Table B.7.13-1 title should be 'Summary of import tolerances on CP4-EPSPS and GOX modified crops', not just 'GOX modified crops'. Soya beans are modified only with CP4-EPSPS, and the maize included in the first DAR was modified with both CP4-EPSPS and GOX.	
(15)	Vol. 3, Annex B.7.13, Proposed EU Import tolerances and justification for the acceptability of those residues, page 303	GTF: The section under 'GAT modified crops' should reflect the Standing Committee decision of February 3-4 2011 and therefore only present OPTION 1.	Refer to further explanations provided under Point (2)
(16)	Vol 3, Annex B.7.14, Basis for differences with Codex MRLs, page 307	GTF: The JMPR 2011 review included glyphosate tolerant (CP4 EPSPS only) sugar beets and sweetcorn, and conventional lentils, in addition to the GAT crops.	
(17)	Vol. 3, Annex B.7.18, Appendix – Supervised field trials, page 353	GTF: Discrepancies were noted in the 'Applicant' and 'Commercial Product' listed in a number of the tables. Each instance is listed below on a separate line with the page number(s) in Column 1 and comment in Column 2.	
(18)	Vol. 3, Annex B.7.18, Appendix – Supervised field trials, pages 354, 358, 370, 374, 380, 405, 410, 413, 422, 427, 441, 445, 448, 522, 525, 531, 533, 751, 931	GTF: The content of a.i. is listed as 355.7 g/l. The value should be 360 g/l.	

Section 6 – Metabolism and Residues Data (B.7)

No.	Column 1 Reference to assessment report *	Column 2 Comment * (restricted to 500 characters, ca. 10 lines)	Column 3 Further explanations
(19)	Vol. 3, Annex B.7.18.2, Pome fruit, page 370	GTF: The commercial product should be Glistar, not Roundup.	
(20)	Vol. 3, Annex B.7.18.3, Stone fruit, page 382	GTF: This study was generated by Monsanto using a Monsanto formulation but Cheminova A/S has joint access. Applicant should also include Cheminova A/S	
(21)	Vol. 3, Annex B.7.18.3, Stone fruit, page 383	GTF: This study was generated by Monsanto using a Monsanto formulation but Cheminova A/S has joint access. Applicant should also include Cheminova A/S	
(22)	Vol. 3, Annex B.7.18, Appendix – Supervised field trials, pages 401, 412, 417, 419, 420, 426, 429, 430, 432, 433, 434, 435, 436, 438, 439, 447, 451, 453, 454, 585, 586, 592, 592, 594, 599, 601, 607, 610, 615, 619, 623, 627, 650, 653, 660, 662, 669, 674, 676, 707, 814, 844, 871, 892, 894, 914, 916, 946, 960	GTF: The formulation is listed as SC. It should be listed as SL. In some instances the formulation type is also listed as SC in Column 10.	
(23)	Vol. 3, Annex B.7.18, Appendix – Supervised field trials, pages 555, 692, 757, 942	GTF: The formulation (MON 78568) is listed as SG. It should be listed as WG.	

Section 6 – Metabolism and Residues Data (B.7)

No.	Column 1 Reference to assessment report *	Column 2 Comment * (restricted to 500 characters, ca. 10 lines)	Column 3 Further explanations
(24)	Vol. 3, Annex B.7.18.18, Barley (Northern Europe), page 563	GTF: Applicant is Cheminova A/S and not Monsanto	
(25)	Vol. 3, Annex B.7.18.18, Barley (Northern Europe), page 574	GTF: The commercial product is missing. It should be MON 52276. The formulation is listed as SC. It should be listed as SL (both in the header and in Column 10).	
(26)	Vol. 3, Annex B.7.18.18, Barley (Northern Europe), page 578	GTF: The commercial product is missing. It should be MON 44068.	
(27)	Vol. 3, Annex B.7.18.20, Oats, page 704	GTF: Commercial Product is CHE 3607	
(28)	Vol. 3, Annex B.7.18.20, Oats, page 711	GTF: Commercial Product is CHE 3607	
(29)	Vol. 3, Annex B.7.18.22, Wheat (Northern Europe), page 771	GTF: The formulation (MON 44068) is listed as SG. It should be listed as WG.	
(30)	Vol. 3, Annex B.7.18.22, Wheat (Northern Europe), page 894	GTF: The commercial product is not listed. It should be MON 14478.	

4. Environmental fate and behaviour (B.8)

No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	List of endpoints, Page 30, In Section "Residues requiring further assessment"	GTF: AMPA should be included in addition to the glyphosate that has been listed for Groundwater.	
(2)	Vol. 1, Level 1, 2.3.4, Summary of observations on other undesirable or unintended side-effects, page 28	GTF: On page 28, it is stated that the soil (field), DT_{50} value for glyphosate "varies from 3 to 174 days depending on edaphic and climatic conditions". However, in Vole. 3, Annex B.8.1.2.2 Field studies, page 111, Table B.8.1-117, the DT_{50} values of all available field soil dissipation studies of glyphosate were reported to be in the range of 5.7 to 40.9 days.	
(3)	Vol. 1, Level 1, 2.8.4, Summary of monitoring data concerning fate and behaviour of the active substance, metabolites, degradation and reaction products, page 112	GTF : on page 112, RMS concludes: ".....that misuses of plant protection products on paved surfaces, which often contain glyphosate as active ingredient, by non-professional users occur to a relatively large extent. Therefore, current discussions in Germany are focusing on whether the findings of glyphosate and its metabolite AMPA in surface waters originate to some extent from these misuses of plant protection products containing glyphosate on paved surfaces by non-professional users." The use of glyphosate based products by non-professional users or even professional users on	

No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		paved surfaces is not part of the representative GAP supporting the glyphosate Annex I renewal submission. Therefore comments, suggestions and recommendations regarding this use are not relevant in the context of the European re-authorisation of the active substance glyphosate. Since this use is out of scope of the joint renewal submission, the GTF has not submitted any data proactively as part of the initial submission and is in no position to do so in the rebuttal of the above claim. The GTF refers to the re-authorization process of individual company's PPPs containing glyphosate under Article 43 to defend this use at zonal/national level. Therefore comments regarding this use in the RAR should not influence the EFSA opinion nor the provisions of the Commissions' review report.	
(4)	Vol. 1, Level 1, 2.8.4, Summary of monitoring data concerning fate and behaviour of the active substance, metabolites, degradation and reaction products, page 113	GTF: on page 113, RMS concludes the following in regard to bank filtration of glyphosate into groundwater: "Within a study from Spain (Sanchís et al., 2012, BVL no 2537361), it is described that surface waters exist in 10 out of 11 sampling sites where glyphosate was (at least partly) detected. Due to this fact, surface run-off and/or drainage into these waters with subsequent bank filtration into groundwater cannot be excluded as pathway. During the EU evaluation of the active substances the pathway surface run-off and drainage into an	

No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		adjacent ditch with subsequent bank filtration into groundwater is not considered until now." The GTF does not concur with the assertion related to the possibility of the movement of glyphosate/AMPA from surface run-off and drainage into groundwater through bank filtration. Conservative experimental data summarized in RAR (Vol.3, Annex B.8.5. Impact on water treatment procedures) show glyphosate and AMPA are removed from water by bank filtration to a large extent (20-50% and 25-95% for glyphosate and AMPA, respectively).	
(5)	Vol. 1, Level 3, 3.1.1.4, Criteria for the approval of an active substance, page 152	GTF: Page 152 under the "Definition of residues for monitoring" glyphosate, AMPA, and HMPA are listed for surface water and sediment compartments. This is not correct and HMPA should not be included in the list since as described correctly on page 131 of the same document and the "List of Endpoints" the residue definitions for monitoring purposes should be glyphosate and AMPA for surface water and sediment.	
(6)	Vol. 3, Annex B.8.1.2.1, Laboratory studies, page 75," RMS Comment and re-calculation"	GTF disagrees with the RMS decision to include data points beyond study duration of 120 days for the studies of Dean, 1995 and Galicia & Morgenroth, 1993. Soil microbial biomass clearly declined in both studies. In addition, total microbial biomass measurement does not guarantee a proportional microbial diversity and	The fact that microbial biomass decreased from beginning to the end of studies is likely to have an impact on the overall degradation rates of glyphosate and AMPA. In the case of the Dean study, biomass was essentially constant through 120 days; thereafter it dropped off by nearly 25%. If OECD guideline 307 do not recommend going beyond 120 days because of concern over soil viability, it seems like the results from the biomass determination confirms this concern and gives us a rationale for

No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		activity, ensuring abundance of glyphosate/AMPA-degrading microorganisms in soil. We note that the RMS re-calculated endpoint from Dean, 1995 study appears to be an outlier in the modelling endpoint Table B.8.1-94 for glyphosate. This observation may suggest that inclusion of data points beyond 120 days resulted in endpoints that are not consistent with the weight of evidence.	excluding data beyond 120 days. For the same reason, we should be able to exclude data beyond 120 days in the Galicia & Morgenroth study, even though there was no biomass determination at 120 day. There should be enough doubt in the viability of soil considering the decline in microbial biomass from the beginning to the end of the study was > 60%.
(7)	Vol. 3, Annex B.8.1.2.1, Laboratory studies, page 83ff	GTF: The RMS has re-calculated the half-life of a number of studies and provided the χ^2 and t-test values for testing the goodness of fit; however, the visual assessment cannot be reviewed as no graphs have been included. Please provide the graphs in addition to other statistics such as confidence intervals so that the fits can be assessed.	
(8)	Vol. 3, Annex B.8.1.2.1, Laboratory studies, page 75	GTF: On page 75, RMS states: "The approach of the study author, to use the overall mass balance as initial glyphosate concentration is not exactly according to FOCUS (2006, 2011) where it is only suggested to convert the initial metabolite concentration to mass parent and to add it to the value measured for the parent". GTF respectfully disagree with this conclusion for the reasons described in Column 3.	FOCUS Kinetics guidance (2011) on pages 76 and 77 provides instructions on how to correct Time 0 in the kinetic analysis for the formation of metabolites and/or bound residues found in the time zero samples. On page 77 the guidance document states: *"Initial concentrations for metabolites and bound residues (in laboratory studies) are expected to be zero. However, the time from application of the parent compound to taking the first soil sample is usually in the range of 0.5-2 hours. Rapidly formed metabolites and bound residues may thus be detectable in the first sample. In this situation, the amount of the parent compound present in soil at time zero should be adjusted during kinetic analysis (i.e., the mass of the metabolite found in the*

No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
			initial sample is converted to mass parent and added to the value measured for the parent compound). The mass of the metabolite should be set to zero. Where possible, this procedure should also be followed if unidentified metabolites or bound residues (sink compartment) are present in the first sample due to rapid formation." In a laboratory soil study, the mass balance at time 0 represents the sum of the concentrations of parent, metabolite(s), and bound residues; therefore, correction for mass balance for Time 0 parent concentration is a valid approach according to FOCUS Kinetics guidance (2011).
(9)	Vol. 3, Annex B.8.1.2.1, Laboratory studies, page 76	GTF: page 76, Table B.8.1-76, Dean, 1995 kinetic re-evaluation for glyphosate - The DFOP rate constants k_1 and k_2 values as reported in Table B.8.1-76 appear to be in error. The DT_{90} value of 300.73 cannot be reproduced by GTF. It appears that RMS re-calculations presented on page 76 (Table B.8.1-76), for Time 0 values (based on the M0 optimized values of about 90%) were not corrected for metabolites and bound residues as described in comment # 3 above.	
(10)	Vol. 3, Annex B.8.1.2.1, Laboratory studies, page 74 and 87	GTF: The modelling DT_{50} value of 300.7 days reported in Table B.8.1-94 for glyphosate from the Dean, 1995 Arrow soil appears to be in error and it appears that this value corresponds to the DT_{90} value as reported in Table B.8.1-76. We note that the RMS re-calculated endpoint from the Dean, 1995 study is clearly an outlier among all the modelling endpoint reported in Table B.8.1-94 for	Time (days) %Glyphosate 0 Day 97.1 3 days 84.6 7 days 74.0 14 days 66.9 30 days 54.3 60 days 39.8 90 days 34.0 120 days 28.6

No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		glyphosate. Visual inspection of the residue data presented in column 3 for this soil highlight the fact that a DT_{50} of 300.7 days could not fit the experimental data. In other words, a DT_{50} of 300.7 days does not make any sense if the experimental data show glyphosate degradation had occurred nearly for two half-lives (75% degradation) during the 180 days of incubation.	180 days 27.1
(11)	Vol. 3, Annex B.8.1.2.1, Laboratory studies, page 79	GTF: page 79, Table B.8.1-82 – Kesterson & Atkins processed residue data – Day 0 residue data for glyphosate is not correct. This study was conducted with radiolabeled glyphosate and quantitation of AMPA was based on applied radioactivity which is independent of the relative mass of AMPA or glyphosate. AMPA % of applied on Day 0 should be added to glyphosate and should not be corrected for the molecular weight ratio of AMPA to glyphosate.	The same is true for the Day0 processed residue data for Lewis & Turnbull study in page 82, Table B.8.1-88. AMPA % of applied at Day 0 should be simply added to the glyphosate % of applied at Day 0, without any mass correction. In addition, the Day 0 concentration of glyphosate should be corrected for Day 0 mass balance based on the rationale provided in comment # 3 above.
(12)	Vol. 3, Annex B.8.2.2, Adsorption and desorption of all relevant metabolites, page 122	GTF: Page 122, Table B.8.2.1 – Waring 1992 study investigated the adsorption properties of glyphosate in 5 soils and one sediment at single concentrations. No isotherm data were provided by the study. GTF believes that a 1/n default value of 1 applied to the soils and sediment from this study should **not** be included in the arithmetic mean calculation considering that numerous valid data are available from other submitted studies.	
(13)	Vol. 3, Annex B.8.4.4,	GTF:	

Section 7 – Environmental fate and behaviour (B.8)

No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	Water/sediment study and also in list of endpoints, page 282	page 282 Persistence endpoints for AMPA (Table B.8.4-70) according to the DG SANCO Working Document on "Evidence needed to identify POP, PBT and vPvB Properties for Pesticides" (rev. 3, 25.09.2012), metabolites should not be included in the assessment against the P-criteria laid down in point 3.7 of Annex II of Regulation (EC) no 1107/2009.	
(14)	Vol. 3, Annex B.8.10.6.2, Literature Review, Monitoring data, pages 188 and 232	GTF: Pages 188 and 232 - Augustin (2003) is not a peer-reviewed publication.	
(15)	Vol. 3, Annex B.8.10.6.2, Literature Review, Monitoring data, pages 230 and 236	GTF: Pages 230 and 236 - Malaguerra et al. (2010) is not a peer reviewed publication.	
(16)	Vol. 3, Annex B.8.10.7, Literature Review, Other studies, pages 298 and 316	GTF: Pages 298 and 316 - The Watts (2009) citation is not peer-reviewed.	

5. Ecotoxicology (B.9)

No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	List of Endpoints, Effects on non-target plants	GTF: An endpoint of ER_{50} = 146 g a.s./ha was used in the original risk assessment, and the notifier submitted an endpoint of HC_5 = 206.35 g a.s./ha for a probabilistic risk assessment. New data is submitted for the representative formulation MON 52776, with for a revised risk assessment below.	Vol. 3, B.9.9.1.5 page 270
(2)	List of Endpoints, toxicity data for aquatic species	GTF: Daphnia, reproduction, glyphosate acid: Change of endpoint (RMS: 12.5 mg/L; notifier: 30 mg/L). Endpoint of Wüthrich, 1990 (250795) was not used, endpoint of Magor, Shillabeer, 1999 (BL6535/B) was used	Vol. 3, B.9.2.1.5 Page 82
(3)	List of Endpoints, Effects on terrestrial vertebrates, Birds	GTF: Long-term endpoints should be 201 mg/kg b.w./d and 300 mg/kg bw/d, based on studies presented	See comments below for Vol. 3 B.9.1.
(4)	List of Endpoints, Effects on terrestrial vertebrates, Mammals	GTF: The acute oral endpoint in the rat should be at the very least >5000 mg/kg bw, not >2000 mg/kg bw. This point was already commented in the mammalian toxicity Section 4.	While > 2000 mg/kg/day is the assigned upper LD_{50} limit for EU classification, these acute data are not applicable to other sections of the dossier. For example, the acute oral LD_{50} data submitted reflect a higher value of > 5000 mg/kg/day as appropriate for use in the acute oral wildlife risk assessment. In addition, other world regions which may have adopted the GHS classification scheme look to the EU for guidance in regulatory reviews. Under representation of the EU limit dose as 2000 mg/kg/day rather than 5000 mg/kg/day for GHS, may undermine other regions with less sophisticated regulatory expertise than the EU, possibly resulting in inappropriate classification of glyphosate acute oral/dermal

No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
			endpoints as GHS category 4 based on LD_{50} > for 2000 mg/kg/day, rather than the appropriate GHS category 5 (not classified) for > 5000 mg/kg/day.
(5)	List of Endpoints, Effects on terrestrial vertebrates, Mammals	GTF: Long-term endpoint for the ecological risk assessment should be at least 985 mg/kg bw, based on no ecologically adverse effect observed up to highest concentration tested in 2-generation rat study ([redacted]. 2000).	See comments below for Vol. 3 B.9.3., Vol. 3 B.6.6.1 (2-gen repro tox in rat), Vol. 3 B.6.6.10 (terato in rat), Vol. 3 B.6.6.11 (terato rabbit).
(6)	Vol. 1, Level 1, 2.9.1 Summary of effects on birds and other terrestrial vertebrates, page 117	GTF: The proposed endpoint should be LD_{50} > 5000 mg/kg bw, not >2000 mg/kg bw.	While > 2000 mg/kg/day is the assigned upper LD 50 limit for EU classification, these acute data are applicable to other sections of the dossier. For example, the acute oral LD50 data submitted reflect a higher value of > 5000 mg/kg/day as appropriate for use in the acute oral wildlife risk assessment. In addition, other world regions which may have adopted the GHS classification scheme look to the EU for guidance in regulatory reviews. Under representation of the EU limit dose as 2000 mg/kg/day rather than 5000 mg/kg/day for GHS, may undermine other regions with less sophisticated regulatory expertise than the EU, possibly resulting in inappropriate classification of glyphosate acute oral/dermal endpoints as GHS category 4 based on LD50 > for 2000 mg/kg/day, rather than the appropriate GHS category 5 (not classified) for > 5000 mg/kg/day.
(7)	Vol. 1, Level 1, 2.9.1 Summary of effects on birds and other terrestrial vertebrates, page 117	GTF: According to EFSA guidance (1438/2009), at the screening level, the lowest endpoint from the 2-generation studies in mammals and the developmental toxicity studies should be considered. The relevance of the selected endpoint should be considered for ecological risk assessment at the Tier1 level.	See comments below for Vol. 3 B.9.3. The use of the teratogenicity endpoint of 50 mg a.i./kg bw/d in the screening risk assessment is in accordance with EFSA/2009/1438. Since this endpoint is from a multi-gavage treatment with an acidic compound, this type of treatment may have adverse effects on the GI tract, and is not representative of the exposure that a herbivore would experience in the wild. Dietary studies are much more relevant for this type of risk assessment.

No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		We also note that the EFSA guidelines state that where there are several studies with overlapping NOAELs and LOAELs the chosen endpoint should be HIGHEST NOAEL that does not exceed the lowest LOAEL.	In addition, the highest NOAEL that does not exceed a LOAEL (100 mg/kg/day in table B.9.3-4) according to Vol1 Table 2.6-12 and Table 2.6-14, is 75 mg/kg/day for maternal effects and 175 mg/kg bw/day for developmental effects, based on a LOAEL of 200 mg/kg/day. However, according to the guidance, it is recommended to use the NOAEL rather than the NOEL. Considering that no reproductive effects could be observed in higher concentrations, over longer periods, and more relevant route of exposure such as in the 2-generation rat study, the endpoint to be used in the reproductive mammal risk assessment at Tier 1 should be based on the 2-generation rat study. The only adverse effect observed in the 2-generation rat studies was a decrease in homogenization resistant spermatids in the *cauda epididymidis* in one study in F0 males at 1000 mg/kg bw/d. However, this does not represent an ecologically relevant effect, as it did not reduce offspring or the fitness of the F1 generation. When considering ecologically relevant endpoints, it should be noted that no ecologically relevant adverse effect could be observed up to 985 mg/kg bw/d, which is the highest concentration tested. This no ecological adverse effect level (NOEAEL) should be used in the Tier 1 reproductive mammal risk assessment.
(8)	Vol. 1, Level 1, 2.9.1 Summary of effects on birds and other terrestrial vertebrates, page 117	GTF: See comment on Vol. 1, Level 1, 2.6.7.2.2 Rabbit developmental toxicity and teratogenicity, regarding [redacted] (1996, ASB2012-11499), page 75. The GTF believes the developmental NOAEL in Coles and Doleman is 400 mg/kg/day, with no evidence to test substance related dose-response, citing the published expert review Kimmel et al., 2013, Evaluation of developmental toxicity studies of glyphosate with attention to	The statistically significant increased post-implantation loss at 200 mg/kg/day with a preponderance of early fetal deaths would be considered relevant if a dose response was noted with early post-implantation loss observed at 400 mg/kg/day. At 200 mg/kg there were early embryonic deaths (slight increase) and at 400 mg/kg there were late embryo/fetal deaths (slight increase). These early and late effects cannot be linked. If there was a true dose response relationship of a single effect one would have seen more early embryonic deaths at 400 mg/kg. Different mechanisms between the two dose levels are attributable to a sudden change in time at which embryos die. Thus a possible mechanism for the early effects at 200 mg/kg/day fails to demonstrate a dose-

No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		cardiovascular development, *Crit Rev Toxicol*, 2013; 43(2): 79–95.	response, while a possible mechanism for the effect on one animal at the high dose with significant late post implantation loss is not statistically significant, although perhaps biologically relevant in the presence of considerable maternal toxicity at 400 mg/kg/day. The detailed expert review publication, Kimmel et al. (2013) notes; "There was a statistically significant increase in embryo/ fetal death and post-implantation loss at 200 mg/kg/day, and a statistically not significant increase at 400 mg/kg/day. The standard deviations within these data are considerable and [redacted] (1996) point out that at 200 mg/kg/day, there was a preponderance of ''early fetal deaths'', and at 400 mg/kg/day, the increase could be attributed to one animal with nine late deaths or a post-implantation loss of 69.2%. If the one litter with high implantation loss is excluded, the mean ± standard deviation for post-implantation loss in the remaining litters is 8.0 ± 10.2. With no consistent, statistically significant dose-response pattern, the biological significance of these data is questionable." Pooling data for **maternal toxicity** in rabbit developmental toxicity studies clearly demonstrates that 75 mg/kg bw/day is the NOAEL for maternal toxicity. As discussed in comment (10), the supplementary Suresh study findings at 100 mg/kg bw/day are not in alignment with other studies and may be considered of questionable reliability for risk assessment purposes. However, in an abundance of caution, if the Suresh dose of 100 mg/kg bw/day is considered the LOAEL for maternal toxicity, additional conservatism by rejecting the Tasker NOAEL of 75 mg/kg bw/day should be considered overly conservative. **Dose (mg/kg bw/d); <u>Maternal</u> Effects; Study (AIR Ref.)** **10**; **No Adverse Effects**; [redacted] (1995, ASB2012-11498) **20**; **No Adverse Effects**; [redacted] (1993, TOX9551106) **50**; **No Adverse Effects**; [redacted] (1996, ASB2012-11499) **50**; **No Adverse Effects**; [redacted] (1991, TOX9552393)

No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
			75; **No Adverse Effects**; [redacted]. (1980, TOX9552392) **100**; **No Adverse Effects**; [redacted] (1995, ASB2012-11498) **100**; **No Adverse Effects**; [redacted](1996, TOX2000-2001) **100**; Mortality (4/16); [redacted] (1993, TOX9551106) **125**; **No Adverse Effects**; [redacted] (1989, TOX9551960) **150**; Reduced feed intake, fecal output and body weight gain. Soft/liquid stools; [redacted] (1991, TOX9552393) **175**; Reduced feed consumption and bw gain, reduced feces, diarrhoea; [redacted] (1996, TOX2000-2001) **175**; Equivocal increase in mortality (2/16), slight increase in soft stools and diarrhoea; [redacted] (1980, TOX9552392) **200**; Slight reduction in bw gain, not statistically significant; [redacted] (1996, ASB2012-11499) **250**; **No Adverse Effects**; [redacted] (1989, TOX9551960) **300**; GI effects (loose stool); [redacted] (1995, ASB2012-11498) **300**; Reduced feed consumption and bw gain, reduced feces, diarrhoea; [redacted] (1996, TOX2000-2001) **350**; Mortality (10/17), increase in soft stools and diarrhoea; [redacted]. (1980, TOX9552392) **400**; Reduced feed consumption and bw gain; [redacted] (1996, ASB2012-11499) **450**; Reduced feed intake, fecal output and body weight gain. Soft/liquid stools; [redacted] (1991, TOX9552393) **500**; Mortality, soft/liquid stool and mucus stool; [redacted] (1993, TOX9551106) **500**; Reduced body weights during study, including Day 0; [redacted] (1989, TOX9551960) If the Rapporteur is to consider the 100 mg/kg bw/day in [redacted] (1993, TOX9551106) as of sufficient merit to select as the LOAEL for maternal toxicity in rabbits, the notifiers believe that equal merit of the maternal

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			toxicity NOAEL established in [redacted] (1980, TOX9552392) should be of equal merit. If both [redacted] (1993, TOX9551106) and [redacted] (1980, TOX9552392) are considered unreliable for establishing the maternal toxicity endpoint, then a NOAEL of 100 mg/kg bw/day as the point of departure. Pooling data for **developmental effects** in rabbits clearly demonstrates that 175 mg/kg bw/day is the NOAEL for developmental toxicity. **Dose (mg/kg bw/d); Developmental Effects; Study (AIR Ref.)** **10**; **No Adverse Effects**; [redacted] (1995, ASB2012-11498) **20**; **No Adverse Effects**; [redacted] (1993, TOX9551106) **50**; **No Adverse Effects**; [redacted] (1996, ASB2012-11499) **50**; **No Adverse Effects** [redacted]. (1991, TOX9552393) **75**; **No Adverse Effects**; [redacted]. (1980, TOX9552392) **100**; **No Adverse Effects**; [redacted] (1995, ASB2012-11498) **100**; **No Adverse Effects**; [redacted] (1996, TOX2000-2001) **100**; **No Adverse Effects** (insufficient number of adults and litters); [redacted] (1993, TOX9551106) **125**; **No Adverse Effects**; [redacted] (1989, TOX9551960) **150**; **No Adverse Effects**; [redacted]. (1991, TOX9552393) **175**; **No Adverse Effects**; [redacted] (1996, TOX2000-2001) **175**; **No Adverse Effects** (supplementary data due to insufficient number of litters); [redacted] (1980, TOX9552392) **200**; Increased post-implantation loss (early foetal death); [redacted] (1996, ASB2012-11499) **250**; **No Adverse Effects**; [redacted] (1989, TOX9551960) **300**; Abortion/premature delivery; [redacted] (1995, ASB2012-11498) **300**; Reduced foetal body weight and reduced ossification; [redacted] (1996, TOX2000-2001) **350**; **No Adverse Effects** (insufficient number of surviving dams and

No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
			thus litters); [redacted]. (1980, TOX9552392) **400**; Increased post-implantation loss (late foetal death); [redacted] (1996, ASB2012-11499) **450**; Reduced feed intake, fecal output and body weight gain. Soft/liquid stools; [redacted]. (1991, TOX9552393) **500**; **No Adverse Effects** (insufficient number adults and litters); [redacted] (1993, TOX9551106) **500**; failed to produce viable litters (aborted or no live fetuses); [redacted] (1989, TOX9551960)
(9)	Vol. 1, Level 1, 2.9.1 Summary of effects on birds and other terrestrial vertebrates, page 118	GTF: Indirect effects via food chain interference	See comments on Vol. 3, B.9.1.7.7.
(11)	Vol. 3, Annex B.9.1.3, Subchronic toxicity and reproduction, Study KIIA 8.1.4/01, page 10	GTF: We believe this study on bobwhite quail was done properly according to the GLP requirements at the time (1999) and that these data are valid for use in the ecological risk assessment. There appears to have been some confusion with the guideline specification from the original 0.25 ft^2 floor area of the cages. 6 mortalities occurred in the control group and 2 mortalities occurred in each of the treatment groups in week 17. These are considered incidental as they were linked to likely hysteria, not diseases or toxic effects. The study should therefore not be invalidated. A detailed explanatory report is available and can be submitted upon request.	The main concern in this 20 week study, where essentially no effects were seen from any of the glyphosate treatments, and the only unexpected mortalities were in the control at week 19. This variability at such a late stage and only in the control population should not be sufficient to invalidate the study, and we believe that repeating such a study on these grounds would be unethical. Consequently the NOEL of 2250 ppm diet (201 mg/kg/day) is valid and should be used in the risk assessment. For pilot reproduction and definitive reproduction studies, adult Northern Bobwhite are housed in battery breeding pens manufactured by GQF Manufacturing Company (Model No. 206 or 0330). Cages of this type have been successfully used to house Northern Bobwhite for more than 40 years. Each pen has floor space that measures approximately 25 x 51 cm (1275 cm^2 or 638 cm^2 per bird). Floors are sloping so that ceiling height will range from approximately 20 to 26 cm. These measurements exceed those recommended in the *Guide for the Care and Use of*

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			Laboratory Animals, the governing animal welfare regulations in the United States, where the study was performed. The area provided also meets or exceeds recommendations of other husbandry resources. A table is attached that lists a compilation of recommended housing sizes for bobwhite from various sources. The OECD Guideline 206 (1984) value of 0.250 m^2 per pair was apparently based upon the value in the 1978 issue of *Guide* (see above) listed as 0.25 ft^2, with the unit inadvertently miscopied. While it would intuitively seem that "bigger" would be better, that is not the case when housing birds designed to be as close to wild type as possible, a requirement of both the USEPA and OECD guidelines. For bobwhite, where the typical escape response is to flush, a bigger cage can result in more injuries, rather than fewer. In the housing currently used the birds have sufficient room to stretch, and make normal comfort movements, but not so much room as to encourage any attempt at flight. Cage size also impacts the ability to catch the birds for necessary handling without causing undue stress. A cage sized so that the bird can be caught gently and efficiently limits the amount of chase and handling time. Additionally, since both control and treated birds are housed identically, any minor differences in environmental conditions observed will be uniform across all groups, and would not impact the interpretations of the study. The study on the bobwhite quail by [redacted]. (1999) should be used in addition to the similar study on same species by [redacted]. (1) The mortalities in the control group can be clearly attributed to an incidental event (hysteria) and diseases or other affections could be excluded as causes for the increased mortalities. Lesions observed on the birds could be attributed to self-inflicted trauma due to hysteria attack. (2) The mortalities occurred late in the study, week 19 out of 20 and have not affected the final outcome of the study. The remaining birds

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			continued fairing perfectly well until the end of the study. (3) The relevant endpoint, reproduction, is measured during a period of 10 weeks and eggs are incubated, hatched and offspring is observed for a 14 day period. (4) In a short report compiled by the authors of the study, which can be readily made available upon request by the RMS, a statistical analysis was conducted over the 10-week and the 8-week egg-laying period versus historical control data. This clearly demonstrates that the "hysteria-attack" related mortalities in week 9 did not affect the mean values in the control group for the parameters Eggs Laid/Maximum Laid, Eggs Cracked/Eggs Laid, Viable Embryos/Eggs Set, Live 3-Wk Embryos/Viable Embryos, Hatchlings/Live 3-Wk Embryos, 14-Day Old Survivors/Hatchlings, and Hatchlings/Eggs Set. Since there were no statistical differences between the control and any of the treatment groups (500, 1000 and 2250 ppm), and the control group did not differ from the historical control data, this study should be considered as valid and the NOEC should be set at 2250 ppm. (5) For pilot reproduction and reproduction studies, adult Northern Bobwhite are housed in battery breeding pens manufactured by GQF Manufacturing Company (Model No. 206 or 0330). Cages of this type have been used to house Northern Bobwhite for more than 40 years. Each pen has floor space that measures approximately 25 x 51 cm (1275 c^{m2} or 638 c^{m2} per bird). Floors are sloping so that ceiling height will range from approximately 20 to 26 cm. These measurements exceed those recommended in the *Guide for the Care and Use of Laboratory Animals*, the governing animal welfare regulations in the United States, where the study was performed. The area provided also meets or exceeds recommendations of other husbandry resources. A table is attached that lists a compilation of recommended housing sizes for bobwhite from various sources. The OECD Guideline 206 (1984) value of 0.250 m^2 per

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			pair was apparently based upon the value in the 1978 issue of *Guide* (see above) listed as 0.25 ft^2, with the unit inadvertently miscopied. While it would intuitively seem that "bigger" would be better, that is not the case when housing birds designed to be as close to wild type as possible, a requirement of both the USEPA and OECD guidelines. For bobwhite, where the typical escape response is to flush, a bigger cage can result in more injuries, rather than fewer. In the housing currently used the birds have sufficient room to stretch, and make normal comfort movements, but not so much room as to encourage any attempt at flight. Cage size also impacts the ability to catch the birds for necessary handling without causing undue stress. A cage sized so that the bird can be caught gently and efficiently limits the amount of chase and handling time. Additionally, since both control and treated birds are housed identically, any minor differences in environmental conditions observed will be uniform across all groups, and would not impact the interpretations of the study.
(12)	Vol. 3, Annex B.9.1.3, Subchronic toxicity and reproduction, Study KIIA 8.1.4/02, page 12	GTF: The significant difference between the control and the highest treatment group should not be considered as an adverse effect. The NOEC for mallard ducks should be set at 2250 ppm	The statistically significant difference in bodyweight of 14-day hatchlings of 10% in the 2250ppm group did not respond to a dose-respondent pattern. Indeed the treatment group of 500 ppm group was also 10% below the control group, while the intermediate dose group (1000 ppm) was just 1% lower than the control group. Additionally, as mentioned in the study report on page 140, the body weight of hatchlings in the 2250 ppm group was the same as the body weight of hatchlings in the control group of a study running simultaneously in the same laboratory, in birds from the same supplier, in the same cohort. Therefore the NOEC should be set at 2250 ppm and the NOEL at 300 mg/kg bw/d.
(13)	Vol. 3, Annex B.9.1.6, Summary of effects on birds, Table 9.1-10, page 21	GTF: As indicated above, the endpoint from the quail long-term study by [redacted] (1999) should be added with NOEC = 2250 ppm. The mallard long-term	Given that the [redacted] 1999 study with the quail is acceptable based on the arguments provided under Vol. 3, 9.1.3 KIIA 8.1.4/01, it should be listed with 2250 ppm as NOEC. Based on the explanations given under Vol. 3., 9.1.3 KIIA 8.1.4/02 regarding the duck 1-gen, the endpoint should be

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		study by [redacted] (1999) endpoint should be NOEC = 2250 ppm. Detailed comments from the study director can be made available upon request.	NOEC = 2250 ppm
(14)	Vol. 3, Annex B.9.1.7, Risk assessment, page 21	GTF: According to the EFSA guidance document, the chronic endpoints of two reproduction studies in the same species can be taken as one study. As there were no ecologically relevant effects in both studies in the quail, and both studies in the mallard, the lowest ecologically relevant endpoint is 201 mg/kg bw/d based on the highest concentration tested in the quail.	EFSA guidance document 1438/2009, p. 23/139, under Point 2.4.3 "How to deal with more than one study on the same species". Quail 1:0, 50, 200, 1000 ppm, no ecologically relevant effects Quail 2: 0, 500, 1000, 2250 ppm, no ecologically relevant effects Duck 1: 0, 50, 200, 1000 ppm, no ecologically relevant effects Duck 2: 0, 500, 1000, 2250 ppm, no ecologically relevant effects Combining both quail and both duck studies, into one respective study for each species results in the following list of test concentrations: Quail: 0, 50, 200, 500, 1000, 2250 ppm, no ecologically relevant effects Duck: 0, 50, 200, 500, 1000, 2250 ppm, no ecologically relevant effects Therefore for both species the highest tested concentration of 2250 ppm is the NOEC. When the daily doses are calculated for species, the Duck results in 300 mg/kg bw/d and the quail in 201 mg/kg bw/d. The lowest reproductive endpoint in birds should be taken for the risk assessment. Based on the data available for glyphosate, the NOEL for the long-term risk assessment should therefore be 201 mg/kg bw/d.
(15)	Vol. 3, Annex B.9.1.7.7, Indirect Effects via trophic interactions, page 31	GTF: We agree as to the importance of this topic and that in Europe the issues of farmland biodiversity and ecosystem services have to be addressed across all member states via Common Agricultural Policy (CAP) and local agro-environmental schemes. We agree that various indirect effects can be attributed to agricultural production in Europe, and the relevant literature shows that there are a variety of causes. However,	As the RMS indicates, CAP reforms and agro-environment schemes, that are proven to promote biodiversity (and maintain ecosystem services), are needed to work alongside integrated high output farming systems. For this a clearly defined strategy for what in the broadest sense Europe wants to produce and protect on its farms and arable land is needed. However, Annex I renewal of one active ingredient is not the adequate forum for such a debate, since one herbicide is only one of a number of tools to remove weeds from cropped fields. In addition, there are numerous publications and assessments which indicate that the use of glyphosate as a chemical method of weed removal protects soil

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		an Annex I renewal procedure of one active ingredient is not the relevant arena for this discussion. A more extended comment on indirect effects of glyphosate can be made available upon request.	biodiversity and improves soil structure, thereby reducing erosion. None of these aspects were taken into consideration by the RMS, which leads to a biased assessment with regard to biodiversity, outside the remit of 91/414/EEC, which is the legal framework where the Annex I renewal process is placed. This is also acknowledged by the RMS in the text. In addition, the potential issues raised by the RMS for glyphosate conceptually also apply to any other herbicide, be it broadband or specific, leading to inconsistent assessment of AIR II substances if only glyphosate is selected as a case.
(16)	Vol. 3, Annex B.9.1.7.7, Indirect Effects via trophic interactions, page 31	GTF: The RMS highlights the importance of glyphosate regarding indirect effects and concludes that "*glyphosate must therefore be considered the most significant herbicide regarding indirect effects*". We regard this conclusion as highly speculative. As indicated above it is necessary to address the issues of food production and ecosystem services on a broader scale. A more extended comment on relevance of indirect effects of glyphosate can be made available upon request.	The notifier acknowledges the statement made in the RAR, and the legislation and guidelines that are referenced. It proposes that the focus on glyphosate is discriminatory and disproportionate. In particular this brief review does not consider the use of selective herbicides in crop. Equal treatment should be given to other herbicides and weed control practices (and indeed to other agricultural practices such as cultivation, cutting and mowing, crop rotation and fertiliser use).
(17)	Vol. 3, Annex B.9.1.7.7, Indirect Effects via trophic interactions, page 35	GTF: The RMS cites a recent report Jahn et al. 2013. We would appreciate this being made available to us and the public.	
(18)	Vol. 3, Annex B.9.3.2, Summary of terrestrial vertebrate toxicity data, Table B.9.3-3, page 165	GTF: The review of reproduction toxicity did not consider ecological relevance in its assessment of the 2-generation studies. For the study by [redacted], the body-weight differences observed in the	In principle, the use of the teratogenicity endpoint in assessing the long-term endpoint for the risk assessment is in accordance with EFSA/2009/1438. However, according to the guidance, it is recommended to use the NOAEL rather than the NOEL. Considering that no reproductive effects could be observed in higher concentrations, over

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		F1 males at 10000 ppm, are not ecologically relevant because less than 5% in magnitude and the difference cannot be observed at the end of the study (weeks 9 and 10). Therefore the NOEAEL should be 10000ppm, i.e. 985 mg a.s./kg b.w./d	longer periods of exposure, and through more relevant routes of exposure such as in the 2-generation rat study, the endpoint to be used in the reproductive mammal risk assessment at Tier 1 should be based on the 2-generation rat study. When considering ecologically relevant endpoints, it should be noted that no ecologically relevant adverse effect could be observed up to 985 mg/kg bw/d, which is the highest concentration tested. This no ecological adverse effect level (NOEAEL) should be used in the Tier 1 reproductive mammal risk assessment. An endpoint is proposed based on a recent multigenerational rat reproduction study [redacted], 2000*)* which was provided in the post Annex I dossier. The toxicological NOAEL level was 3000 ppm (299 - 323 mg/kg bw/d; male-female), but for this ecotoxicological risk assessment the highest rate in the study 10000 ppm (985 - 1054 mg/kg bw/d; male-female), is used as the NOEAEL based on ecologically significant effects. Continuous feeding at this rate had no effect on the propagation of two generations in the rat. The fertility and reproductive performance of each generation of parental animals and the clinical condition and survival of their offspring were not adversely affected. The only effect of treatment observed was a statistically relevant, but not biologically relevant reduction in the bodyweight of the F1A pups in the 10000 ppm glyphosate acid group with a subsequent reduction in bodyweight of the selected F1 parent males for the duration of the pre-mating period. This is not considered to be ecologically relevant. In the study by [redacted] (1992), the effects observed at the highest treatment dose were not ecologically relevant, as they did not affect the reproduction or general fitness of the animals. In addition, the increase in food and water consumption was not of biological relevance in its size. The observation of salivary gland and parotid are not of relevance when considering population-relevant endpoints as it is the case in the ecological risk assessment.

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			For more detail, the endpoints which need to be carefully considered and weighted for ecological risk assessment for mammals are listed in EFSA/2009/1438 on page 41/139 under Step 9 of Module 4.4. Further comments on teratogenicity of glyphosate in rabbits under Vol. 3 B.6.6.11, in rats under Vol. 3 B.6.6.10, and reproductive toxicity under Vol. 3 B.6.6.1. Note that endpoints deemed as relevant for the individual human risk assessment are not automatically relevant for the population wild mammal risk assessment.
(19)	Vol. 3, Annex B.9.3.3, Risk assessment – mammal acute endpoint, page 167	GTF: The acute endpoint for mammals should be >5000 mg/kg bw, not >2000 mg/kg bw. No mortalities were observed in all studies considered valid. The only study with mortalities at this dose is [redacted] (1979) but it is considered supplementary.	
(20)	Vol. 3, Annex B.9.3.3, Risk assessment – mammal reproductive endpoint, page 167	GTF: The ecologically relevant endpoint for the reproductive mammal risk assessment should be 985 mg a.s./kg bw/d, based on 2-generation NOEAEL in the rat [redacted], 2000), not 50 mg/kg bw/d based on developmental study in rabbit.	The use of the 2-generation rat study endpoint is more relevant, mainly because the exposure is much longer (2 generations) and through a more relevant route (dietary). In addition, 20x higher doses were achieved over much longer exposure times without causing reduced litter size, indicating that the developmental endpoint chosen by the RMS is overly conservative and ecologically not relevant.
(21)	Vol. 3, Annex B.9.3.3, Risk assessment, Table B.9.3-5, page 169	GTF: Using the correct acute endpoint for mammals, i.e. >5000 mg/kg bw/d, the TER for the vole in scenario “all crops, preplanting, 2x2160g/ha” would result in 16, above trigger value 10, including conservative assumption of DT_{50} in foliage = 10 d.	All other acute mammal TER values would result higher, indicating no risk from acute exposure to glyphosate based on conservative screening step default assumptions.
(22)	Vol. 3, Annex B.9.3.3, Risk assessment, Table B.9.3-5, page 158	GTF: Since voles are not required as focal species in all EU-member states, a more detailed risk	

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		assessment with additional generic focal species would be helpful for a possible risk envelope approach	
(23)	Vol. 3, Annex B.9.3.3, Risk assessment, Table B.9.3-6, page 158	GTF: If using the correct reproductive endpoint (ecologically relevant NOEAEL = 985 mg/kg bw/d) the lowest TER value in the screening assay would be 13.22 (All crops, all seeded or transplanted crops) pre planting of crop, at 2x2160 g/ha).	Based on the very conservative screening step assumptions, using the relevant endpoint (NOEAEL = 985 mg/kg bw/d, based on no effects at highest dose in Moxon 2-generation rat study), all scenarios would result in values higher than the trigger TER of 5, by margins of more than 2. This indicates low risk from chronic exposure of wild mammals to glyphosate residues.
(24)	Vol. 3, Annex B.9.3.3.2, page 171	GTF: Since voles are not required as focal species in all EU-member states, a more detailed risk assessment with additional generic focal species would be helpful for a possible risk envelope approach	
(25)	Vol. 3, Annex B.9.3.3.4, (chronic orchards) page 173	GTF: Further refinement for small herbivores: The initial risk assessment for small mammals is based on the worst-case assumptions that herbivores consume 100% treated food in their diet over a 3-week period with no food sourced from adjacent hedges, untreated grassy alleys, grassy field margins or adjacent fields, and no avoidance of dead vegetation. Glyphosate treated weeds are rapidly desiccated and will become unpalatable, and hence are unlikely to be consumed in large quantities.	Further refinement for small herbivores: The refined TER for small herbivores is considered to be worst case for the following reasons. Treated vegetation will not remain palatable for more than 7-10 days after treatment and this will lead to avoidance of such dead weeds. In orchards, as glyphosate is not applied to the grassy alleys between the tree lines (or the foliage of the trees) there will be other non-contaminated vegetation for herbivores to graze. Also we need to consider the unpalatability of treated vegetation. Following application of glyphosate, treated weeds will desiccate in 5-10 days and as a result become unpalatable to herbivores, which will then avoid grazing on such vegetation. In the long-term risk assessment it is recommended to consider a period of at least 21 days exposure, but for glyphosate the unpalatability factor will result in the herbivores not feeding on treated plants for such a long period. In this scenario it is reasonable to apply an

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			"unpalatability" factor to the risk assessment as there would as a rule be only 7 days feeding, not 21, resulting in a factor equal to 7/21 or 0.33. Applying this refinement (x 0.33) will result in a proportionate increase in the refined TERs to give TERs of 7.7, 6.1, 10.2 and 15.3 for the 4 small herbivore scenarios based on the calculation used in the original table. With this additional refinement the lowest TER_{LT} value of 6.1 for small herbivores in orchards is above the trigger of 5, indicating no unacceptable risk to small herbivores for this use.
(26)	Vol. 3, Annex B.9.3.3.4, Refined risk assessment, page 173	GTF: If not done already at the screening step (as recommended above), at this stage of the risk assessment additional refinement should be made by using a rodent endpoint, i.e. endpoint from 2-generation rat study [redacted], 2000) of NOEAEL=985 mg/kg bw/d instead of developmental endpoint NOEL=50 mg/kg based on the rabbit.	In addition to the more relevant route of exposure, the longer exposure time, the more population-relevant endpoints, the rat is a taxonomically more relevant species for the vole scenario than the rabbit. Note that in the EFSA RUD table the maximum chronic exposure for a rodent (vole) in the orchards scenario is 72.3, whereas as for a lagomorph it is only 14.3. Consequently the DDD for rodents will be 19.78 (= 2.88 x 0.5 x 72.3 x 0.19), but for lagomorphs 3.91 (= 2.88 x 0.5 x 14.3 x 0.19). Using these values the TERs are 50 (= 985/19.78) for voles and 26 (= 100/3.91) for rabbits. Both of these values are well above the trigger value of 5.
(27)	Vol. 3, Annex B.9.5.6, Risk assessment, Table B.9.5-7, page 221	GTF: We consider that the use of a MAF value of 1.7 on foliage and 1.9 on soil is over conservative with respect to glyphosate, when the application interval indicated in the GAP is a minimum of 21 days.	We calculate that a 10-day half-life and interval of 21 days (a ratio of 1:2) would give a MAF of 1.23 for 2 sprays and 1.29 for 3 sprays (1.3 in ESCORT2). This is conservative given the average DT50 of 2.8 days on foliage referred to in B.9.1.7.3, which we calculate to give a MAF of 1.006 and consequently results in an in-field PER foliar of 2173 g a.s./ha and not 3672 g a.s./ha.
(28)	Vol. 3, Annex B.9.5.6, Risk assessment, Table B.9.5-8, page 222	GTF: We consider that the use of a MAF value of 1.7 on foliage and 1.9 on soil is over conservative with respect to glyphosate, when the application interval indicated in the GAP is a minimum of 21	The respective in-field HQ values need to be recalculated based on the corrected MAF and in-field PER values, respectively.

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		days.	
(29)	Vol. 3, Annex B.9.5.6, Risk assessment, Table B.9.5-9, page 223	GTF: We consider that the use of a MAF value of 1.7 on foliage is over conservative with respect to glyphosate, when the application interval indicated in the GAP is a minimum of 21 days.	The respective off-field HQ values need to be recalculated based on the corrected MAF and in-field and off-field PER values, respectively.
(30)	Vol. 3, Annex B.9.5, Effects on other arthropod species (Annex IIA 8.3.2; Annex IIIA 10.5), Table B.9.5-9, page 210	GTF: The RMS argues that a vegetation distribution factor of only 5 (rather than 10) should be considered. This is not in agreement with risk assessment procedures as laid out in the relevant guidance document ESCORT 2	The vegetation distribution factor of 10 as proposed by the GTF is to be maintained in the off-field PER and HQ calculation.
(31)	Vol. 3, Annex B.9.5, Effects on other arthropod species (Annex IIA 8.3.2; Annex IIIA 10.5), Table B.9.5-9, page 210	GTF: The RMS argues that for use on desiccation of mature crops a higher drift rate (2 x 2.77% = 5.54%) should be considered. This is not in agreement with risk assessment procedures as laid out in the relevant guidance document ESCORT 2, where for field crops 2.77% drift are considered for one application and 2.38% for two applications.	The calculation of the off-field PER and HQ should be based on adopted drift rates.
(32)	Vol. 3, Annex B.9.5.6, Risk assessment, page 220	GTF: We consider that the use of a MAF value of 1.7 is over conservative with respect to glyphosate, when the application interval indicated in the GAP is a minimum of 21 days.	We calculate that a 10-day half-life and interval of 21 days (a ratio of 1:2) would give a MAF of 1.23 for 2 sprays and 1.29 for 3 sprays (1.3 in ESCORT2). This is conservative given the average DT50 of 2.8 days on foliage referred to in B.9.1.7.3, which we calculate to give a MAF of 1.006.
(33)	Vol. 3, Annex B 9.8.1, Laboratory testing, page 253	GTF: KIIA 8.10.1/01: N-transformation study was considered invalid and need for generation of further data was identified.	The following data was given in the first review of glyphosate: no adverse effects at 28.8 mg glyphosate acid/kg dry soil

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		A new GLP study has been generated and can be made available upon request.	
(34)	Vol. 3, Annex B.9.9.1.1, Seedling emergence, Study KIIA 8.12/01, page 268	GTF: We accept that this 1996 seedling emergence study preceded the current OECD guidelines, but still see this 28 day study is a valid test to show that glyphosate is very much less active pre-emergence than post-emergence.	The reasons for rejecting this study include "no data on visible phytotoxic effects and mean survival of emerged seedlings". This data is presented in Tables 8, 11, 12 and 13, of the original report. These results confirm that there are no treatment related effects from pre-emergence treatments of glyphosate... The temperature variation was a function of natural sunshine in a glasshouse experiment, so outside the control of the study team.
(35)	Vol. 3, Annex B.9.9.1.4, Summary of results on non-target plants, page 281	GTF: The limitations of the seedling emergence study are discussed above, but we believe that this study clearly shows that glyphosate has very little activity as a pre-emergence herbicide, and therefore the risk assessment should focus on the post-emergence data.	Further support for this may be taken from the standard weed science reference book called "The Herbicide Glyphosate" – page 3 – "Glyphosate exhibits many unique biological properties. It is a broad-spectrum post-emergence herbicide[...]In contrast to its high unit activity, when applied post-emergence, glyphosate shows no pre-emergence or residual activity. This is because the herbicide is tenaciously bound to soil particles and is readily degraded by soil microorganisms[...]"
(36)	Vol. 3, Annex B.9.9.1.4, Summary of results on non-target plants, page 281	GTF: The RMS argues that for use on desiccation of mature crops a higher drift rate (2 x 2.77% = 5.54%) should be considered. This is not in agreement with risk assessment procedures as laid out in the relevant guidance document, where for field crops 2.77% drift are considered for one application and 2.38% for two applications.	The TER calculation should be based on adopted drift rates.
(37)	Vol. 3, Annex B.9.9.1.5, Risk assessment for non-target plants, page 282	GTF: We consider that the use of a MAF value of 1.7 is over conservative with respect to glyphosate on foliage, when the application interval indicated in the GAP is a minimum of 21 days.	We calculate that a 10-day half-life and interval of 21 days would give a MAF of 1.23 for 2 sprays and 1.29 for 3 sprays (or 1.3 as given in the ESCORT2 tables for a 14 day interval). This is conservative given the average DT_{50} of 2.8 days on foliage referred to in B.9.1.7.3, which we calculate to give a MAF of 1.006. As indicated above glyphosate has little activity on plants from natural soils.

<table>
<tr><th>No.</th><th>Column 1
Reference to assessment report</th><th>Column 2
Comment (restricted to 500 characters, ca.10 lines)</th><th>Column 3
Further explanations</th></tr>
<tr><td>(38)</td><td>Vol. 3, Annex B.9.9.1.5, Risk assessment for non-target plants, page 282</td><td>GTF:
An endpoint of ER_{50} = 146 g a.s./ha was used for risk assessment: Notifier submitted a probabilistic endpoint of HC_5 = 206.35 g a.s./ha.
New data is available upon request for the representative formulation MON 52776 for a revised risk assessment below</td><td></td></tr>
<tr><td>(39)</td><td>Vol. 3, Annex B.9.9.1.5, NTP probabilistic risk assessment, page 282</td><td>GTF:
The GTF submitted a probabilistic risk assessment in line with the Guidance Document on Terrestrial Ecotoxicology (SANCO/10329/2002 rev 2 final) page 32. This analysis uses the data from 15 species to calculate the exposure level that is protective of 95% of species.
The owner of the representative formulation has finalized a study on MON 52276 which can be made available upon request.</td><td>For this analysis, the notifier suggest using the endpoints based on dry weight assessment for the two studies with the active substance considered as acceptable by the RMS. Dry weight is the relevant endpoint considering ecological relevance, as primary producers support the ecosystem by producing biomass. Additionally, only in few cases did the biomass endpoint exceed other endpoints. Therefore, it can be considered as sensitive in the majority of cases. For the species which were measured in both studies, a geometric mean is derived. This geometric mean of species with two ER_{50} (dry weight) and the values measured once in either of both studies are then plotted to derive an HC_5.
<table>
<tr><th>ER_{50} kg/ha</th><th>Species</th></tr>
<tr><td>0.146</td><td>Tomato</td></tr>
<tr><td>0.149</td><td>Oilseed rape</td></tr>
<tr><td>0.242</td><td>Winter wheat</td></tr>
<tr><td>0.346</td><td>Okra</td></tr>
<tr><td>0.377</td><td>Sugar beet</td></tr>
<tr><td>0.386</td><td>Maize</td></tr>
<tr><td>0.515</td><td>Radish</td></tr>
<tr><td>0.553</td><td>Lettuce</td></tr>
<tr><td>0.567</td><td>Cucumber</td></tr>
<tr><td>0.573</td><td>Oat</td></tr>
<tr><td>0.591</td><td>Soybean</td></tr>
</table>
</td></tr>
</table>

<table>
<tr><th>No.</th><th>Column 1
Reference to assessment report</th><th>Column 2
Comment (restricted to 500 characters, ca.10 lines)</th><th>Column 3
Further explanations</th></tr>
<tr><td></td><td></td><td></td><td>
<table>
<tr><td>0.739</td><td>Cabbage</td></tr>
<tr><td>0.75</td><td>Corn</td></tr>
<tr><td>1.253</td><td>Purple nutsedge</td></tr>
<tr><td>1.344</td><td>Ryegrass</td></tr>
<tr><td>1.792</td><td>Onion</td></tr>
</table>

Based on the endpoints listed above, using the RIVM program ETX 2.0, the median HC_5 value is 0.155 kg a.s./ha and this can be used in a probabilistic risk assessment. According to the Terrestrial Guidance Document, the risk to terrestrial plants is considered to be acceptable if the ER_{50} for less than 5% of species is above the highest predicted exposure level. In this case we propose using this HC_5 endpoint for the risk assessment of MON 52776, and a much more conservative trigger TER of 3. This revised TER calculation is shown below:
<table>
<tr><th rowspan="2">App. rate</th><th rowspan="2">Distance (m)</th><th rowspan="2">Drift rate (%)</th><th rowspan="2">HC_{05} (g a.s./ha)</th><th colspan="4">TER (g a.s./ha) for nozzle type</th></tr>
<tr><th>conventional</th><th>50% drift red.</th><th>75% drift red.</th><th>90% drift red.</th></tr>
<tr><td rowspan="2">2880</td><td>1</td><td>2.77</td><td rowspan="2">155</td><td>1.9</td><td>3.9</td><td>7.8</td><td>19</td></tr>
<tr><td>5</td><td>0.57</td><td>9.4</td><td>19</td><td>38</td><td>94</td></tr>
</table>
The table shows that a safe use can be identified for applications at the maximum single application rate of 2880 g/ha with a 5m buffer strip without drift reduction nozzles (TER = 9.4).
At 1m with 50% drift reduction nozzles this probabilistic risk assessment results in a TER of 3.9 and indicates acceptable risk when used with this mitigation for all of the application scenarios listed in table B.9.9-7.
In addition it should be noted, that the guidance SANCO/10329/2002 rev</td></tr>
</table>

No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
			2 final does not specify an increase of the trigger TER for the non-target plant risk assessment. Given the fact that ten plant species were tested with glyphosate, rather than six, in fact a reduction of the trigger TER should be considered, since the level of uncertainty is clearly lower for the deterministic approach.
(40)	Vol. 3, B.9.9.1.5, NTP risk assessment, page 282	GFT: A new GLP OECD 227 study performed by the owner of representative formulation MON 52276 is available for submission upon request. The risk assessment for non-target plants has been updated.	The risk assessment for non-target plants has been updated using the new dataset. This can be made available upon request.
(41)	Vol. 3, Annex B.9.11.1, Literature Review, page 294	GTF: The inclusion of extensive review of a surfactant system which is contained in a plant protection product which is not the representative formulation and therefore not up for review in the Annex I Renewal process is questionable and should be revised by the RMS.	The representative formulation (MON52276) that is the basis of this submission does not contain POEA, and consequently is not likely to pose unacceptable risk to aquatic organisms.
(42)	Vol. 3, Annex B.9.12, References relied on, page 300	GTF: The study Annex point is not written out, i.e. needs the final number per annex point. Given that there are many studies for several annex points, adding the final number should help readability.	
(43)	Vol. 3, Annex B.9.12, References relied on, page 300	GTF: Legend of owner acronyms is incorrect, i.e. ALS = Arysta Lifesciences SAS, MON = Monsanto, SYN = Syngenta. MOT is not correct	Please refer to the Glyphosate Task Force member companies for the correct denomination of the company owning the study.
(44)	Vol. 3, Annex B.9, Evaluation of peer-	GTF: The notifier acknowledges the thorough review	It should be noted that inconsistency of conclusions regarding reliability and relevance assessments of studies reviewed by both UBA and BfR

No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	reviewed literature regarding ecotoxicity of glyphosate, page 1	performed by the RMS of the available literature, while disagreeing with several of the specific evaluations made of individual articles.	can be observed. The RMS devised a new categorisation system which does not align with the one submitted by the notifier. According to the RMS, more articles are "UBA2" – i.e. 18 supporting information, vs only three according to the notifier (see submitted dossier AII, Section 6, pp.288-651). The main difference lies in that POEA-containing formulations as test substance were considered relevant by the RMS, when the representative formulation MON 52276 does not contain POEA, hence the notifier is of the opinion that only the representative formulation and the active substance glyphosate should be taken into consideration when assessing the environmental safety for Annex I renewal of glyphosate. In addition, several studies with evident experimental deficiencies were considered as very relevant and reliable by the RMS. The notifier has pointed out the deficiencies of these studies in the submitted dossier. However, they were not taken into account at their full rate. From a regulatory point of view however, it is paramount that studies which are used for risk assessment follow validated protocols, accurate materials and method description, are reported transparently and present appropriate analytical data.

Confidential Volume 4 – Annex C

Vol. 4 General information, Annex C: Summary, Scientific Evaluation and Assessment

Vol. 4, Annex C			
No.	Column 1 Reference to assessment report*	Column 2 Comments* from Member States and/or applicant	Column 3 Further explanations
(1)	Vol. 4, C.1.1	**RMS:** It seems that neither the DAR (1998) nor the subsequent Addenda contained evaluations whether (1) the material used in toxicological studies is representative for the (reference) specification or (2) whether the impurities are relevant. For the renewal procedure (2013), none of the applicants provided sufficient information/data, which would allow to judge whether the impurities are relevant. Hence, it cannot be evaluated, whether the material used in toxicological studies is representative for the proposed specification or the reference specification derived during the previous EU evaluation. **GTF:** Additional data/information could be submitted upon request which will allow to judge whether the impurities are of toxicological relevance or not with regard to the impurities of the reference source. Furthermore, the applicant can provide data/information demonstrating that the material used in toxicological studies is representative for the proposed specification upon request.	
(2)	Vol. 4, C.1.1	**RMS:** No data or information was submitted that would allow setting maximum limits for relevant impurities. In summary, based on the currently available data and information, safe maximum levels for relevant impurities cannot be derived. **GTF:** Additional data can be submitted upon request.	

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Vol. 4, Annex C: Summary, Scientific Evaluation and Assessment

<table>
<tr><th colspan="4">Vol. 4, Annex C</th></tr>
<tr><th>No.</th><th>Column 1
Reference to assessment report</th><th>Column 2
Comments from Member States and/or applicant</th><th>Column 3
Further explanations</th></tr>
<tr><td>(1)</td><td>Vol. 4,
C.1.2.4
Comparison of the analytical profile of batches</td><td>RMS: The maximum content of [redacted] and formaldehyde in the corresponding equivalence Report [AFRASA EQUIVALENCE_ES_2013_april] is slightly lower ([redacted]). Clarification is needed which values are correct.

INA: During the evaluation of the equivalence by Spain, the specification was adjusted to the results obtained in the five batch analysis.
The correct specification is proposed in the next table:</td><td>The specification proposed is:
<table><tr><td>Glyphosate</td><td>min 950 g/kg</td></tr><tr><td>[redacted]</td><td>[redacted]</td></tr><tr><td>[redacted]</td><td>[redacted]</td></tr><tr><td>Formaldehyde</td><td>max. 0.6 g/kg</td></tr><tr><td>N-Nitrosoglyphosate</td><td>Max. 1 ppm</td></tr></table></td></tr>
</table>

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Vol. 4, Annex C			
No.	Column 1 Reference to assessment report	Column 2 Comments from Member States and/or applicant	Column 3 Further explanations
(2)	Vol. 4, C.1.2.4., Toxicological evaluation of specification (2013)	**RMS:** The applicant provided no information/data, which would allow to judge whether the impurities are relevant. **INA:**: Industrias AFRASA conducted one study to assess the toxicity, that was considered valid by the Spanish authorities, that considered this source equivalent: a) *Reverse Mutation Assay using Bacteria (Salmonella typhirium) with Glyphosate (BSL Bioservice Report nr 126159)* This study is available for prompt submission on request. Additional data/information could be submitted which allow judging whether the impurities are of toxicological relevance or not with regard to the impurities of the reference source.	In addition to this Industrias AFRASA performed a QSAR analysis of the impurity [redacted] to predict the mutagenic potential of the technical material. No alert was identified. b) *Glyphosate: Tier 2: Evaluation of toxicological Properties of Impurities; GABConsulting GmbH, Report nr 616141-A2-0501-01 by Eurotox registred Toxicologist.* This study is available for prompt submission on request.

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Vol. 4, Annex C			
No.	Column 1 Reference to assessment report	Column 2 Comments from Member States and/or applicant	Column 3 Further explanations
(3)	Vol. 4, C.1.2.4 Comparison of the analytical profile of batches - Toxicological evaluation of specification (2013):	**RMS:** The notifier provided no evaluation, whether the material used in toxicological studies is representative for the proposed specification. **INA:** The technical material (batch nr 20110107-2) used in the above mentioned Reverse Mutation Toxicological Study (Report nr 126159), was one of the five batches of the 5-batch-GLP (Report nr DNA1300). This demonstrates that the material used in toxicological studies is representative for the proposed specification.	

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Vol. 4, Annex C			
No.	Column 1 Reference to assessment report	Column 2 Comments from Member States and/or applicant	Column 3 Further explanations
(4)	Vol. 4, C.1.2.4 Comparison of the analytical profile of batches - Ecotoxicology	**RMS:** Based on the available studies, a conclusion on the equivalence of the Afrasa source cannot be made. **INA:** The questions arisen on ecotoxicology are adequately addressed, for the [redacted] further ecotoxicological assessment is not required as the evaluation according to SANCO/10597/2003 rev10.1 showed that the increase in toxicity is not serious in comparison to the reference specification.	**INA:** We kindly ask the authorities to close this point and conclude that the source is equivalent from the ECOTOXICOLOGICAL point of view.

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Vol. 4, Annex C			
No.	Column 1 Reference to assessment report	Column 2 Comments from Member States and/or applicant	Column 3 Further explanations
(1)	Vol. 4, C.1.2.4 Comparison of the analytical profile of batches - Toxicological evaluation of specification (2013):	**RMS:** The applicant provided no information/data, which would allow to judge whether the impurities are relevant. The notifier provided no evaluation, whether the material used in tox studies is representative for the proposed specification. Based on the available studies submitted, a conclusion on the equivalence of the Agria source cannot be made. **AGR:** Additional data/information will be submitted which allow judging whether the impurities are of toxicological relevance or not with regard to the impurities of the reference source. Furthermore, the applicant will provide data/information demonstrating that the material used in toxicological studies is representative for the proposed specification.	

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Vol. 4, Annex C			
No.	Column 1 Reference to assessment report	Column 2 Comments from Member States and/or applicant	Column 3 Further explanations
(1)	Vol. 4, C.1.2.4 Comparison of the analytical profile of batches - Toxicological evaluation of specification (2013):	**RMS:** The applicant provided no information/data, which would allow to judge whether the impurities are relevant. The notifier provided no evaluation, whether the material used in tox studies is representative for the proposed specification. Based on the available studies submitted, a conclusion on the equivalence of the Agrichem source cannot be made. **AGI:** Additional data/information will be submitted which allow judging whether the impurities are of toxicological relevance or not with regard to the impurities of the reference source. Furthermore, the applicant will provide data/information demonstrating that the material used in toxicological studies is representative for the proposed specification.	

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Vol. 4, Annex C: Summary, Scientific Evaluation and Assessment

Vol. 4, Annex C			
No.	Column 1 Reference to assessment report	Column 2 Comments from Member States and/or applicant	Column 3 Further explanations
(1)	Vol. 4, C.1.2.4 Comparison of the analytical profile of batches - Toxicological evaluation of specification (2013):	**RMS:** The applicant provided no information/data, which would allow to judge whether the impurities are relevant. The applicant provided no evaluation, whether the material used in tox studies is representative for the proposed specification. Based on the available studies submitted, a conclusion on the equivalence of the Agro source cannot be made. **AGT:** Additional data/information will be submitted which allow judging whether the impurities are of toxicological relevance or not with regard to the impurities of the reference source. Furthermore, the applicant will provide data/information demonstrating that the material used in toxicological studies is representative for the proposed specification.	

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Vol. 4, Annex C			
No.	Column 1 Reference to assessment report	Column 2 Comments from Member States and/or applicant	Column 3 Further explanations
(1)	Vol. 4, C.1.2.4 Comparison of the analytical profile of batches	**RMS:** The applicant provided no information/data, which would allow to judge whether the impurities are relevant. The applicant provided no evaluation, whether the material used in toxicological studies is representative for the proposed specification. Based on the available studies, a conclusion on the equivalence of the Albaugh source cannot be made. **ALB:** Additional data/information will be submitted which allow judging whether the impurities are of toxicological relevance or not with regard to the impurities of the reference source. Furthermore, the applicant could provide data/information demonstrating that the material used in toxicological studies is representative for the proposed specification.	

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Vol. 4, Annex C			
No.	Column 1 Reference to assessment report	Column 2 Comments from Member States and/or applicant	Column 3 Further explanations
(1)	C.1.2.4 Comparison of the analytical profile of batches - Toxicological evaluation of specification (2013):	**RMS:** The applicant provided no information/data, which would allow to judge whether the impurities are relevant. The applicant provided no evaluation, whether the material used in tox studies is representative for the proposed specification. It is noted, that most/all impurities are specified in higher levels than they were present in material used in tox studies. Impurity 6 was reported as "< LOQ of 0.19" in the tox batch but was foreseen to be specified. Additionally, the min purity in the specification is slightly below the amount in some of the materials used in tox studies (95% vs. 97.4%). Additionally, the mentioned batches were used only in a limited set of studies. Impurities 10 and 17 are specified in significantly higher amounts than listed in the reference specification. The notifier has submitted a statement. However, RMS indicates that "the mentioned data/information has not been submitted for the present EU procedure. Hence RMS's tox risk assessor cannot confirm that there is no significant increase in toxicity due to the presence of the impurities". In summary, it cannot be evaluated, whether the material used in toxicological studies is representative for the proposed specification. Based on the available studies submitted, a conclusion on the equivalence of the Arysta sources cannot be made. **AAP:** Regarding the impurities 6, 10 and 17 additional data could be submitted. Furthermore, sufficient information/data could be submitted for the present EU procedure which allow judging whether the impurities are toxicologically relevant or not with regard to the impurities of the reference source.	

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Vol. 4, Annex C			
No.	Column 1 Reference to assessment report	Column 2 Comments from Member States and/or applicant	Column 3 Further explanations
(2)	C.1.2.4 Comparison of the analytical profile of batches – Ecotoxicological evaluation of specification (2013):	**RMS:** For the impurity 10, further ecotox assessment is required as the evaluation according to SANCO/10597/2003 rev 10.1. The impurity 10 is present in the specification from the manufacturer [redacted] and the manufacturer [redacted] at [redacted] respectively. The equivalence of this source to the reference source cannot be substantiated with sufficient certainty; additional information addressing the ecotox representativeness of the specification is required. Based on the available studies submitted, a conclusion on the equivalence of the Arysta sources cannot be made. **AAP:** Additional data will be provided	
(3)	C.1.3-1 Analytical methods. Validation data for the determination of the impurity 6	**RMS:** In case of impurity 6 the determination of the precision cannot be regarded as acceptable as matrix effects and sample preparation are not taken into account. **AAP:** In Guidance document SANCO 3030/99 rev. 4 it is stated under 3.1.2 (iii) that the accuracy of the method for s**ignificant and/or relevant impurities** should be reported as mean recovery ± relative standard deviation in the technical material. Arysta provided two analytical method validations (Schoop 2004 and 2006): In the validation report from 2004 [redacted] was found to be below the LOQ of 0.019 mg/kg. Therefore, [redacted] is not a significant impurity and the validation using a calibration solution should be acceptable. Nevertheless, in the second validation the precision was measured with five preparations of glyphosate in concentration ranges of [redacted]. Therefore the matrix effects were taken into account.	

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No.	Column 1 Reference to assessment report	Column 2 Comments from Member States and/or applicant	Column 3 Further explanations
(4)	C.1.3-3 Analytical methods. Validation data for the determination of the impurity 2	**RMS:** With respect to validation data for the determination of the impurity 2, the method should be described in detail by the applicant. The use of the reaction solution is not mentioned within the sample preparation. **AAP:** Additional data will be submitted.	
(5)	C.1.3-9 Analytical methods. Validation data for the determination of the impurity 21	**RMS:** With respect to validation data for the determination of the impurity 21, the fortification levels for the determination of the accuracy should be given by the applicant with respect to glyphosate technical in %. **AAP:** Additional data will be submitted.	

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Vol. 4, Annex C			
No.	Column 1 Reference to assessment report	Column 2 Comments from RMS and/or applicant	Column 3 Further explanations
(1)	Vol 4 C.1.2.4 Comparison of the analytical profile of batches (5-batch analysis)	**RMS:** The maximum content of the impurity 20 should be clarified. The maximum content is amended to be in compliance with the analytical data. However, an updated Document J should be submitted by the applicant. **BCL:** Additional data will be submitted.	The [redacted] content has been amended to 0.0004g/kg (0.4mg/kg).
(2)	Vol 4 C.1.2.4 Comparison of the analytical profile of batches - Toxicological evaluation of specification (2013):	**RMS:** The applicant provided no information/data, which would allow to judge whether the impurities are relevant The applicant provided no evaluation, whether the material used in tox studies is representative for the proposed specification. Based on the submitted data, a conclusion on the equivalence of the Barclay sources cannot be made. **BCL:** Additional data/information will be submitted which allow judging whether the impurities are of toxicological relevance or not with regard to the impurities of the reference source. Furthermore, the applicant could provide data/information demonstrating that the material used in toxicological studies is representative for the proposed specification.	

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Vol. 4, Annex C			
No.	Column 1 Reference to assessment report	Column 2 Comments from RMS and/or applicant	Column 3 Further explanations
(3)	Vol 4, C.1.3.7 - Validation data for the determination of the impurity 21	**RMS:** The applicability of the method must be demonstrated. Appropriate chromatograms have to be submitted by the applicant. The applicant stated that representative chromatograms are available if required. **BCL:** Additional data will be submitted.	

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<table>
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<tr><th>No.</th><th>Column 1
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Comments from Member States and/or applicant</th><th>Column 3
Further explanations</th></tr>
<tr><td>(1)</td><td>Vol 4
C.1.1.2</td><td>RMS: The applicant has to clarify whether or not the starting materials are commercially available.

BRO: All starting materials indicated are common components and they can be easily bought in the market.</td><td></td></tr>
<tr><td>(2)</td><td>Vol 4
C.1.2.3</td><td>RMS: No information on the date of production of the batches has been stated.

BRO: Please see production date of the five batches samples in column 3.</td><td><table><tr><th>Batch number</th><th>Production date</th></tr><tr><td>071600</td><td>Aug. 25, 2007</td></tr><tr><td>072020</td><td>Sep. 3, 2007</td></tr><tr><td>072380</td><td>Sep. 9, 2007</td></tr><tr><td>072682</td><td>Sep. 14, 2007</td></tr><tr><td>073112</td><td>Sep. 21, 2007</td></tr></table></td></tr>
<tr><td>(3)</td><td>Vol 4
C.1.2.4
Comparison of the analytical profile of batches</td><td>RMS: The applicant has only given the minimum purity of the technical active substance. Maximum contents of the significant impurity 3, 9, 20 and 21 are required.

BRO:
- Maximum contents of the significant/relevant impurities above mentioned were provided to RMS/EFSA.
- The data provided were the same as the data provided for the application of equivalence of Brokden glyphosate source in CRD UK. In these specifications the maximum contents of the significant/relevant impurities were declared.</td><td></td></tr>
</table>

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Vol. 4, Annex C			
No.	Column 1 Reference to assessment report	Column 2 Comments from Member States and/or applicant	Column 3 Further explanations
(4)	Vol 4 C.1.2.4 Comparison of the analytical profile of batches - Toxicological evaluation of specification (2013):	**RMS:** The applicant provided no information/data, which would allow to judge whether the impurities are relevant. The applicant provided no evaluation, whether the material used in tox studies is representative for the proposed specification. Based on the data submitted, a conclusion on the equivalence of the Brokden source cannot be made. **BRO:** Additional data/information will be submitted which allow judging whether the impurities are of toxicological relevance or not with regard to the impurities of the reference source. Furthermore, the applicant will provide data/information demonstrating that the material used in toxicological studies is representative for the proposed specification.	
(5)	Vol 4 C.1.2.4 Comparison of the analytical profile of batches - Toxicological evaluation of specification (2013):	**RMS:** Based on the data submitted, a conclusion on the equivalence of the Brokden source cannot be made. **BRO:** Data for relevant impurities were provided.	

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Vol. 4, Annex C			
No.	Column 1 Reference to assessment report	Column 2 Comments from Member States and/or applicant	Column 3 Further explanations
(1)	Vol 4, C.1.2.4 Comparison of the analytical profile of batches	**RMS:** The proposed levels for impurity 15 and impurity 26 are higher than the batch data indicate are necessary. A justification is needed by the applicant why the proposed maximum contents for those impurities are necessary. **BSJ:** Additional information will be submitted.	The specification provided to RMS was not in line with Manual on development and use of FAO and WHO specifications for pesticides and proposed levels for impurity 15 and impurity 26 were miscalculated. BSJ, if requested can submit corrected manufacturing specification, which is mainly based on the 5-batch mean values of the content for each impurity plus / minus 3 standard deviations.

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Vol. 4, Annex C			
No.	Column 1 Reference to assessment report	Column 2 Comments from Member States and/or applicant	Column 3 Further explanations
(2)	Vol 4, C.1.2.4 Comparison of the analytical profile of batches - Toxicological evaluation of specification (2013):	**RMS:** The applicant provided no information/data, which would allow to judge whether the impurities are relevant. The applicant provided no evaluation, whether the material used in tox studies is representative for the proposed specification. The impurities 10, 15 and 26 are specified in significantly higher amounts than listed in the reference specification. For the impurity 15, further tox assessment is required according to the criteria given in SANCO/10597/2003. Statements have been reported by the notifier; however, the RMS indicates that "the mentioned data/information has not been submitted for the present EU procedure. Hence it cannot confirm that there is no significant increase in toxicity due to the presence of the impurities." The applicant provided no evaluation, whether the material used in toxicological studies is representative for the proposed specification. Based on the available studies which were submitted for the renewal of glyphosate, a conclusion on the equivalence of the Bros source cannot be made. **BSJ:** Additional data/information could be submitted which allow judging whether the impurities are of toxicological relevance or not with regard to the impurities of the reference source. Furthermore, GTF will provide data/information demonstrating that the material used in toxicological studies is representative for the proposed specification.	In July 2013 BSJ informed RMS that additional data (including a Position Paper on impurities, based on available, supporting evidence and literature data) could be submitted, when requested by RMS. BSJ proposed the date of submission, but there was no formal request from RMS to provide this data. To our knowledge it is not possible to submit any additional information for EU procedure without a formal request from relevant authority. When requested by EFSA, abovementioned data could be submitted, including reports from GLP acute toxicity studies of BSJ glyphosate. The glyphosate batch used in these studies was covered by BSJ glyphosate specification.

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No.	Column 1 Reference to assessment report	Column 2 Comments from Member States and/or applicant	Column 3 Further explanations
(3)	Vol 4, C.1.2.4 Comparison of the analytical profile of batches - Ecotoxicology	**RMS:** For the impurity 15, further ecotox assessment is required as the evaluation according to SANCO/10597/2003- rev10.1, since representativeness of this source cannot substantiated with sufficient certainty; additional information addressing the ecotox representativeness of the specification is required. Based on the available studies, a conclusion on the equivalence of the Bros source cannot be made. **BSJ:** Additional data/information could be submitted.	In July 2013 BSJ informed RMS that additional data (including a Position Paper on impurities, based on available, supporting evidence and literature data) could be submitted, when requested by RMS. BSJ proposed the date of submission, but there was no formal request from RMS to provide this data. To our knowledge it is not possible to submit any additional information for EU procedure without a formal request from relevant authority. Results of study on Algae for Impurity 15 or BSJ glyphosate with determined content of Impurity 15could be submitted, when requested by EFSA.

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No.	Column 1 Reference to assessment report	Column 2 Comments from Member States and/or applicant	Column 3 Further explanations
(4)	Vol 4, C.1.3-1 Analytical methods. Methods of analysis for the determination of impurities 1 and 26	**RMS**: The analytical method for the determination of impurity 1 and impurity 26 is not acceptably validated as the test for accuracy was conducted with standard solutions which cannot be regarded as a representative sample. Matrix effects are not taken into account by the analysis of standard solutions. **BSJ:** Additional data/information could be submitted.	In July 2013 the following comment was provided to RMS by BSJ: "The accuracy was tested by measuring the recovery and RSD% of Impurity sample, which was prepared by spiking impurity analytical standard into the solvent blank, not the standard addition method in a sample matrix without the presence of the analyte. Use of standard solutions instead of standard addition method is not inconsistent with SANCO/3030/99 rev.4 Appendix 2 of the SANCO 3030 states that "However a well characterised sample must be used. An example of this would be a reference standard." - The main reason is that a sample matrix without the presence of the analyte was not avaliable. - Specificity for each Impurity indicated the Impurity peak was not attributable to more than one component in the Glyphosate manufactured by BSJ, so the sample matrix has no interference with the Impurities, the background of solvent blank and the sample matrix have the same effect. - According to published literature data addition of isotope standard caused ionization suppression of glyphosate, with matrix effect of 7,4%, therefore was not included in further analyses. -One can argue whether spiking the analyte with standards would further bring more data concerning matrix effect, but we believe that our current method is sufficiently reliable and reproductible, while the achieved process efficiency is high with efficiency of sample preparation shows acceptable RSD% (according to Horwitz equation), with negligible analyte ionization variability." RMS did not reference this comment directly in RAR. Thus BSJ cannot judge if this justification is considered acceptable or not. If EFSA requests, new validation could be performed with accuracy data measured with the technical material.

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No.	Column 1 Reference to assessment report	Column 2 Comments from Member States and/or applicant	Column 3 Further explanations
(5)	Vol 4, C.1.3-2 Analytical methods. Methods of analysis for the determination of impurity 10	**RMS**: The analytical method for the determination of impurity 10 is not acceptably validated as the test for accuracy was conducted with standard solutions which cannot be regarded as a representative sample. Matrix effects are not taken into account by the analysis of standard solutions. **BSJ:** Additional data/information could be submitted.	See above.
(6)	Vol 4, C.1.3-3 Analytical methods. Validation data for the determination of the impurity 15	**RMS:** The analytical method for the determination of impurity 15 is not acceptably validated as the test for accuracy was conducted with standard solutions which cannot be regarded as a representative sample. Matrix effects are not taken into account by the analysis of standard solutions. **BSJ:** Additional data/information could be submitted.	See above.
(7)	Vol 4, C.1.3-4 Analytical methods. Validation data for the determination of the impurity 16	**RMS:** The analytical method for the determination of impurity 16 is not acceptably validated as the test for accuracy was conducted with standard solutions which cannot be regarded as a representative sample. Matrix effects are not taken into account by the analysis of standard solutions. **BSJ:** Additional data/information could be submitted.	See above.

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Vol. 4, Annex C			
No.	Column 1 Reference to assessment report	Column 2 Comments from Member States and/or applicant	Column 3 Further explanations
(1)	Vol 4, C.1.2.4 Comparison of the analytical profile of batches - Toxicological evaluation of specification (2013):	**RMS:** The applicant provided no information/data, which would allow to judge whether the impurities are relevant. The applicant provided no evaluation, whether the material used in tox studies is representative for the proposed specification. It is noted, that several impurities are specified in higher levels than they were present in material used in tox studies. Impurity 5 was not reported in the tox batches but is foreseen to be specified. Also, the min purity in the specification is slightly below the amount in materials used in tox studies (97% - 98% vs. 98.5% - 92.2%). Additionally, the mentioned batches were used only in a limited set of studies. In summary, it cannot be evaluated, whether the material used in tox studies is representative for the proposed specification. Based on the available data submitted, a conclusion on the equivalence of the Cheminova sources cannot be made. **CHE:** Additional data/information could be submitted which allow judging whether the impurities are of toxicological relevance or not with regard to the impurities of the reference source. Furthermore, the applicant could provide data/information demonstrating that the material used in toxicological studies is representative for the proposed specification.	For the first Annex I listing of glyphosate, Cheminova was one of the notifying companies and Cheminova's technical glyphosate was considered as fully equivalent to the established reference profile. The specifications supporting Cheminova's technical glyphosate for Annex I Renewal are considered to fall within the specification supported at the first Annex I listing and are supported by an updated confidential dossier (Doc J) included with the current submission.

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No.	Column 1 Reference to assessment report	Column 2 Comments from Member States and/or applicant	Column 3 Further explanations
(1)	Vol. 4, C.1.2.4 Comparison of the analytical profile of batches	**RMS:** With respect to the determination of the impurity 20 in the technical material, it should be noted that the usage of analytical method CH-141/2001 was stated for both glyphosate sources. However, this method differs from method CH-141/2001 which was submitted for monitoring purposes concerning the used HPLC column, eluent and detection wavelength. Only the specificity and the linearity of the method were demonstrated. **DOW:** Further data will be provided.	DAS will provide a new study.
(2)	Vol. 4, C.1.2.4 Comparison of the analytical profile of batches - Toxicological evaluation of specification (2013):	**RMS:** The applicant provided no information/data, which would allow to judge whether the impurities are relevant. Impurities 4, 10, 13 and 14 are specified in significantly higher amounts than listed in ref specification. The applicant informed that equivalency is being confirmed from DAS and response will be available by July 31, 2013. But the mentioned data/inform has not been submitted for the present EU procedure. Hence, it cannot be evaluated/ confirmed that there is no significant increase in toxicity due to the presence of the impurities. The applicant provided no evaluation, whether the material used in tox studies is representative for the proposed specification. **DOW:** Additional data/information will be submitted which allow judging whether the impurities are of toxicological relevance or not with regard to the impurities of the reference source. Furthermore, the applicant will provide data/information demonstrating that the material used in toxicological studies is representative for the proposed specification.	

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No.	Column 1 Reference to assessment report	Column 2 Comments from Member States and/or applicant	Column 3 Further explanations
(3)	Vol. 4, C.1.2.4 Comparison of the analytical profile of batches - Ecotoxicology	**RMS:** For the impurity 10 and 13 methyl ester further ecotox assessment is required as the evaluation according to SANCO/10597/2003 rev 10.1. The impurity 10 was present in the specifications at [redacted] and impurity 13 at [redacted] respectively. The equivalence of both sources to the reference source cannot be substantiated with sufficient certainty; additional information addressing the ecotox representativeness of the specifications is required. Based on the available studies which were submitted for the renewal of glyphosate, a conclusion on the equivalence of the DOW sources cannot be made. **DOW:** Further data will be provided	
(4)	Vol. 4, C.1.3.2 Analytical methods. Validation data for the determination of the impurity 20	**RMS:** The repeatability of the method was not determined although spiking of technical glyphosate with impurity 1 was possible. Therefore, the method as a whole cannot be regarded as acceptable. The applicant stated that data on the repeatability could be provided by December 2013. **DOW:** Further data will be provided.	

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No.	Column 1 Reference to assessment report	Column 2 Comments from Member States and/or applicant	Column 3 Further explanations
(1)	Vol. 4, Table C.1.2-1: Analytical profile of batches and specification	**RMS:** Clarification by the applicant is needed concerning the fact that the account of three batches is lower than 980 g/kg. **XLE:** Additional data will be submitted.	**New GLP 5-Batch study has been initiated by Excel Crop Care (Europe) NV, the final report is expected to be in hand by July/August 2014 and will be submitted.**
(2)	Vol. 4 , C.1.2.4 Comparison of the analytical profile of batches - Toxicological evaluation of specification (2013):	**RMS:** The applicant provided no information/data, which would allow to judge whether the impurities are relevant. The applicant provided no evaluation, whether the material used in tox studies is representative for the proposed specification. Impurity 5 and impurity 20 were not reported in the tox batch but are foreseen to be specified. The min purity in the specification is slightly below the amount in material used in tox studies (95% vs. 96%). Additionally, the mentioned batches were used only in a limited set of studies. The notifier provided no evaluation, whether the material used in tox studies is representative for the proposed specification. In summary, it cannot be evaluated, whether the material used in tox studies is representative for the proposed specification. Based on the available studies which were submitted for the renewal of glyphosate, a conclusion on the equivalence of the Excel source cannot be made. **XLE:** Additional data/information will be submitted which allow judging whether the impurities are of toxicological relevance or not with regard to the impurities of the reference source. Furthermore, the applicant will provide data/information demonstrating that the material used in toxicological studies is representative for the proposed specification.	**Fresh acute mammalian toxicity studies using counter sample from one of the batches from the new 5-Batch study is being undertaken by Excel Crop Care (Europe) NV, these reports will be submitted together with the new 5-Batch study.**

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No.	Column 1 Reference to assessment report	Column 2 Comments from Member States and/or applicant	Column 3 Further explanations
(3)	Vol. 4, C.1.3-2 Validation data for the determination of the impurity 5 in technical glyphosate	**RMS:** The RSD of the repeatability of 5.8 % at a content of 0.41 % slightly exceeds the corresponding modified Horwitz RSD value of 3.1 %. Nevertheless, the method can be regarded as fit for purpose for the determination of the impurity 5 in the technical material. **XLE:** Additional data will be submitted.	
(4)	Vol. 4, C.1.3-3 Validation data for the determination of the impurity 20 in technical glyphosate	**RMS:** As the LOQ exceeds the proposed max content of 1 ppm impurity 20 in the tech material, the applicant has to demonstrate that this value can be monitored with the method. The applicant stated that a report could be provided to extend the LOQ investigation and to confirm that the lower level could be accurately quantified. **XLE:** Additional data will be submitted.	
(5)	Vol. 4, C.1.3.2 Validation data for the determination of the impurity 2 and 5 in technical glyphosate	**RMS:** This method did not meet the requirements of Guidance Document SANCO9303/99 rev. 4 and so cannot be considered acceptable for the determination of impurity2 and impurity 5 in the technical material. **XLE:** Impurity2 is not part of the specification of the technical material provided by Excl. Therefore no an analytical method for monitoring is not required. For impurity 5 an analytical method is provided and accepted by the RMS (see C.3 of the RAR).	

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No.	Column 1 Reference to assessment report	Column 2 Comments from Member States and/or applicant	Column 3 Further explanations
(1)	Vol. 4, C.1.2.4 Comparison of the analytical profile of batches - Toxicological evaluation of specification (2013):	**RMS:** The applicant provided no information/data, which would allow to judge whether the impurities are relevant. The applicant provided no evaluation, whether the material used in tox studies is representative for the proposed specification. It is noted, that some impurities are specified in higher levels than they were present in material used in tox studies. Impurity 21 was not reported in the tox batches but is foreseen to be specified. The min purity in the specification is slightly below the amount in material used in tox studies (95% vs. 96.8% - 99.2). Additionally, the mentioned batches were used only in a limited set of studies. In summary, it cannot be evaluated, whether the material used in tox studies is representative for the proposed specification. Based on the available studies, a conclusion on the equivalence of the Feinchemie source cannot be made. **FCS:** Additional data/information will be submitted which allow judging whether the impurities are of toxicological relevance or not with regard to the impurities of the reference source. Concerning the representativity of the material used in the tox studies we refer to the argumentation presented in more detail in point Vol 4, C.1.5. What impurity 21 is concerned we would like to point out that the specified content is based on the FAO specification for glyphosate and that the actual content in the technical material is less than 25% of the specified value.	

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No.	Column 1 Reference to assessment report	Column 2 Comments from Member States and/or applicant	Column 3 Further explanations
(2)	Vol. 4, C.1.3-1 Analytical methods. Validation data for the determination of the impurities 2 and 3	**RMS:** With respect to validation data for the determination of the impurities 2 and 3, the applicant should explain the different RSD values of the repeatability of the fortified and not fortified samples. **FCS:** The determination of the RSD of the method was done on an unspiked study sample in an analytical sequence run on June 28th 2009, when the response of the detector was optimum and signal / noise ratio of the chromatograms was very high. The accuracy of the method was determined in a sequence run on August 1st. At this time, the detector's response was much less sensitive, as can be seen on sample chromatograms given in appendix G3, page 173 and following pages. The higher background noise resulted in a less precise integration of the signals, resulting in turn in a higher variability of the results. However the accuracy calculated with these analyses was found acceptable. Moreover, on study sample run in the same sequence gave results very close to the results of the batches run in the previous sequence, which is a confirmation of the validity of the august 1st analytical sequence.	Comment supplied by Christian Wasser, the Scientific director of Anadiag, where the study was performed. He also added the following: "I need to add that these analyses are very delicate, since large amounts of glyphosate are injected in the system, which may contribute to alter the column and MS source".

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No.	Column 1 Reference to assessment report	Column 2 Comments from Member States and/or applicant	Column 3 Further explanations
(3)	Vol. 4, C.1.5 Other confidential information	**RMS:** It seems that the batches 1993 and 1998 cannot be correlated with batches used in toxicological studies. **FCS:** As well as the batches characterized in 1993 and 1998 the technical material used in the toxicological studies was manufactured by M/S Epic-Schwebda Chemicals. Since in addition the same route of synthesis was kept over the period of toxicity testing it can be assumed that the impurity profile of the batches used in the toxicological studies is within the range of these specifications, incl. for impurities nos. 3, 9, 11 and 20, which were only determined in the 1998 analysis but which can be assumed to have been present also in the 1993 and earlier batches. As a conclusion, the impurity profile of the batches used in the toxicological studies can be assumed to be properly described by the impurity profiles of the batches analysed in 1993 and 1998 presented in table C.1.5-1.	

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No.	Column 1 Reference to assessment report	Column 2 Comments from Member States and/or applicant	Column 3 Further explanations
(1)	Vol. 4, C.1.2.4 Comparison of the analytical profile of batches - Toxicological evaluation of specification (2013):	**RMS:** The applicant provided no information/data, which would allow to judge whether the impurities are relevant. The applicant provided no evaluation, whether the material used in tox studies is representative for the proposed specification. It is noted, that several impurities are specified in higher levels than they were present in material used in tox studies. Impurity 5 was not reported in the tox batches but is foreseen to be specified. Additionally, the min purity in the specification is slightly below the amount in material used in tox studies (e.g., 95.0% vs. 96.7%). Additionally, the mentioned batches were used only in a limited set of acute tox studies which are less relevant to assess the specification. Based on the available studies submitted, a conclusion on the equivalence of the Helm sources cannot be made. **HEL:** Additional data/information will be submitted which allow judging whether the impurities are of toxicological relevance or not with regard to the impurities of the reference source. Furthermore, the applicant will provide data/information demonstrating that the material used in toxicological studies is representative for the proposed specification.	

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No.	Column 1 Reference to assessment report	Column 2 Comments from Member States and/or applicant	Column 3 Further explanations
(2)	Vol. ,4 C.1.2.4 Comparison of the analytical profile of batches - Toxicological evaluation of specification (2013):	**RMS:** Impurities 10 and 17 are specified in significantly higher amounts than listed in the reference specification. Regarding these impurities, the applicant did not submit any comment/information/data. **HEL:** Additional data will be submitted.	
(3)	Vol. 4, C.1.2.4 Comparison of the analytical profile of batches - Toxicological evaluation of specification (2013):	**RMS:** The impurity 10 is specified with [redacted] depending on the source. According to SANCO/10597/2003 – rev. 10.1, depending on the amount of a new / increased impurity, different data/information need to be provided. An Ames test with technical material has been submitted. This single study might be sufficient to assess the amount the impurity 10 in the source [redacted] But this study is not sufficient to assess the amount in the sources 2, 4 and 6 because there this impurity is specified in amounts > 1 %. Nevertheless, considering, that the technical material was tested, it was not addressed whether the highest dose was high enough to adequately investigate the mutagenic potential of the impurity being present at low levels. Based on the available studies submitted, a conclusion on the equivalence of the Helm sources cannot be made. **HEL:** Additional data will be submitted.	

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No.	Column 1 Reference to assessment report	Column 2 Comments from Member States and/or applicant	Column 3 Further explanations
(4)	Vol. 4, C.1.2.4 Comparison of the analytical profile of batches - Toxicological evaluation of specification (2013):	**RMS:** Currently, the no data/information has been submitted for the present EU procedure regarding impurity 17. Hence RMS's toxicological risk assessor cannot confirm that there is no significant increase in toxicity due to the presence of the impurities. Based on the available studies submitted, a conclusion on the equivalence of the Helm sources cannot be made. **HEL:** Additional data will be submitted.	
(5)	Vol. 4, C.1.2.4 Comparison of the analytical profile of batches – Ecotoxicology:	**RMS:** For the impurity 17 at source 4 further ecotox assessment is required as the evaluation according to SANCO/10597/2003 rev 10.1. The equivalence of this source to the reference source cannot be substantiated with sufficient certainty; additional information addressing the ecotox representativeness of the specification is required. Based on the available studies submitted, a conclusion on the equivalence of the Helm sources cannot be made. **HEL:** Additional data will be submitted.	Please provide study on alage according to OECD 201 for Impurity 17 [redacted]
(6)	Vol. 4, C.1.3-11 Analytical methods. Validation data for the determination of the impurity 21 (source 3)	**RMS:** In case of the determination of the accuracy only the concentration in the spiked solutions has been given. The applicant should state the fortification levels in relation to the technical material (in %). **HEL:** Additional data will be submitted.	This should be clarified (maybe the laboratory can provide a statement).

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No.	Column 1 Reference to assessment report	Column 2 Comments from Member States and/or applicant	Column 3 Further explanations
(7)	Vol. 4, C.1.3-12 Analytical methods. Validation data for the determination of the impurity 1 (source 4)	**RMS:** There seems to be an interference of [redacted] with the glyphosate peak in the chromatogram. The applicant should demonstrate that the specificity of the method is ensured. **HEL:** Additional data will be submitted.	This should be clarified (maybe the laboratory can provide a statement).
(8)	Vol. 4, C.1.3-23 Analytical methods. Validation data for the determination of the impurity 21 (source 5)	**RMS:** The LOQ was only determined as the lowest concentration of the calibration standard (1.28 mg/L). In order to take matrix effects into account the applicant should determine the LOQ in relation to the technical material. The lowest levels used for the determination of the accuracy and repeatability exceed the proposed maximum content of 0.8 g/kg formaldehyde in the technical material. **HEL:** Additional data will be submitted.	This should be clarified.
(9)	Vol. 4, C.1.3 Determination of impurity 23 (source 5)	**RMS:** The content of water was determined by loss on drying which is not specific to water. **HEL:** Additional data will be submitted.	This should be clarified.

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No.	Column 1 Reference to assessment report	Column 2 Comments from Member States and/or applicant	Column 3 Further explanations
(10)	Vol. 4, C.1.3-27 Analytical methods. Validation data for the determination of the impurity 20 (source 6)	**RMS:** The applicant should explain why standard addition was not used for the determination of the repeatability. The fortification levels for the determination of the accuracy have not been stated explicitly, the levels should be clarified. **HEL:** Additional data will be submitted.	This should be clarified (maybe the laboratory can provide a statement).
(11)	Vol. 4, C.1.3-28 Analytical methods. Validation data for the determination of the impurity 21 (source 6)	**RMS:** With respect to linearity and accuracy and repeatability the method for the determination of impurity 21 in the tech material can be considered acceptably validated. However, the applicant should explain why standard addition was not used for the determination of the repeatability. **HEL:** Additional data will be submitted.	This should be clarified (maybe the laboratory can provide a statement).
(12)	Vol. 4, C.1.3 Determination of impurity 23 (source 5)	**RMS:** The content of water was determined by loss on drying which is not specific to water. **HEL:** Additional data will be submitted.	This should be clarified.

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No.	Column 1 Reference to assessment report	Column 2 Comments from Member States and/or applicant	Column 3 Further explanations
(1)	Vol. 4, C.1.2.4 Comparison of the analytical profile of batches	**RMS:** Glyphosate was determined in the batches by the analytical method PC-ME-0765. The validation data are acceptable. It should be noted that the method PC-ME-0765 needs to be submitted in the EU process; so far it was submitted only in the context of national authorisations. **MOD:** PC-ME-0765 can be submitted upon request	

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No.	Column 1 Reference to assessment report	Column 2 Comments from Member States and/or applicant	Column 3 Further explanations
(2)	Vol. 4, C.1.2.4 Comparison of the analytical profile of batches - Toxicological evaluation of specification (2013):	**RMS:** The applicant provided no information/data, which would allow to judge whether the impurities are relevant. **MOD:** Although some information was available and has been submitted in AII DOC J, additional data/information can be submitted upon request which will allow judging whether the impurities are of toxicological relevance or not with regard to the impurities of the reference source.	• **Relevant impurities**. Two impurities of substances of well known toxicity, namely formaldehyde and an N-nitroso substance, N-nitroso glyphosate (NNG). Existing thresholds were used by the FAO evaluator to define their maximum concentration, and the same evaluator reviewed the data for Annex I inclusion in 2002. o The FAO evaluation report notes that "for formaldehyde the limit was set to 1.3 g/kg on a glyphosate acid basis, according to the rules of the FAO as published in the Manual. This limit corresponds closely to the limit in the US OSHA regulations and was set on an 'as is' basis not on an 'acid basis'." o The limit for NNG was derived from a US EPA limit: "the Agency has determined that technical glyphosate contains N-nitroso glyphosate (NNG) as a contaminant of 0.1 ppm or less. The Agency has determined that oncogenicity testing of N-nitroso contaminants will be required only in those cases in which the level of nitroso compounds exceeds 1.0 ppm (see 'Pesticide Contaminated with N-nitroso Compounds, proposed policy 45 FR 42854 (June 25, 1980))". The EU now takes a similar view, as in the Guidance Document on Equivalence SANCO/10597/2003-rev.10.1 "If analytical results indicate that total nitrosamine levels exceed 1 mg/kg in the technical material, the following toxicological requirements must be addressed".

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			Thus the maximum concentrations of these substances are set at levels which are not considered to be toxic. Although the FAO Specification refers to them as 'relevant' impurities, according to the FAO Guidance Document they are not relevant unless they exceed the limits. Data can be submitted upon request. • **Impurities considered to be non-relevant** [redacted] Based on the conclusions in the RAR, AMPA should be considered non-relevant from a tox-ecotox perspective. [redacted] Data were submitted in Doc J for these impurities because our increased specification levels (mean +3 SD) were beyond the FAO specification/equivalence threshold. Based on this information the RMS concluded "According to the criteria given in Tier I of Guidance Document SANCO/10597/2003 rev 10.1 the proposed specification is regarded as equivalent to the reference source." In addition, the RMS stated that "The maximum content of [redacted] is regarded as acceptable as [redacted] is a biosynthesised amino acid which acts as a precursor for proteins and is an approved food additive according to Directive 95/2/EC."

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			[redacted]: these impurities were new compared to the reference specification. A further toxicological and ecotoxicological assessment is not deemed to be required (as suggested by the RMS in C.1.2.4 Conclusions of the RAR) due to the nature of these compounds. These and the other inorganic substances are well-known chemicals that are commonly encountered in many foods and environmental samples. [redacted]: This impurity was determined in the batches but was not specified in the reference specification. However, based on the submitted batch data the RMS considered there is no need to specify a limit for the impurity (same reference as above). **Other impurities**: The report by Wratten et al (2013) assesses the occurrence and toxicology of all the impurities in the MON specification (relevant impurities, non-relevant including inorganic, glyphosate related at high prominence and glyphosate related at low levels). This report has already been submitted (in an earlier version) in AII Doc J but an updated version is available upon request. It should be referenced as a justification of the non-relevance of these impurities.

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(3)	Vol. 4, C.1.2.4 Comparison of the analytical profile of batches - Toxicological evaluation of specification (2013):	**RMS:** The applicant provided no evaluation, whether the material used in tox studies is representative for the proposed specification. It is noted, that several impurities are specified in higher levels than they were present in material used in tox studies. The min purity in the specification is slightly below the amount in material used in tox studies (95% vs. ~ 96%). Additionally, the mentioned batches were used only in a limited set of studies. In summary, it cannot be evaluated, whether the material used in toxicological studies is representative for the proposed specification Based on the available studies submitted, a conclusion on the equivalence of the Monsanto sources cannot be made. **MOD:** Upon request, **t**he applicant can provide data/information demonstrating that the material used in toxicological studies is representative for the proposed specification.	The specification is **minimum** 95% glyphosate on a dry basis. Therefore, the concentration in manufactured technical glyphosate and the test substances will be greater than 95%.
(4)	Vol. 4, C.1.3-1 Analytical methods. Validation data for the determination of the impurity 1	**RMS:** The applicant stated that a revised evaluation of the precision of method [redacted] with respect to the impurity 1 has been conducted and could be submitted. The precision has been considerably improved compared to the previous precision. **MOD:** Additional data can be submitted upon request.	

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No.	Column 1 Reference to assessment report	Column 2 Comments from Member States and/or applicant	Column 3 Further explanations
(5)	Vol. 4, C.1.4-1 Identity, content and function of formulants	**RMS:** It should be noted that the MSDS of the formulants are not in compliance with the requirements according to REACH. However, the applicant stated that MSDSs which are in line with the requirements for REACH for the [redacted] and its components [redacted] and [redacted] could be submitted. **MOD:** Additional data can be submitted upon request	

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No.	Column 1 Reference to assessment report	Column 2 Comments from Member States and/or applicant	Column 3 Further explanations
(1)	Vol. 4, C.1.2.4 Comparison of the analytical profile of batches - Toxicological evaluation of specification (2013):	**RMS:** The applicant provided no information/data, which would allow to judge whether the impurities are relevant. It is noted, that some impurities are specified in higher levels than they were present in material used in toxicological studies Impurity 1 was not reported in the tox batches but is foreseen to be specified. Impurity 20 was reported as "< 0.0001 %" in the tox batches but is foreseen to be specified. Additionally, in case [redacted] can be correlated with tox batches used in specific tox studies, the mentioned batches were used only in a limited set of studies In summary, it cannot be evaluated, whether the material used in toxicological studies is representative for the proposed specification. Based on the available studies submitted, a conclusion on the equivalence of the Nufarm source cannot be made. **NUF:** Additional data/information will be submitted which allow judging whether the impurities are of toxicological relevance or not with regard to the impurities of the reference source. Furthermore, the applicant will provide data/information demonstrating that the material used in toxicological studies is representative for the proposed specification.	

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No.	Column 1 Reference to assessment report	Column 2 Comments from Member States and/or applicant	Column 3 Further explanations
(2)	Vol. 4, C.1. 5.1 Tox profile	**RMS:** It seems difficult to correlate the batches [redacted] with the batch numbers given in the study reports. It is noted that [redacted]" is correlated once with batch H05H016A and another time with batch H95D161A. In summary, the meaning of [redacted] seems unclear **NUF: [redacted] were suppliers of glyphosate technical to Nufarm in the past. A number of tox studies were carried out with the [redacted] technical material characterized by a typical batch identification starting with H+ 2 digits for the year + mixture of letter and numbers; whilst [redacted] had their own identification of batches starting with the year + 5 digits.** .	The meaning of [redacted] can be explained as follows: [redacted] the full name of the [redacted] is: [redacted]
(3)	Vol. 4, C.1. 5.1 Tox profile	**RMS: the purity of the technical grade for [redacted] source is given as 94.7%.** **NUF: the value is not correct. All studies were run with Batch H05H016A containing 95.7%. or batch H95D161A containing 95.3%.**	

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(4)	Vol. 4, C.1. 5. Page 15	**RMS: Information, which batch has been used in the respective studies** **NUF: a number of major toy studies have not been listed in the table. Following studies run with batch H05H016A (95.7%) are missing:** **IIA, 5.5.2/08: Glyphosate Technical: Dietary Combined Chronic Toxicity/Carcinogenicity in the Rat, 2009a, [redacted] *et al.*** **IIA, 5.5.3/02: Glyphosate technical: Dietary Carcinogenicity Study in the Mouse, 2009b, [redacted]**	

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Vol. 4, Annex C			
No.	Column 1 Reference to assessment report	Column 2 Comments from Member States and/or applicant	Column 3 Further explanations
(1)	Vol. 4, C.1.2.4 Comparison of the analytical profile of batches - Toxicological evaluation of specification (2013):	**RMS:** The applicant provided no information/data, which would allow to judge whether the impurities are relevant. The applicant provided no evaluation, whether the material used in toxicological studies is representative for the proposed specification. Hence, it cannot be evaluated, whether the material used in tox studies is representative for the proposed specification. Based on the available studies submitted, a conclusion on the equivalence of the Rotam source cannot be made. **RTA:** Additional data/information will be submitted which allow judging whether the impurities are of toxicological relevance or not with regard to the impurities of the reference source. Furthermore, the applicant will provide data/information demonstrating that the material used in toxicological studies is representative for the proposed specification.	

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Vol. 4, Annex C			
No.	Column 1 Reference to assessment report	Column 2 Comments from Member States and/or applicant	Column 3 Further explanations
(1)	Vol. 4, C.1.2.4 Comparison of the analytical profile of batches - Toxicological evaluation of specification (2013):	**RMS:** The applicant provided no information/data, which would allow to judge whether the impurities are relevant. The applicant provided no evaluation, whether the material used in tox studies is representative for the proposed specification. Based on the available studies submitted, a conclusion on the equivalence of the Sabero source cannot be made. **SAO:** Additional data/information will be submitted which allow judging whether the impurities are of toxicological relevance or not with regard to the impurities of the reference source. Furthermore, the applicant will provide data/information demonstrating that the material used in toxicological studies is representative for the proposed specification.	
(2)	Vol. 4, C.1.3-1 Comparison of the analytical profile of batches - Validation data for the determination of impurities 1 and 9:	**RMS:** Regarding the validation data for the determination of impurities 1 and 9, the peaks of those impurities in the chromatograms show a considerable interference with other compounds. The applicant stated that a new study can be submitted by December 2013 in order to demonstrate that the specificity of the method is ensured. **SAO:** New information will be submitted	

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No.	Column 1 Reference to assessment report	Column 2 Comments from Member States and/or applicant	Column 3 Further explanations
(3)	Vol. 4, C.1.3-2 Comparison of the analytical profile of batches - Validation data for the determination of impurity 2:	**RMS:** Regarding the validation data for the determination of impurity 2, the RSD of the repeatability exceeds the Horwitz value which is 4.2 % at 0.5 g/kg and 3.1 % at 4 g/kg. The applicant stated that a new study can be submitted by December 2013 in order to demonstrate that the precision of the method is acceptable. **SAO:** New information will be submitted	
(4)	Vol. 4, C.1.3-6 Comparison of the analytical profile of batches - Validation data for the determination of impurity 21:	**RMS:** Regarding the validation data for the determination of impurity 21, the RSD of the repeatability slightly exceeds the Horwitz value which is 3.9 % at 0.8 g/kg and 3.4 % at 1.9 g/kg. The applicant stated that a new study can be submitted by December 2013 in order to demonstrate that the precision of the method is acceptable. **SAO:** New information will be submitted	
(5)	Vol. 4, C.1.3 Determination of impurity 23:	**RMS:** The content of water was determined by loss on drying which is not specific to water. The applicant stated that a more specific method, such as a Karl Fischer titration can be submitted by December 2013. **SAO:** New information will be submitted	

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No.	Column 1 Reference to assessment report	Column 2 Comments from Member States and/or applicant	Column 3 Further explanations
(1)	Vol. 4, C.1.2.3, Analytical profile of batches	**SAP:** Where it is stated "*The batches were analysed for (…)* [redacted] ***(Imp 9)***, [redacted] *Imp 9) (…)*", should be written "*The batches were analysed for (…)* [redacted] ***(Imp 3)***, [redacted] *(Imp 9) (…)*"**.**	
(2)	Vol. 4, C.1.3.1, Methods of analysis for the determination of impurities	**SAP:** In table C.1.3-3, column "*Recovery*", please replace the values of ***104.3%*** and ***122.9%*** for ***122.9%*** and ***104.3%***, respectively.	
(3)	Vol. 4, C.1.2.4 Comparison of the analytical profile of batches - Toxicological evaluation of specification (2013):	**RMS:** The applicant provided no information/data, which would allow to judge whether the impurities are relevant. The applicant provided no evaluation, whether the material used in toxicological studies is representative for the proposed specification. Based on the available studies submitted, a conclusion on the equivalence of the Sapec source cannot be made. **SAP:** Additional data/information will be submitted which allow judging whether the impurities are of toxicological relevance or not with regard to the impurities of the reference source. Furthermore, the applicant will provide data/information demonstrating that the material used in toxicological studies is representative for the proposed specification.	

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No.	Column 1 Reference to assessment report	Column 2 Comments from Member States and/or applicant	Column 3 Further explanations
(1)	Vol. 4, C.1.2.4 Comparison of the analytical profile of batches	**RMS:** According to the criteria given in Tier I of Guidance Document SANCO/10597/2003 rev 10.1 the proposed specification cannot be regarded as equivalent to the reference source as the specified value for impurity 3 is outside of the acceptable tolerance. A Tier II assessment is necessary **SFP:** Additional data will be submitted. However, SFP wants also to underline that comments performed during RAR seem to have not been taken into account by the RMS. We showed that there are a lot of publically available data on the compound of concern (ECHA and EPA data basis in particular), showing its non-relevance. These data are very old (all before 1990) but conducted under GLP procedure and considered reliable by both EPA and ECHA during registration process of the concerned compound.	

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No.	Column 1 Reference to assessment report	Column 2 Comments from Member States and/or applicant	Column 3 Further explanations
(2)	Vol. 4, C.1.2.4 Comparison of the analytical profile of batches - Toxicological evaluation of specification (2013):	**RMS:** The applicant provided no information/data, which would allow to judge whether the impurities are relevant. Impurity 3 is specified in significantly higher amounts than listed in the reference specification. Regarding this issue, the applicant has submitted a statement but RMS also indicates that "currently, the mentioned data/information has not been submitted for the present EU procedure. Hence RMS cannot confirm that there is no significant increase in toxicity due to the presence of the impurity." The applicant provided no evaluation, whether the material used in tox studies is representative for the proposed specification. Based on the available studies submitted, a conclusion on the equivalence of the SFP source cannot be made **SFP:** Additional data/information will be submitted which allow judging whether the impurities are of toxicological relevance or not with regard to the impurities of the reference source. SFP will also demonstrate that data submitted for registration of this compound [redacted]) under EPA and ECHA processes, showing the non-relevance of this impurity, can not be considered as being still under protection. Otherwise, agreement for the access to these data will be discussed and found with their owners.	
(3)	Vol. 4, C.1.2.4 Comparison of the analytical profile of batches - Ecotoxicology	**RMS:** Based on the available studies, which were submitted for the renewal of glyphosate, a conclusion on the equivalence of the SFP source cannot be made. **SFP:** SFP did not perform any ecotox study with its technical ingredient, so there is no need and no possibility to demonstrate such a reliability.	

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No.	Column 1 Reference to assessment report	Column 2 Comments from Member States and/or applicant	Column 3 Further explanations
(4)	Vol. 4, C.1.3-2 Analytical methods. Validation data for the determination of the impurity 9	**RMS:** With respect to validation data for the determination of the impurity 9, Clarification is needed concerning the fortification levels used for the determination of the accuracy and repeatability. It seems that pure standard solutions have been used for the measurements. However, the accuracy and repeatability should be determined with spiked technical material. The fortification levels should be stated in % related to the tech material. **SFP:** In appendix 2 of SANCO 3030/99 rev. 4 it is stated that "accuracy may be measured in different ways(…). Assessment may be made by analysing a sample of known concentration and comparing the measured value to the true value. However a well characterized sample must be used. An example of this would be a reference standard." Usual validation for impurities request two fortifications. In this validation, 6 levels were tested with two determinations each time. RSD was estimated on all levels ensuring a worst case as a simple repeatability on one level. Therefore, the validation should be considered as acceptable. Anyway, if necessary, further validation data will be provided.	

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No.	Column 1 Reference to assessment report	Column 2 Comments from Member States and/or applicant	Column 3 Further explanations
(1)	Vol. 4, C.1.2.4 Comparison of the analytical profile of batches - Toxicological evaluation of specification (2013):	**RMS:** The applicant provided no information/data, which would allow to judge whether the impurities are relevant. The applicant provided no evaluation, whether the material used in tox studies is representative for the proposed specification. Based on the available studies submitted, a conclusion on the equivalence of the Sinon source cannot be made. **SNN:** Additional data/information will be submitted which allow judging whether the impurities are of toxicological relevance or not with regard to the impurities of the reference source. Furthermore, the applicant will provide data/information demonstrating that the material used in toxicological studies is representative for the proposed specification.	
(2)	Vol. 4, C.1.3-1 Analytical methods. Validation data for the determination of the impurity 1	**RMS:** Clarification is needed concerning the fortification levels for the determination of the accuracy. The applicant stated that the standard addition level (%) was done at 37%, 47% and 54%. However, these values seem to be not reliable and the sample preparation, i.e. weighing and dilution of the technical material, is not described. The fortification levels have to be stated in % related to the technical material. The RSD of the precision exceeds the Horwitz value which is 2.7% for a concentration of 1%. According to SANCO/3030/99 an explanation is required by the applicant. **SNN:** Additional data/information will be submitted.	

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No.	Column 1 Reference to assessment report	Column 2 Comments from Member States and/or applicant	Column 3 Further explanations
(3)	Vol. 4, C.1.3-2 Analytical methods. Validation data for the determination of the impurities 6 and 9	**RMS:** With respect to validation data for the determination of the impurities 6 and 9, the fortification levels are not appropriate to the specified values of 0.1% and 0.3%, respectively. Furthermore, the determination of the repeatability by repeated injection of a standard solution is not acceptable. A minimum of five replicate determinations in the tech material must be made. **SNN:** Additional data/information will be submitted.	
(4)	Vol. 4, C.1.3-3 Analytical methods. Validation data for the determination of the impurity 3	**RMS:** With respect to validation data for the determination of the impurity 3, clarification is needed concerning the fortification levels for the determination of the accuracy. The applicant stated that the standard addition level (%) was done at 32%, 41% and 49%. However, these values seem to be not reliable and the sample preparation, i.e. weighing and dilution of the tech material, is not described. The fortification levels have to be stated in % related to the technical material. The RSD of the precision exceeds the Horwitz value which is 3.7% for a concentration of 0.12%. According to SANCO/3030/99 an explanation is required by the applicant. **SNN:** Additional data/information will be submitted.	

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No.	Column 1 Reference to assessment report	Column 2 Comments from Member States and/or applicant	Column 3 Further explanations
(6)	Vol. 4, C.1.3-4 Analytical methods. Validation data for the determination of the impurity 20	**RMS:** The fortification levels are not appropriate to the specified value of 1 ppm. Furthermore, the determination of the repeatability by repeated injection of a standard solution is not acceptable. A min of 5 replicate determinations in the tech material must be made. **SNN:** Additional data/information will be submitted.	
(7)	Vol. 4, C.1.3-5 Analytical methods. Validation data for the determination of the impurity 20	**RMS:** Clarification is needed concerning the fortification levels for the determination of the accuracy. The applicant stated that the standard addition level (%) was done at 52 %, 57 % and 69 %. However, these values seem to be not reliable and the sample preparation, i.e. weighing and dilution of the technical material, is not described. The fortification levels have to be stated in % related to the tech material. **SNN:** Additional data/information will be submitted.	

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No.	Column 1 Reference to assessment report	Column 2 Comments from Member States and/or applicant	Column 3 Further explanations
(1)	Vol. 4, C.1.1, Toxicological evaluation of specification	Applicant: Syngenta acknowledges the RMS comment "For the renewal procedure (2013), none of the applicants provided sufficient information/data, which would allow to judge whether the impurities are relevant. It is noted that Syngenta submitted a case on relevance of impurities; this case is evaluated in the respective Vol. 4."	Dr Knoell will address this on behalf of the Task Force.
(2)	Vol. 4, C.1.1, Toxicological evaluation of specification	Applicant: Syngenta acknowledges the RMS comment "For the renewal procedure (2013), none of the applicants provided a sufficient evaluation, whether the material used in toxicological studies is representative for the respectively proposed specifications or the reference specification derived during the previous EU evaluation. Hence, it cannot be evaluated, whether the material used in toxicological studies is representative for the proposed specification or the reference specification derived during the previous EU evaluation"	Dr Knoell will address this on behalf of the Task Force.
(3)	Vol. 4, C.1.1, Toxicological evaluation of specification	Applicant: Syngenta acknowledges the RMS comment "No data or information was submitted that would allow setting maximum limits for relevant impurities. In summary, based on the currently available data and information, safe maximum levels for relevant impurities [[redacted] and formaldehyde] cannot be derived.	Dr Knoell will address this on behalf of the Task Force.
(4)	Vol. 4, C1.2.4, Comparison of the analytical profile of batches	Applicant: Syngenta acknowledges the RMS comment that in respect of the proposed specification clause "insolubles in NaOH" that is has been removed from the proposed specification by the RMS. However, it should be noted that the specification is therefore not consistent with the FAO specification which requires insolubles to be listed.	

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No.	Column 1 Reference to assessment report	Column 2 Comments from Member States and/or applicant	Column 3 Further explanations
(5)	Vol. 4, C1.2.4, Comparison of the analytical profile of batches – [redacted]	Applicant: Syngenta acknowledges the RMS comment that in respect of the proposed specification for the [redacted] technical material that a Tier II assessment is necessary in respect of the [redacted]	Syngenta will provide, on request, a Tier II toxicological assessment according to guidance document SANCO 10597 in respect of the [redacted], to demonstrate equivalence to the reference source and that there is no significant increase in toxicty as a result of the proposed specification limits, for the noted impurities.
(6)	Vol. 4, C1.2.4, Comparison of the analytical profile of batches – toxicological equivalence	Applicant: Syngenta acknowledges the RMS comment "the information provided by the applicant is not sufficient to establish relevance/non-relevance of impurities". Syngenta has tried to address this by the use of QSAR analysis and specific toxicological data where that is available but it recognises that there is no specific guidance relating to how to address relavance/non-relevance of impurities. Please can the RMS comment – how should this be assessed?	Dr Knoell will address this on behalf of the Task Force.
(7)	Vol. 4, C1.2.4, Comparison of the analytical profile of batches – toxicological equivalence	Applicant: Syngenta acknowledges the RMS comment "Impurities formaldehyde (impurity 21) and *N*-nitrosoglyphosate (impurity 20) were reported as "not analysed" in the tox. Batches but are foreseen to be specified" However, this is because the analysis of most of the toxicological batches was conducted before the analysis of relevant impurities was a formal requirement. However, it is clear that these known toxicologically relevant impurities are specified in the FAO specification which must be respected and that the impurities are controlled below the agreed (FAO) specification limits as demonstrated by the batch analysis.	

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No.	Column 1 Reference to assessment report	Column 2 Comments from Member States and/or applicant	Column 3 Further explanations
(8)	Vol. 4, C1.2.4, Comparison of the analytical profile of batches – toxicological equivalence	Applicant: Syngenta acknowledges the RMS comment [redacted] (impurity 14, SYN545862), [redacted] (impurity 16) and [redacted] (impurity 17) were reported as "not analysed" in the tox. batch Bx20100609 from the [redacted] but are foreseen to be specified"	For SYN545862 this was mistakenly reported as "NA" when it is clear from the analytical report it should be "ND" - which is not detected. SYN545862 was however detected in batch Bx 20070911 also used in toxicity testing. Whilst [redacted] (impurity 16) and [redacted] (impurity 17) were not analysed in this particular batch, other batches used for toxicological studies did contain these two impurities which were analysed and reported.
(9)	Vol. 4, C1.2.4, Comparison of the analytical profile of batches – toxicological equivalence	Applicant: Syngenta acknowledges the RMS comment "Impurities [redacted] (impurity 3 R25029), [redacted] (impurity 4, R153382) are intended to be specified with 10g/kg but were reported to be present in the tox batch P24 with only 3.4 g/kg or 1.3 g/kg, respectively. Additionally the results of an Ames test are available. For the evaluation of an impurity above/equal to 10 g/kg, the results of the in vitro genotoxicity testing battery are needed"	Syngenta is currently considering the implications of this request related to the impurities [redacted] (impurity 3 R25029), and [redacted] (impurity 4, R153382) and is reviewing different options to address the reviewer's concern. Syngenta commits to providing further information on this point.
(10)	Vol. 4, C1.2.4, Comparison of the analytical profile of batches – toxicological equivalence	Applicant: Syngenta acknowledges the RMS comment "[redacted] (impurity 10) is intended to be specified with 30 g/kg ([redacted] but was reported to be present in the tox batch Bx20070911 with only 21.2 g/kg. Additionally the results of an Ames test are available. For the evaluation of an impurity above 10 g/kg, the results of the in vitro genotoxicity testing battery are needed. Tox batch Bx20070911 was mainly used for acute toxicity studies and one Ames test"	R71181 was present in batch Bx20070911 at 21.2 g/kg, which tested negative in an Ames study and an *in vivo* mouse micronucleus assay. In addition, a bacterial reverse mutation assay has been conducted on R71181 in six bacterial strains (Reynolds and Riach, 1988). The results of these studies demonstrate that R71181 has no bacterial mutagenic activity or clastogenicity activity *in vivo*. Syngenta commits to providing the additional genotoxicity data to support glyphosine at the level in the proposed specification.

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No.	Column 1 Reference to assessment report	Column 2 Comments from Member States and/or applicant	Column 3 Further explanations
(11)	Vol. 4, C1.2.4, Comparison of the analytical profile of batches – toxicological equivalence	Applicant: Syngenta acknowledges the RMS comment "[redacted] (impurity 14 SYN545862) is intended to be specified with 5 g/kg [redacted]) but was reported to be present in the tox batch Bx20070911 with only 2.9 g/kg. Tox batch Bx20070911 was mainly used for acute toxicity studies and an Ames test. The intended amount would be within the acceptable increase for non-relevant impurities according Tier I of SANCO/10597/2003 – rev. 10.1"	Syngenta commits to providing further data to demonstrate that SYN545862 is indeed not relevant and therefore the proposed specification limit of 5g/kg will be supported by the existing toxicological study database according to a Tier I assessment using SANCO/10597/2003 – rev. 10.1. Dr Knoell will address this on behalf of the Task Force.
(12)	Vol. 4, C1.2.4, Comparison of the analytical profile of batches – toxicological equivalence	Applicant: Syngenta acknowledges the RMS comment "[redacted] (impurity 16) is intended to be specified with 8 g/kg [redacted]) but was reported to be present in the tox batch Bx20070911 with only 6.9 g/kg. Tox batch Bx20070911 was mainly used for acute toxicity studies and one Ames test. The intended amount would be within the acceptable increase for non-relevant impurities according Tier I of SANCO/10597/2003 – rev. 10.1."	Syngenta commits to providing further data to demonstrate that [redacted] is indeed not relevant and therefore the proposed specification limit of 8g/kg will be supported by the existing toxicological study database according to a Tier I assessment using SANCO/10597/2003 – rev. 10.1. Dr Knoell will address this on behalf of the Task Force.
(13)	Vol. 4, C1.2.4, Comparison of the analytical profile of batches – toxicological equivalence	Applicant: Syngenta acknowledges the RMS comment "[redacted] (impurity 16) is intended to be specified with 8 g/kg [redacted]) but was reported to be present in the tox batch Bx20070911 with only 6.9 g/kg. Tox batch Bx20070911 was mainly used for acute toxicity studies and one Ames test. The intended amount would be within the acceptable increase for non-relevant impurities according Tier I of SANCO/10597/2003 – rev. 10.1."	Syngenta commits to providing further data to demonstrate that [redacted] is indeed not relevant and therefore the proposed specification limit of 8g/kg will be supported by the existing toxicological study database according to a Tier I assessment using SANCO/10597/2003 – rev. 10.1. Dr Knoell will address this on behalf of the Task Force.
(14)	Vol. 4, C1.2.4, Comparison of the analytical profile of batches – toxicological equivalence	Applicant: Syngenta acknowledges the RMS comment "[redacted] (impurity 17) is intended to be specified with 5 g/kg ([redacted] but was reported to be present in the tox batch Bx20070911 with only 1.1 g/kg. Tox batch Bx20070911 was mainly used for acute toxicity studies and one Ames test. The intended amount would be outside the acceptable increase for non-relevant impurities according Tier I of SANCO/10597/2003 – rev. 10.1."	After extensive discussions with the supplier it has been agreed to reduce the proposed specification limit for [redacted] to 4g/kg. Syngenta therefore respectfully submits that the existing toxicological database supports this limit for triethylamine.

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No.	Column 1 Reference to assessment report	Column 2 Comments from Member States and/or applicant	Column 3 Further explanations
(15)	Vol. 4, C1.2.4, Comparison of the analytical profile of batches – ecotoxicological equivalence	Applicant: Syngenta acknowledges the RMS comment "The impurity 10 [redacted] (R71181) was present in batches Bx20070911 and Bx20100609 at 21.2 and 20.0 g/kg respectively, which were used in several toxicological studies. Eco-toxicological studies were performed with the batches P24 and P30, which do not contain this impurity. Thus, the equivalence of this source *(Glycine)* to the reference source cannot be substantiated with sufficient certainty; additional information addressing the ecotoxicological representativeness of the specification is required. If this information is not available an appropriate bridging study is required according to guideline OECD 201 (due to animal welfare reasons and the specific mode of action of glyphosate other studies are not required) to prove the eco-toxicological representativeness"	Syngenta is currently considering the implications of this request and will provide further information related to impurity 10 ([redacted] to address this concern on request.
(16)	Vol. 4, C1.3-1, Validation data for the determination of impurities in technical glyphosate	RMS: The analytical methods are acceptably validated and allow the determination of the impurities in the technical material. However, clarification on the concentration levels in mg/mL used for the linearity test of the impurities impurity 6, impurity 10 and impurity 14 is still needed. Applicant: Data can be provided on request	

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Vol. 4, Annex C			
No.	Column 1 Reference to assessment report	Column 2 Comments from Member States and/or applicant	Column 3 Further explanations
(1)	Vol. 4, C.1.2.4 Comparison of the analytical profile of batches - Toxicological evaluation of specification (2013):	**RMS:** The applicant provided no information/data, which would allow to judge whether the impurities are relevant. The applicant provided no evaluation, whether the material used in tox studies is representative for the proposed specification. Hence, it cannot be evaluated, whether the material used in tox studies is representative for the proposed specification. Based on the available studies submitted, a conclusion on the equivalence of the UPL source cannot be made **UPL:** Additional data/information will be submitted which allow judging whether the impurities are of toxicological relevance or not with regard to the impurities of the reference source. Furthermore, the applicant will provide data/information demonstrating that the material used in toxicological studies is representative for the proposed specification.	

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No.	Column 1 Reference to assessment report	Column 2 Comments from Member States and/or applicant	Column 3 Further explanations
(2)	Vol. 4, C.1.3-4 Analytical methods. Validation data for the determination of the impurity 20	RMS: With respect to validation data for the determination of the impurity 20, the method for the determination of the impurity 20 in the tech material is considered not acceptably validated as the fortification level for the accuracy test is not appropriate to the specified value of 0.7 ppm. UPL: In appendix 2 of SANCO 3030/99 rev. 4 it is stated that "accuracy may be measured in different ways(…). Assessment may be made by analysing a sample of known concentration and comparing the measured value to the true value. However a well characterized sample must be used. An example of this would be a reference standard." The validation of the method was done with preparations of glyphosate technical material and the reference material of impurity 20. The concentration of impurity 20 was well known during the validation. Therefore, the method should be acceptable.	

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No.	Column 1 Reference to assessment report	Column 2 Comments from Member States and/or applicant	Column 3 Further explanations
(1)	Vol. 4, C.1.2.4 Comparison of the analytical profile of batches - Toxicological evaluation of specification (2013):	**RMS:** The applicant provided no information/data, which would allow to judge whether the impurities are relevant. The applicant provided no evaluation, whether the material used in toxicological studies is representative for the proposed specification Based on the available studies which were submitted for the renewal of glyphosate, a conclusion on the equivalence of the Wynca source cannot be made. **WYC:** Additional data/information will be submitted which allow judging whether the impurities are of toxicological relevance or not with regard to the impurities of the reference source. Furthermore, the applicant will provide data/information demonstrating that the material used in toxicological studies is representative for the proposed specification.	
(2)	Vol. 4, C.1.3-4 Methods of analysis for the determination of impurities- Validation data for the determination of the impurities 1 and 9	**RMS:** The method is not acceptably validated, but can be used to confirm the results for the determination of the impurities 1 and 9 by NMR analysis. **WYC:** Other acceptable methods have already been provided.	As there are other methods provided for the determination of [redacted] and [redacted], no further action is needed

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Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)

Identity (B.1, Annex C)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Physical and chemical properties of the active substance (B.2.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Physical, chemical and technical properties of the formulation (B.2.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

Further information (B.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Methods of analysis (B.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Other comments (B.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol.3, B.6, Toxicology and metabolism, page 2	PAN-Europe: in the classification of studies the categories 2,3 and E are made subject to the so-called Klimisch-criteria. We do not agree with using Klimisch criteria since it uses no test protocol criteria, just the circular logic that OECD/GLP = good . Academic studies rarely use these standard protocols as they restrict the testing of hypothesis. Do the hundreds of thousands scientists in academia do irrelevant or poor work? RMS say yes, but do not prove it	Studies need to be assessed on their scientific value and not dismissed without reading because not being GLP/OECD. Next a 'weight of the evidence' approach should be followed, including all scientifically qualified studies available, especially independent studies.
2.	Vol.3, B 6	PAN-Europe: Industry's financial interests in	White, J. and Bero, L.A., 2010, 'Corporate manipulation of research:

Other comments (B.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		selling their products conflicts with the interests of truth when they perform the agent's safety tests. Specific techniques are used to allow their mission of getting products approved to prevail. White, 2010, extends the well-known strategies of the tobacco industry to other sectors. A RMS must be ready to counter these strategies, yet we didn't note a very critical approach of RMS to the applicant.	Strategies are similar across five industries', *Stanford Law & Policy Review*, (21/1) 105–134. We are fi. disappointed that the RMS agreed on the completeness of the dossier while demanding extra tests and confirmatory information would be the proper approach, especially in case the outcome of industry-sponsored studies differ from academic studies.
3.	Vol.3, B.6	The tests performed by the applicants will probably be based on good laboratory practice (GLP), but this doesn't guarantee quality and reliability. In the past several cases of industry laboratory fraud (IBT, Craven) were discovered by regulators (including tests on Glyphosate). Although these fraudulent tests were replaced by new ones, we still have our doubts on their quality and reliability. GLP, in the end, is just a management system, forcing laboratories to be transparent, but no-one can guarantee what is written down exactly, and what happened or is observed in the tests.	Commission therefore needs to explain what guarantees they have used to ensure quality and reliability of tests, both old and new. Many outcomes of studies comparing GLP-studies and studies from open (independent) literature have different outcomes, an unaddressed concern.

2. Mammalian toxicology (B.6)

Toxicokinetics (B.6.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Acute toxicity (B.6.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol.3, B.6.2.3, page 240	PAN-Europe, we do not understand that the exposure of test animals at 1000 ppm is called "low". With a current ADI of 0,3 ppm we challenge the value of this type of experiments with extreme high doses. This also means that effects seen at doses people are exposed to in practice are not tested and given the fact that Glyphosate has endocrine disrupting properties, adverse effects of low doses at vulnerable periods of development cannot be excluded.	We do not understand what we can learn from exposure of 20.000 ppm. Can any effect seen at this unrealistic dose be extrapolated to lower doses, thousand times lower and more, to predict an effect? We do not think that this type of mechanistic linear dose-response thinking has any basis in science. A body is no machine but an interrelated system with three major communication systems with triggers and feedback. OECD-tests are very insensitive and should be replaced by realistic dose tests on those elements (with very specific and sensitive endpoints) derived from the hazard assessment (mainly based on academic studies)

Section 2 - Mammalian toxicology (B.6)

Short-term toxicity (B.6.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Genotoxicity (B.6.4)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
1.	Vol.3, B.6.4, genotoxicty, page 359	PAN-Europe: In Table B 6.4-15 an experiment is disqualified for having too low doses. This is difficult to understand since the dose is still above ADI and far more relevant than the many dozens studies at extreme high dose.	Also remarkable is that at these doses effects are seen. They are subsequently qualified as not relevant using an industry-invented tool called "historical control data" allowing adverse effects being dismissed. Historical control data are never used by active scientists; they rely on normal controls.
2.	Vol.3, B.6.4, genotoxicty, page 382	PAN-Europe: The study discussed showing clastogenicity is done at lower levels than usual. It concludes that effects are seen al lower levels while no effects are seen at higher levels. This again would be reason to reconsider the old paradigms of linear dose-response and use of high unrealistic doses.	
3.	Vol.3, B.6.4, genotoxicity, page 384	PAN-Europe: the study of Clemens shows mutagenicity in tadpoles and the occurrence of this effect is not excluded by the RMS. However in the next lines many questionable assumptions and reasoning are added by the	We think the only proper approach in case of uncertainties would be to demand the test to be repeated and confirmed in independent laboratories and blind testing. And the process of approval halted until more clarity is given.

Genotoxicity (B.6.4)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		RMS and finally the effects dismissed for humans. We cannot agree with assumptions being made of questionable grounds; expert judgement should be based on science and not feelings.	
4.	Vol.3, B.6.4, genotoxicty, page 385	PAN-Europe: we think it is not justified to dismiss studies (genotoxic effects in germ cells in Drosophila) that challenge industry findings by immediately pointing at the "large database of existing studies`. This gives the impression the RMS had already made up his mind about mutagenicity and is now just looking for reasons to dismiss studies not confirming the RMS´s feelings.	All studies should be used for a weight of the evidence approach in an open scientific approach without prior opinions or feelings. We think independent experts are needed to do this weight of the evidence evaluation, who were not involved in drafting the RAR and contacts with industry. The same biased approach is taken on page 386 for another critical study.
5.	Vol.3, B.6.4, genotoxicty, page 386	PAN-Europe: we can understand that the applicant will claim that any adverse effect seen is due to the co-formulant tallowene and as such these studies should not count. We do not understand the claim of the RMS that it can "certainly be assumed" that an effect will be caused by the co-formulant. RMS's should not assume but assess. And if they have no data to prove it was the co-formulant, the effects should be counted for the active ingredient.	Again, there is all reason to demand the applicant to repeat academic studies showing adverse effects by exposing the active substance. This should be done in an independent laboratory with blind testing.
6.	Vol.3, B.6.4, genotoxicty, page 389	PAN-Europe: The claim in the RAR of a lack of mutagenicity or even that results of studies are	Literature references will be provided by PAN Europe on request but should also be part of the review of the applicant on peer-reviewed

Genotoxicity (B.6.4)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		consistently and unequivocally negative (Vol.1) is false. Genotoxic effects on the contrary are already long known and available to the reviewers. Kale, 1995, showed mutations in fruit flies, Vigfussen, 1980, showed sister chromatin exchanges in human lymphocytes, just as Bolognesi in 1997. Peluso in 1998 showed increased DNA adducts in mice. Gasnier, 2009, showed DNA damage, as well as Manas, 2009. Some are captured in the industry review, others not, for unknwon reason. All are dismissed in the end. Numerous other studies have confirmed DNA damage in mouse, bovine, fish, caiman, tadpole, fruit fly, sea urchin, onion, and bacterial cells.	literature. We only mention, Grisolia, 2002, Sivikova, 2006, Belle, 2007, Cavas, 2007, Cavalcante, 2008, Guilherme, 2009, Poletta, 2009, Monroy, 2005. It is really a joke the RMS uses the unscientific Klimisch-criteria for academic studies. Anyone knows the outcome: all dismissed! Given the conflict of interest of the applicant on safety testing, and the potential bias in studies or interpretation of studies, we propose EFSA starts her peer-review with independent literature for doing a hazard assessment. Independent literature has less chance on bias because of lacking motives and should be qualified as more reliable than industry-sponsored studies with an inherent conflict of interest. It is strange to note that Table 2.6-6 in Volume 1 only summarises industry-sponsored studies.
7.	Vol.3, B.6.4.8.10, weight of the evidence	PAN-Europe: While the RMS discusses a few of the academic studies that show adverse effects, in the 'weight of the evidence' approach taken by the RMS as a standard procedure plays down the positive effects seen by assumptions and reasoning's such as the effects being indirect, or being beyond a certain threshold, not relevant for humans, suggests that the effect are toxic but not mutagenic. None of these assumptions is based on science but just part of the old paradigm used by regulators.	The RMS has high confidence in industry-sponsored studies and very low in academic studies, with the result only industry-sponsored studies with their favourable outcome for industry are counted in the final evaluation.

Section 2 - Mammalian toxicology (B.6)

Genotoxicity (B.6.4)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations

Long-term toxicity and carcinogenicity (B.6.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
1	Vol 3, B 6.5. Long-term toxicity and carcinogenicity, page 435	PAN-Europe: A major failure in the testing systems used is the lack of exposure in-utero of the test animals. It is well-known that many chronic diseases develop in-utero (not only for cancer) and as such tests lacking in-utero exposure cannot be qualified as a 'state-of-the art' scientific approach. The conclusion that the substance is not carcinogen needs to be justified. We therefore propose EFSA requires the applicant to test again with in-utero exposure, performed with blind testing in an independent laboratory.	EU legislation provides for a high level of human health protection based on the precautionary principle and requires special attention for the vulnerable, the unborn and the elderly. The test system disregards the effects on the vulnerable groups in society.
2	Vol 3, B 6.5. Long-term toxicity and carcinogenicity, page 435	PAN-Europe: Next point is the extreme high doses used in notifier's testing. More and evidence is available in literature (see Vandenberg et al. 2012 review) that low doses can harm, many times in the developing phase of the organism and many times for endocrine	EFSA should require the applicant to do new testing of the substance including a range of low doses.

Long-term toxicity and carcinogenicity (B.6.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		disrupting chemicals. Since Glyphosate has endocrine disrupting properties, EFSA should perform a thorough review ion the data in independent literature, and require applicant to do a series of low dose testing on endocrine adverse effects.	
3	Vol 3, B 6.5. Long-term toxicity and carcinogenicity, page 435	PAN-Europe: Another point on carcinogenicity is the need to expose and follow test animals during their entire lifetime. Most diseases develops after notifier's tests incinerate the test animals (e.g. ACS (American Cancer Society): *Cancer Facts & Figures 2012*. Atlanta: American Cancer Society; 2012. [http://cancer.org/acs/groups/content/@epidemiologysurveilance/documents/document/acspc-031941.pdf].	EFSA should require the applicant to do new testing of the substance including lifetime exposure and monitoring.
4.	Vol 3, B 6.5. Long-term toxicity and carcinogenicity, page 502	PAN Europe: No evidence in rat according to the RAR (only industry-sponsored studies analysed) but the malignant lymphoma seen in mice were dismissed. It was not the chemical (Glyphosate) that should be blamed according to the RMS but the strain of mice. We think this has nothing to do with a scientific evaluation but more with a determination to get to a certain outcome. Given the many articles in peer-reviewed literature on long-term effects	We propose that based on the studies in open literature a hazard assessment is done to find out what long-term effects and cancers can be expected to occur by the use of Glyphosate. Next, an analysis need to be done if the long-term and carcinogenicity animal tests will really capture the expected effects. And finally those long-term and carcinogenicity tests qualifying for capturing the adverse effects should be used for a final conclusion. No study should be dismissed for being non-GLP or non-OECD. Every study counts, also the one of Seralini. While the Rapporteur might not like the outcome, there is no scientific failure in the tests of Seralini.

Long-term toxicity and carcinogenicity (B.6.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		and cancer, a more balanced approach would have been justified.	
5.	Vol 3, B 6.5. Long-term toxicity and carcinogenicity, page 502	PAN-Europe: Glyphosate has a history of links with cancer. The first carcinogenicity study submitted to US-EPA (1981) by applicant Monsanto showed an increase in testicular tumours in male rats as well as an increase in the frequency of a thyroid cancer in females. Both results occurred at the highest dose tested (30 mg/kg of body weight per day). The second study (1983) found an increasing trend in the frequency of a rare kidney tumour in male mice. A later study (1990) found an increase in pancreas and liver tumours in male rats together with an increase of the same thyroid cancer found in the 1983 study in females.	We ask EFSA to take a look at these older studies. There is good reason for EFSA to start the cancer analysis from scratch including all evidence from the past and from independent literature. Knowing the potential of Glyphosate to cause these effects, are the currently evaluated safety tests designed to capture these effects?
6.	Vol 3, B 6.5. Long-term toxicity and carcinogenicity page 524	PAN-Europe: In the RAR all epidemiology studies showing a relation between Glyphosate and cancer are considered irrelevant, such as the Hardell-studies on the link with non-Hodgkin's, and even the unscientific Klimisch-approach is used for this qualification. This is unjustified. Now industry has created a situation in which people are exposed to thousands of chemicals at the same time, epidemiology studies cannot by nature be	Industry should monitor the use of Glyphosate, analyse all environmental compartments and organisms, and do a large epidemiology study focussed on clarifying the evidence available. There is good evidence on the relation with non-Hodgkin's lymphoma, Nordstrom, 1998, Hardell, 1999 and 2002, McDuffie, 2001, De Roos, 2003 and Eriksson, 2008, and multiple myeloma, De Roos, 2005, and a large study should be initiated to find out more.

Long-term toxicity and carcinogenicity (B.6.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		sensitive anymore. This means if a relation is shown, even weak, this should be reason for concern and reason to demand the applicant to do independent monitoring to et more information	
7.			

Reproductive toxicity (B.6.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
1	Vol.3 B.6.6 Reproductive toxicity. page 538	PAN-Europe: a big omission in the German RAR is the lack of a hazard characterization of Glyphosate. In many EFSA opinions it is stated that the first step of risk assessment is the hazard characterization. We observe that Germany just moves on directly to risk characterisation and standard setting, and ignores the evidence on hazards	A hazard characterization is important to learn about the mechanism of toxicity of Glyphosate. Without the knowledge of the hazards it will be difficult to select in the next steps of risk assessment what data are useful and not. Germany just puts all evidence in the "Klimisch-mill" with the obvious effect of all independent science disregarded.
2	Vol.3 B.6.6 Reproductive toxicity. page 538	PAN-Europe: We urge EFSA to include a hazard characterisation in the peer-review. This should be done by using all in-vitro studies available, disregarding none, and all mechanistic studies	The study of Paganelli et al. 2010 presents interesting evidence on the mechanism of action. During early embryonic development, retinoic acid generated in a specific region of the embryo helps determine position along the embryonic anterior/posterior axis by serving as an

Reproductive toxicity (B.6.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		available. The peer-review should focus on what mechanistic evidence is present on teratogenicity, on DNA-damage., etc.?	intercellular signaling molecule that guides development of the posterior portion of the embryo. It acts through Hox genes, which ultimately control anterior/posterior patterning in early developmental stages. The findings of Marc et al. '05 support this, offering a general mechanism of action for teratogenicity.
3.	Vol.3 B.6.6 Reproductive toxicity. page 539	PAN-Europe: many multi-generation tests in the RAR with their very high (and unrealistic) doses, endpoints which are not the state-of-the-art cannot provide for the final answer on reproductive toxicity. The results are not clear anyway with a study that shows effects at low doses but is dismissed in the end by the Rapporteur. And studies showing effects on the offspring also accepted because they are observed at high doses. Combined with the many studies in open literature on malformations of the offspring and developmental effects, a peer-review by EFSA of all evidence is more than necessary.	The industry-sponsored OECD tests are known for their insensitivity and this could explain the very remarkable difference seen between the industry-sponsored studies and independent literature. The high doses used are close to the acute poisoning doses and poisoning effects are common in these tests, while more subtle effects could be missed.
4	Vol.3 B.6.6 Reproductive toxicity. page 548	PAN-Europe, we again question the use of extreme high exposure doses such as 15.000 ppm or 1000 mg/kg, more than 1000x the ADI. Animals should be tested at realistic doses and no extrapolation used	The high doses are close to the acute poisoning doses used and poisoning effects are common in these tests, while more subtle effects could be missed.
5	Vol.3 B.6.6 Reproductive toxicity.	PAN-Europe: We especially encourage EFSA to take a look at teratogenicity. The pre-2001	In the first DAR on Glyphosate in 2001, the UK experts commented that -based on the Monsanto studies- a single study might not raise

Reproductive toxicity (B.6.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	page 596	studies of Monsanto show teratogen effects, a range of independent studies report these effects, these effects are also observed in areas with Roundup monocultures (soy) in epidemiology studies and even in bioindustry where piglets fed on soy have these effects.	concerns, but that the teratogenic effects that kept being observed in the Monsanto-studies, pointed at a pattern that should not be dismissed in the risk assessment. EFSA should asses if in the two-generation studies the animals are properly exposed during vulnerable windows during development and if a large range and relevant endpoints are considered for teratogenicity and development during later life of the offspring.
6.	Vol.3 B.6.6.9, Reproductive toxicity. page 597	PAN-Europe: specific endocrine disrupting tests should be demanded from the applicant. Just basing conclusions on outdated OECD-protocols on reproduction and development is not justified. The science on endocrine disruption differs a lot from other fields and specific exposure windows, doses and specific endpoints should be used. In the traditional tests with traditional experts these effects will be missed.	
7.	Vol.3 B.6.6.9 Reproductive toxicity. page 597	PAN-Europe: A large body of evidence on endocrine disrupting effects of Glyphosate is disregarded and dismissed in the RAR. Walsh, 2002 showed the disruption of the steroid hormone progesterone, as well as Romano, 2010 on testosterone. Richard, 2005 also concludes Glyphosate is an endocrine disruptor by affecting aromatase at very low doses. Also Benachour, 2005 and Gasnier, 2007 came to	Hokanson, 2007, demonstrated a synergistic effect of Glyphosate with oestrogen, with implications for pregnancy-induced hypertension and foetal growth retardation. The implications of these effects on reproduction and the developing foetus are profound, with work by Mose, 2008, confirming that Glyphosate does cross the placenta.

Reproductive toxicity (B.6.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		the same conclusion.	
8	Vol.3 B.6.6.10 Reproductive toxicity. page 613	PAN-Europe: the study in rabbits shows that at a level of 10 mg/kg 20% of the litters have malformations while this is 5% in the control (this also counts for the foetus, 3,1% vs. 0,7%). While this dose is at least less enormous than the regular dose, it is still above a realistic dose and we think additional studies should be done with lower and m	The malformations should be more thoroughly investigated and this study already shows that the LOAEL of 10 mg/kg should be adopted for standard setting. A suggesting NOEAL of 100 mg/kg by the applicant is absurd.
9.	Vol.3 B.6.6.10 Reproductive toxicity. page 619	PAN-Europe: this study in rabbit again shows most effects at the lowest dose tested (18 vs. 13 of the litters tested with malformations), 50 mg/kg. While this dose is still unrealistic high, lower doses should be tested on malformations of the foetus.	
10.	Vol.3 B.6.6.10 Reproductive toxicity. page 629	PAN-Europe: this study in rabbit also shows malformations at the lowest level tested (82 foetus with 'minor' defects vs, 58 in the control), 100 mg/kg. This "low" dose is of course unrealistically high.	There is a clear pattern of malformations of the foetus in all rabbit studies.
11.	Vol.3 B.6.6.10 Reproductive toxicity. page 642	PAN-Europe: this study confirms previous observations that malformations of the foetus is highest in the lowest dose tested, 50 mg/kg, (17.7% vs. 11,7% in the control). We object to the use of historical control data. The only scientific approach is to compare the	Why the RMS values historical control data over the normal (negative|) control is a mystery. While it is highly questionable if the industry-sponsored studies are reproducible at all, historical control data mix different labs, operators, protocols and strains and create an unrealistic wide range of "controls'. No scientist will ever use this type of tools.

Reproductive toxicity (B.6.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		outcome in the tests against the control.	
12.	Vol.3 B.6.6.10 Reproductive toxicity. page 650	PAN-Europe: also this study shows effects at the lowest dose tested, 20 mg/kg, upper cleft palate, 15% vs. 5% in the control, and dilated heart, 23,1% vs. 0% in the control.	There is a clear pattern of malformations of the foetus in all rabbit studies.
13.	Vol.3 B.6.6.12, Reproductive toxicity, Published data, page 658	PAN-Europe: it is remarkable that the RMS now easily rejects all claims made by EOS in their report "is the public kept in the dark" and let most independent literature fall under the 'Klimisch-axe". In their reaction in July 2011, the RMS called the report: The recently published report "Roundup and birth defects: Is the public kept in the dark?" is a challenging critical summary of adverse health (mainly teratological and reproductive) findings that are attributed by the authors to the compound glyphosate and/or to herbicides such as Roundup that contain glyphosate as active ingredient.	The RMS ends their report by saying: An adequate response to the criticism and the many accusations in the report would require a general discussion of the established paradigms for the toxicological evaluation of chemicals. These general discussions should be initiated by the Commission before we start with the re-evaluation of glyphosate within the AIR2 project. We fail to have seen any general discussion on established paradigms, not by the RMS and not by Commission. We therefore urge EFSA to start such a discussion before drafting the peer review on Glyphosate.
14.	Vol.3 B.6.6.12, Reproductive toxicity, Published data, page 658	PAN-Europe: it is sad to note that the industry review made by the applicant is not commented by the RMS. Given the many missing studies and the standard use of Klimisch to dismiss studies on a large scale, an intervention of the RMS was needed very much.	We urge EFSA to review all independent studies and stop using the entirely unscientific Klimisch-tool and do a purely scientific assessment of each study looking at the quality of the study, disregarding protocols and GLP-administration systems.

Section 2 - Mammalian toxicology (B.6)

Neurotoxicity (B.6.7)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
1.	Vol.3, B.6.7.1, Neurotoxicity, Published data, page 702.	PAN Europe: Epidemiology studies have been published pointing at Glyphosate of causing mental disorders of children born to pesticide applicators in the US, Garry, 2002. Even acute poisoning could lead to brain damage, Barbosa, 2001. Animal studies have demonstrated that Glyphosate depletes serotonin and dopamine, Anadon, 2008, and causes a loss of mitochondrial transmembrane potential in rat brain cells, especially in the substantia nigra region of the brain, Astiz, 2009.	There is evidence of developmental neurotoxicity of Glyphosate and EFSA should pay good attention to this adverse effect in their peer-review.
2.	Vol.3, B.6.7.1, Neurotoxicity, Published data, page 702.	PAN-Europe: We regret that an assessment of the literature by the RMS is missing. We think the assessment of the applicant is totally inadequate, playing down any adverse effects and using the "Klimisch-axe" to ensure it is ignored. This abrogates the idea of scientific evaluation.	

Other toxicological studies & Medical data (B.6.8-B.6.9)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data	<< Identifier >>: <<comment>>	

Section 2 - Mammalian toxicology (B.6)

Other toxicological studies & Medical data (B.6.8-B.6.9)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	point>>, <<description>>		

Summary of mammalian toxicology and setting ADI, AOEL, ARfD (B.6.10)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Toxicity of the product(s) (B.6.11)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Dermal absorption (B.6.12)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data	<< Identifier >>: <<comment>>	

Section 2 - Mammalian toxicology (B.6)

Dermal absorption (B.6.12)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	point>>, <<description>>		

Toxicity of non-active substances (B.6.13)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Exposure data (B.6.14)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol.3, B.6 review public	PAN-Europe: We did our own literature search	To check compliance with the new mandate on literature review,

Section 2 - Mammalian toxicology (B.6)

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	data	(see explanations) and found remarkable differences with the one conducted by the applicant.The notifier only found 52% of the 145 significant glyphosate toxicity studies we found, despite the mandate to find all. Worse– the notifier finds a published study but never mentions it (not even placing its main numerical finding in a table, as sometimes occurred). So the fraction of those we found that were also discussed is just 31%.	we performed a simple search of PubMed: "<pesticide common name> toxicity". The later is a specific keyword in PubMed, while almost all studies use, inter alia, the common name of a chemical. In our experience this simple search term captures on average 95% of all *published* studies relating to the risks of a chemical. After eliminating the obviously irrelevant, we saved the remaining abstracts (by publication date) as a public PubMed collection, and listed by endpoint in a table the studies that the notifier and RMS did & did not find or discuss, critiquing the reasons for the former.

5. Ecotoxicology (B.9)

Birds and mammals (B.9.1 and B.9.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Aquatic organisms (B.9.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Bees and non-target arthropods (B.9.4 and B.9.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.9.4	PAN-Europe: the endocrine disrupting effects of Glyphosate on birds and other non-target organisms are disregarded.	

Section 5 - Ecotoxicology (B.9)

Earthworms and other soil non-target organisms (macro and micro) (B.9.6, B.9.7 and B.9.8)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Other non-target organisms (flora and fauna), sewage treatment (B.9.9 and B.9.10)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.9, Annex, page 298	PAN-Europe: many studies show that Glyphosate has endocrine disrupting properties. The RMS conveniently states that all endocrine disrupting effects are likely caused by the surfactant. The study of Paganelli, 2010, for instance clealrly shows that formulations and active substance have the same adverse effect, and clearly point at Glyphosate as being an endocrine disruptor.	EFSA should demand studies from the applicant (in independent laboratories, blind testing) for a range of endocrine disruption screening test for Glyphosate.

Section 2 - Mammalian toxicology (B.6)

Reproductive toxicity (B.6.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 1, <<2.6.7.2.2 Rabbit>>, <<Studies with formulations/Published data>>	<< Gerhart Ryffel >>: The data of Paganelli et al 2010 are summarized in a misleading manner. From a scientific point of view they prove the teratogenic property of glyphosate in the frog Xenopus with most convincing experiments. The application into the water is a most natural way for developing frogs. The documented interference with retinoic acid signalling establishes that glyphosate interferes with a basic developmental pathway common to all vertebrates including humans.	A cautionary interpretation of these basic experiments in the frog is essential. The result of Paganelli et al 2010 documents that a highly conserved pathway is specifically affected by glyphosate. It would be imperative to exclude that this effect cannot happen in mammals including humans. Concerning environmental effects it would be essential to determine the lowest concentration of glyphosate interfering with embryogenesis. Negative effects of glyphosate on amphibian has been reported, e.g. Howe et al 2004, Relyea et al 2012, Lanctot et al 2013.

Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)

Identity (B.1, Annex C)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Physical and chemical properties of the active substance (B.2.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Physical, chemical and technical properties of the formulation (B.2.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Further information (B.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations

Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

Further information (B.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Methods of analysis (B.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Other comments (B.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol.3, B.6, Toxicology and metabolism, page 2	EGM: in the classification of studies the categories 2,3 and E are made subject to the so-called Klimisch-criteria. We do not agree with using Klimisch criteria since it uses no test protocol criteria, just the circular logic that OECD/GLP = good . Academic studies rarely use these standard protocols as they restrict the testing of hypothesis. Do the hundreds of thousands scientists in academia do irrelevant or poor work? RMS say yes, but do not prove it	Studies need to be assessed on their scientific value and not dismissed without reading because not being GLP/OECD. Next a 'weight of the evidence' approach should be followed, including all scientifically qualified studies available, especially independent studies.
(2)	Vol.3, B 6	EGM: industry's financial interest in selling their products conflicts with the interests of truth when they perform the agent’s safety tests. Specific techniques are used to allow their mission of getting products approved to prevail. White, 2010,	White, J. and Bero, L.A., 2010, 'Corporate manipulation of research: Strategies are similar across five industries', Stanford Law & Policy Review, (21/1) 105–134. We are fi. disappointed that the RMS agreed on the completeness of the dossier while demanding extra tests and confirmatory information would

Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

Other comments (B.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		extends the well-known strategies of the tobacco industry to other sectors. A RMS must be ready to counter these strategies, yet we didn't note a very critical approach of RMS to the applicant.	be the proper approach, especially in case the outcome of industry-sponsored studies differ from academic studies.
(3)	Vol.3, B.6	The tests performed by the applicants will probably be based on good laboratory practice (GLP), but this doesn't guarantee quality and reliability. In the past several cases of industry laboratory fraud (IBT, Craven) were discovered by regulators (including tests on Glyphosate). Although these fraudulent tests were replaced by new ones, we still have our doubts on their quality and reliability. GLP, in the end, is just a management system, forcing laboratories to be transparent, but no-one can guarantee what is written down exactly, and what happened or is observed in the tests.	Commission therefore needs to explain what guarantees they have used to ensure quality and reliability of tests, both old and new. Many outcomes of studies comparing GLP-studies and studies from open (independent) literature have different outcomes, an unaddressed concern.

2. Mammalian toxicology (B.6)

Toxicokinetics (B.6.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Acute toxicity (B.6.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol.3, B.6.2.3, page 240	EGM: we do not understand that the exposure of test animals at 1000 ppm is called "low". With a current ADI of 0,3 ppm we challenge the value of this type of experiments with extreme high doses. This also means that effects seen at doses people are exposed to in practice are not tested and given the fact that Glyphosate has endocrine disrupting properties, adverse effects of low doses at vulnerable periods of development cannot be excluded.	We do not understand what we can learn from exposure of 20.000 ppm. Can any effect seen at this unrealistic dose be extrapolated to lower doses, thousand times lower and more, to predict an effect? We do not think that this type of mechanistic linear dose-response thinking has any basis in science. A body is no machine but an interrelated system with three major communication systems with triggers and feedback. OECD-tests are very insensitive and should be replaced by realistic dose tests on those elements (with very specific and sensitive endpoints) derived from the hazard assessment (mainly based on academic studies)

Short-term toxicity (B.6.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Genotoxicity (B.6.4)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol.3, B.6.4, genotoxicty, page 359	EGM: In Table B 6.4-15 an experiment is disqualified for having too low doses. This is difficult to understand since the dose is still above ADI and far more relevant than the many dozens studies at extreme high dose.	Also remarkable is that at these doses effects are seen. They are subsequently qualified as not relevant using an industry-invented tool called "historical control data" allowing adverse effects being dismissed. Historical control data are never used by active scientists; they rely on normal controls.
(2)	Vol.3, B.6.4, genotoxicty, page 382	EGM: The study discussed showing clastogenicity is done at lower levels than usual. It concludes that effects are seen al lower levels while no effects are seen at higher levels. This again would be reason to reconsider the old paradigms of linear dose-response and use of high unrealistic doses.	
(3)	Vol.3, B.6.4, genotoxicity, page 384	EGM: the study of Clemens shows mutagenicity in tadpoles and the occurrence of this effect is not excluded by the RMS. However in the next lines many questionable assumptions and reasoning are added by the RMS and finally the effects dismissed for humans. We cannot agree with assumptions being made of questionable grounds; expert judgement should be based on science and not feelings.	We think the only proper approach in case of uncertainties would be to demand the test to be repeated and confirmed in independent laboratories and blind testing. And the process of approval halted until more clarity is given.
(4)	Vol.3, B.6.4, genotoxicty, page 385	EGM: we think it is not justified to dismiss studies (genotoxic effects in germ cells in Drosophila) that challenge industry findings by immediately pointing at the "large database of existing	All studies should be used for a weight of the evidence approach in an open scientific approach without prior opinions or feelings. We think independent experts are needed to do this weight of the evidence evaluation, who were not involved in drafting the RAR and contacts

Genotoxicity (B.6.4)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		studies`. This gives the impression the RMS had already made up his mind about mutagenicity and is now just looking for reasons to dismiss studies not confirming the RMS´s feelings.	with industry. The same biased approach is taken on page 386 for another critical study.
(5)	Vol.3, B.6.4, genotoxicty, page 386	EGM: we can understand that the applicant will claim that any adverse effect seen is due to the co-formulant tallowene and as such these studies should not count. We do not understand the claim of the RMS that it can "certainly be assumed" that an effect will be caused by the co-formulant. RMS's should not assume but assess. And if they have no data to prove it was the co-formulant, the effects should be counted for the active ingredient.	Again, there is all reason to demand the applicant to repeat academic studies showing adverse effects by exposing the active substance. This should be done in an independent laboratory with blind testing.
(6)	Vol.3, B.6.4, genotoxicty, page 389	EGM: The claim in the RAR of a lack of mutagenicity or even that results of studies are consistently and unequivocally negative (Vol.1) is false. Genotoxic effects on the contrary are already long known and available to the reviewers. Kale, 1995, showed mutations in fruit flies, Vigfussen, 1980, showed sister chromatin exchanges in human lymphocytes, just as Bolognesi in 1997. Peluso in 1998 showed increased DNA adducts in mice. Gasnier, 2009, showed DNA damage, as well as Manas, 2009. Some are captured in the	It is unacceptable that RMS uses the Klimisch-criteria for academic studies. Anyone knows the outcome: all dismissed! Given the conflict of interest of the applicant on safety testing, and the potential bias in studies or interpretation of studies, we propose EFSA starts her peer-review with independent literature for doing a hazard assessment. Independent literature has less chance on bias because of lacking motives and should be qualified as more reliable than industry-sponsored studies with an inherent conflict of interest. It is strange to note that Table 2.6-6 in Volume 1 only summarises industry-sponsored studies.

Genotoxicity (B.6.4)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		industry review, others not, for unknwon reason. All are dismissed in the end. Numerous other studies have confirmed DNA damage in mouse, bovine, fish, caiman, tadpole, fruit fly, sea urchin, onion, and bacterial cells.	
(7)	Vol.3, B.6.4.8.10, weight of the evidence	EGM: While the RMS discusses a few of the academic studies that show adverse effects, in the 'weight of the evidence' approach taken by the RMS as a standard procedure plays down the positive effects seen by assumptions and reasoning's such as the effects being indirect, or being beyond a certain threshold, not relevant for humans, suggests that the effect are toxic but not mutagenic. None of these assumptions is based on science but just part of the old paradigm used by regulators.	The RMS has high confidence in industry-sponsored studies and very low in academic studies, with the result only industry-sponsored studies with their favourable outcome for industry are counted in the final evaluation.

Long-term toxicity and carcinogenicity (B.6.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol 3, B 6.5. Long-term toxicity and carcinogenicity, page 435	EGM: A major failure in the testing systems used is the lack of exposure in-utero of the test animals. It is well-known that many chronic diseases develop in-utero (not only for cancer) and as such tests lacking in-utero exposure cannot be	EU legislation provides for a high level of human health protection based on the precautionary principle and requires special attention for the vulnerable, the unborn and the elderly. The test system disregards the effects on the vulnerable groups in society.

Long-term toxicity and carcinogenicity (B.6.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		qualified as a 'state-of-the art' scientific approach. The conclusion that the substance is not carcinogen needs to be justified. We therefore propose EFSA requires the applicant to test again with in-utero exposure, performed with blind testing in an independent laboratory.	
(2)	Vol 3, B 6.5. Long-term toxicity and carcinogenicity, page 435	EGM: Next point is the extreme high doses used in notifier's testing. More and evidence is available in literature (see Vandenberg et al. 2012 review) that low doses can harm, many times in the developing phase of the organism and many times for endocrine disrupting chemicals. Since Glyphosate has endocrine disrupting properties, EFSA should perform a thorough review ion the data in independent literature, and require applicant to do a series of low dose testing on endocrine adverse effects.	EFSA should require the applicant to do new testing of the substance including a range of low doses.
(3)	Vol 3, B 6.5. Long-term toxicity and carcinogenicity, page 435	EGM: Another point on carcinogenicity is the need to expose and follow test animals during their entire lifetime. Most diseases develops after notifier's tests incinerate the test animals (e.g. ACS (American Cancer Society): *Cancer Facts & Figures 2012*. Atlanta: American Cancer Society; 2012. [http://cancer.org/acs/groups/content/@epidemiologysurveilance/documents/document/ac	EFSA should require the applicant to do new testing of the substance including lifetime exposure and monitoring.

Long-term toxicity and carcinogenicity (B.6.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		spc-031941.pdf].	
(4)	Vol 3, B 6.5. Long-term toxicity and carcinogenicity, page 502	EGM: No evidence in rat according to the RAR (only industry-sponsored studies analysed) but the malignant lymphoma seen in mice were dismissed. It was not the chemical (Glyphosate) that should be blamed according to the RMS but the strain of mice. We think this has nothing to do with a scientific evaluation but more with a determination to get to a certain outcome. Given the many articles in peer-reviewed literature on long-term effects and cancer, a more balanced approach would have been justified.	We propose that based on the studies in open literature a hazard assessment is done to find out what long-term effects and cancers can be expected to occur by the use of Glyphosate. Next, an analysis need to be done if the long-term and carcinogenicity animal tests will really capture the expected effects. And finally those long-term and carcinogenicity tests qualifying for capturing the adverse effects should be used for a final conclusion. No study should be dismissed for being non-GLP or non-OECD. Every study counts, also the one of Seralini. While the Rapporteur might not like the outcome, there is no scientific failure in the tests of Seralini.
(5)	Vol 3, B 6.5. Long-term toxicity and carcinogenicity, page 502	EGM: Glyphosate has a history of links with cancer. The first carcinogenicity study submitted to US-EPA (1981) by applicant Monsanto showed an increase in testicular tumours in male rats as well as an increase in the frequency of a thyroid cancer in females. Both results occurred at the highest dose tested (30 mg/kg of body weight per day). The second study (1983) found an increasing trend in the frequency of a rare kidney tumour in male mice. A later study (1990) found an increase in pancreas and liver tumours in male rats together with an increase of the same thyroid cancer found in the 1983 study in	We ask EFSA to take a look at these older studies. There is good reason for EFSA to start the cancer analysis from scratch including all evidence from the past and from independent literature. Knowing the potential of Glyphosate to cause these effects, are the currently evaluated safety tests designed to capture these effects?

Long-term toxicity and carcinogenicity (B.6.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		females.	
(6)	Vol 3, B 6.5. Long-term toxicity and carcinogenicity page 524	EGM: In the RAR all epidemiology studies showing a relation between Glyphosate and cancer are considered irrelevant, such as the Hardell-studies on the link with non-Hodgkin's, and even the unscientific Klimisch-approach is used for this qualification. This is unjustified. Now industry has created a situation in which people are exposed to thousands of chemicals at the same time, epidemiology studies cannot by nature be sensitive any more. This means if a relation is shown, even weak, this should be reason for concern and reason to demand the applicant to do independent monitoring to et more information	Industry should monitor the use of Glyphosate, analyse all environmental compartments and organisms, and do a large epidemiology study focussed on clarifying the evidence available. There is good evidence on the relation with non-Hodgkin's lymphoma, Nordstrom, 1998, Hardell, 1999 and 2002, McDuffie, 2001, De Roos, 2003 and Eriksson, 2008, and multiple myeloma, De Roos, 2005, and a large study should be initiated to find out more.

Reproductive toxicity (B.6.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol.3 B.6.6 Reproductive toxicity. page 538	EGM: a big omission in the German RAR is the lack of a hazard characterization of Glyphosate. In many EFSA opinions it is stated that the first step of risk assessment is the hazard characterization. We observe that Germany just	A hazard characterization is important to learn about the mechanism of toxicity of Glyphosate. Without the knowledge of the hazards it will be difficult to select in the next steps of risk assessment what data are useful and not. Germany just puts all evidence in the "Klimisch-mill" with the obvious effect of all independent science disregarded.

Reproductive toxicity (B.6.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		moves on directly to risk characterisation and standard setting, and ignores the evidence on hazards	
(2)	Vol.3 B.6.6 Reproductive toxicity. page 538	EGM: We urge EFSA to include a hazard characterisation in the peer-review. This should be done by using all in-vitro studies available, disregarding none, and all mechanistic studies available. The peer-review should focus on what mechanistic evidence is present on teratogenicity, on DNA-damage., etc.?	The study of Paganelli et al. 2010 presents interesting evidence on the mechanism of action. During early embryonic development, retinoic acid generated in a specific region of the embryo helps determine position along the embryonic anterior/posterior axis by serving as an intercellular signaling molecule that guides development of the posterior portion of the embryo. It acts through Hox genes, which ultimately control anterior/posterior patterning in early developmental stages. The findings of Marc et al. '05 support this, offering a general mechanism of action for teratogenicity.
(3)	Vol.3 B.6.6 Reproductive toxicity. page 539	EGM: many multi-generation tests in the RAR with their very high (and unrealistic) doses, endpoints which are not the state-of-the-art cannot provide for the final answer on reproductive toxicity. The results are not clear anyway with a study that shows effects at low doses but is dismissed in the end by the Rapporteur. And studies showing effects on the offspring also accepted because they are observed at high doses. Combined with the many studies in open literature on malformations of the offspring and developmental effects, a peer-review by EFSA of all evidence is more than necessary.	The industry-sponsored OECD tests are known for their insensitivity and this could explain the very remarkable difference seen between the industry-sponsored studies and independent literature. The high doses used are close to the acute poisoning doses and poisoning effects are common in these tests, while more subtle effects could be missed.

Reproductive toxicity (B.6.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(4)	Vol.3 B.6.6 Reproductive toxicity. page 548	EGM: we again question the use of extreme high exposure doses such as 15.000 ppm or 1000 mg/kg, more than 1000x the ADI. Animals should be tested at realistic doses and no extrapolation used	The high doses are close to the acute poisoning doses used and poisoning effects are common in these tests, while more subtle effects could be missed.
(5)	Vol.3 B.6.6 Reproductive toxicity. page 596	EGM: We especially encourage EFSA to take a look at teratogenicity. The pre-2001 studies of Monsanto show teratogen effects, a range of independent studies report these effects, these effects are also observed in areas with Roundup monocultures (soy) in epidemiology studies and even in bioindustry where piglets fed on soy have these effects.	In the first DAR on Glyphosate in 2001, the UK experts commented that -based on the Monsanto studies- a single study might not raise concerns, but that the teratogenic effects that kept being observed in the Monsanto-studies, pointed at a pattern that should not be dismissed in the risk assessment. EFSA should asses if in the two-generation studies the animals are properly exposed during vulnerable windows during development and if a large range and relevant endpoints are considered for teratogenicity and development during later life of the offspring.
(6)	Vol.3 B.6.6.9, Reproductive toxicity. page 597	EGM: specific endocrine disrupting tests should be demanded from the applicant. Just basing conclusions on outdated OECD-protocols on reproduction and development is not justified. The science on endocrine disruption differs a lot from other fields and specific exposure windows, doses and specific endpoints should be used. In the traditional tests with traditional experts these effects will be missed.	
(7)	Vol.3 B.6.6.9 Reproductive toxicity. page 597	EGM: A large body of evidence on endocrine disrupting effects of Glyphosate is disregarded and dismissed in the RAR. Walsh, 2002 showed	Hokanson, 2007, demonstrated a synergistic effect of Glyphosate with oestrogen, with implications for pregnancy-induced hypertension and foetal growth retardation.

Reproductive toxicity (B.6.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		the disruption of the steroid hormone progesterone, as well as Romano, 2010 on testosterone. Richard, 2005 also concludes Glyphosate is an endocrine disruptor by affecting aromatase at very low doses. Also Benachour, 2005 and Gasnier, 2007 came to the same conclusion.	The implications of these effects on reproduction and the developing foetus are profound, with work by Mose, 2008, confirming that Glyphosate does cross the placenta.
(8)	Vol.3 B.6.6.10 Reproductive toxicity. page 613	EGM: the study in rabbits shows that at a level of 10 mg/kg 20% of the litters have malformations while this is 5% in the control (this also counts for the foetus, 3,1% vs. 0,7%). While this dose is at least less enormous than the regular dose, it is still above a realistic dose and we think additional studies should be done with lower and m	The malformations should be more thoroughly investigated and this study already shows that the LOAEL of 10 mg/kg should be adopted for standard setting. A suggesting NOEAL of 100 mg/kg by the applicant is absurd.
(9)	Vol.3 B.6.6.10 Reproductive toxicity. page 619	EGM: this study in rabbit again shows most effects at the lowest dose tested (18 vs. 13 of the litters tested with malformations), 50 mg/kg. While this dose is still unrealistic high, lower doses should be tested on malformations of the foetus.	
(10)	Vol.3 B.6.6.10 Reproductive toxicity. page 629	EGM: this study in rabbit also shows malformations at the lowest level tested (82 foetus with 'minor' defects vs, 58 in the control), 100 mg/kg. This "low" dose is of course unrealistically high.	There is a clear pattern of malformations of the foetus in all rabbit studies.

Reproductive toxicity (B.6.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(11)	Vol.3 B.6.6.10 Reproductive toxicity. page 642	EGM: this study confirms previous observations that malformations of the foetus is highest in the lowest dose tested, 50 mg/kg, (17.7% vs. 11,7% in the control). We object to the use of historical control data. The only scientific approach is to compare the outcome in the tests against the control.	Why the RMS values historical control data over the normal (negative|) control is a mystery. While it is highly questionable if the industry-sponsored studies are reproducible at all, historical control data mix different labs, operators, protocols and strains and create an unrealistic wide range of "controls'. No scientist will ever use this type of tools.
(12)	Vol.3 B.6.6.10 Reproductive toxicity. page 650	EGM: also this study shows effects at the lowest dose tested, 20 mg/kg, upper cleft palate, 15% vs. 5% in the control, and dilated heart, 23,1% vs. 0% in the control.	There is a clear pattern of malformations of the foetus in all rabbit studies.
(13)	Vol.3 B.6.6.12, Reproductive toxicity, Published data, page 658	EGM: it is remarkable that the RMS now easily rejects all claims made by EOS in their report "is the public kept in the dark" and let most independent literature fall under the 'Klimisch-axe". In their reaction in July 2011, the RMS called the report: The recently published report "Roundup and birth defects: Is the public kept in the dark?" is a challenging critical summary of adverse health (mainly teratological and reproductive) findings that are attributed by the authors to the compound glyphosate and/or to herbicides such as Roundup that contain glyphosate as active ingredient.	The RMS ends their report by saying: An adequate response to the criticism and the many accusations in the report would require a general discussion of the established paradigms for the toxicological evaluation of chemicals. These general discussions should be initiated by the Commission before we start with the re-evaluation of glyphosate within the AIR2 project. We fail to have seen any general discussion on established paradigms, not by the RMS and not by Commission. We therefore urge EFSA to start such a discussion before drafting the peer review on Glyphosate.
(14)	Vol.3 B.6.6.12, Reproductive toxicity,	EGMEGM : it is sad to note that the industry review made by the applicant is not commented	We urge EFSA to review all independent studies and stop using the entirely unscientific Klimisch-tool and do a purely scientific

Reproductive toxicity (B.6.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	Published data, page 658	by the RMS. Given the many missing studies and the standard use of Klimisch to dismiss studies on a large scale, an intervention of the RMS was needed very much.	assessment of each study looking at the quality of the study, disregarding protocols and GLP-administration systems.

Neurotoxicity (B.6.7)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol.3, B.6.7.1, Neurotoxicity, Published data, page 702.	PAN Europe: Epidemiology studies have been published pointing at Glyphosate of causing mental disorders of children born to pesticide applicators in the US, Garry, 2002. Even acute poisoning could lead to brain damage, Barbosa, 2001. Animal studies have demonstrated that Glyphosate depletes serotonin and dopamine, Anadon, 2008, and causes a loss of mitochondrial transmembrane potential in rat brain cells, especially in the substantia nigra region of the brain, Astiz, 2009.	There is evidence of developmental neurotoxicity of Glyphosate and EFSA should pay good attention to this adverse effect in their peer-review.

Comments of Eco Centre Wales on the Renewal Assessment Report on Glyphosate 06. 05. 2014

1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)

Identity (B.1, Annex C)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Physical and chemical properties of the active substance (B.2.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Physical, chemical and technical properties of the formulation (B.2.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Further information (B.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, Annex B.3 Data	***Eco Centre Wales***: Worldwide there are at least 28	In Europe, there are more cases of glyphosate resistance than depicted in

Further information (B.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	on application and further information, page 7-8	weed species (not only 24) for which glyphosate-resistance has been documented, comprising more than 200 populations and infesting millions of hectares (Heap 2014). Although countries with RRcrop cultivation are affected most heavily, cases of glyphosate-resistant weed species are increasingly reported from other countries too. As a result, a massive increase in herbicide amounts applied has been documented. To stop the pesticide treadmill, glyphosate use has to be restricted.	the RAR (16 cases instead of 10 and 6 species instead of 5). Contrary to the RAR, glyphosate-resistant weed species have not been found exclusively in orchards, vineyards or olive groves, but also in other crops, e.g. asparagus (Lolium rigidum in France) and alfalfa (Conyza canadensis in Greece). And Northern and Central Europe will also be affected, with Poland being already the second country after the Czech Republic to report glyphosate-resistant weeds. It will be a question of time when glyphosate-resistant weed biotypes will show up in countries such as Germany. Therefore, evolution of glyphosate-resistance will speed up in Europe too, unless use of glyphosate is severely restricted.

Methods of analysis (B.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

5. Ecotoxicology (B.9)

Birds and mammals (B.9.1 and B.9.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Aquatic organisms (B.9.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	B.9.2.2 Summary of aquatic toxicity data Page 132	***Eco Centre Wales*** : In particular, amphibians, many of which are endangered, have been shown to be affected by glyphosate-based herbicides, possibly both their larval and adult stages (Wagner et al. 2013). Reviewing peer-reviewed studies on glyphosate impacts on amphibian, Plötner and Matschke (2012) concluded that glyphosate is itself toxic to amphibians, and surfactants such as POEA are even more so leading to abnormal behaviour, teratogenic effects and developmental failures. In addition, toxicity of glyphosate and Roundup to aquatic invertebrates such as *Daphnia magna* has been underestimated (Cuhra et al. 2013). Toxicity classification has to be revised.	Cuhra et al. (2013) found EC50 (48) values for glyphosate IPA in *Daphnia magna* that were significantly lower than the values depicted in table B.9.2-59. Testing glyphosate and Roundup for 55 days (instead of only 21 days tested in the long-term studies referred to in table B.9.2-59) led to significant reduction in juvenile size even at the lowest test concentration of 0.05 mg a.i./L. About ten times higher concentrations of Roundup affected fecundity, growth and abortion rate and at1.35 and 4.05 mg a.i./L of both glyphosate and Roundup significant negative effects were seen on most tested parameters, including mortality. Thus even low ambient concentrations of glyphosate will affect aquatic invertebrate ecology.

Section 5 - Ecotoxicology (B.9)

Bees and non-target arthropods (B.9.4 and B.9.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Earthworms and other soil non-target organisms (macro and micro) (B.9.6, B.9.7 and B.9.8)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.9.8 Effects on soil non-target micro-organisms	***Eco Centre Wales***: As stated in the RAR and reported by Kremer & Means (2009), glyphosate leads to significant shifts in bacterial community composition but it also affects importantfungal species, e.g. beneficial mycorrhizal fungi (Druille et al. 2013a,b). Previous use of glyphosate has been linked to increased Fusarium infection of wheat and barley (Fernandez et al. 2009). Thus impacts of glyphosate use on bacterial and fungal species that are linked to plant health and disease have to be considered too.	

Other non-target organisms (flora and fauna), sewage treatment (B.9.9 and B.9.10)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.9.9.1.4	***Eco Centre Wales***:	Adverse impacts of (repeated) glyphosate use on the health of non-target

Other non-target organisms (flora and fauna), sewage treatment (B.9.9 and B.9.10)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	Summary of results on non-target plants	Glyphosate can adversely impact micronutrient uptake in plants as it is a strong metal chelator (Tesfamariam et al. 2009, Cakmak et al. 2009). Even low levels of residual glyphosate in soil can greatly impede the availability and uptake of Mn, Fe, Cu, and Zn by plants and lead to their undersupply with these nutrients. Reduced disease resistance and plant growth may be the result (Johal & Huber 2009).	plants have to be taken into account, as reduced disease resistance most likely will increase use of other pesticides, e.g. fungicides that may be highly toxic too.
	Vol. 3, B.9.9.1.6 Indirect effects via trophic interactions	The Farm Scale Evaluations have shown that the quantitative loss of weeds reduces number and diversity of arthropods heavily and interrupts the food chain for farmland birds and mammals. Ample evidence of negative impacts of glyphosate on biodiversity has been collected in areas where glyphosate is used extensively, e.g. in combination with genetically modified glyphosate-resistant crops. The all-time low in the number of monarch butterflies in 2013/2014 has been attributed to the loss of their food plant (*Asclepias syriaca*) in vast areas of the United States where glyphosate-resistant crops are grown (Wade 2014).	As glyphosate is the herbicide most widely used, these massive negative impacts on biodiversity have to be considered and used as reason not to re-authorize the substance. Mitigation measures, such as buffer strips, that would be up to the individual member states will not reduce the risk of impacting biodiversity to an acceptable level – even if farmers accepted to spare buffer strips from glyphosate application which they often don't.

Section 5 - Ecotoxicology (B.9)

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	B.9.11 Surface-active substances in glyphosate-based formulations	***Eco Centre Wales:*** There is ample evidence that formulated products can exhibit higher toxicity. In particular, polyethoxylated alkylamines (POEA) are known to be highly toxic to cells and organisms (Mesnage et al. 2013). Glyphosate has endocrine disrupting properties which cannot only be attributed to the surfactants. Paganelli et al (2010) showed that both formulated products and the active substance have adverse effects and that glyphosate acts as an endocrine disruptor. To make agriculture in Europe more environmentally benign, it is of utmost importance that pesticide use is restricted to a much greater extent than it is actually the case. As herbicides make up the largest share of pesticides and glyphosate is the most used herbicide, regulators are obliged to not renew the approval of this chemical.	To argue, that the lead formulation MON52276 for the assessment of glyphosate does not contain POEA and that POEA-formulated products "are not expected to be neither notified nor registered in the future", is not comforting, as such products are still on the market and data about the nature and toxicity of other surfactants that replace POEA are not provided to the public. In addition, predicted environmental concentrations for glyphosate and its metabolite AMPA do not take into account the highly toxic surfactants that are released into the environment in combination with the active ingredient. Therefore, data about environmental concentrations of surfactants should have been collected and their impact on the environment should have been considered before drafting the RAR .

Eco Centre Wales: Comments to the Renewal Assessment Report (RAR) – Glyphosate

Introduction

The Renewal Assessment Report (RAR) prepared by the Rapporteur Member State (RMS) has been opened by EFSA to comments from the public. Some parts of the final report have been blackened, presumably names that refer to studies provided by the applicants. Unfortunately, in **Volume 1 Report and Proposed Decision** the very last chapter, **3.2 Proposed Decision,** has been blackened too. This means the public will not get informed about what kind of decision the RMS and the Co-RMS propose. Thus the public can only speculate about details of the proposal.

Eco Centre Wales is commenting on specific sections of the renewal assessment report (RAR), in particular those that deal with environmental impacts of glyphosate.

Development of resistance

In **Volume 1, Section 2.3.2 Summary of information on the development of resistance**, and **Volume 3 Annex B.3 Data on application and further information**, the topics "development of resistance and appropriate management strategies" are being discussed.

Comments:

The simplicity and effectiveness of weed control through glyphosate will be undermined by shifts in weed communities and populations resulting from the selection pressure of the applied herbicides. Glyphosate has long been considered to be a low risk herbicide in terms of the evolution of resistant weed populations (Beckie 2006), but ever increasing use of glyphosate has favored the development of glyphosate-resistance in weeds. It has taken 8-20 years of glyphosate use in conventional systems until the first glyphosate-resistant weed, rigid ryegrass (*Lolium rigidum*), was found in 1996 in Australia (Pratley et al. 1999). Since then, at least 28 cases of glyphosate-resistant weed species (comprising more than 200 populations) have been recorded worldwide (Heap 2014). The resistant weeds infest millions of hectares at many different places in various countries. Although countries, such as the US, Argentina, Australia, and Brazil, where glyphosate-resistant crops are cultivated are affected most heavily, countries without GM crop cultivation increasingly report cases of glyphosate-resistant weed species.

Glyphosate-resistance in weeds has been found to be based on several mechanisms, such as target site insensitivity, overproduction of the target protein EPSPS (5-enolpyruvylshikimate-3-phosphate synthase), amplification of the EPSPS gene, reduced glyphosate translocation, and increased sequestration of glyphosate in plant cell vacuoles (Perez-Jones & Mallory-Smith 2010). Resistance mechanisms can co-occur, in particular, when related resistant weed species hybridize. In addition, multiple-resistance to other herbicide mode of actions than glyphosate has been reported too (Heap 2014).

In the RAR, reference is made to the development of glyphosate-resistance in Europe. But in reality, the situation is far more severe than depicted in the RAR document (as of September 2012). There are not only 10 cases of resistance known in Europe, but meanwhile the number is 16 and it is not

only five species that have been found, but there are six (Heap 2014). With five resistant species that have infested hundreds of hectares, Spain is the most afflicted country. Contrary to the RAR presentation, glyphosate-resistant weed species have not been found exclusively in orchards, vineyards or olive groves, but also in other crops such as asparagus (*Lolium rigidum* in France) and alfalfa (*Conyza canadensis* in Greece). It is also not quite true, that "*Apart from one case (C. canadensis) in the Czech Republic, Northern and Central Europe are not affected by glyphosate resistance up to now*", since resistant *C. canadensis* has also been reported from Poland railways. This indicates that evolution of glyphosate-resistance will speed up in Europe too, unless use of glyphosate is severely restricted.

In the US, not only the broad adoption of glyphosate-resistant crops but also the continuous rise in the number of resistant species and areas inflicted by resistant weeds has resulted in a massive increase in herbicide amounts applied (Benbrook 2012a). A similar scenario has been depicted for Europe in case genetically modified glyphosate-resistant crops would be authorized for cultivation here too (Benbrook 2012b). Therefore, to stop the pesticide treadmill, glyphosate use has to be restricted.

Environmental effects

In **Volume 1, Section 2.9 Effects on non-target species and Volume 3, Annex B.9 Ecotoxicology),** data on ecotoxicology studies are discussed, evaluated, and summarized.

Environmental impacts on non-target organisms

The risk assessment for birds and mammals is based on the active ingredient glyphosate acid in the product MON 52276 for the intended uses in several crops including pre-planting, pre-emergence, pre-harvest and row-application in orchards and vineyards. From the data provided by the applicants, the RMS comes to the conclusion that after use of the lead formulation MON 52276 in the indications according to the label there is an acceptable acute risk for birds and mammals due to uptake of contaminated food and an acceptable risk resulting from an exposure of small herbivorous mammals, non-target arthropods, and aquatic organisms. Use under the proposed conditions will result in a negligible exposure of honeybees or has no unacceptable acute or chronic effects on colony survival and development. The RMS concludes further, that for the evaluation of the formulation MON 52276 on non-target plants data are still required, in particular, as a valid study with this product to non-target plants is lacking and the formulants in the product may enhance toxicity.

The RMS concedes that, depending on the agricultural and ecological conditions, the use of glyphosate may affect populations of non-target terrestrial arthropods and vertebrate species (especially farmland birds) via trophic interactions and suggests mitigation measures. The RAR reads at this point: *These effects trace back to the intended effect of the herbicides – eliminating competing plants – and the interruption of the food web going along with it*.

In Volume 1, Section 3 Proposed decision, the RMS states: *It is considered that Article 4 of Regulation (EC) No 1107/2009 is complied with. Specifically the RMS considers that authorization in at least one Member State is expected to be possible for at least one plant protection product containing the active substance for at least one of the representative uses*. But the approval should be subject to conditions and restrictions. According to the RMS, glyphosate is not a candidate for substitution.

This statement has been made although the RMS identifies data gaps with regard to the ecotoxicology risk assessment (e.g. aquatic organisms, microorganisms, and non-target plants such as tomato) and concludes that certain areas of the risk assessment could not be finalized on the basis of the available data, among them effects of glyphosate towards microorganisms, on non-target plants and on biodiversity.

For all uses, the RMS acknowledges that the impacts of glyphosate on biodiversity is a critical area of concern and recommends that member states should pay attention to such potential indirect effects and may consider adequate risk mitigation measures.

Comments

It is not acceptable that glyphosate that is known to negatively impact biodiversity to such an extent should be re-authorized in the EU. Glyphosate exhibits acute and chronic toxicity, in particular, to aquatic species and non-target plants. As stated in the RAR and reported by Kremer & Means (2009), glyphosate leads to significant shifts in bacterial community composition but it also affects some fungal species, e.g. beneficial mycorrhizal fungi (Druille et al. 2013a,b). Previous use of glyphosate has been linked to increased Fusarium infection of wheat and barley (Fernandez et al. 2009). Amphibians, many of which are endangered, have been shown to be affected, possibly both their larval and adult stages (Wagner et al. 2013). Plötner and Matschke (2012) concluded that glyphosate is itself toxic to amphibians, and surfactants such as POEA are even more so causing abnormal behavior, teratogenic effects and developmental failures.

Glyphosate can adversely impact micronutrient uptake in plants as it is a strong metal chelator (Tesfamariam et al. 2009, Cakmak et al. 2009). Even low levels of residual glyphosate in soil can greatly impede the availability and uptake of Mn, Fe, Cu, and Zn by plants and lead to their undersupply with these nutrients. Reduced disease resistance and plant growth may be the result (Johal & Huber 2009). Adverse impacts of (repeated) glyphosate use on the health of non-target plants have to be taken into account, as reduced disease resistance most likely will increase use of other pesticides, e.g. fungicides that may be highly toxic too.

It is well known that weeds offer considerable benefits for the agro ecosystem, as they support a range of organisms, among them decomposers, predators, pollinators, and parasitoids, by providing food and shelter for them (Marshall et al. 2003). The Farm Scale Evaluations performed in the UK showed that broad-spectrum herbicides such as glyphosate impact abundance and diversity of weeds more severely than conventional herbicide regimes (Heard et al. 2003). The quantitative loss of weeds reduces number and diversity of arthropods heavily and interrupts the food chain for farmland birds and mammals. Ample evidence of negative impacts of glyphosate on biodiversity has been collected in areas where glyphosate is used extensively, e.g. in combination with genetically modified glyphosate-resistant crops. The all-time low in the number of monarch butterflies in the winter 2013/2014 has been attributed to the loss of their food plant (*Asclepias syriaca*) in vast areas of the United States where glyphosate-resistant crops are grown (Wade 2014).

As glyphosate is the herbicide most widely used, these massive negative impacts on biodiversity have to be considered and used as reason not to re-authorize the substance. Mitigation measures, such as buffer strips, that would be up to the individual member states could not reduce the risk of impacting

biodiversity to an acceptable level – even if farmers accepted to spare buffer strips from glyphosate application which they often don't.

Subclause: Formulated glyphosate products (Annex B.9.11 Surface-active substances in glyphosate-based formulations)

In the RAR, solely the active ingredient glyphosate is being considered for authorization, although in the field, only formulated products are applied. The final glyphosate products contain high amounts of surfactants that have surface-active properties. According to the German government[1], in addition to the 5000 t of glyphosate used in Germany in 2010, 1700 t of polyethoxylated alkylamines (POEA) had been applied. Therefore, it is of importance to not only test the toxicity of the active ingredient glyphosate but to take into account the toxicity of the various formulated products that are used.

There is ample evidence that formulated products can exhibit higher toxicity. In particular, polyethoxylated alkylamines (POEA) are known to be highly toxic to cells and organisms (Mesnage et al. 2013). The RMS considers several of the observed effects on endpoints regarding genotoxicity, mutagenicity, and development or reproduction of non-target organisms to be mediated by the surfactant included in the formulations. Thus the RMS concedes that "*the toxicity of glyphosate-based products is greatly enhanced if the active substance is formulated with alkylamine ethoxylates"* and "*the authorization of glyphosate-based products with alkylamine ethoxylated surfactants might require the generation of further data*". But to argue, that the lead formulation MON52276 for the assessment of glyphosate does not contain this surfactant and that nowadays POEA-formulated products "*are not expected to be neither notified nor registered in the future"*, are not comforting statements, as such products are still on the market and data about the nature and toxicity of other surfactants that replace POEA are not provided to the public. In addition, predicted environmental concentrations for glyphosate and its metabolite AMPA are calculated only for these substances, not taking into account the highly toxic surfactants that are released into the environment together with the active ingredient. Therefore, it is important to collect data about environmental concentrations of surfactants and to consider their impact on the environment already during the authorization process.

Conclusions

To make agriculture in Europe more environmentally benign, it is of utmost importance that pesticide use is restricted to a much greater extent than it is actually the case. As herbicides make up the largest share of pesticides and glyphosate, in particular, is the most used herbicide, regulators are obliged to not renew the approval of this chemical.

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Comments of BUND Germany on the Renewal Assessment Report on Glyphosate 06. 05. 2014

1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)

Identity (B.1, Annex C)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Physical and chemical properties of the active substance (B.2.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Physical, chemical and technical properties of the formulation (B.2.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Further information (B.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, Annex B.3 Data on application and further	BUND: Worldwide there are at least 28 weed species (not only 24) for which glyphosate-resistance has	In Europe, there are more cases of glyphosate resistance than depicted in the RAR (16 cases instead of 10 and 6 species instead of 5). Contrary to

Further information (B.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	information, page 7-8	been documented, comprising more than 200 populations and infesting millions of hectares (Heap 2014). Although countries with RRcrop cultivation are affected most heavily, cases of glyphosate-resistant weed species are increasingly reported from other countries too. As a result, a massive increase in herbicide amounts applied has been documented. To stop the pesticide treadmill, glyphosate use has to be restricted.	the RAR, glyphosate-resistant weed species have not been found exclusively in orchards, vineyards or olive groves, but also in other crops, e.g. asparagus (Lolium rigidum in France) and alfalfa (Conyza canadensis in Greece). And Northern and Central Europe will also be affected, with Poland being already the second country after the Czech Republic to report glyphosate-resistant weeds. It will be a question of time when glyphosate-resistant weed biotypes will show up in countries such as Germany. Therefore, evolution of glyphosate-resistance will speed up in Europe too, unless use of glyphosate is severely restricted.

Methods of analysis (B.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

5. Ecotoxicology (B.9)

Birds and mammals (B.9.1 and B.9.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Aquatic organisms (B.9.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	B.9.2.2 Summary of aquatic toxicity data Page 132	BUND: In particular, amphibians, many of which are endangered, have been shown to be affected by glyphosate-based herbicides, possibly both their larval and adult stages (Wagner et al. 2013). Reviewing peer-reviewed studies on glyphosate impacts on amphibian, Plötner and Matschke (2012) concluded that glyphosate is itself toxic to amphibians, and surfactants such as POEA are even more so leading to abnormal behaviour, teratogenic effects and developmental failures. In addition, toxicity of glyphosate and Roundup to aquatic invertebrates such as *Daphnia magna* has been underestimated (Cuhra et al. 2013). Toxicity classification has to be revised.	Cuhra et al. (2013) found EC50 (48) values for glyphosate IPA in *Daphnia magna* that were significantly lower than the values depicted in table B.9.2-59. Testing glyphosate and Roundup for 55 days (instead of only 21 days tested in the long-term studies referred to in table B.9.2-59) led to significant reduction in juvenile size even at the lowest test concentration of 0.05 mg a.i./L. About ten times higher concentrations of Roundup affected fecundity, growth and abortion rate and at1.35 and 4.05 mg a.i./L of both glyphosate and Roundup significant negative effects were seen on most tested parameters, including mortality. Thus even low ambient concentrations of glyphosate will affect aquatic invertebrate ecology.

Section 5 - Ecotoxicology (B.9)

Bees and non-target arthropods (B.9.4 and B.9.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Earthworms and other soil non-target organisms (macro and micro) (B.9.6, B.9.7 and B.9.8)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.9.8 Effects on soil non-target micro-organisms	BUND: As stated in the RAR and reported by Kremer & Means (2009), glyphosate leads to significant shifts in bacterial community composition but it also affects importantfungal species, e.g. beneficial mycorrhizal fungi (Druille et al. 2013a,b). Previous use of glyphosate has been linked to increased Fusarium infection of wheat and barley (Fernandez et al. 2009). Thus impacts of glyphosate use on bacterial and fungal species that are linked to plant health and disease have to be considered too.	

Other non-target organisms (flora and fauna), sewage treatment (B.9.9 and B.9.10)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.9.9.1.4	BUND:	Adverse impacts of (repeated) glyphosate use on the health of non-target

Other non-target organisms (flora and fauna), sewage treatment (B.9.9 and B.9.10)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	Summary of results on non-target plants	Glyphosate can adversely impact micronutrient uptake in plants as it is a strong metal chelator (Tesfamariam et al. 2009, Cakmak et al. 2009). Even low levels of residual glyphosate in soil can greatly impede the availability and uptake of Mn, Fe, Cu, and Zn by plants and lead to their undersupply with these nutrients. Reduced disease resistance and plant growth may be the result (Johal & Huber 2009).	plants have to be taken into account, as reduced disease resistance most likely will increase use of other pesticides, e.g. fungicides that may be highly toxic too.
	Vol. 3, B.9.9.1.6 Indirect effects via trophic interactions	The Farm Scale Evaluations have shown that the quantitative loss of weeds reduces number and diversity of arthropods heavily and interrupts the food chain for farmland birds and mammals. Ample evidence of negative impacts of glyphosate on biodiversity has been collected in areas where glyphosate is used extensively, e.g. in combination with genetically modified glyphosate-resistant crops. The all-time low in the number of monarch butterflies in 2013/2014 has been attributed to the loss of their food plant (*Asclepias syriaca*) in vast areas of the United States where glyphosate-resistant crops are grown (Wade 2014).	As glyphosate is the herbicide most widely used, these massive negative impacts on biodiversity have to be considered and used as reason not to re-authorize the substance. Mitigation measures, such as buffer strips, that would be up to the individual member states will not reduce the risk of impacting biodiversity to an acceptable level – even if farmers accepted to spare buffer strips from glyphosate application which they often don't.

Section 5 - Ecotoxicology (B.9)

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	B.9.11 Surface-active substances in glyphosate-based formulations	BUND: There is ample evidence that formulated products can exhibit higher toxicity. In particular, polyethoxylated alkylamines (POEA) are known to be highly toxic to cells and organisms (Mesnage et al. 2013). Glyphosate has endocrine disrupting properties which cannot only be attributed to the surfactants. Paganelli et al (2010) showed that both formulated products and the active substance have adverse effects and that glyphosate acts as an endocrine disruptor. To make agriculture in Europe more environmentally benign, it is of utmost importance that pesticide use is restricted to a much greater extent than it is actually the case. As herbicides make up the largest share of pesticides and glyphosate is the most used herbicide, regulators are obliged to not renew the approval of this chemical.	To argue, that the lead formulation MON52276 for the assessment of glyphosate does not contain POEA and that POEA-formulated products “are not expected to be neither notified nor registered in the future”, is not comforting, as such products are still on the market and data about the nature and toxicity of other surfactants that replace POEA are not provided to the public. In addition, predicted environmental concentrations for glyphosate and its metabolite AMPA do not take into account the highly toxic surfactants that are released into the environment in combination with the active ingredient. Therefore, data about environmental concentrations of surfactants should have been collected and their impact on the environment should have been considered before drafting the RAR .

BUND: Comments to the Renewal Assessment Report (RAR) – Glyphosate

Introduction

The Renewal Assessment Report (RAR) on glyphosate prepared by the Rapporteur Member State (RMS) Germany and the Co-RMS Slovakia has been opened by EFSA to comments from the public. Some parts of the final report have been blackened, presumably names that refer to studies provided by the applicants. Unfortunately, in **Volume 1 Report and Proposed Decision** the very last chapter, **3.2 Proposed Decision,** has been blackened too. This means the public will not get informed about what kind of decision the RMS and the Co-RMS propose. Thus the public can only speculate about details of the proposal.

BUND Germany (Bund für Umwelt und Naturschutz Deutschland) is commenting on specific sections of the renewal assessment report (RAR), in particular those that deal with environmental impacts of glyphosate.

Development of resistance

In **Volume 1, Section 2.3.2 Summary of information on the development of resistance**, and **Volume 3 Annex B.3 Data on application and further information**, the topics "development of resistance and appropriate management strategies" are being discussed.

BUND Comments:

The simplicity and effectiveness of weed control through glyphosate will be undermined by shifts in weed communities and populations resulting from the selection pressure of the applied herbicides. Glyphosate has long been considered to be a low risk herbicide in terms of the evolution of resistant weed populations (Beckie 2006), but ever increasing use of glyphosate has favored the development of glyphosate-resistance in weeds. It has taken 8-20 years of glyphosate use in conventional systems until the first glyphosate-resistant weed, rigid ryegrass (*Lolium rigidum*), was found in 1996 in Australia (Pratley et al. 1999). Since then, at least 28 cases of glyphosate-resistant weed species (comprising more than 200 populations) have been recorded worldwide (Heap 2014). The resistant weeds infest millions of hectares at many different places in various countries. Although countries, such as the US, Argentina, Australia, and Brazil, where glyphosate-resistant crops are cultivated are affected most heavily, countries without GM crop cultivation increasingly report cases of glyphosate-resistant weed species.

Glyphosate-resistance in weeds has been found to be based on several mechanisms, such as target site insensitivity, overproduction of the target protein EPSPS (5-enolpyruvylshikimate-3-phosphate synthase), amplification of the EPSPS gene, reduced glyphosate translocation, and increased sequestration of glyphosate in plant cell vacuoles (Perez-Jones & Mallory-Smith 2010). Resistance mechanisms can co-occur, in particular, when related resistant weed species hybridize. In addition, multiple-resistance to other herbicide mode of actions than glyphosate has been reported too (Heap 2014).

In the RAR, reference is made to the development of glyphosate-resistance in Europe. But in reality, the situation is far more severe than depicted in the RAR document (as of September 2012). There

are not only 10 cases of resistance known in Europe, but meanwhile the number is 16 and it is not only five species that have been found, but there are six (Heap 2014). With five resistant species that have infested hundreds of hectares, Spain is the most afflicted country. Contrary to the RAR presentation, glyphosate-resistant weed species have not been found exclusively in orchards, vineyards or olive groves, but also in other crops such as asparagus (*Lolium rigidum* in France) and alfalfa (*Conyza canadensis* in Greece). It is also not quite true, that "*Apart from one case (C. canadensis) in the Czech Republic, Northern and Central Europe are not affected by glyphosate resistance up to now*", since resistant *C. canadensis* has also been reported from Poland railways. This indicates that evolution of glyphosate-resistance will speed up in Europe too, unless use of glyphosate is severely restricted.

In the US, not only the broad adoption of glyphosate-resistant crops but also the continuous rise in the number of resistant species and areas inflicted by resistant weeds has resulted in a massive increase in herbicide amounts applied (Benbrook 2012a). A similar scenario has been depicted for Europe in case genetically modified glyphosate-resistant crops would be authorized for cultivation here too (Benbrook 2012b). Therefore, to stop the pesticide treadmill, glyphosate use has to be restricted.

Environmental effects

In **Volume 1, Section 2.9 Effects on non-target species and Volume 3, Annex B.9 Ecotoxicology),** data on ecotoxicology studies are discussed, evaluated, and summarized.

Environmental impacts on non-target organisms

The risk assessment for birds and mammals is based on the active ingredient glyphosate acid in the product MON 52276 for the intended uses in several crops including pre-planting, pre-emergence, pre-harvest and row-application in orchards and vineyards. From the data provided by the applicants, the RMS comes to the conclusion that after use of the lead formulation MON 52276 in the indications according to the label there is an acceptable acute risk for birds and mammals due to uptake of contaminated food and an acceptable risk resulting from an exposure of small herbivorous mammals, non-target arthropods, and aquatic organisms. Use under the proposed conditions will result in a negligible exposure of honeybees or has no unacceptable acute or chronic effects on colony survival and development. The RMS concludes further, that for the evaluation of the formulation MON 52276 on non-target plants data are still required, in particular, as a valid study with this product to non-target plants is lacking and the formulants in the product may enhance toxicity.

The RMS concedes that, depending on the agricultural and ecological conditions, the use of glyphosate may affect populations of non-target terrestrial arthropods and vertebrate species (especially farmland birds) via trophic interactions and suggests mitigation measures. The RAR reads at this point: *These effects trace back to the intended effect of the herbicides – eliminating competing plants – and the interruption of the food web going along with it*.

In Volume 1, Section 3 Proposed decision, the RMS states: *It is considered that Article 4 of Regulation (EC) No 1107/2009 is complied with. Specifically the RMS considers that authorization in at least one Member State is expected to be possible for at least one plant protection product containing the*

active substance for at least one of the representative uses. But the approval should be subject to conditions and restrictions. According to the RMS, glyphosate is not a candidate for substitution.

This statement has been made although the RMS identifies data gaps with regard to the ecotoxicology risk assessment (e.g. aquatic organisms, microorganisms, and non-target plants such as tomato) and concludes that certain areas of the risk assessment could not be finalized on the basis of the available data, among them effects of glyphosate towards microorganisms, on non-target plants and on biodiversity.

For all uses, the RMS acknowledges that the impacts of glyphosate on biodiversity is a critical area of concern and recommends that member states should pay attention to such potential indirect effects and may consider adequate risk mitigation measures.

BUND Comments

It is not acceptable that glyphosate that is known to negatively impact biodiversity to such an extent should be re-authorized in the EU. Glyphosate exhibits acute and chronic toxicity, in particular, to aquatic species and non-target plants. As stated in the RAR and reported by Kremer & Means (2009), glyphosate leads to significant shifts in bacterial community composition but it also affects some fungal species, e.g. beneficial mycorrhizal fungi (Druille et al. 2013a,b). Previous use of glyphosate has been linked to increased Fusarium infection of wheat and barley (Fernandez et al. 2009). Amphibians, many of which are endangered, have been shown to be affected, possibly both their larval and adult stages (Wagner et al. 2013). Plötner and Matschke (2012) concluded that glyphosate is itself toxic to amphibians, and surfactants such as POEA are even more so causing abnormal behavior, teratogenic effects and developmental failures.

Glyphosate can adversely impact micronutrient uptake in plants as it is a strong metal chelator (Tesfamariam et al. 2009, Cakmak et al. 2009). Even low levels of residual glyphosate in soil can greatly impede the availability and uptake of Mn, Fe, Cu, and Zn by plants and lead to their undersupply with these nutrients. Reduced disease resistance and plant growth may be the result (Johal & Huber 2009). Adverse impacts of (repeated) glyphosate use on the health of non-target plants have to be taken into account, as reduced disease resistance most likely will increase use of other pesticides, e.g. fungicides that may be highly toxic too.

It is well known that weeds offer considerable benefits for the agro ecosystem, as they support a range of organisms, among them decomposers, predators, pollinators, and parasitoids, by providing food and shelter for them (Marshall et al. 2003). The Farm Scale Evaluations performed in the UK showed that broad-spectrum herbicides such as glyphosate impact abundance and diversity of weeds more severely than conventional herbicide regimes (Heard et al. 2003). The quantitative loss of weeds reduces number and diversity of arthropods heavily and interrupts the food chain for farmland birds and mammals. Ample evidence of negative impacts of glyphosate on biodiversity has been collected in areas where glyphosate is used extensively, e.g. in combination with genetically modified glyphosate-resistant crops. The all-time low in the number of monarch butterflies in the winter 2013/2014 has been attributed to the loss of their food plant (*Asclepias syriaca*) in vast areas of the United States where glyphosate-resistant crops are grown (Wade 2014).

As glyphosate is the herbicide most widely used, these massive negative impacts on biodiversity have to be considered and used as reason not to re-authorize the substance. Mitigation measures, such as

buffer strips, that would be up to the individual member states could not reduce the risk of impacting biodiversity to an acceptable level – even if farmers accepted to spare buffer strips from glyphosate application which they often don't.

Subclause: Formulated glyphosate products (Annex B.9.11 Surface-active substances in glyphosate-based formulations)

In the RAR, solely the active ingredient glyphosate is being considered for authorization, although in the field, only formulated products are applied. The final glyphosate products contain high amounts of surfactants that have surface-active properties. According to the German government[1], in addition to the 5000 t of glyphosate used in Germany in 2010, 1700 t of polyethoxylated alkylamines (POEA) had been applied. Therefore, it is of importance to not only test the toxicity of the active ingredient glyphosate but to take into account the toxicity of the various formulated products that are used.

There is ample evidence that formulated products can exhibit higher toxicity. In particular, polyethoxylated alkylamines (POEA) are known to be highly toxic to cells and organisms (Mesnage et al. 2013). The RMS considers several of the observed effects on endpoints regarding genotoxicity, mutagenicity, and development or reproduction of non-target organisms to be mediated by the surfactant included in the formulations. Thus the RMS concedes that "*the toxicity of glyphosate-based products is greatly enhanced if the active substance is formulated with alkylamine ethoxylates"* and "*the authorization of glyphosate-based products with alkylamine ethoxylated surfactants might require the generation of further data*".

But to argue, that the lead formulation MON52276 for the assessment of glyphosate does not contain this surfactant and that nowadays POEA-formulated products "*are not expected to be neither notified nor registered in the future"*, are not comforting statements, as such products are still on the market and data about the nature and toxicity of other surfactants that replace POEA are not provided to the public. In addition, predicted environmental concentrations for glyphosate and its metabolite AMPA are calculated only for these substances, not taking into account the highly toxic surfactants that are released into the environment together with the active ingredient. Therefore, it is important to collect data about environmental concentrations of surfactants and to consider their impact on the environment already during the authorization process.

Conclusions

To make agriculture in Europe more environmentally benign, it is of utmost importance that pesticide use is restricted to a much greater extent than it is actually the case. As herbicides make up the largest share of pesticides and glyphosate, in particular, is the most used herbicide, regulators are obliged to not renew the approval of this chemical.

[1] http://dipbt.bundestag.de/dip21/btd/17/071/1707168.pdf

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Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 1, 3.1.5	Public: despite the huge number of taskforce members, it is very surprising, that not a single acceptable specification exists from a toxicological point of view. Even safe maximum levels for relevant impurities could not be derived. From the text it is unclear, whether the specification(s) is/are considered safe from an ecotoxicological point of view.	
	Vol. 1, 2.10 (classification)	Public: It is unclear which classification is intended for glyphosate (acid). In the beginning of section 2.10.1, classification for serious eye damage is mentioned but in the table at the end of this section, this classification is not given. In section 2.10.2, it seems that only the need for toxicological classification was evaluated.	

2. Mammalian toxicology (B.6)

Reproductive toxicity (B.6.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.6.6.11	Public: In the study IIA 5.6.11/05 (TOX9552391) heart-related malformations (interventricular septal defects, enlarged left/reduced right ventricles, retro-oesophageal right subclavian artery and narrowed/dilated aortic arch/pulmonary trunk/arterial trunk) in several foetuses/several litters were observed. Some of these findings occurred in incidences above historical control range. According to RMS's summary, dose levels leading to malformations did not seem excessively toxic to does. These findings might be relevant for a classification as a developmental toxicant (at least H361d/Cat. 2)	TOX9551106 dilated heart (p. 651) TOX9551960 Ventricular septal defects (p. 655)

Toxicity of the product(s) (B.6.11)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.6.11	Public: throughout chapter B.6, studies describing adverse effects induced by commercial formulations are summarised (e.g., CMR properties). Based on these findings, RMS concludes that glyphosate-containing formulations (may) exhibit more severe or other effects than explained by glyphosate alone. Based on which evidence can the relevance of findings	According to regulation (EU) No 545/2011 (section 7: "If possible, additional information on mode of toxic action, toxicological profile and all other known toxicological aspects of the active substance shall be submitted."), it is necessary to require further data in case the toxicological properties cannot be sufficiently evaluated with the standard tests for formulations.

Section 2 - Mammalian toxicology (B.6)

Toxicity of the product(s) (B.6.11)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		in open literature for “MON 52276” be excluded? Considering the indications from open literature, a more thorough evaluation of the possible effects induced by “MON 52276” should be conducted.	

Dermal absorption (B.6.12)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.6.12.1	Public: variability of results (i.e., SD) was not reported in the evaluation and should be reported. In case large variability of absorption was observed, this should be taken into account appropriately. The number of skin donors and their body parts should be given. Was it confirmed that the receptor fluid did not act as a diffusion barrier and how?	

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.6	Public: An extensive set of published literature was described in the throughout chapter B.6 of the DRAR. Could you please confirm that the notifiers provided a systematic review? Was this systematic review conducted and reported	

Section 2 - Mammalian toxicology (B.6)

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		according to the relevant EFSA guidance? How was it ensured that no bias was introduced in search strategy and study evaluation?	

Comments of Hnutí DUHA - Friends of the Earth Czech Republic on the Renewal Assessment Report on Glyphosate 06. 05. 2014

1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)

Identity (B.1, Annex C)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Physical and chemical properties of the active substance (B.2.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Physical, chemical and technical properties of the formulation (B.2.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Further information (B.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, Annex B.3 Data	***Hnutí DUHA - Friends of the Earth Czech***	In Europe, there are more cases of glyphosate resistance than depicted in

Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

Further information (B.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	on application and further information, page 7-8	***Republic***: Worldwide there are at least 28 weed species (not only 24) for which glyphosate-resistance has been documented, comprising more than 200 populations and infesting millions of hectares (Heap 2014). Although countries with RRcrop cultivation are affected most heavily, cases of glyphosate-resistant weed species are increasingly reported from other countries too. As a result, a massive increase in herbicide amounts applied has been documented. To stop the pesticide treadmill, glyphosate use has to be restricted.	the RAR (16 cases instead of 10 and 6 species instead of 5). Contrary to the RAR, glyphosate-resistant weed species have not been found exclusively in orchards, vineyards or olive groves, but also in other crops, e.g. asparagus (Lolium rigidum in France) and alfalfa (Conyza canadensis in Greece). And Northern and Central Europe will also be affected, with Poland being already the second country after the Czech Republic to report glyphosate-resistant weeds. It will be a question of time when glyphosate-resistant weed biotypes will show up in countries such as Germany. Therefore, evolution of glyphosate-resistance will speed up in Europe too, unless use of glyphosate is severely restricted.

Methods of analysis (B.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Section 5 - Ecotoxicology (B.9)

5. Ecotoxicology (B.9)

Birds and mammals (B.9.1 and B.9.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Aquatic organisms (B.9.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	B.9.2.2 Summary of aquatic toxicity data Page 132	***Hnutí DUHA - Friends of the Earth Czech Republic*** : In particular, amphibians, many of which are endangered, have been shown to be affected by glyphosate-based herbicides, possibly both their larval and adult stages (Wagner et al. 2013). Reviewing peer-reviewed studies on glyphosate impacts on amphibian, Plötner and Matschke (2012) concluded that glyphosate is itself toxic to amphibians, and surfactants such as POEA are even more so leading to abnormal behaviour, teratogenic effects and developmental failures. In addition, toxicity of glyphosate and Roundup to aquatic invertebrates such as *Daphnia magna* has been underestimated (Cuhra et al. 2013). Toxicity classification has to be revised.	Cuhra et al. (2013) found EC50 (48) values for glyphosate IPA in *Daphnia magna* that were significantly lower than the values depicted in table B.9.2-59. Testing glyphosate and Roundup for 55 days (instead of only 21 days tested in the long-term studies referred to in table B.9.2-59) led to significant reduction in juvenile size even at the lowest test concentration of 0.05 mg a.i./L. About ten times higher concentrations of Roundup affected fecundity, growth and abortion rate and at1.35 and 4.05 mg a.i./L of both glyphosate and Roundup significant negative effects were seen on most tested parameters, including mortality. Thus even low ambient concentrations of glyphosate will affect aquatic invertebrate ecology.

Section 5 - Ecotoxicology (B.9)

Bees and non-target arthropods (B.9.4 and B.9.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Earthworms and other soil non-target organisms (macro and micro) (B.9.6, B.9.7 and B.9.8)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.9.8 Effects on soil non-target micro-organisms	***Hnutí DUHA - Friends of the Earth Czech Republic***: As stated in the RAR and reported by Kremer & Means (2009), glyphosate leads to significant shifts in bacterial community composition but it also affects importantfungal species, e.g. beneficial mycorrhizal fungi (Druille et al. 2013a,b). Previous use of glyphosate has been linked to increased Fusarium infection of wheat and barley (Fernandez et al. 2009). Thus impacts of glyphosate use on bacterial and fungal species that are linked to plant health and disease have to be considered too.	

Other non-target organisms (flora and fauna), sewage treatment (B.9.9 and B.9.10)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.9.9.1.4	***Hnutí DUHA - Friends of the Earth Czech Republic***:	Adverse impacts of (repeated) glyphosate use on the health of non-target plants have to be taken into account, as reduced disease resistance most

Section 5 - Ecotoxicology (B.9)

Other non-target organisms (flora and fauna), sewage treatment (B.9.9 and B.9.10)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	Summary of results on non-target plants	Glyphosate can adversely impact micronutrient uptake in plants as it is a strong metal chelator (Tesfamariam et al. 2009, Cakmak et al. 2009). Even low levels of residual glyphosate in soil can greatly impede the availability and uptake of Mn, Fe, Cu, and Zn by plants and lead to their undersupply with these nutrients. Reduced disease resistance and plant growth may be the result (Johal & Huber 2009).	likely will increase use of other pesticides, e.g. fungicides that may be highly toxic too.
	Vol. 3, B.9.9.1.6 Indirect effects via trophic interactions	The Farm Scale Evaluations have shown that the quantitative loss of weeds reduces number and diversity of arthropods heavily and interrupts the food chain for farmland birds and mammals. Ample evidence of negative impacts of glyphosate on biodiversity has been collected in areas where glyphosate is used extensively, e.g. in combination with genetically modified glyphosate-resistant crops. The all-time low in the number of monarch butterflies in 2013/2014 has been attributed to the loss of their food plant (*Asclepias syriaca*) in vast areas of the United States where glyphosate-resistant crops are grown (Wade 2014).	As glyphosate is the herbicide most widely used, these massive negative impacts on biodiversity have to be considered and used as reason not to re-authorize the substance. Mitigation measures, such as buffer strips, that would be up to the individual member states will not reduce the risk of impacting biodiversity to an acceptable level – even if farmers accepted to spare buffer strips from glyphosate application which they often don't.

Section 5 - Ecotoxicology (B.9)

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	B.9.11 Surface-active substances in glyphosate-based formulations	***Hnutí DUHA - Friends of the Earth Czech Republic:*** There is ample evidence that formulated products can exhibit higher toxicity. In particular, polyethoxylated alkylamines (POEA) are known to be highly toxic to cells and organisms (Mesnage et al. 2013). Glyphosate has endocrine disrupting properties which cannot only be attributed to the surfactants. Paganelli et al (2010) showed that both formulated products and the active substance have adverse effects and that glyphosate acts as an endocrine disruptor. To make agriculture in Europe more environmentally benign, it is of utmost importance that pesticide use is restricted to a much greater extent than it is actually the case. As herbicides make up the largest share of pesticides and glyphosate is the most used herbicide, regulators are obliged to not renew the approval of this chemical.	To argue, that the lead formulation MON52276 for the assessment of glyphosate does not contain POEA and that POEA-formulated products "are not expected to be neither notified nor registered in the future", is not comforting, as such products are still on the market and data about the nature and toxicity of other surfactants that replace POEA are not provided to the public. In addition, predicted environmental concentrations for glyphosate and its metabolite AMPA do not take into account the highly toxic surfactants that are released into the environment in combination with the active ingredient. Therefore, data about environmental concentrations of surfactants should have been collected and their impact on the environment should have been considered before drafting the RAR .

Hnutí DUHA - Friends of the Earth Czech Republic: Comments to the Renewal Assessment Report (RAR) – Glyphosate

Introduction

The Renewal Assessment Report (RAR) prepared by the Rapporteur Member State (RMS) has been opened by EFSA to comments from the public. Some parts of the final report have been blackened, presumably names that refer to studies provided by the applicants. Unfortunately, in **Volume 1 Report and Proposed Decision** the very last chapter, **3.2 Proposed Decision,** has been blackened too. This means the public will not get informed about what kind of decision the RMS and the Co-RMS propose. Thus the public can only speculate about details of the proposal.

Hnutí DUHA - Friends of the Earth Czech Republic is commenting on specific sections of the renewal assessment report (RAR), in particular those that deal with environmental impacts of glyphosate.

Development of resistance

In **Volume 1, Section 2.3.2 Summary of information on the development of resistance**, and **Volume 3 Annex B.3 Data on application and further information**, the topics "development of resistance and appropriate management strategies" are being discussed.

Comments:

The simplicity and effectiveness of weed control through glyphosate will be undermined by shifts in weed communities and populations resulting from the selection pressure of the applied herbicides. Glyphosate has long been considered to be a low risk herbicide in terms of the evolution of resistant weed populations (Beckie 2006), but ever increasing use of glyphosate has favored the development of glyphosate-resistance in weeds. It has taken 8-20 years of glyphosate use in conventional systems until the first glyphosate-resistant weed, rigid ryegrass (*Lolium rigidum*), was found in 1996 in Australia (Pratley et al. 1999). Since then, at least 28 cases of glyphosate-resistant weed species (comprising more than 200 populations) have been recorded worldwide (Heap 2014). The resistant weeds infest millions of hectares at many different places in various countries. Although countries, such as the US, Argentina, Australia, and Brazil, where glyphosate-resistant crops are cultivated are affected most heavily, countries without GM crop cultivation increasingly report cases of glyphosate-resistant weed species.

Glyphosate-resistance in weeds has been found to be based on several mechanisms, such as target site insensitivity, overproduction of the target protein EPSPS (5-enolpyruvylshikimate-3-phosphate synthase), amplification of the EPSPS gene, reduced glyphosate translocation, and increased sequestration of glyphosate in plant cell vacuoles (Perez-Jones & Mallory-Smith 2010). Resistance mechanisms can co-occur, in particular, when related resistant weed species hybridize. In addition, multiple-resistance to other herbicide mode of actions than glyphosate has been reported too (Heap 2014).

In the RAR, reference is made to the development of glyphosate-resistance in Europe. But in reality, the situation is far more severe than depicted in the RAR document (as of September 2012). There are not only 10 cases of resistance known in Europe, but meanwhile the number is 16 and it is not

only five species that have been found, but there are six (Heap 2014). With five resistant species that have infested hundreds of hectares, Spain is the most afflicted country. Contrary to the RAR presentation, glyphosate-resistant weed species have not been found exclusively in orchards, vineyards or olive groves, but also in other crops such as asparagus (*Lolium rigidum* in France) and alfalfa (*Conyza canadensis* in Greece). It is also not quite true, that "*Apart from one case (C. canadensis) in the Czech Republic, Northern and Central Europe are not affected by glyphosate resistance up to now*", since resistant *C. canadensis* has also been reported from Poland railways. This indicates that evolution of glyphosate-resistance will speed up in Europe too, unless use of glyphosate is severely restricted.

In the US, not only the broad adoption of glyphosate-resistant crops but also the continuous rise in the number of resistant species and areas inflicted by resistant weeds has resulted in a massive increase in herbicide amounts applied (Benbrook 2012a). A similar scenario has been depicted for Europe in case genetically modified glyphosate-resistant crops would be authorized for cultivation here too (Benbrook 2012b). Therefore, to stop the pesticide treadmill, glyphosate use has to be restricted.

Environmental effects

In **Volume 1, Section 2.9 Effects on non-target species and Volume 3, Annex B.9 Ecotoxicology),** data on ecotoxicology studies are discussed, evaluated, and summarized.

Environmental impacts on non-target organisms

The risk assessment for birds and mammals is based on the active ingredient glyphosate acid in the product MON 52276 for the intended uses in several crops including pre-planting, pre-emergence, pre-harvest and row-application in orchards and vineyards. From the data provided by the applicants, the RMS comes to the conclusion that after use of the lead formulation MON 52276 in the indications according to the label there is an acceptable acute risk for birds and mammals due to uptake of contaminated food and an acceptable risk resulting from an exposure of small herbivorous mammals, non-target arthropods, and aquatic organisms. Use under the proposed conditions will result in a negligible exposure of honeybees or has no unacceptable acute or chronic effects on colony survival and development. The RMS concludes further, that for the evaluation of the formulation MON 52276 on non-target plants data are still required, in particular, as a valid study with this product to non-target plants is lacking and the formulants in the product may enhance toxicity.

The RMS concedes that, depending on the agricultural and ecological conditions, the use of glyphosate may affect populations of non-target terrestrial arthropods and vertebrate species (especially farmland birds) via trophic interactions and suggests mitigation measures. The RAR reads at this point: *These effects trace back to the intended effect of the herbicides – eliminating competing plants – and the interruption of the food web going along with it*.

In Volume 1, Section 3 Proposed decision, the RMS states: *It is considered that Article 4 of Regulation (EC) No 1107/2009 is complied with. Specifically the RMS considers that authorization in at least one Member State is expected to be possible for at least one plant protection product containing the active substance for at least one of the representative uses*. But the approval should be subject to conditions and restrictions. According to the RMS, glyphosate is not a candidate for substitution.

This statement has been made although the RMS identifies data gaps with regard to the ecotoxicology risk assessment (e.g. aquatic organisms, microorganisms, and non-target plants such as tomato) and concludes that certain areas of the risk assessment could not be finalized on the basis of the available data, among them effects of glyphosate towards microorganisms, on non-target plants and on biodiversity.

For all uses, the RMS acknowledges that the impacts of glyphosate on biodiversity is a critical area of concern and recommends that member states should pay attention to such potential indirect effects and may consider adequate risk mitigation measures.

Comments

It is not acceptable that glyphosate that is known to negatively impact biodiversity to such an extent should be re-authorized in the EU. Glyphosate exhibits acute and chronic toxicity, in particular, to aquatic species and non-target plants. As stated in the RAR and reported by Kremer & Means (2009), glyphosate leads to significant shifts in bacterial community composition but it also affects some fungal species, e.g. beneficial mycorrhizal fungi (Druille et al. 2013a,b). Previous use of glyphosate has been linked to increased Fusarium infection of wheat and barley (Fernandez et al. 2009). Amphibians, many of which are endangered, have been shown to be affected, possibly both their larval and adult stages (Wagner et al. 2013). Plötner and Matschke (2012) concluded that glyphosate is itself toxic to amphibians, and surfactants such as POEA are even more so causing abnormal behavior, teratogenic effects and developmental failures.

Glyphosate can adversely impact micronutrient uptake in plants as it is a strong metal chelator (Tesfamariam et al. 2009, Cakmak et al. 2009). Even low levels of residual glyphosate in soil can greatly impede the availability and uptake of Mn, Fe, Cu, and Zn by plants and lead to their undersupply with these nutrients. Reduced disease resistance and plant growth may be the result (Johal & Huber 2009). Adverse impacts of (repeated) glyphosate use on the health of non-target plants have to be taken into account, as reduced disease resistance most likely will increase use of other pesticides, e.g. fungicides that may be highly toxic too.

It is well known that weeds offer considerable benefits for the agro ecosystem, as they support a range of organisms, among them decomposers, predators, pollinators, and parasitoids, by providing food and shelter for them (Marshall et al. 2003). The Farm Scale Evaluations performed in the UK showed that broad-spectrum herbicides such as glyphosate impact abundance and diversity of weeds more severely than conventional herbicide regimes (Heard et al. 2003). The quantitative loss of weeds reduces number and diversity of arthropods heavily and interrupts the food chain for farmland birds and mammals. Ample evidence of negative impacts of glyphosate on biodiversity has been collected in areas where glyphosate is used extensively, e.g. in combination with genetically modified glyphosate-resistant crops. The all-time low in the number of monarch butterflies in the winter 2013/2014 has been attributed to the loss of their food plant (*Asclepias syriaca*) in vast areas of the United States where glyphosate-resistant crops are grown (Wade 2014).

As glyphosate is the herbicide most widely used, these massive negative impacts on biodiversity have to be considered and used as reason not to re-authorize the substance. Mitigation measures, such as buffer strips, that would be up to the individual member states could not reduce the risk of impacting

biodiversity to an acceptable level – even if farmers accepted to spare buffer strips from glyphosate application which they often don't.

Subclause: Formulated glyphosate products (Annex B.9.11 Surface-active substances in glyphosate-based formulations)

In the RAR, solely the active ingredient glyphosate is being considered for authorization, although in the field, only formulated products are applied. The final glyphosate products contain high amounts of surfactants that have surface-active properties. According to the German government[1], in addition to the 5000 t of glyphosate used in Germany in 2010, 1700 t of polyethoxylated alkylamines (POEA) had been applied. Therefore, it is of importance to not only test the toxicity of the active ingredient glyphosate but to take into account the toxicity of the various formulated products that are used.

There is ample evidence that formulated products can exhibit higher toxicity. In particular, polyethoxylated alkylamines (POEA) are known to be highly toxic to cells and organisms (Mesnage et al. 2013). The RMS considers several of the observed effects on endpoints regarding genotoxicity, mutagenicity, and development or reproduction of non-target organisms to be mediated by the surfactant included in the formulations. Thus the RMS concedes that "*the toxicity of glyphosate-based products is greatly enhanced if the active substance is formulated with alkylamine ethoxylates"* and "*the authorization of glyphosate-based products with alkylamine ethoxylated surfactants might require the generation of further data*". But to argue, that the lead formulation MON52276 for the assessment of glyphosate does not contain this surfactant and that nowadays POEA-formulated products "*are not expected to be neither notified nor registered in the future"*, are not comforting statements, as such products are still on the market and data about the nature and toxicity of other surfactants that replace POEA are not provided to the public. In addition, predicted environmental concentrations for glyphosate and its metabolite AMPA are calculated only for these substances, not taking into account the highly toxic surfactants that are released into the environment together with the active ingredient. Therefore, it is important to collect data about environmental concentrations of surfactants and to consider their impact on the environment already during the authorization process.

Conclusions

To make agriculture in Europe more environmentally benign, it is of utmost importance that pesticide use is restricted to a much greater extent than it is actually the case. As herbicides make up the largest share of pesticides and glyphosate, in particular, is the most used herbicide, regulators are obliged to not renew the approval of this chemical.

[1] http://dipbt.bundestag.de/dip21/btd/17/071/1707168.pdf

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1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)

Identity (B.1, Annex C)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Physical and chemical properties of the active substance (B.2.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Physical, chemical and technical properties of the formulation (B.2.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

Further information (B.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Methods of analysis (B.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Other comments (B.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol.3, B.6, Toxicology and metabolism, page 2	PAN UK: in the classification of studies the categories 2,3 and E are made subject to the so-called Klimisch-criteria. We do not agree with using Klimisch criteria since it uses no test protocol criteria, just the circular logic that OECD/GLP = good . Academic studies rarely use these standard protocols as they restrict the testing of hypothesis. Do the hundreds of thousands scientists in academia do irrelevant or poor work? RMS say yes, but do not prove it	Studies need to be assessed on their scientific value and not dismissed without reading because not being GLP/OECD. Next a 'weight of the evidence' approach should be followed, including all scientifically qualified studies available, especially independent studies.
2.	Vol.3, B 6	PAN UK: Industry's financial interests in selling	White, J. and Bero, L.A., 2010, 'Corporate manipulation of research:

Other comments (B.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		their products conflicts with the interests of truth when they perform the agent's safety tests. Specific techniques are used to allow their mission of getting products approved to prevail. White, 2010, extends the well-known strategies of the tobacco industry to other sectors. A RMS must be ready to counter these strategies, yet we didn't note a very critical approach of RMS to the applicant.	Strategies are similar across five industries', *Stanford Law & Policy Review*, (21/1) 105–134. We are fi. disappointed that the RMS agreed on the completeness of the dossier while demanding extra tests and confirmatory information would be the proper approach, especially in case the outcome of industry-sponsored studies differ from academic studies.
3.	Vol.3, B.6	The tests performed by the applicants will probably be based on good laboratory practice (GLP), but this doesn't guarantee quality and reliability. In the past several cases of industry laboratory fraud (IBT, Craven) were discovered by regulators (including tests on Glyphosate). Although these fraudulent tests were replaced by new ones, we still have our doubts on their quality and reliability. GLP, in the end, is just a management system, forcing laboratories to be transparent, but no-one can guarantee what is written down exactly, and what happened or is observed in the tests.	Commission therefore needs to explain what guarantees they have used to ensure quality and reliability of tests, both old and new. Many outcomes of studies comparing GLP-studies and studies from open (independent) literature have different outcomes, an unaddressed concern.

2. Mammalian toxicology (B.6)

Toxicokinetics (B.6.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Acute toxicity (B.6.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol.3, B.6.2.3, page 240	PAN UK, we do not understand that the exposure of test animals at 1000 ppm is called "low". With a current ADI of 0,3 ppm we challenge the value of this type of experiments with extreme high doses. This also means that effects seen at doses people are exposed to in practice are not tested and given the fact that Glyphosate has endocrine disrupting properties, adverse effects of low doses at vulnerable periods of development cannot be excluded.	We do not understand what we can learn from exposure of 20.000 ppm. Can any effect seen at this unrealistic dose be extrapolated to lower doses, thousand times lower and more, to predict an effect? We do not think that this type of mechanistic linear dose-response thinking has any basis in science. A body is no machine but an interrelated system with three major communication systems with triggers and feedback. OECD-tests are very insensitive and should be replaced by realistic dose tests on those elements (with very specific and sensitive endpoints) derived from the hazard assessment (mainly based on academic studies)

Short-term toxicity (B.6.3)

No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Genotoxicity (B.6.4)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
1.	Vol.3, B.6.4, genotoxicty, page 359	PAN UK: In Table B 6.4-15 an experiment is disqualified for having too low doses. This is difficult to understand since the dose is still above ADI and far more relevant than the many dozens studies at extreme high dose.	Also remarkable is that at these doses effects are seen. They are subsequently qualified as not relevant using an industry-invented tool called "historical control data" allowing adverse effects being dismissed. Historical control data are never used by active scientists; they rely on normal controls.
2.	Vol.3, B.6.4, genotoxicty, page 382	PAN UK: The study discussed showing clastogenicity is done at lower levels than usual. It concludes that effects are seen al lower levels while no effects are seen at higher levels. This again would be reason to reconsider the old paradigms of linear dose-response and use of high unrealistic doses.	
3.	Vol.3, B.6.4, genotoxicity, page 384	PAN UK: the study of Clemens shows mutagenicity in tadpoles and the occurrence of this effect is not excluded by the RMS. However in the next lines many questionable assumptions and reasoning are added by the RMS and finally the effects dismissed for	We think the only proper approach in case of uncertainties would be to demand the test to be repeated and confirmed in independent laboratories and blind testing. And the process of approval halted until more clarity is given.

Genotoxicity (B.6.4)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		humans. We cannot agree with assumptions being made of questionable grounds; expert judgement should be based on science and not feelings.	
4.	Vol.3, B.6.4, genotoxicty, page 385	PAN UK: we think it is not justified to dismiss studies (genotoxic effects in germ cells in Drosophila) that challenge industry findings by immediately pointing at the "large database of existing studies`. This gives the impression the RMS had already made up his mind about mutagenicity and is now just looking for reasons to dismiss studies not confirming the RMS´s feelings.	All studies should be used for a weight of the evidence approach in an open scientific approach without prior opinions or feelings. We think independent experts are needed to do this weight of the evidence evaluation, who were not involved in drafting the RAR and contacts with industry. The same biased approach is taken on page 386 for another critical study.
5.	Vol.3, B.6.4, genotoxicty, page 386	PAN UK: we can understand that the applicant will claim that any adverse effect seen is due to the co-formulant tallowene and as such these studies should not count. We do not understand the claim of the RMS that it can "certainly be assumed" that an effect will be caused by the co-formulant. RMS's should not assume but assess. And if they have no data to prove it was the co-formulant, the effects should be counted for the active ingredient.	Again, there is all reason to demand the applicant to repeat academic studies showing adverse effects by exposing the active substance. This should be done in an independent laboratory with blind testing.
6.	Vol.3, B.6.4, genotoxicty, page 389	PAN UK: The claim in the RAR of a lack of mutagenicity or even that results of studies are consistently and unequivocally negative (Vol.1)	Literature references will be provided by PAN UK on request but should also be part of the review of the applicant on peer-reviewed literature. We only mention, Grisolia, 2002, Sivikova, 2006, Belle,

Genotoxicity (B.6.4)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		is false. Genotoxic effects on the contrary are already long known and available to the reviewers. Kale, 1995, showed mutations in fruit flies, Vigfussen, 1980, showed sister chromatin exchanges in human lymphocytes, just as Bolognesi in 1997. Peluso in 1998 showed increased DNA adducts in mice. Gasnier, 2009, showed DNA damage, as well as Manas, 2009. Some are captured in the industry review, others not, for unknwon reason. All are dismissed in the end. Numerous other studies have confirmed DNA damage in mouse, bovine, fish, caiman, tadpole, fruit fly, sea urchin, onion, and bacterial cells.	2007, Cavas, 2007, Cavalcante, 2008, Guilherme, 2009, Poletta, 2009, Monroy, 2005. It is really a joke the RMS uses the unscientific Klimisch-criteria for academic studies. Anyone knows the outcome: all dismissed! Given the conflict of interest of the applicant on safety testing, and the potential bias in studies or interpretation of studies, we propose EFSA starts her peer-review with independent literature for doing a hazard assessment. Independent literature has less chance on bias because of lacking motives and should be qualified as more reliable than industry-sponsored studies with an inherent conflict of interest. It is strange to note that Table 2.6-6 in Volume 1 only summarises industry-sponsored studies.
7.	Vol.3, B.6.4.8.10, weight of the evidence	PAN UK: While the RMS discusses a few of the academic studies that show adverse effects, in the 'weight of the evidence' approach taken by the RMS as a standard procedure plays down the positive effects seen by assumptions and reasoning's such as the effects being indirect, or being beyond a certain threshold, not relevant for humans, suggests that the effect are toxic but not mutagenic. None of these assumptions is based on science but just part of the old paradigm used by regulators.	The RMS has high confidence in industry-sponsored studies and very low in academic studies, with the result only industry-sponsored studies with their favourable outcome for industry are counted in the final evaluation.

Section 2 - Mammalian toxicology (B.6)

Genotoxicity (B.6.4)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations

Long-term toxicity and carcinogenicity (B.6.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
1	Vol 3, B 6.5. Long-term toxicity and carcinogenicity, page 435	PAN UK: A major failure in the testing systems used is the lack of exposure in-utero of the test animals. It is well-known that many chronic diseases develop in-utero (not only for cancer) and as such tests lacking in-utero exposure cannot be qualified as a 'state-of-the art' scientific approach. The conclusion that the substance is not carcinogen needs to be justified. We therefore propose EFSA requires the applicant to test again with in-utero exposure, performed with blind testing in an independent laboratory.	EU legislation provides for a high level of human health protection based on the precautionary principle and requires special attention for the vulnerable, the unborn and the elderly. The test system disregards the effects on the vulnerable groups in society.
2	Vol 3, B 6.5. Long-term toxicity and carcinogenicity, page 435	PAN UK: Next point is the extreme high doses used in notifier's testing. More and evidence is available in literature (see Vandenberg et al. 2012 review) that low doses can harm, many times in the developing phase of the organism and many times for endocrine disrupting chemicals. Since Glyphosate has endocrine	EFSA should require the applicant to do new testing of the substance including a range of low doses.

Long-term toxicity and carcinogenicity (B.6.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		disrupting properties, EFSA should perform a thorough review ion the data in independent literature, and require applicant to do a series of low dose testing on endocrine adverse effects.	
3	Vol 3, B 6.5. Long-term toxicity and carcinogenicity, page 435	PAN UK: Another point on carcinogenicity is the need to expose and follow test animals during their entire lifetime. Most diseases develops after notifier's tests incinerate the test animals (e.g. ACS (American Cancer Society): *Cancer Facts & Figures 2012*. Atlanta: American Cancer Society; 2012. [http://cancer.org/acs/groups/content/@epidemiologysurveilance/documents/document/acspc-031941.pdf].	EFSA should require the applicant to do new testing of the substance including lifetime exposure and monitoring.
4.	Vol 3, B 6.5. Long-term toxicity and carcinogenicity, page 502	PAN-UK: No evidence in rat according to the RAR (only industry-sponsored studies analysed) but the malignant lymphoma seen in mice were dismissed. It was not the chemical (Glyphosate) that should be blamed according to the RMS but the strain of mice. We think this has nothing to do with a scientific evaluation but more with a determination to get to a certain outcome. Given the many articles in peer-reviewed literature on long-term effects and cancer, a more balanced approach would have been justified.	We propose that based on the studies in open literature a hazard assessment is done to find out what long-term effects and cancers can be expected to occur by the use of Glyphosate. Next, an analysis need to be done if the long-term and carcinogenicity animal tests will really capture the expected effects. And finally those long-term and carcinogenicity tests qualifying for capturing the adverse effects should be used for a final conclusion. No study should be dismissed for being non-GLP or non-OECD. Every study counts, also the one of Seralini. While the Rapporteur might not like the outcome, there is no scientific failure in the tests of Seralini.

Long-term toxicity and carcinogenicity (B.6.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
5.	Vol 3, B 6.5. Long-term toxicity and carcinogenicity, page 502	PAN UK: Glyphosate has a history of links with cancer. The first carcinogenicity study submitted to US-EPA (1981) by applicant Monsanto showed an increase in testicular tumours in male rats as well as an increase in the frequency of a thyroid cancer in females. Both results occurred at the highest dose tested (30 mg/kg of body weight per day). The second study (1983) found an increasing trend in the frequency of a rare kidney tumour in male mice. A later study (1990) found an increase in pancreas and liver tumours in male rats together with an increase of the same thyroid cancer found in the 1983 study in females.	We ask EFSA to take a look at these older studies. There is good reason for EFSA to start the cancer analysis from scratch including all evidence from the past and from independent literature. Knowing the potential of Glyphosate to cause these effects, are the currently evaluated safety tests designed to capture these effects?
6.	Vol 3, B 6.5. Long-term toxicity and carcinogenicity page 524	PAN UK: In the RAR all epidemiology studies showing a relation between Glyphosate and cancer are considered irrelevant, such as the Hardell-studies on the link with non-Hodgkin's, and even the unscientific Klimisch-approach is used for this qualification. This is unjustified. Now industry has created a situation in which people are exposed to thousands of chemicals at the same time, epidemiology studies cannot by nature be sensitive anymore. This means if a relation is shown, even weak, this should be reason for concern and reason to demand the	Industry should monitor the use of Glyphosate, analyse all environmental compartments and organisms, and do a large epidemiology study focussed on clarifying the evidence available. There is good evidence on the relation with non-Hodgkin's lymphoma, Nordstrom, 1998, Hardell, 1999 and 2002, McDuffie, 2001, De Roos, 2003 and Eriksson, 2008, and multiple myeloma, De Roos, 2005, and a large study should be initiated to find out more.

Long-term toxicity and carcinogenicity (B.6.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		applicant to do independent monitoring to et more information	
7.			

Reproductive toxicity (B.6.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
1	Vol.3 B.6.6 Reproductive toxicity. page 538	PAN UK: a big omission in the German RAR is the lack of a hazard characterization of Glyphosate. In many EFSA opinions it is stated that the first step of risk assessment is the hazard characterization. We observe that Germany just moves on directly to risk characterisation and standard setting, and ignores the evidence on hazards	A hazard characterization is important to learn about the mechanism of toxicity of Glyphosate. Without the knowledge of the hazards it will be difficult to select in the next steps of risk assessment what data are useful and not. Germany just puts all evidence in the "Klimisch-mill" with the obvious effect of all independent science disregarded.
2	Vol.3 B.6.6 Reproductive toxicity. page 538	PAN UK: We urge EFSA to include a hazard characterisation in the peer-review. This should be done by using all in-vitro studies available, disregarding none, and all mechanistic studies available. The peer-review should focus on what mechanistic evidence is present on teratogenicity, on DNA-damage., etc.?	The study of Paganelli et al. 2010 presents interesting evidence on the mechanism of action. During early embryonic development, retinoic acid generated in a specific region of the embryo helps determine position along the embryonic anterior/posterior axis by serving as an intercellular signaling molecule that guides development of the posterior portion of the embryo. It acts through Hox genes, which ultimately control anterior/posterior patterning in early developmental

Reproductive toxicity (B.6.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
			stages. The findings of Marc et al. '05 support this, offering a general mechanism of action for teratogenicity.
3.	Vol.3 B.6.6 Reproductive toxicity. page 539	PAN UK: many multi-generation tests in the RAR with their very high (and unrealistic) doses, endpoints which are not the state-of-the-art cannot provide for the final answer on reproductive toxicity. The results are not clear anyway with a study that shows effects at low doses but is dismissed in the end by the Rapporteur. And studies showing effects on the offspring also accepted because they are observed at high doses. Combined with the many studies in open literature on malformations of the offspring and developmental effects, a peer-review by EFSA of all evidence is more than necessary.	The industry-sponsored OECD tests are known for their insensitivity and this could explain the very remarkable difference seen between the industry-sponsored studies and independent literature. The high doses used are close to the acute poisoning doses and poisoning effects are common in these tests, while more subtle effects could be missed.
4	Vol.3 B.6.6 Reproductive toxicity. page 548	PAN UK, we again question the use of extreme high exposure doses such as 15.000 ppm or 1000 mg/kg, more than 1000x the ADI. Animals should be tested at realistic doses and no extrapolation used	The high doses are close to the acute poisoning doses used and poisoning effects are common in these tests, while more subtle effects could be missed.
5	Vol.3 B.6.6 Reproductive toxicity. page 596	PAN UK: We especially encourage EFSA to take a look at teratogenicity. The pre-2001 studies of Monsanto show teratogen effects, a range of independent studies report these effects, these effects are also observed in areas with Roundup	In the first DAR on Glyphosate in 2001, the UK experts commented that -based on the Monsanto studies- a single study might not raise concerns, but that the teratogenic effects that kept being observed in the Monsanto-studies, pointed at a pattern that should not be dismissed in the risk assessment.

Reproductive toxicity (B.6.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		monocultures (soy) in epidemiology studies and even in bioindustry where piglets fed on soy have these effects.	EFSA should asses if in the two-generation studies the animals are properly exposed during vulnerable windows during development and if a large range and relevant endpoints are considered for teratogenicity and development during later life of the offspring.
6.	Vol.3 B.6.6.9, Reproductive toxicity. page 597	PAN UK: specific endocrine disrupting tests should be demanded from the applicant. Just basing conclusions on outdated OECD-protocols on reproduction and development is not justified. The science on endocrine disruption differs a lot from other fields and specific exposure windows, doses and specific endpoints should be used. In the traditional tests with traditional experts these effects will be missed.	
7.	Vol.3 B.6.6.9 Reproductive toxicity. page 597	PAN UK: A large body of evidence on endocrine disrupting effects of Glyphosate is disregarded and dismissed in the RAR. Walsh, 2002 showed the disruption of the steroid hormone progesterone, as well as Romano, 2010 on testosterone. Richard, 2005 also concludes Glyphosate is an endocrine disruptor by affecting aromatase at very low doses. Also Benachour, 2005 and Gasnier, 2007 came to the same conclusion.	Hokanson, 2007, demonstrated a synergistic effect of Glyphosate with oestrogen, with implications for pregnancy-induced hypertension and foetal growth retardation. The implications of these effects on reproduction and the developing foetus are profound, with work by Mose, 2008, confirming that Glyphosate does cross the placenta.
8	Vol.3 B.6.6.10 Reproductive toxicity.	PAN UK: the study in rabbits shows that at a level of 10 mg/kg 20% of the litters have	The malformations should be more thoroughly investigated and this study already shows that the LOAEL of 10 mg/kg should be adopted

Reproductive toxicity (B.6.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	page 613	malformations while this is 5% in the control (this also counts for the foetus, 3,1% vs. 0,7%). While this dose is at least less enormous than the regular dose, it is still above a realistic dose and we think additional studies should be done with lower and m	for standard setting. A suggesting NOEAL of 100 mg/kg by the applicant is absurd.
9.	Vol.3 B.6.6.10 Reproductive toxicity. page 619	PAN UK: this study in rabbit again shows most effects at the lowest dose tested (18 vs. 13 of the litters tested with malformations), 50 mg/kg. While this dose is still unrealistic high, lower doses should be tested on malformations of the foetus.	
10.	Vol.3 B.6.6.10 Reproductive toxicity. page 629	PAN UK: this study in rabbit also shows malformations at the lowest level tested (82 foetus with 'minor' defects vs, 58 in the control), 100 mg/kg. This "low" dose is of course unrealistically high.	There is a clear pattern of malformations of the foetus in all rabbit studies.
11.	Vol.3 B.6.6.10 Reproductive toxicity. page 642	PAN UK: this study confirms previous observations that malformations of the foetus is highest in the lowest dose tested, 50 mg/kg, (17.7% vs. 11,7% in the control). We object to the use of historical control data. The only scientific approach is to compare the outcome in the tests against the control.	Why the RMS values historical control data over the normal (negative|) control is a mystery. While it is highly questionable if the industry-sponsored studies are reproducible at all, historical control data mix different labs, operators, protocols and strains and create an unrealistic wide range of "controls'. No scientist will ever use this type of tools.
12.	Vol.3 B.6.6.10 Reproductive toxicity.	PAN UK: also this study shows effects at the lowest dose tested, 20 mg/kg, upper cleft	There is a clear pattern of malformations of the foetus in all rabbit studies.

Reproductive toxicity (B.6.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	page 650	palate, 15% vs. 5% in the control, and dilated heart, 23,1% vs. 0% in the control.	
13.	Vol.3 B.6.6.12, Reproductive toxicity, Published data, page 658	PAN UK: it is remarkable that the RMS now easily rejects all claims made by EOS in their report "is the public kept in the dark" and let most independent literature fall under the 'Klimisch-axe". In their reaction in July 2011, the RMS called the report: The recently published report "Roundup and birth defects: Is the public kept in the dark?" is a challenging critical summary of adverse health (mainly teratological and reproductive) findings that are attributed by the authors to the compound glyphosate and/or to herbicides such as Roundup that contain glyphosate as active ingredient.	The RMS ends their report by saying: An adequate response to the criticism and the many accusations in the report would require a general discussion of the established paradigms for the toxicological evaluation of chemicals. These general discussions should be initiated by the Commission before we start with the re-evaluation of glyphosate within the AIR2 project. We fail to have seen any general discussion on established paradigms, not by the RMS and not by Commission. We therefore urge EFSA to start such a discussion before drafting the peer review on Glyphosate.
14.	Vol.3 B.6.6.12, Reproductive toxicity, Published data, page 658	PAN UK: it is sad to note that the industry review made by the applicant is not commented by the RMS. Given the many missing studies and the standard use of Klimisch to dismiss studies on a large scale, an intervention of the RMS was needed very much.	We urge EFSA to review all independent studies and stop using the entirely unscientific Klimisch-tool and do a purely scientific assessment of each study looking at the quality of the study, disregarding protocols and GLP-administration systems.

Neurotoxicity (B.6.7)

Section 2 - Mammalian toxicology (B.6)

No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
1.	Vol.3, B.6.7.1, Neurotoxicity, Published data, page 702.	PAN UK: Epidemiology studies have been published pointing at Glyphosate of causing mental disorders of children born to pesticide applicators in the US, Garry, 2002. Even acute poisoning could lead to brain damage, Barbosa, 2001. Animal studies have demonstrated that Glyphosate depletes serotonin and dopamine, Anadon, 2008, and causes a loss of mitochondrial transmembrane potential in rat brain cells, especially in the substantia nigra region of the brain, Astiz, 2009.	There is evidence of developmental neurotoxicity of Glyphosate and EFSA should pay good attention to this adverse effect in their peer-review.
2.	Vol.3, B.6.7.1, Neurotoxicity, Published data, page 702.	PAN UK: We regret that an assessment of the literature by the RMS is missing. We think the assessment of the applicant is totally inadequate, playing down any adverse effects and using the "Klimisch-axe" to ensure it is ignored. This abrogates the idea of scientific evaluation.	

Other toxicological studies & Medical data (B.6.8-B.6.9)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Summary of mammalian toxicology and setting ADI, AOEL, ARfD (B.6.10)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Toxicity of the product(s) (B.6.11)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Dermal absorption (B.6.12)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Section 2 - Mammalian toxicology (B.6)

Toxicity of non-active substances (B.6.13)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Exposure data (B.6.14)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol.3, B.6 review public data	PAN UK: We did our own literature search (see explanations) and found remarkable differences with the one conducted by the applicant.The notifier only found 52% of the 145 significant glyphosate toxicity studies we found, despite the mandate to find all. Worse–the notifier finds a published study but never mentions it (not even placing its main numerical finding in a table, as sometimes occurred). So the fraction	To check compliance with the new mandate on literature review, we performed a simple search of PubMed: "<pesticide common name> toxicity". The later is a specific keyword in PubMed, while almost all studies use, inter alia, the common name of a chemical. In our experience this simple search term captures on average 95% of all *published* studies relating to the risks of a chemical. After eliminating the obviously irrelevant, we saved the remaining abstracts (by publication date) as a public PubMed collection, and listed by endpoint in a table the studies that the notifier and RMS

Section 2 - Mammalian toxicology (B.6)

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		of those we found that were also discussed is just 31%.	did & did not find or discuss, critiquing the reasons for the former.

5. Ecotoxicology (B.9)

Birds and mammals (B.9.1 and B.9.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Aquatic organisms (B.9.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Bees and non-target arthropods (B.9.4 and B.9.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.9.4	PAN UK: the endocrine disrupting effects of Glyphosate on birds and other non-target organisms are disregarded.	

Section 5 - Ecotoxicology (B.9)

Earthworms and other soil non-target organisms (macro and micro) (B.9.6, B.9.7 and B.9.8)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Other non-target organisms (flora and fauna), sewage treatment (B.9.9 and B.9.10)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.9, Annex, page 298	PAN UK: many studies show that Glyphosate has endocrine disrupting properties. The RMS conveniently states that all endocrine disrupting effects are likely caused by the surfactant. The study of Paganelli, 2010, for instance clealrly shows that formulations and active substance have the same adverse effect, and clearly point at Glyphosate as being an endocrine disruptor.	EFSA should demand studies from the applicant (in independent laboratories, blind testing) for a range of endocrine disruption screening test for Glyphosate.

Comments of Eco Centre Wales on the Renewal Assessment Report on Glyphosate 06. 05. 2014

1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)

Identity (B.1, Annex C)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Physical and chemical properties of the active substance (B.2.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Physical, chemical and technical properties of the formulation (B.2.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Further information (B.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, Annex B.3 Data	***Eco Centre Wales***: Worldwide there are at least 28	In Europe, there are more cases of glyphosate resistance than depicted in

Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

Further information (B.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	on application and further information, page 7-8	weed species (not only 24) for which glyphosate-resistance has been documented, comprising more than 200 populations and infesting millions of hectares (Heap 2014). Although countries with RRcrop cultivation are affected most heavily, cases of glyphosate-resistant weed species are increasingly reported from other countries too. As a result, a massive increase in herbicide amounts applied has been documented. To stop the pesticide treadmill, glyphosate use has to be restricted.	the RAR (16 cases instead of 10 and 6 species instead of 5). Contrary to the RAR, glyphosate-resistant weed species have not been found exclusively in orchards, vineyards or olive groves, but also in other crops, e.g. asparagus (Lolium rigidum in France) and alfalfa (Conyza canadensis in Greece). And Northern and Central Europe will also be affected, with Poland being already the second country after the Czech Republic to report glyphosate-resistant weeds. It will be a question of time when glyphosate-resistant weed biotypes will show up in countries such as Germany. Therefore, evolution of glyphosate-resistance will speed up in Europe too, unless use of glyphosate is severely restricted.

Methods of analysis (B.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

5. Ecotoxicology (B.9)

Birds and mammals (B.9.1 and B.9.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Aquatic organisms (B.9.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	B.9.2.2 Summary of aquatic toxicity data Page 132	***Eco Centre Wales*** : In particular, amphibians, many of which are endangered, have been shown to be affected by glyphosate-based herbicides, possibly both their larval and adult stages (Wagner et al. 2013). Reviewing peer-reviewed studies on glyphosate impacts on amphibian, Plötner and Matschke (2012) concluded that glyphosate is itself toxic to amphibians, and surfactants such as POEA are even more so leading to abnormal behaviour, teratogenic effects and developmental failures. In addition, toxicity of glyphosate and Roundup to aquatic invertebrates such as *Daphnia magna* has been underestimated (Cuhra et al. 2013). Toxicity classification has to be revised.	Cuhra et al. (2013) found EC50 (48) values for glyphosate IPA in *Daphnia magna* that were significantly lower than the values depicted in table B.9.2-59. Testing glyphosate and Roundup for 55 days (instead of only 21 days tested in the long-term studies referred to in table B.9.2-59) led to significant reduction in juvenile size even at the lowest test concentration of 0.05 mg a.i./L. About ten times higher concentrations of Roundup affected fecundity, growth and abortion rate and at1.35 and 4.05 mg a.i./L of both glyphosate and Roundup significant negative effects were seen on most tested parameters, including mortality. Thus even low ambient concentrations of glyphosate will affect aquatic invertebrate ecology.

Section 5 - Ecotoxicology (B.9)

Bees and non-target arthropods (B.9.4 and B.9.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Earthworms and other soil non-target organisms (macro and micro) (B.9.6, B.9.7 and B.9.8)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.9.8 Effects on soil non-target micro-organisms	***Eco Centre Wales***: As stated in the RAR and reported by Kremer & Means (2009), glyphosate leads to significant shifts in bacterial community composition but it also affects importantfungal species, e.g. beneficial mycorrhizal fungi (Druille et al. 2013a,b). Previous use of glyphosate has been linked to increased Fusarium infection of wheat and barley (Fernandez et al. 2009). Thus impacts of glyphosate use on bacterial and fungal species that are linked to plant health and disease have to be considered too.	

Other non-target organisms (flora and fauna), sewage treatment (B.9.9 and B.9.10)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.9.9.1.4	***Eco Centre Wales***:	Adverse impacts of (repeated) glyphosate use on the health of non-target

Section 5 - Ecotoxicology (B.9)

Other non-target organisms (flora and fauna), sewage treatment (B.9.9 and B.9.10)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	Summary of results on non-target plants	Glyphosate can adversely impact micronutrient uptake in plants as it is a strong metal chelator (Tesfamariam et al. 2009, Cakmak et al. 2009). Even low levels of residual glyphosate in soil can greatly impede the availability and uptake of Mn, Fe, Cu, and Zn by plants and lead to their undersupply with these nutrients. Reduced disease resistance and plant growth may be the result (Johal & Huber 2009).	plants have to be taken into account, as reduced disease resistance most likely will increase use of other pesticides, e.g. fungicides that may be highly toxic too.
	Vol. 3, B.9.9.1.6 Indirect effects via trophic interactions	The Farm Scale Evaluations have shown that the quantitative loss of weeds reduces number and diversity of arthropods heavily and interrupts the food chain for farmland birds and mammals. Ample evidence of negative impacts of glyphosate on biodiversity has been collected in areas where glyphosate is used extensively, e.g. in combination with genetically modified glyphosate-resistant crops. The all-time low in the number of monarch butterflies in 2013/2014 has been attributed to the loss of their food plant (*Asclepias syriaca*) in vast areas of the United States where glyphosate-resistant crops are grown (Wade 2014).	As glyphosate is the herbicide most widely used, these massive negative impacts on biodiversity have to be considered and used as reason not to re-authorize the substance. Mitigation measures, such as buffer strips, that would be up to the individual member states will not reduce the risk of impacting biodiversity to an acceptable level – even if farmers accepted to spare buffer strips from glyphosate application which they often don't.

Section 5 - Ecotoxicology (B.9)

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	B.9.11 Surface-active substances in glyphosate-based formulations	***Eco Centre Wales:*** There is ample evidence that formulated products can exhibit higher toxicity. In particular, polyethoxylated alkylamines (POEA) are known to be highly toxic to cells and organisms (Mesnage et al. 2013). Glyphosate has endocrine disrupting properties which cannot only be attributed to the surfactants. Paganelli et al (2010) showed that both formulated products and the active substance have adverse effects and that glyphosate acts as an endocrine disruptor. To make agriculture in Europe more environmentally benign, it is of utmost importance that pesticide use is restricted to a much greater extent than it is actually the case. As herbicides make up the largest share of pesticides and glyphosate is the most used herbicide, regulators are obliged to not renew the approval of this chemical.	To argue, that the lead formulation MON52276 for the assessment of glyphosate does not contain POEA and that POEA-formulated products "are not expected to be neither notified nor registered in the future", is not comforting, as such products are still on the market and data about the nature and toxicity of other surfactants that replace POEA are not provided to the public. In addition, predicted environmental concentrations for glyphosate and its metabolite AMPA do not take into account the highly toxic surfactants that are released into the environment in combination with the active ingredient. Therefore, data about environmental concentrations of surfactants should have been collected and their impact on the environment should have been considered before drafting the RAR .

GM-Free Cymru: Comments to the Renewal Assessment Report (RAR) – Glyphosate. 08/04/2014

Introduction

The Renewal Assessment Report (RAR) prepared by BfR and Germany as the Rapporteur Member State (RMS) has been opened by EFSA to "peer review" comments from the public. Some parts of the final report have been blackened, presumably names that refer to studies provided by the applicants. Unfortunately, in Volume 1 Report and Proposed Decision the very last chapter, 3.2 Proposed Decision, has been blackened too. This means the public will not get informed about what kind of decision the RMS and the Co-RMS propose. Thus the public can only speculate about details of the proposal.

That having been said, there is absolutely no doubt that the BfR has signed up to the rebuttal of all "inconvenient" research and has slavishly followed the wishes of the biotechnology and pesticides industries in recommending that glyphosate should be approved for future use in Europe.:

http://www.bfr.bund.de/en/
the_bfr_has_finalised_its_draft_report_for_the_re_evaluation_of_glyphosate-188632.html
http://www.bfr.bund.de/en/
frequently_asked_questions_on_the_health_assessment_of_glyphosate-127871.html

Press release

The BfR has finalised its draft report for the re-evaluation of glyphosate

Glyphosate in an active substance widely used in herbicides and is currently subject to a comprehensive re-evaluation process by the European Union (EU). This regular re-assessment of active ingredients in plant protection products is a routine procedure controlled by the European Commission. Within this re-evaluation new findings in research and development as well as new aspects in the risk assessment are taken into consideration. As a result of this re-evaluation, the Commission will decide whether or not the active substance may be applied in plant protection products in future.

During this re-evaluation procedure Germany evaluates glyphosate and a sample formulation of a plant protection product containing glyphosate. In this framework Germany acts as Rapporteur Member State (RMS) writing a draft re-assessment report.
Several competent authorities in Germany are involved in the writing process (i.e., the Federal Institute for Risk Assessment -BfR-, the Federal Environment Agency, the Julius Kuehn-Institute and the Federal Office of Consumer Protection and Food Safety). After the establishment of a draft re-assessment report this report will be send to the European Food Safety Authority (EFSA).

The Federal Institute for Risk Assessment (BfR) has already completed the draft re-assessment report on health risk assessment. For this purpose, more than 150 new

toxicological studies were evaluated for the first time and are described in detail in the draft report by BfR. In addition, all available toxicological studies (nearly 300) were re-assessed from the point of view of compliance with actual quality standards in study conduction and confirmation of interpreted results. Furthermore, about 900 publications from scientific journals have been considered in the draft report and more than 200 publications were reviewed in detail. In conclusion of this re-evaluation process of the active substance glyphosate by BfR the available data do not show carcinogenic or mutagenic properties of glyphosate nor that glyphosate is toxic to fertility, reproduction or embryonal/fetal development in laboratory animals. As a result of the re-assessment for the active substance BfR proposes slight amendments of the reference values. BfR believes that there is convincing evidence that the measured toxicity of some glyphosate containing herbicides is the result of the co-formulants in the plant protection products (e.g., tallowamines used as surfactants). Therefore BfR calls special attention to the co-formulants and incorporated a toxicological assessment of tallowamines in its draft report. A research project initiated by BfR and performed by the University of Veterinary Medicine in Hanover investigated the influence of a glyphosate containing herbicide on microbial metabolism and communities in ruminants. The results of this study are summarised in the draft suggesting that there is no negative impact on the microflora in the rumen. In particular, there was no indication that Clostridium bacteria might multiply under the influence of glyphosate.

After sending the draft re-assessment report of glyphosate to EFSA, it will constitute the basis for the public consultation with all interested stakeholders as well as for the so-called "peer review procedure" by experts from other EU member states. After commenting of the draft, the RMS will incorporate all final comments and remarks. EFSA is steering the re-assessment procedure and will establish an "EFSA conclusion" on basis of the German draft re-assessment report and the comments of the other stakeholders by the end of 2014. The Commission will then take a decision on the future approval of the active ingredient glyphosate on the basis of the EFSA conclusion. All re-assessment reports and scientific opinions which are intended for the public consultation will become publicly available on the EFSA website.

BfR continues its active investigation on possible effects of glyphosate-containing pesticides on humans and farm animals in close co-operations with German and foreign research institutes. To support public debate on the risk assessment of glyphosate, the BfR will held a scientific symposium on 20th January 2014 about the "Safety of plant protection products containing glyphosate" at ICC Berlin, Germany during Green Week (17-26 January 2014).

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We also note the powerful role played by the "Glyphosate Task Force" -- involved in the high-profile and slick marketing of glyphosate -- and we note its rebuttals of all "inconvenient" research.....

http://www.glyphosate.eu/news/re-evaluation-glyphosate-german-authorities-confirm-previous-evaluations

The Glyphosate Information Portal is an initiative of the European Glyphosate Task Force (GTF), a consortium of companies joining resources and efforts in order to renew the European glyphosate registration with a joint submission. This consortium is not to be considered a legal entity.

The following companies are confirmed member of the GTF (as of December 2nd, 2011):

Agria S.A., Agro Trade GmbH, Albaugh UK Limited, Arysta Lifesciences SAS, Barclay Chemicals (Manufacturing) Ltd., Brokden SL, Bros Spolka Jawna B. P. Miranowscy, Cheminova A/S, Dow AgroSciences LLC., EXCEL CROP CARE(Europe) NV, Feinchemie Schwebda GmbH, Helm AG, Industrias Afrasa S.A., Monsanto Europe S.A./ N.V., Nufarm GmbH & Co KG, Pinus TKI d.d., Rotam Agrochemical Europe Limited, Sabero Organics Gujarat Limited, Sapec Agro S.A., Sinon Corporation, Société Financière de Pontarlier, Syngenta Limited, United Phosphorus Ltd, Wynca UK Limited

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Their comment on the German Re-evaluation:

Re-evaluation of glyphosate: German authorities confirm previous evaluations

Early 2014 the German Federal Institute for Risk Assessment (BfR) and other German safety authorities have published their draft re-assessment report on the health risk assessment of glyphosate, re-assessing hundreds of studies and public domain literature. The draft report is an important step in the process to re-register active substances of pesticides, such as glyphosate. The substance glyphosate was granted EU-wide approval in 2002 and is currently undergoing a renewal process controlled by the European commission.

In the case of glyphosate, Germany is the Rapporteur Member State (RMS) who has submitted the draft of the re-evaluation report to the European Food Safety Authority (EFSA). In conclusion of the re-evaluation process by BfR, the available data confirms the previous evaluation: Glyphosate does not show carcinogenic or mutagenic properties, has no toxic effect on fertility, reproduction or embryonal/fetal development in laboratory animals and is not considered to pose any risk to human health.

The sub report by BfR is now available for consultation with interested stakeholders and will go into the "peer review procedure" by experts from other EU Member States.

More information about the draft re-evaluation report on glyphosate:

* *Draft report for the re-evaulation of glyphosate by the German Federal Institute for Risk Assessment (BfR): BfR press release*
* *Re-evaluation of glyphosate enters the next phase. (Press release of the German Federal Office of Consumer Protection and Food Safety (BVL); 6th January 2014; in German only)*

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Industry Task Force welcomes important step in the EU review of glyphosate

The Glyphosate Task Force welcomes the finalisation of the assessment report of glyphosate by Germany, the rapporteur Member State appointed to review existing and new data relating to the human and environmental safety profile of glyphosate.
The re-evaluation of glyphosate is part of a standard procedure for crop protection products, which have to undergo a renewal process controlled by the European Commission.

The assessment report drafted by Germany is now available on the website of the European Food Safety Authority (EFSA) and all interested parties and stakeholders are invited to comment on its contents and conclusions.

The Glyphosate Task Force, which comprises 24 member companies, especially welcomes the fact that the assessment report drafted by Germany provides a comprehensive and detailed review of new studies, peer reviewed literature and additional information - including that submitted by stakeholders.

The Glyphosate Task Force notes that the report's conclusions broadly confirm earlier regulatory assessments regarding glyphosate's safety profile, in particular that it has limited toxicity for man, animals and the environment; is not neurotoxic, carcinogenic or mutagenic; is not toxic to reproduction or development, does not have endocrine disrupting properties; is not bio-accumulative or persistent and has minimal toxicity for bees.

Finalisation of the assessment report represents the beginning of a new phase in the renewal process for glyphosate. In this regard, the Glyphosate Task Force awaits EFSA's conclusions which are expected later this year.

On the basis that the report's conclusions "broadly confirm earlier regulatory assessments regarding glyphosate's safety profile, in particular that it has limited toxicity for man, animals and the environment; is not neurotoxic, carcinogenic or mutagenic; is not toxic to reproduction or development, does not have endocrine disrupting properties; is not bio-accumulative or persistent and has minimal toxicity for bees" **we wish to state categorically that we do not agree with those assessments or conclusions, which have more to do with the wishes of industry than they do with public and environmental health and the Precautionary Principle.**

It seems to us to be hardly credible that the BfR assessment relates to glyphosate, the very same active substance that hundreds of research scientists now see as highly toxic and dangerous to the environment, to farm animals and to public health.

WE WISH TO HAVE IT PLACED ON RECORD THAT IN OUR VIEW, FROM A LONG STUDY OF THE RELEVANT LITERATURE, GLYPHOSATE AND ROUNDUP SHOULD BE IMMEDIATELY BANNED THROUGHOUT THE EU.

Below, GM-Free Cymru is commenting on specific sections of the renewal assessment report (RAR), in particular those that deal with health effects and the environmental impacts of glyphosate.

HEALTH EFFECTS --- ref B.6.4 - B.6.13

Summary 1

Glyphosate is the active ingredient in the herbicide Roundup. It is a broad-spectrum herbicide, considered to be nearly nontoxic to humans (Williams et al., 2000). However, a recent paper (Samsel & Seneff, 2013), argued that glyphosate may be a key contributor to the obesity epidemic and the autism epidemic in the United States, as well as to several other diseases and conditions, such as Alzheimer's disease, Parkinson's disease, infertility, depression, and cancer. Glyphosate suppresses 5-enolpyruvylshikimic acid-3-phosphate synthase (EPSP synthase), the rate-limiting step in the synthesis of the aromatic amino acids, tryptophan, tyrosine, and phenylalanine, in the shikimate pathway of bacteria, archaea and plants (de María et al., 1996). In plants, aromatic amino acids collectively represent up to 35% of the plant dry mass (Franz, 1997). This mode of action is unique to glyphosate among all emergent herbicides. Humans do not possess this pathway, and therefore we depend upon our ingested foodand our gut microbes to provide these essential nutrients. Glyphosate, patented as an antimicrobial (Monsanto Technology LLC, 2010), has been shown to disrupt gut bacteria in animals, preferentially killing beneficial forms and causing an overgrowth of pathogens. Two other properties of glyphosate also negatively impact human health – chelation of minerals such as iron and cobalt, and interference with cytochrome P450 (CYP) enzymes, which play many important roles in the body. (Samsel and Seneff, 2013)

Summary 2

People, plants and animals can be exposed to glyphosate and Roundup in many ways. Farmers, bystanders and other operators can be exposed during its application, and neighbouring natural habitats by drift from the area where it is being applied. Aerial application is used on some crops, such as on the vast monoculture plantations of GM RR soya in the Americas, which greatly increases the chances of accidental exposure of neighbouring populations or habitats. Exposure to glyphosate and Roundup also occurs via their residues, frequently found in food and the environment. The Maximum Residue Levels (MRLs) in food for glyphosate and its breakdown product were agreed by the UN-based Codex Alimentarius Commission in 2006, but appear to be related more to the type of agricultural practices characteristic of each food crop rather than to safety thresholds for human health. In light of the new scientific evidence on the health and environmental impacts of glyphosate it is essential to re-evaluate MRLs in order to align them with updated safety assessments.

In the environment, glyphosate can be held in the soil by binding to particles but, depending on soil chemistry, can also leach into groundwater. Glyphosate can also wash directly into drains and surface waters and it has been detected in both. Glyphosate and its degradation product have been detected in studies of drainage surface waters in Canada, the US and Denmark. These finding have implications for surface water quality

and drinking water quality. Given the evidence that glyphosate can cause harm to health and the environment, the leaching of glyphosate has also serious implications for aquatic life. Glyphosate is present in soils, waters and our food as a result of its use as a herbicide. Therefore, rigorous assessment of the safety of glyphosate to plant, humans and animals is of great importance.

Human health problems related to glyphosate: Independent scientific studies are underscoring the call for an urgent reassessment of glyphosate and its related products. These studies associate exposure to glyphosate with a number of negative effects on human and animal health, including long term or chronic effects:

▪▪ Birth defects in the Argentinean state of Chaco, where GM soya and rice crops are heavily sprayed with glyphosate, increased nearly fourfold over the years 2000 to 2009. Similar defects were also found in women from Paraguay exposed to glyphosate-based herbicides during pregnancy. These defects were compatible with those induced in laboratory experiments at much lower concentrations than normal commercial glyphosate concentrations.

▪▪ Glyphosate is a suspected endocrine disruptor. This means it could disrupt production of vital reproductive hormones, such as progesterone and oestrogen. Published studies demonstrate various endocrine effects in animals and human cells associated with glyphosate.

▪▪ Studies of illness patterns in human populations (epidemiological studies) have linked glyphosate exposure to non-Hodgkin's lymphoma (a type of blood cancer) whilst laboratory studies have confirmed that glyphosate and/or its associated products exhibit characteristics typical of cancer causing agents (i.e. genotoxicity or mutagenicity) in both humans and animals. Together, these studies suggest that glyphosate may contribute to cancer. Evidence that glyphosate may also affect the nervous system and may even be implicated in Parkinson's disease. Scientific evidence highlighting these health effects must be taken very seriously. An urgent reassessment of the health impacts of glyphosate and its related products must take place. (Greenpeace /GMFreeze, 2011)

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OCCURRENCE AND FATE OF THE HERBICIDE GLYPHOSATE AND ITS DEGRADATE AMINOMETHYLPHOSPHONIC ACID IN THE ATMOSPHERE
FENG-CHIH CHANG, MATT F. SIMCIK, and PAUL D. CAPEL
Environmental Toxicology and Chemistry, Vol. 30, No. 3, pp. 548–555, 2011

Glyphosate has strongly negative effects on crops and field ecology
Scientists finding many negative impacts of Roundup Ready GM crops
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Visceral botulism at dairy farms in Schleswig Holstein, Germany - Prevalence of Clostridium botulinum in feces of cows, in animal feeds, in feces of the farmers, and in house dust
by Monika Krüger, Anke Große-Herrenthey, Wieland Schrödl, Achim Gerlach, Arne Rodloff
Anaerobe 18 (2012) 221e223

Why Is Damning New Evidence About Monsanto's Most Widely Used Herbicide Being Silenced?
It turns out that Monsanto's Roundup herbicide might not be nearly as safe as people have thought, but the media is staying mum on the revelation.
by Jill Richardson AlterNet Apr 27, 2011 http://www.alternet.org/story/150733/
why_is_damning_new_evidence_about_monsanto%27s_most_wide
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The woes of GMOs - Glyphosate and GMOs Impact on Crops, Soils, Animals and Man
Dr. Don M. Huber, Emeritus Professor of Plant Pathology, Purdue University
http://www.gmfreecymru.org.uk/pivotal_papers/glyphosate_toxic_food.html

Increased Cancer Burden Among Pesticide Applicators and Others Due to Pesticide Exposure
Michael C. R. Alavanja, Dr PH; Matthew K. Ross, PhD; Matthew R. Bonner, PhD, MPH
CA Cancer J Clin 2013 Jan 15. doi: 10.3322/caac.21170. 23 pp.

THE DANGERS OF GLYPHOSATE:
Letter to Ventura County supervisor Steve Bennett
ISIS Letter 5 September 2011

To: Supervisor Steve Bennett, L-1900 800 S. Victoria Ave Venura, CA 93009
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5 September 2011

Roundup residues interfere with multiple metabolic pathways
Citation: M Malatesta, F Perdoni, G Santin, S Battistelli, S Muller, M Biggiogera (2008). Hepatoma tissue culture (HTC) cells as a model for investigating the effects of low concentrations of herbicide on cell structure and function.
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Glyphosate Toxic to Mouth Cells & Damages DNA, Roundup Much Worse
Further evidence of genotoxic and cytotoxic effects – a prelude to cancer, birth defects and reproductive problems by Dr Eva Sirinathsinghji
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Jeffrey Smith January 14, 2011 Institute for Responsible Technology
For photos, graphs etc please go to this web site: http://www.responsibletechnology.org/blog/664

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Reduction in urinary organophosphate pesticide metabolites in adults after a week-long organic diet
4th May 2014
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ENVIRONMENTAL EFFECTS -- ref B.8.1 - B.8.9 and Ecotoxicology ref B.9

Development of resistance

In Volume 1, Section 2.3.2 Summary of information on the development of resistance, and Volume 3 Annex B.3 Data on application and further information, the topics “development of resistance and appropriate management strategies” are discussed. GM-Free Cymru supports FoE Europe, and its submission is reproduced here with minor changes.

Comments:

The simplicity and effectiveness of weed control through glyphosate will be undermined by shifts in weed communities and populations resulting from the selection pressure of the applied herbicides. Glyphosate has long been considered to be a low risk herbicide in terms of the evolution of resistant weed populations (Beckie 2006), but ever increasing use of glyphosate has favored the development of glyphosate-resistance in weeds. It has taken 8-20 years of glyphosate use in conventional systems until the first glyphosate-resistant weed, rigid ryegrass (Lolium rigidum), was found in 1996 in Australia (Pratley et al. 1999). Since then, at least 28 cases of glyphosate-resistant weed species (comprising more than 200 populations) have been recorded worldwide (Heap 2014). The resistant weeds infest millions of hectares at many different places in various countries. Although countries, such as the US, Argentina, Australia, and Brazil, where glyphosate-resistant crops are cultivated are affected most heavily, countries without GM crop cultivation increasingly report cases of glyphosate-resistant weed species.

Glyphosate-resistance in weeds has been found to be based on several mechanisms, such as target site insensitivity, overproduction of the target protein EPSPS (5-enolpyruvylshikimate-3-phosphate synthase), amplification of the EPSPS gene, reduced glyphosate translocation, and increased sequestration of glyphosate in plant cell vacuoles (Perez-Jones & Mallory-Smith 2010). Resistance mechanisms can co-occur, in particular, when related resistant weed species hybridize. In addition, multiple-resistance to other herbicide mode of actions than glyphosate has been reported too (Heap 2014).

In the RAR, reference is made to the development of glyphosate-resistance in Europe. But in reality, the situation is far more severe than depicted in the RAR document (as of September 2012). There are not only 10 cases of resistance known in Europe, but meanwhile the number is 16 and it is not only five species that have been found, but there are six (Heap 2014). With five resistant species that have infested hundreds of hectares, Spain is the most afflicted country. Contrary to the RAR presentation, glyphosate-resistant weed species have not been found exclusively in orchards, vineyards or olive groves, but also in other crops such as asparagus (Lolium rigidum in France) and alfalfa (Conyza canadensis in Greece). It is also not quite true, that “Apart from one case (C. canadensis) in the Czech Republic, Northern and Central Europe are not affected by glyphosate resistance up to now”, since resistant C. canadensis has also been reported

from Poland railways. This indicates that evolution of glyphosate-resistance will speed up in Europe too, unless use of glyphosate is severely restricted.

In the US, not only the broad adoption of glyphosate-resistant crops but also the continuous rise in the number of resistant species and areas inflicted by resistant weeds has resulted in a massive increase in herbicide amounts applied (Benbrook 2012a). A similar scenario has been depicted for Europe in case genetically modified glyphosate-resistant crops would be authorized for cultivation here too (Benbrook 2012b). Therefore, to stop the pesticide treadmill, glyphosate use has to be restricted.

Environmental effects

In Volume 1, Section 2.9 Effects on non-target species and Volume 3, Annex B.9 Ecotoxicology), data on ecotoxicology studies are discussed, evaluated, and summarized.

Environmental impacts on non-target organisms

The risk assessment for birds and mammals is based on the active ingredient glyphosate acid in the product MON 52276 for the intended uses in several crops including pre-planting, pre-emergence, pre-harvest and row-application in orchards and vineyards. From the data provided by the applicants, the RMS comes to the conclusion that after use of the lead formulation MON 52276 in the indications according to the label there is an acceptable acute risk for birds and mammals due to uptake of contaminated food and an acceptable risk resulting from an exposure of small herbivorous mammals, non-target arthropods, and aquatic organisms. Use under the proposed conditions will result in a negligible exposure of honeybees or has no unacceptable acute or chronic effects on colony survival and development. The RMS concludes further, that for the evaluation of the formulation MON 52276 on non-target plants data are still required, in particular, as a valid study with this product to non-target plants is lacking and the formulants in the product may enhance toxicity.

The RMS concedes that, depending on the agricultural and ecological conditions, the use of glyphosate may affect populations of non-target terrestrial arthropods and vertebrate species (especially farmland birds) via trophic interactions and suggests mitigation measures. The RAR reads at this point: These effects trace back to the intended effect of the herbicides – eliminating competing plants – and the interruption of the food web going along with it.

In Volume 1, Section 3 Proposed decision, the RMS states: It is considered that Article 4 of Regulation (EC) No 1107/2009 is complied with. Specifically the RMS considers that authorization in at least one Member State is expected to be possible for at least one plant protection product containing the active substance for at least one of the representative uses. But the approval should be subject to conditions and restrictions. According to the RMS, glyphosate is not a candidate for substitution.

This statement has been made although the RMS identifies data gaps with regard to the ecotoxicology risk assessment (e.g. aquatic organisms, microorganisms, and non-target plants such as tomato) and concludes that certain areas of the risk assessment could not be finalized on the basis of the available data, among them effects of glyphosate towards microorganisms, on non-target plants and on biodiversity.

For all uses, the RMS acknowledges that the impacts of glyphosate on biodiversity is a critical area of concern and recommends that member states should pay attention to such potential indirect effects and may consider adequate risk mitigation measures.

Comments

It is not acceptable that glyphosate that is known to negatively impact biodiversity to such an extent should be re-authorized in the EU. Glyphosate exhibits acute and chronic toxicity, in particular, to aquatic species and non-target plants. As stated in the RAR and reported by Kremer & Means (2009), glyphosate leads to significant shifts in bacterial community composition but it also affects some fungal species, e.g. beneficial mycorrhizal fungi (Druille et al. 2013a,b). Previous use of glyphosate has been linked to increased Fusarium infection of wheat and barley (Fernandez et al. 2009). Amphibians, many of which are endangered, have been shown to be affected, possibly both their larval and adult stages (Wagner et al. 2013). Plötner and Matschke (2012) concluded that glyphosate is itself toxic to amphibians, and surfactants such as POEA are even more so causing abnormal behavior, teratogenic effects and developmental failures.

Glyphosate can adversely impact micronutrient uptake in plants as it is a strong metal chelator (Tesfamariam et al. 2009, Cakmak et al. 2009). Even low levels of residual glyphosate in soil can greatly impede the availability and uptake of Mn, Fe, Cu, and Zn by plants and lead to their undersupply with these nutrients. Reduced disease resistance and plant growth may be the result (Johal & Huber 2009). Adverse impacts of (repeated) glyphosate use on the health of non-target plants have to be taken into account, as reduced disease resistance most likely will increase use of other pesticides, e.g. fungicides that may be highly toxic too.

It is well known that weeds offer considerable benefits for the agro ecosystem, as they support a range of organisms, among them decomposers, predators, pollinators, and parasitoids, by providing food and shelter for them (Marshall et al. 2003). The Farm Scale Evaluations performed in the UK showed that broad-spectrum herbicides such as glyphosate impact abundance and diversity of weeds more severely than conventional herbicide regimes (Heard et al. 2003). The quantitative loss of weeds reduces number and diversity of arthropods heavily and interrupts the food chain for farmland birds and mammals. Ample evidence of negative impacts of glyphosate on biodiversity has been collected in areas where glyphosate is used extensively, e.g. in combination with genetically modified glyphosate-resistant crops. The all-time low in the number of monarch butterflies in the winter 2013/2014 has been attributed to the loss of their food plant (Asclepias syriaca) in vast areas of the United States where glyphosate-resistant crops are grown (Wade 2014).

As glyphosate is the herbicide most widely used, these massive negative impacts on biodiversity have to be considered and used as reason not to re-authorize the substance. Mitigation measures, such as buffer strips, that would be up to the individual member states could not reduce the risk of impacting biodiversity to an acceptable level – even if farmers accepted to spare buffer strips from glyphosate application which they often don't.

Subclause: Formulated glyphosate products (Annex B.9.11 Surface-active substances in glyphosate-based formulations)

In the RAR, solely the active ingredient glyphosate is being considered for authorization, although in the field, only formulated products are applied. The final glyphosate products

contain high amounts of surfactants that have surface-active properties. According to the German government[1], in addition to the 5000 t of glyphosate used in Germany in 2010, 1700 t of polyethoxylated alkylamines (POEA) had been applied. Therefore, it is of importance to not only test the toxicity of the active ingredient glyphosate but to take into account the toxicity of the various formulated products that are used.

There is ample evidence that formulated products can exhibit higher toxicity. In particular, polyethoxylated alkylamines (POEA) are known to be highly toxic to cells and organisms (Mesnage et al. 2013). The RMS considers several of the observed effects on endpoints regarding genotoxicity, mutagenicity, and development or reproduction of non-target organisms to be mediated by the surfactant included in the formulations. Thus the RMS concedes that “the toxicity of glyphosate-based products is greatly enhanced if the active substance is formulated with alkylamine ethoxylates” and “the authorization of glyphosate-based products with alkylamine ethoxylated surfactants might require the generation of further data”. But to argue, that the lead formulation MON52276 for the assessment of glyphosate does not contain this surfactant and that nowadays POEA-formulated products “are not expected to be neither notified nor registered in the future”, are not comforting statements, as such products are still on the market and data about the nature and toxicity of other surfactants that replace POEA are not provided to the public. In addition, predicted environmental concentrations for glyphosate and its metabolite AMPA are calculated only for these substances, not taking into account the highly toxic surfactants that are released into the environment together with the active ingredient. Therefore, it is important to collect data about environmental concentrations of surfactants and to consider their impact on the environment already during the authorization process.

Conclusions

Glyphosate demonstrably does great damage to wildlife and the environment. To make agriculture in Europe more environmentally benign, it is of utmost importance that pesticide use is restricted to a much greater extent than it is actually the case. As herbicides make up the largest share of pesticides and glyphosate, in particular, is the most used herbicide, and one of the most dangerous, **regulators are now obliged to refuse to renew the approval of this chemical.**

References --ref B.8.1 - B.8.9 and Ecotoxicology ref B.9

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Chapter 5

Pesticides and Agricultural Work Environments in Argentina

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Additional information is available at the end of the chapter

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1. Introduction

The use of chemical pesticides has brought benefits such as the increase of agricultural production, soil productivity and product quality, which is reflected in economic benefits, vector disease control and in general, in public health. However, given that only 10 percent of applied pesticides reach the target organism, a high percentage is deposited on non target-areas (soil, water, sediments) and, as well as affecting public health, impacts non-target organisms such as wild life [1]. Also, the extended use of pesticides commonly results in residues in foods [2] generating continued human exposure by different pathways, which has led to widespread concern over the potentially adverse effects of these chemicals on human health.

Pesticides are an important aspect of agricultural practice in both developed and developing countries and, despite the many technological advances brought by the modern intensification of agriculture, the increased yields were achieved primarily through the use of fertilizers and pesticides [3].

Argentina is one of the major crop producers in Latin America, with the export of cereals and oilseeds being one of the principal axes of the national economy. The frontiers of farming have expanded greatly in the past 30 years, from 15 to the current 30 million hectares, with an increase of the area planted for grain production, particularly for soybeans, from 34,700 ha in the 1969/70 season to about 18 million ha in 2011/12 [4]. Today, Argentina is the world's leading producer of vegetable oils, the fourth largest producer and second largest exporter of sun-

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flower oil, and the fourth producer and leading exporter of soybean oil. The country has one of the highest yields in the world in soybean, corn and wheat [5].

Argentina's extensive production of cereals and oilseeds for the international market coexists with intensive horticulture and family farming, with wide geographical distribution, mainly close to urban centers, and diversity of cultivated species, occupying an area of about 230,000 ha [6], giving an annual production of over 10,000,000 tons, primarily for domestic consumption.

Crop production has been accompanied by a steady increase in the use of agrochemicals; pesticide marketing has grown strongly, from 155 million pounds in 1995 up to 700 m.p. in 2012 [7]. In technology used for spraying pesticides, the country has a wide variety of equipment ranging from self-propelled sprayers, which also involve high technological complexity, with filtered air cabins, to activated charcoal filters, spray drag and power and manual backpacks used particularly in intensive farming. Each of these different technological environments is associated with different health and environmental risks.

The Province of Córdoba is in the central region of Argentina, with a total area of 165,321 km². Its location, as well as its political and physical characteristics, make this province a hub of articulation between different natural regions of the country. It has a population of 3,304,825 inhabitants, 88.7% of whom live in urban areas and 11.3% in rural areas [8]. Among the inhabitants of rural areas, 45.9% live in towns of less than 2,000 inhabitants, and the rest dispersed in the open countryside [9]. The northern and western areas are less populated and are the ones which concentrate most indicators of structural and cyclical poverty. The agricultural roots of this province mean that the settlements are mixed with agricultural developments, increasing the risk of non-occupational exposure of communities adjacent to cultivated fields.

The rural area in Cordoba devoted to extensive crops (soybean, maize, sorghum, peanut, wheat and sunflower), has expanded from 3,397,050 ha in 1994/95 to 7,300,000 ha in 2011/2012 [4].

The country's extensive agricultural model, based on glyphosate-resistant transgenic soybean farming, no-till and the intensive use of fertilizers and pesticides [10], is highly dependent on modern technologies [11]. In contrast, intensive crops such as fruits and vegetables are characterized by high demand of labor per unit of output. Typically, this is a small-scale activity usually performed by the peasant family production unit [12, 13], with all its members participating. The incidence of pesticide poisoning in these agricultural settings includes non-intentional child exposure, occupational exposure of young farm laborers, para-occupational exposure of the farm workers and their families and the adjacent community, and exposure to banned pesticides [14].

In Córdoba Province, exposure to different pesticides linked to agricultural production has long been recognized [10, 15-16], as well as the unavoidable soil contamination even decades after its application [17]. Our previous results of a population-based study in the province of terrestrial applicators of pesticides in extensive crops (n=880), emphasized that workers were highly exposed to pesticides, and we studied various determinants of this exposure, including the pesticides most frequently used or still in use by the applicators. We also reported the

negative health consequences associated with their employment status. The weakness of compliance with the rules governing the activity was also highlighted as a factor that increases the health risk of agricultural workers and the general population [10].

The greenbelt surrounding the provincial capital is a zone of fruit and vegetable farming, providing fresh food to the local urban population. Its extension includes neighboring towns, forming a strongly integrated commercial and productive system. Almost 90% of the fruits and vegetables it provides are produced within the urban area [17]. Horticultural smallholders and farmworkers are often immigrant workers from neighboring countries [18-20]: according to the Ministry of Education [21], sixty percent of them are Bolivian citizens, which increases their risk of environmental and occupational illness and injury, as well as the health disparities typically associated with poverty [22].

This chapter offers a comparative analysis of two widely different agricultural settings (extensive and horticultural crops) and characterizes the pesticide applicator populations in each, including the health conditions associated with occupational pesticide use. We introduce two pesticide exposure assessment proposals, consisting of intensity and accumulated exposure indexes for both scenarios. The proposals include new results about the pesticide applicators of extensive crops, including an update of the differential characteristics of worker populations in homogeneous ecological areas of the province. We also introduce a new scenario consisting of horticultural smallholders and farmworkers, and describe their working conditions. The study and comparison of these different work settings allows us to tailor the exposure indexes developed in our previous publication [10] to the particular pesticide exposure of greenbelt situations, as well as to develop proposals for preventive measures for the reduction of human exposure and environmental impact, according to each scenario.

2. Materials and methods

2.1. Population studies

We conducted a population-based study in Córdoba Province, Argentina, with two principal target populations: a) terrestrial applicators of pesticides of extensive crops; b) smallholders and farmworkers of the greenbelt of its capital city, Córdoba.

a. In the first case, all the applicators attending the mandatory courses for obtaining the applicator license, provided by the Agriculture, Livestock and Food Ministry, were asked to participate in the survey, during the period 2007-2012. A self-administered questionnaire was used to obtain demographic data, pesticides and technologies used, crops sprayed, workers' lifestyle and family health information, as already described in a previous publication [10]. From 1479 completed questionnaires, a consistency analysis for several responses was carried out, with a sample size of 1327 for further analysis. We also performed a stratified analysis taking into account the Homogeneous Ecological Areas (HEAs) divisions of the province in order to describe differences between these.

b. In the second case, 101 smallholders and farmworkers were contacted in Cordoba's wholesale fruit and vegetables market and in the greenbelt setting itself. The above questionnaire was adapted for this specific population, after an exploratory study through in-depth interviews during 2011. As described in the literature, the exploratory study shows that this is a difficult-to-reach population due to their migratory status and unstable working conditions.

2.2. Variables

2.2.1. Terrestrial applicators of pesticides of extensive crops

a. Social and demographic variables: age (in years, as from birth date), education level (highest level of educational attainment in the formal system) and marital status (married or cohabiting and others).

b. Technological and working practices variables: pesticide spray equipment (self-propelled crop sprayer with cab and activated charcoal filter; trailed crop sprayer with cab and activated charcoal filter), area worked (average hectares applied in the last year), seniority in the job (years mixing/applying), written pesticide prescription signed by an agricultural engineer (yes/no).

To assess the level of protection implemented by the terrestrial applicators, we adopt the proposal in [23], considering eight categories of personal protective equipment (PPE) used, alone or in combination: waterproof clothing, gas mask, chemical-resistant gloves, face shields or goggles, hat or helmet and other protective clothes (boots, apron, waterproof pants). The weighting of PPE elements is based on monitoring and measurement of occupational exposure during the task. A new measure called protection level was constructed [10]: unprotected (0% protection), partially protected (20 to 70% protection) and protected (90% protection).

These variables were analyzed comparatively between homogeneous ecological areas (HEAs) of the province, according to soil and climatic characteristics, land use and production activities, as described in [10].

c. Good agricultural practices: we considered two practices included in the local regulation aimed at reducing human risks and negative environmental impacts [24]: a) the triple washing of pesticide containers (yes/no). This practice consists in washing the empty container three times and draining for thirty seconds in upload position; and b) correct end use of pesticide containers (yes/no): properly cleaned containers must be transferred to an authorized registered storage center, to be destroyed in a pyrolytic oven; burial, burning, storage, sale or reuse are prohibited.

2.2.2. Smallholders and farm workers of the greenbelt surrounding the capital city of Cordoba

To highlight the particularities of the horticultural work scenario and its worker population, new variables were incorporated into the analysis when necessary.

a. Socio-demographic variables: age, education and marital status are described as mentioned above; origin (country and province of birth); household (members and their participation in horticultural work). Dwelling infrastructure and public services: running water installed (yes/no), bathroom installed (yes/no), domestic gas distribution network (yes/no); public service of urban solid waste collection (yes/no).

b. Work practices, technology and other exposure variables: pesticides sprayed, use of PPE (as described above); crops grown in the last year (type of crop and annual average harvests); greenhouse for crop (yes/no); household distance to the nearest crop (meters); extension of the productive unit in hectares: small: up to 10 ha; medium: between 11 to 40 ha; and large, more than 40 ha [25]: seniority in the job (years mixing/applying); pesticide spray equipment (self-propelled crop sprayer with cab and activated charcoal filter; trailed crop sprayer with cab and air intake activated charcoal filter or without air intake filter; trailed crop machine without cabin, manual and engine backpack).

c. Good agricultural practices (as described above).

2.2.3. Health worker conditions in both agricultural settings

a. Symptoms: Perception of acute and sub-acute manifestations: Irritative symptoms (skin, nose and eye irritation, nausea or vomiting, chest discomfort); fatigue/tiredness; nervousness or depression; headache; excessive sweating. Occurrence of symptoms: Never/Rarely/Sometimes/Frequently;

b. Medical consultations related to pesticide use effects: yes/no; and Hospitalization linked to tasks with pesticides: yes/no;

c. Workers' risk perception of different pesticides: not dangerous/slightly dangerous/dangerous/highly dangerous.

2.3. Exposure assessment

Based on proposed indexes of our previous work [10], the present study incorporates intensity level (ILE) and accumulated exposure (CEI) indexes into pesticide exposure, adapted to the smallholder and farmworker population of the greenbelt of Cordoba city, describing the principal differences among them. These indexes measure instantaneous exposure intensity and cumulative exposure taking into account the life years of worker exposure. To use these indexes in the horticultural worker population, we have carefully adapted the weighting score procedure to this particular context.

2.4. Statistical analysis for association

We used a modeling approach to check differences between ecological areas. Assuming counts or frequencies in each category of the variables as the outcome, we fitted Poisson and Gamma generalized models to estimate the parameters (effects). The latter was used since the empirical distributions of both indexes presented skewness. Association between two or three variables

was studied through log-linear models in order to estimate the odds ratio as association measures.

3. Results

3.1. Population of extensive crops

In a previous work [10] we identified different agricultural settings in the province, based on homogeneous ecological area (HEAs) divisions (Figure 1). Differences in basic characteristics of this population, such as their average age, instruction level and length of occupational exposure to pesticides allow us to hypothesize the existence of diverse risk scenarios in the province. In this chapter, an update of the characterization of workers was performed with an increased sample size, n=1327.

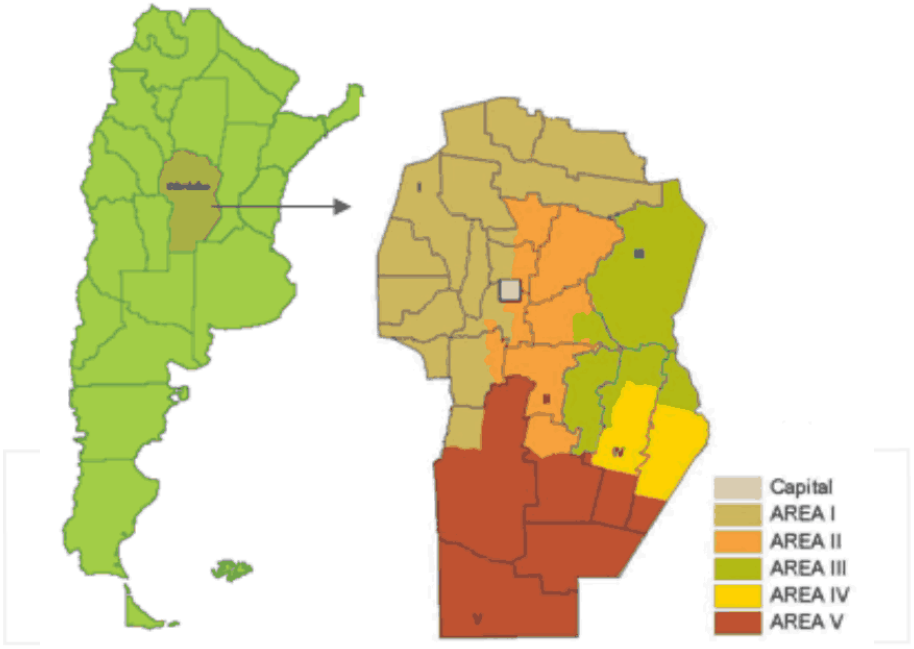

Figure 1. Homogeneous ecological areas (HEAs) of Córdoba province.

Significant differences among HEAs were found for age ($p<0.01$), education level ($p=0.03$) and marital status ($p<0.01$), as well as for seniority in the task ($p<0.05$), average/year of hectares sprayed ($p<0.03$), use of pesticides with written prescription signed by an agricultural engineer ($p<0.03$), and self-propelled crop sprayer with cab and activated charcoal filter ($p<0.03$) (Table

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1). Protection level ($p<0.05$) also showed differences between HEAs I, II, III and HEA V ($p<0.05$), the latter having the fewest completely protected workers (31%). Only trailed crop sprayer with cab and activated charcoal filter results were similar in all the areas. It is important to highlight that HEA I showed the lowest percentage of applicators with complete secondary school level or higher (29.2%) and in subjects married or cohabiting (56.8%), but the most workers using complete protection (54%) and using pesticides with written prescription (58.1%) followed by HEA II (54.8%)

	AREAS					
	I	**II**	**III**	**IV**	**V**	**Total**
n	41	641	230	156	259	1327
Age (years)						
Mean	32.3	35.8	34.9	37.6	34.8	35.6
Standard Deviation	8.6	11.6	9.9	10.9	11.9	11.3
14 – 24	16.2	16.5	16.1	12.8	21.2	16.9
25 – 24	48.6	36.0	38.1	30.2	32.8	35.4
35 – 44	27.0	24.9	28.7	30.2	25.2	26.3
> 45	8.1	22.6	17.0	26.8	20.8	21.4
Marital Status (%)[1]						
Married or cohabiting	56.8	66.8	61.7	78.9	58.6	65.5
Unmarried, separated, divorced or widower	43.2	33.2	38.3	21.1	41.4	34.5
Education (%)						
Incomplete Primary	2.4	11.1	13.5	7.1	10.8	10.7
Complete Primary	29.3	27.9	27.8	29.5	32.0	28.9
Incomplete Secondary	39.0	26.6	21.3	22.4	23.9	25.1
Complete Secondary, Technical or University studies	29.2	34.3	37.4	41.0	33.2	35.2

[1]Percentage considering the total of responses.

Table 1. Sociodemographic characteristics of pesticide applicators by Homogeneous Ecological Areas. Córdoba, Argentina. 2007- 2012.

Pesticide with prescription signed by an agricultural engineer was used by only 33.7% of applicators in HEA V, which was different from the others ($p<0,03$); self-propelled crop sprayer with cab and activated charcoal filter was highest in HEA III (74,1%) and this was significantly different from HEAs II and V ($p<0,05$). No significant differences were found between areas in the use of the trailed crop sprayer with cab and activated charcoal filter, but this is a crop sprayer that is very little used in all the areas (Table 2).

	AREAS					
	I	II	III	IV	V	Total
N	41	641	230	156	259	1327
Protection Level (%)[1]						
Unprotected	12.2	12.5	12.2	9.0	17	12.9
Partially Protected	34.1	48.8	46.1	55.8	52.1	49.4
Protected	53.7	38.7	41.7	35.3	30.9	37.8
Average area/year applied (ha)						
Mean	9717	5226	9923	6535	7182	6767
Years personally mixed/applied pesticides (%)						
≤ 1	26.3	11.2	22.4	10.3	17.0	14.6
2 – 5	36.8	31.6	34.5	27.7	38.3	33.1
6 – 10	18.4	23.5	23.8	23.9	21.3	23.0
11 – 20	10.5	21.4	13.5	23.9	15.8	18.9
21 - ≥ 30	2.6	11.7	5.4	14.2	6.3	9.5
Use pesticides with prescription signed by an agricultural engineer (%)						
Yes	58.3	54.8	46.4	53.8	33.7	49.9
Apply with Self-propelled Crop Sprayer with Cab and Activated Charcoal Filter (%)						
Yes	63.9	49.7	74.1	67.9	63.2	58.7
Apply with Trailed Crop Sprayer with Cab and Activated Charcoal Filter (%)						
Yes	2.9	8.4	4.9	6.2	7.9	7.3

[1]Percentage considering the total of responses.

Table 2. Protection Level, Area/year applied Seniority in the Job and Technology in the different Homogeneous Ecological Areas. Córdoba, Argentina, 2007-2012.

Good agricultural practices were established to reduce the contamination that may be caused by empty pesticide containers and their geographical dispersion. Not all applicators carry out the triple washing of pesticide containers (89.9% do so), and only 10.5% are included in formally regulated programs to ensure the correct end use of empty pesticide containers; in many cases, empty containers of chemicals are burned, buried or reused.

3.2. Population of smallholders and farmworkers of the green belt around the capital city of Córdoba

The green belt, in place since the founding of the city, has seen its landscape transformed over time through a steady process of land use change [26], extending to the nearby towns.

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Currently, the green belt is situated within an urban area with a sum of overlapping environmental hazards caused by agricultural activity and industrial activity (Figure 2).

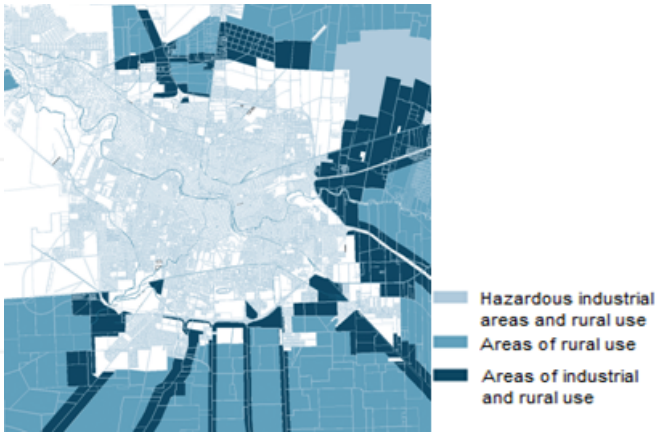

Figure 2. Land use map of the urban area of the city of Córdoba. Municipality of Córdoba, 2004 [17].

Our population consisted of male subjects, with only a single registered female. The mean age was 42.94 years (SD: 13.34), with 67% over 35 years (Table 3). 52% of subjects achieved low levels of education, with 24% who did not complete primary school and 28% who completed only this level. 71% were Argentine and 29% Bolivians. Of the Argentine farmers and workers, 13% were migrants from other provinces. One of the distinguishing characteristics of horticultural farms was their family origin, and this situation, with variations, was maintained over time [27]. 23% of respondents lived alone, while the remaining 77% lived with family members. Of these, 11% lived only with their partner, while 66% also lived with children and 14% with extended family members (older adults, uncles/aunts, cousins). In 31% of families, all took part in the horticultural work with different tasks and hourly loads (involving spouses, children and extended family members).

Among the job roles reported by the horticulturists are the owner, tenant, “mediero” and permanent or temporary employee, and combinations of the above. "Mediería" is a form of associative contract farming: the existence of a partner who provides land and part of the capital, while the other participant contributes labor and other inputs, sharing the product between them.

Part of the population of these small farmers and workers had unsatisfied basic needs, lacking such basic public services as a water network (23%) and a bathroom installed within the dwelling (13%). Precarious living conditions were associated with employment status and land tenure, with the “medieros” and employees having the highest chance of not satisfying these needs ($p < 0.048$), as well as with nationality, to the detriment of the Bolivian-born small farmers ($p < 0.014$, Table 3). An urban solid waste collection service was absent in 23% of cases and domestic gas network provision was lacking in large areas of the green belt (80%).

Sociodemographic characteristics	Number	Valid (%)[1]
Age (years)		
Mean	42.94	
Standard Deviation	13.34	
≤ 25	13	13
26 – 34	20	20
35 – 44	19	19
45 – 54	26	26
> 55	22	22
Education		
Incomplete Primary	24	24
Complete Primary	28	28
Incomplete Secondary	18	18
Complete Secondary, Technical or University studies	31	30
Marital Status		
Married or cohabiting	75	77
Unmarried, separated, divorced or widowed	22	23
Other members of the household working in crops		
Yes	33	31
Running water installed in the household		
Yes	75	77
Bathroom installed in the household		
Yes	85	87
Domestic gas distribution network		
Yes	20	20
Public service of urban solid waste collection		
Yes	66	67
Country of origin and internal migration		
Bolivia	29	29
Argentina	71	71
Born in Cordoba	62	87
Internal migrants	9	13

[1]Percentage considering the total of responses.

Table 3. Social and demographic characteristics of smallholders and farm workers of the Córdoba capital city green belt. 2012.

Table 4 shows that 58% of the productive units were classified as small in extension. Most of the smallholders and farm workers had long experience in the field, 61% with more than 15 years. 69% had their and their family's dwelling within the production unit where they work. 38% of the dwellings were located in close proximity to crops (less than 100 meters) and 50% within 500 m. The pesticide sprayer used by almost all the smallholders and farmworkers in the greenbelt was the backpack (85%), with the self-propelled crop sprayer with cab and

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activated charcoal filter reported by only one farmer. 13% of the productive units grew crops in greenhouses in the last year.

Work characteristics	Number	Valid (%)[1]
Extension of the productive unit (hectares)		
Small (≤ 10 ha)	57	58
Medium (11 to 40 ha)	34	33
Large (≥ 41 ha)	9	9
Area cultivated by worker (ha)		
≤ 10	70	71
11 - 20	11	11
21 - 40	9	9
≥ 41	7	6
Seniority in the horticultural work		
Average (years) 21.34 (SD: 14.58)		
≤ 5	15	17
6 - 10	13	14
11- 15	8	9
16 - 20	14	16
> 20	40	44
Dwelling distance to the nearest crop (meters)		
≤ 50	16	25
51 - 100	8	13
101 - 500	7	11
≥ 501	32	51
Greenhouse for crops in the productive unit		
Yes	13	13
Pesticide spray equipment		
Manual backpacks	77	77
Motor backpacks	7	7
Trailer crop sprayer without cab	28	31

[1]Percentage considering the total of responses.

Table 4. Work practices and technology used by smallholders and farm workers of the Córdoba capital city greenbelt. 2012.

The main vegetable crops cultivated in the green belt of Cordoba are leafy vegetables (Table 5): chard, lettuce, spinach, etc., with the particularity that they are grown throughout the year in a phased manner (Table 5). This means that on the farm at the same time there will be a patch prepared, a patch with the crop planted, another patch growing and another being harvested. These farms, located primarily in the northern greenbelt, are diversified with a large number of crops in many small lots. In these units, the farmer, tenant, and "mediero" work

with their families or with hired laborers, carrying out the various farming tasks: transplanting, manual weed control, irrigation, pest control with manual (backpacks) sprays, harvesting, packing for market, loading and transport. The type of contract may be daily or for quantities.

In the southern area of the green belt, specialized farms have developed, devoted to potatoes as their main activity (22%) and rotation is incorporated into the production system with carrots (10%), wheat (9%) and soybeans (9%) variably according to the conditions of each crop year. These are large production units, with a greater degree of mechanization and automation. Most of the tasks are carried out with machinery, and pesticide application is performed with tractor-drawn and in some cases self-propelled machines. In these cases, labor is incorporated as needed, for example: chopping the seed potatoes and preparing them for planting, and harvesting at the manual collection stage. While potato harvester machines exist, they are not widespread in the green belt. The situation with carrots is similar.

Crops sprayed	Number	Valid (%)[1]	Average harvests per year
Chard *Beta vulgaris L. var. cicla*	71	75	3.75
Spinach *Spinacia oleracera L.*	70	69	3.28
Chicory *Cichorium intybus L.*	64	68	3.34
Scallion *Welsh onion Allium cepa L.*	68	67	2.79
Summer squash *Cucúrbita maxima*	66	65	2.46
Broccoli *Brassica oleracea L.*	65	64	2.93
Parsley *Petroselinum sativum Hoffm.*	62	61	2.98
White cabbage *Brassica oleracea*	61	60	3.22
Butterhead lettuce *Lactuca sativa L. var. Romana*	59	58	3.47
Lettuce *Lactuca sativa L. var. crispa*	58	57	3.83
Lettuce *Lactuca sativa L. var. capitata*	57	56	3.61
Leek *Allium porrum L.*	56	55	2.13
Beet *Beta vulgaris L.*	56	55	3.59
Purple cabbage *Brassica oleracea L. var. capitata*	55	54	3.11
Arugula *Eruca sativa L.*	55	54	4.08
Eggplant *Solanum melongena L.*	47	47	1.61
Cauliflower *Brassica oleracea var. botrytis L. subvar. Cauliflora*	41	41	2.40
Chinese cabbage *Brassica chinensis L.*	35	38	2.54
Radish *Raphanus sativus L.*	38	38	3.04

[1]Percentage considering the total of responses.

Table 5. Principal crops grown in Córdoba capital city green belt, 2012.

The most frequently used pesticides were herbicides (Table 6): glyphosate for 81% of the responses and metolachlor for 65%. In the group of insecticides, those most commonly handled were deltamethrin (72%), cypermethrin (65%), Imidacloprid (66%) and Chlorpyrifos (57%).

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The fungicides most frequently used were cabendazin (71%), mancozeb (63%), zineb (62%), and captan (50%).

Pesticides	(%)[1]
Insecticides	
Deltamethrin	72
Cypermethrin	65
Lambda-cyhalotrin	33
Cartap	40
Carbofuran	36
Carbaryl	34
Methiocarb	25
Chlorpyrifos	57
Dimethoate	50
Methamidophos	23
Imidacloprid	66
Endosulfan	46
Abamectine	35
Fungicides	
Azoxystrobin	47
Azoxystrobin + Ciproconazole	23
Carbendazim + Epoxiconazole	9
Mancozeb	63
Zineb	62
Maneb	15
Carbendazim	71
Captan	50
Chlorothanolil	38
Herbicides	
Glyphosate	81
Fluazifop p butil	46
Metolaclhor	65
2,4 D	19
Atrazine	12
Dicamba	14
Phenmediphan	27
Linuron	61
Metribuzin	31

[1]Percentage considering the total of responses.

Table 6. Most frequently used pesticides in the Córdoba capital city green belt, 2012.

The use (current or past) of banned pesticides was also surveyed: 33% reported having used Parathion, 16% Lindane, 10% Monocrotophos, 8% Methyl Bromide, 7% Malathion, 5% Aldicarb. Current use of Aldicarb was reported by two farmworkers; Monocrotophos and Aldrin were reported by a single case. Regarding good agricultural practices in this setting, 90% performed the triple washing of pesticide containers; but this was not accompanied by correct end use of the empty containers: 57% were stored, 17% were burned, 7% buried, and there were other misuses of contaminated containers.

3.3. Exposure assessment

In a previous work [10], we proposed two indexes to describe pesticide exposure in applicators. The Intensity Level of pesticide Exposure (ILE) index measures instantaneous exposure intensity and the Cumulative Exposure Index (CEI) takes into account the average period of exposure, including the previous ILE information. Both indexes were constructed based on the Dosemeci proposal [23], carefully adapting the weighting procedure to our own context, and particularly to local professional opinion. The expressions of these measures are as follows:

$$ILE = (mix * PPE) + (\sum_{i=1}^{n} \frac{meth * PPE}{\#\, meth}) + (repair * PPE) + house_dist$$

$$CEI = ILE + (\sum_{i=1}^{n} \log(1 + \frac{Ha / year}{55})$$

where *mix* represents a dichotomic response about mixing pesticides, *meth* the category of the method used with a certain *PPE*, *repair* the binary variable for which success is the positive response, *house_dist* the score indicating the applicator dwelling proximity to the nearest crop, and *55* the average of ha treated with a single load in the crop sprayer. These measures were denoted ILE_{EC} and CEI_{EC} for extensive crop worker's population. Lantieri et al. [10] calculated both measures for all subjects in the opening sample of terrestrial pesticide applicators of extensive crops (n=880) and using Bootstrap and Monte Carlo resampling methods, identified the most suitable theoretical stochastic distribution for each measure. In the present work, we assessed the two indexes once again but on a larger sample of applicators (n=1327) and stratifying by HEAs.

The ILE_{EC} and CEI_{EC} indexes were adapted to assess the specific exposure conditions of the population involved of farmworkers and smallholders in the green belt of Cordoba city. The methodology and definition criteria for the preliminary version of these two indexes were as described in [10]. These indexes are presented bellow (ILE_{GB} and CEI_{GB}):

$$IL\ E_{GB} = \left[(mix / load\ * \text{syst}) + \sum_{i=1}^{n} \frac{(meth_apl)}{\#\, meth} \right] * PPE1 + (wash * PPE2) + (\text{rep} * PPE3) * h\,\text{yg} * spill$$

$$CE\,I_{GB} = IL\ E_{GB} * Duration * Frequency$$

where *mix/load* represents a dichotomic response about mixing or loading pesticide; *syst* the sprayer system (open or closed); *meth_apl* the method of performing pesticide application; *PPE*1, the score of use of Personal Protective Equipment for spraying crops, as described before;

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wash is also a dichotomic variable for washing the pesticide application equipment (backpack or machine); *PPE*2, the score of use of Personal Protective Equipment, as described before, for washing the machine and/or backpack; *Rep*, whether repairing application equipment; *PPE*3, the score of use of Personal Protective Equipment for repairing equipment; *hyg* hygiene mode after completing the task with pesticides; and *spill* the behavior during a pesticide spill on clothing, thus, whether the worker changes clothes immediately after the spill or not. The cumulative exposure index incorporates the intensity level of pesticide exposure, the *duration* (years) and *frequency* of exposures (number of days of applications per year).

Tables 7 and 8 show summary statistics for both the measures, constructed for exposure assessment in first population (extensive crops). As can be seen, mean values for both indexes were generally quite different from their medians, indicating empirical distributions different from the normal distribution. Significant differences between ecological areas were found for ILE_{EC} ($p=0.013$) and CEI_{EC} ($p=0.003$). For the former, areas I and III showed the lower and similar values ($p=0.201$) for exposure index, while area V had the highest average ($p<0.01$). As an intermediate group, there was no difference between areas II and IV ($p=0.203$), and these yielded higher values than those obtained in areas I and III ($p<0.001$).

	AREAS					
	I	**II**	**III**	**IV**	**V**	**Total**
n	41	641	230	156	259	1327
Statistics	**Exposure Index distribution**					
Mean	2.04	3.02	2.37	2.76	3.59	2.92
Standard Deviation	2.14	2.36	2.29	2.19	2.57	2.40
Median	0.94	2.61	0.94	2.49	3.24	2.6
Standard Error	0.29	0.09	0.13	0.17	0.15	0.06
p25	0.61	0.86	0.72	0.84	0.89	0.82
p75	2.61	4.47	3.66	3.74	5.66	4.34
Minimum	0	0	0	0	0	0
Maximun	8.80	10.15	9.23	8.94	10.93	10.93

Table 7. Summary statistics of Exposure Index distribution based on pesticide applicators of Extensive Crops (EI_{EC}) information, regarding to Homogeneous Ecological Area Classification. Córdoba, Argentina.

	AREAS					
	I	II	III	IV	V	Total
N	41	641	230	156	259	1327
Statistics	**Cumulative Exposure Index distribution**					
Mean	23.28	44.43	42.34	62.13	59.97	48.02
Standard Deviation	56.46	67.88	66.84	78.25	86.38	72.76
Median	2.18	16.18	13.80	28.52	27.56	17.83
Standard Error	7.61	2.61	3.70	6.17	5.14	1.88
p25	0	0	0	4.31	2.58	0
p75	21.48	56.98	50.62	89.15	84.61	62.36
Minimum	0	0	0	0	0	0
Maximun	383.3	534.877	383.34	370.96	514.2	534.87

Table 8. Summary statistics of Cumulative Exposure Index distribution based on pesticide applicators of Extensive Crops (EI_{EC}) information, regarding to Homogeneous Ecological Areas Classification. Córdoba, Argentina.

For the cumulative exposure index, the differences structure between areas was slightly different. Only areas II and IV were similar (p=0.270) showing intermediate values, while areas I and V yielded lower and higher averages (p<0.001) of the cumulative exposure measure. Figure 3 (first row) presents the box plots for both indexes for the five ecological areas.

When the log of applicator age was included as a covariate, the above results held. The estimate of regression coefficient (slope) for this covariate was equal to b=-0.40 (SE 0.15) and significant (p=0.044), showing that there is an inverse ratio between the exposure index and the log of age. Since the log is a mathematical monotone (increasing) function, this coefficient indicates that the younger workers have higher exposure. In contrast, the age pattern for the cumulative exposure index indicated a direct ratio: the coefficient estimate was 0.43 (SE 0.18), which means that, as expected, that older workers have higher values of cumulative exposure. Figure 3 (second row) illustrates this behavior.

Finally, personal protection was strongly associated with the differences between the areas for both indexes (p<0.001), indicating that in ecological areas with rural workers with lower cumulative exposure, the protection feature used was ideal (Figure 4). There was no association (p=0.695) between CEI_{EC} and the marital status of subjects.

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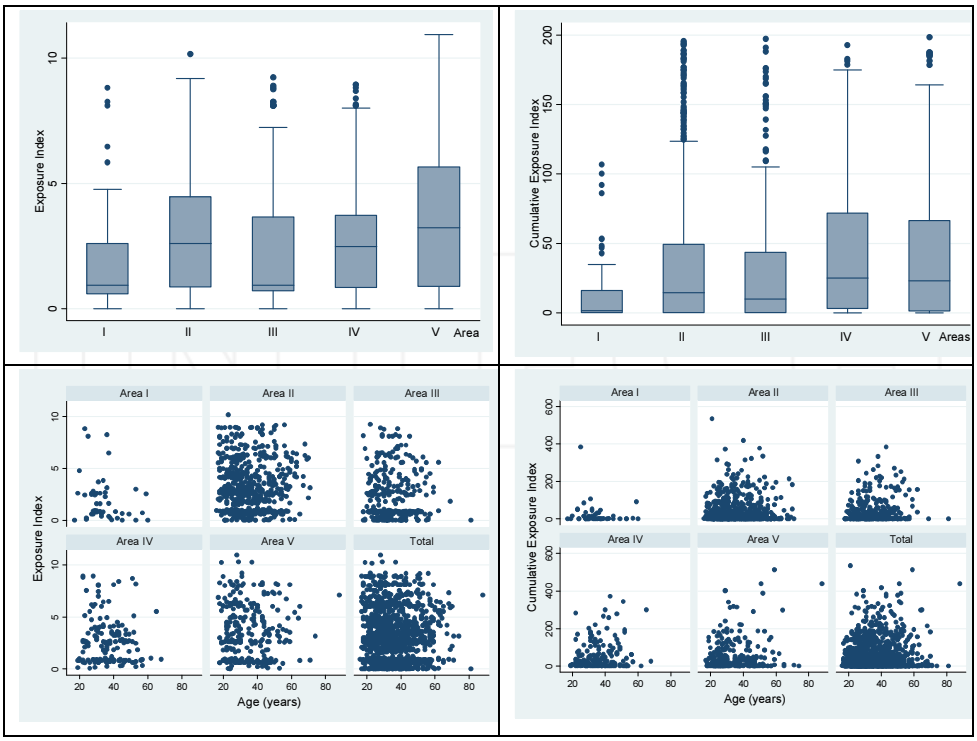

Figure 3. Box plots (above) of Exposure Index (EI_{EC}) and Cumulative Exposure Index (CEI_{EC}) and scatter plots (below) for these indexes *versus* age (years) of workers, for Ecological Areas.

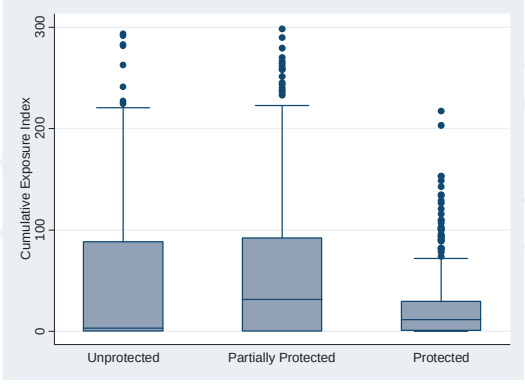

Figure 4. Box plot of Cumulative Exposure Index (CEI_{EC}) in terms of the personal protection category, Córdoba, Argentina.

3.4. Health status of workers related to pesticide exposure

a. Extensive crop pesticide applicator population.

A previous study reported a high prevalence of symptoms: 47.4% with occasional or frequent irritative symptoms, 35.5% fatigue, 40.4% headache and 27.6% anxiety or depression [1]. Increased frequency of medical consultation and hospitalization was associated with the use of chlorpyrifos ($p<0.001$ and $p=0.05$) and endosulfan ($p<0.001$ and $p=0.021$) insecticides, exposure to multiple pesticides ($p<0.001$) and seniority in the job ($p<0.001$). Only 32% of workers were adequately protected. The proper use of Personal Protective Equipment (PPE) (OR: 0.45, SE. 1.56) and marital status (OR 0.16, SE. 1.62) were protective factors for hospitalization.

Within HEAs, there was a difference between Homogeneous Ecological Areas II and III in the probability of medical consultation at least once for reasons related to occupational exposure to pesticides ($p<0.02$), with agricultural workers of HEA III having more probability of medical consultation. In the other health-related variables, no statistical differences were found.

b. Smallholders and farmworkers of the green belt population

In this sensitive population, occasional or frequent manifestation of irritative symptoms affected 49.3%, fatigue 35.6%, headache 52.6%, nervousness or depression 30.6%, dizziness 13.7% and excessive sweating 16.7%, and 18% had had an accident with pesticides. The prevalence of medical consultation and hospitalization was lower than expected: 22.2% and 4% respectively (Table 9). No statistical association was found between these two variables and exposure to specific pesticides.

Symptoms	Never / Rarely	Sometimes / Frequently	Number
Fatigue - tiredness	64.4	35.6	73
Nervousness ordepression	69.4	30.6	72
Headache	47.4	52.6	73
Irritative Symptoms	50.7	49.3	73
Dizziness or vertigo	86.3	13.7	73
Excessive sweating	83.3	16.7	72
Health assistance	**Never**	**Once or more times**	**Number**
Medical consultation	78.8	22.2	80
Hospitalization	96.0	4.0	75
Accident with pesticide			
Yes	82	18	95

[1]Percentage considering the total of responses.

Table 9. Prevalence of symptoms, health assistance and accidents related to occupational exposure among smallholders and farmworkers of the Córdoba capital city green belt. 2012

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c. Workers' risk perception of different agrochemicals

We studied the perceived threat level of pesticides used. In the extensive crop pesticide applicator population, there was a high perception of danger (85.76 - 98%) only for insecticides, with the highest perception of danger for organophosphate. Herbicides and fungicides were considered less hazardous (35.09% - 91.54% and 49.07 - 58.55% respectively). Glyphosate, the most widely used pesticide in crops (98% use in the past year), was considered hardly or not at all dangerous. The level of protection used did not vary according to the perception of risk.

Among workers and smallholders of intensive crops, the insecticide group was also seen as presenting the highest perception of risk: between 33.3% and 86% felt that they are dangerous or very dangerous, with organophosphates and organochlorines seen as the most dangerous. Fungicides and herbicides were perceived as less dangerous (29% - 38% and 33% - 65%).

4. Discussion

This work presents an interesting update of our previous work on extensive crops of Córdoba province, stratified by the Homogeneous Ecological Areas (HEAs) [10]. It also includes, for first time in our country, a characterization of the horticultural smallholder and farmworker populations of the greenbelt of the provincial capital, both settings being recognized as vastly different in pesticide exposure determinants, based on professional judgment. The analysis of each agricultural scenario enabled groups with occupational exposure to pesticides to be identified in each particular labor context (extensive and horticultural crops), as well as the health conditions associated with occupational agrochemical use.

When evaluating the pesticide applicator population of extensive crops, we founded statistically significant differences between areas in age, education, marital status, seniority in the task, average/year of hectares sprayed, use of pesticides with prescription signed by an agricultural engineer, self-propelled crop sprayer with cab and activated charcoal filter, and protection level. Only trailed crop sprayer with cab and activated charcoal filter was similar in all the areas. Self-propelled and trailed crop sprayer combined showed an average 55.5% use in all areas, which means that a large percentage of workers used unsafe machinery, i.e., sprayer with no cab or cab without activated charcoal filter, and this was an important determinant of exposure and was more pronounced in HEA II ("Middle Agricultural and Livestock Area"), followed by HEA V ("South-eastern Agricultural and Livestock Area"). HEA I ("North-western Extensive Livestock Area") was traditionally characterized by grazing cattle but it is now a newly developed agricultural region, due to the nationwide agriculturization process. This area's applicators had the highest level of personal protection and of using pesticides with written prescription, followed by HEA II. Others areas with a historical agricultural tradition, such as HEA IV ("South-eastern Agricultural Area") and HEA V, did not have similar protective measures or a safe work

environment; in fact, the highest rates of unprotected or partially protected applicators were found in these areas.

Our current results confirm previous works [10, 16] and MacFarlane's study [28] reporting no association between instruction level and personal protection. Indeed, HEA IV, with the highest percentage of applicators that had completed secondary school or higher, had only 35.3% of workers completely protected during the task. Likewise, we found no association between marital status and PPE use, as in the case of HEA IV, with the highest percentage of married or cohabiting subjects.

Based on two indexes proposed in previous work [10] for the assessment of pesticide exposure risk, the intensity and accumulated exposure indexes (ILE and CEI), the current assessment was performed in a larger sample of terrestrial pesticide applicators of extensive crops, stratifying by HEAs and showing significant differences among these for ILE_{EC} ($p=0.013$) and CEI_{EC} ($p=0.003$). The results reinforce the previous hypothesis of the emergence of different new risk scenarios in the province. As expected, HEA V yielded the highest averages for both indexes, followed by areas II and IV. It should be stressed that the differences between areas in both measures were strongly associated with the personal protection used (PPE).

As reported in a previous study, we continue to find a lack of enforcement of existing regulations (Law Nº 9164) in all the agricultural settings of the province, with low use of pesticide prescriptions signed by an agricultural engineer, and poor implementation of good agricultural practices such as triple washing of pesticide containers and their correct disposal. Burning, burying or reusing agrochemical containers, a common practice in the study populations, add other risk factors for applicators, as well as abiotic and biotic environmental contamination.

As expected, in contrast with extensive crop settings, wide differences were found in exposure determinants in the greenbelt population of Cordoba city, between their social and demographical characteristics and compared with other agricultural scenarios of the province, as shown above and in previous works [10, 16]. Horticultural workers had a greater average age, long experience in the task, lower educational level, and a high proportion of Bolivian workers and national migrants. Part of the population had unsatisfied basic needs: 23% lacked a running water supply and 13% a bathroom in the dwelling. Precarious living conditions were associated with being a "mediero" (see below), or an employee and a migrant, particularly Bolivian. It is thus a heterogeneous and highly vulnerable population, which favors lax labor structures for their work, leading to scenarios in which a higher rate of occupational health risk is to be expected. Seniority in the job was associated with higher cumulative exposure to pesticides, in turn associated with various deleterious effects on health [29].

The heterogeneity of this population is also seen in the different job roles, employment status and land tenure conditions of the smallholders and farmworkers. The agrarian structure has become dominated by family farms, giving rise to processes of social

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differentiation, concentration of land and capital, and the emergence of a new social actor: the “mediero”, a kind of sharecropper that almost monopolizes the supply of labor by having their family take part in the work. This has transformed the social organization of horticultural work and is extremely functional [30] in that the existence of "medieros” often hides the figure of an unregistered employee, with the advantage for the farmers of transferring some of the risk, while avoiding compliance with labor legislation, social security and occupational risk prevention [31]. It enables them to turn fixed labor costs into variable costs, distribute downward the fluctuations in prices and profitability that are typical of fresh vegetable production, obtain a more stable workforce, delegate responsibilities and reduce the need for control, among others.

The active participation of the family (31%), as in the greenbelt, and the short distance from the home to the cultivation sites (38% less than 100 m), as also reported by applicators in extensive crops, (almost half of them live within 500 m of the nearest crop), leads to non-occupational exposure of the worker after work and para-occupational exposure of the other family members. McCurdy et al., Chaio-Cheng et al., Clifford et al., Loewenherz et al, and Lu et al., [as cited by 32] reported studies suggesting a take-home pathway for pesticides. Applicators and farmworkers accumulate chemicals on their clothing and skin, and can carry these into their homes. The homes of agricultural workers have higher pesticide concentrations in house dust than other homes in the same agricultural community. Children living there have elevated urinary metabolites of organophosphorus pesticides. Regarding dwelling location, higher levels of pesticides were found in dust samples in farmers' dwellings and non-agricultural reference homes closer to orchards [33].

In the greenbelt, the staggered mode in which a diversity of crops are grown allows farmers to grow a large number of crops in small plots, leading to a higher frequency of pesticide application. There is thus a heavy burden of pesticides in both scenarios: in extensive crops, due to the extensive areas sprayed, and in horticultural crops, to the process of spraying throughout the year. This also implies significant environmental pollution, with approximately 47% of the product deposited in adjacent soils and waters or dispersed in the atmosphere [34], depending on climatic conditions such as rain and wind direction, geological features such as soil type and the presence of water currents, and other factors such as the formula and presentation of the product as well as the application technique. Other phenomena promoting environmental spread are photodegradation and volatilization, leaching and surface soil washing, both related to streams and rainfall [35].

Other modern phenomena aggravate the level of pollution and affect the dynamics of farming in the greenbelt. The advance of crops such as cereals and oilseeds, mainly soybeans, over horticultural production, causes the greenbelt to shift towards other neighbouring districts [36]. Moreover, the increase of housing and of informal settlements in urban residential areas, coupled with inadequate planning and land management, further reduces and displaces horticultural production [37]. This is exacerbated by industrial development: the dominant industrial area (including dangerous industrial areas), in-

creased from 8,000 ha (15.1%) to 12,000 (21%) between 2004 and 2012, while the predominantly rural area fell from 29% to 27.5% in the same period [38]. While about 40% of the area sown in the Capital Department is horticultural production [39], it is estimated that it has fallen from 11,000 hectares in 2004 [40] to an area of 5,500 hectares in 2012 [36]. Thus the greenbelt is now located in an urban area with a sum of overlapping environmental risks (caused by agriculture and pesticide pollution as well industrial pollution), making the Capital Department of Cordoba an area of high environmental risk [41].

The informality and precariousness of the situation endured by greenbelt workers is more complex than that of those in extensive crops, whose working conditions are more modern, regulated and safer. The wide diversity of greenbelt workers' tasks in contact with pesticides, the greater burden of insecticides resulting from the type of crops grown, and the application of risky technologies such as spraying with backpacks, also make this group of workers more vulnerable. The broad spectrum herbicide glyphosate, the most frequently used pesticide in this setting, is applied in the vicinity of the crops. Insecticides are also used several times during the crop cycle, as well as fungicides. The level of exposure and the likelihood of acute poisoning in these groups are thus substantially higher due to the continuous contact [34], which is for relatively short periods but is still intense and repetitive during the work day, causing toxic effects that vary depending on the type and amount of pesticide.

Work activity as a source of exposure to pesticides has been widely recognized in farm workers who mix, transport, carry, store or apply them [42]. The magnitude and severity of occupational pesticide exposure, its effects and consequences, cannot be measured exclusively by the classical indicators of mortality and morbidity. The apparent underreporting of cases of acute pesticide poisoning [43] hides the true extent of the problem in rural areas, where some authors report a deficit of up to 50% in reporting these events [44]. The adverse health effects reported in this study show a serious impact on exposed workers. The prevalence of acute and subacute symptoms reported in our study in both groups – extensive and intensive farming – with 47.4% and 49.3% irritative symptoms, 35.5% and 35.6% fatigue, 40.4% and 52.6% headache, 27.6% and 30.6% nervousness or depression, 35.6% and 22.2% rate of activity-related medical consultation, and 5.4% and 4% of hospitalization, respectively, show the high occupational exposure, and may be categorized as indirect indicators of the exposure level, unlike the recording of cases of pesticide poisoning. Argentina reported one of the highest indexes of agricultural accidents at work (94.8‰), with a mortality rate of 195 cases per million workers, only surpassed by the construction sector (229‰) [45]. The Province of Córdoba concentrates 88% of the labor sector in that area.

There are several factors involved in the occurrence of these high levels of accidents. The higher consumption of pesticides (kg/year), the toxicity and diversity of agrochemicals applied, the extent of the areas sprayed, the laxity of State monitoring, the prevailing weather conditions and, particularly, the everyday working conditions of applicators, are

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among the main variables that shape the patterns of occupational exposure to pesticides. This study provides evidence for this hypothesis and helps to analyze the risk. The association between the symptoms reported, as well as the increased hospitalizations and medical consultation among those exposed to certain insecticides, such as chlorpyrifos and endosulfan, as observed previously [46], provide evidence in this regard. Symptoms reported here, and the frequency of their occurrence, match other reports in Argentina and elsewhere showing a positive correlation between health effects and occupational exposure to pesticides [47-50].

Pesticide hazard perception can be associated with the occupational exposure risk prevention in agricultural settings. Our study found a low perception of hazard in relation to herbicides and fungicides and a higher perception to the group of insecticides in both populations, although the smallholders and farmworkers reported lower risk perceptions in all pesticide groups than terrestrial applicators of extensive crops. But it should be noted that the different risk perception reported in our study did not lead to variations in PPE. The hazard perception of insecticides may be explained by the acute toxicological data, and not by the volumes applied, the possibility of dispersal, environmental persistence and the likelihood of chronic health effects. Another explanation proposed for this behaviour is that the pesticide use in agriculture is not perceived as risky for the environment due basically to trust in the improvement of product quality, in the technological innovation that has taken place in the last few years and in the work of official agencies responsible for approving pesticides [51].

The absence of the agrochemical prescription, as well as the lack of implementation of formally regulated programs to ensure the correct end use of empty pesticide containers in both agricultural settings studied, indicate the weakness of compliance with the provincial regulations in force [24].

The results of the two subject groups present a picture of highly vulnerable populations, which must be considered in risk assessment, and in particular in the implementation of prevention strategies. Comprehensive knowledge of the study population is a priority in designing and strengthening protective measures for improving the health and safety conditions of workers and their families. The presence of highly vulnerable groups, such as women of childbearing age and children at all stages of growth, must be taken into account in assessing the problem, including approach strategies [14].

We proposed an analytical approach to assess workers' exposure to pesticides that takes advantage of existing comprehensive information about pesticide uses as well as about the main working habits of subjects, which is of relatively simple application. The information from assessing the indexes includes some observations relative to the specific local exposure scenario [10] in which the different variables that influence or determine exposure have been weighted and combined. Even though this approach does not give accurate estimates of individual exposure but rather pragmatic information on the risks faced by the workers and, consequently, of the presence or absence of a need for preventive interventions, we believe that these measures provide a valuable monitoring tool in our context.

There are some limitations to this study. Because of the complexity described in labor relations in the greenbelt, there is some selection bias in this study population due to difficulties in accessing directly exposed workers. The laxity in the employment relationship, the informality with which employment contracts are made, the uncertainty regarding operating times and the undocumented status of many of these workers [18], are some of the reasons for this, as has also been reported by other authors [52]. Secondly, information on pesticide use and on PPE, as well as some work practices, was based on self-reporting in the interview questionnaires. Thus, errors in recall and reporting may have occurred. A preliminary validation study was conducted, though only for the population of extensive crop workers (n=60), using a short version of questionnaire. Results (not shown here) indicated that the match between the volunteer farmers' questionnaire responses on both occasions was acceptable. Finally, the potential for differential exposure misclassification as reported by terrestrial applicators has been recognized in the present study by proposing the assessment of specific indexes describing the exposure. However, these measures weight, substantially, the use and the amount of pesticides applied in their usual work. Data from the National Cancer Institute studies found little evidence for differential recall of pesticides by farmers [53]. Since applicators are heavily involved in all aspects of pesticide manipulation/operation and this is practically their single occupation, they have a good memory for all the pesticides used. Further research will be carried out explore this in our populations.

5. Conclusion

The evidence presented describes a problem whose complexity is difficult to cover through the usual approaches. Exposure to pesticides in workers responsible for applying these is high. A variety of economic and socio-cultural factors affect exposure and only through a proper evaluation can its true dimension be identified and quantified. The assessment and monitoring of these populations allows us to obtain information about the risk factors associated with occupational exposure and the consequent health damage.

Recognizing the complexity of the processes underlying the vulnerability of these populations to pesticide exposure is a first step to significant change in preventive health. Adopting a comprehensive view of the different aspects of the problem will favor the reception of preventive proposals and their chances of application. The exposure reported here seriously conspires against this activity's desired goal of sustainability, creating serious health and environmental risks with costs that are underestimated in the balance of these operating models. From an economic perspective, action to reduce the risks of exposure and adverse effects of the use of pesticides and to contribute to maintaining and improving public health and the quality of life, supports economic development in all sectors of the country, especially in production. Workers and their families improve their quality of life and their family's economy and social security. Companies do not incur high costs of care for acute and chronic intoxication, disability and compensation. Employers benefit from a real decrease in absenteeism and staff turnover, and the country has a more dynamic and competitive work force. Consequently, such action is a factor that strengthens the development of the country.

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Europe's pesticide and food safety regulators

Who do they work for?

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Earth Open Source

Europe's pesticide and food safety regulators – Who do they work for?

by Claire Robinson

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Claire Robinson is a freelance researcher and writer. She works for NGOs that advocate for public health and the environment.

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Earth Open Source uses open source collaboration to engage individuals, farmers, communities, corporations, universities, and governments in programmes to achieve breakthrough advances that help nourish humanity, increase equity, support food security, and preserve the Earth.

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Summary

The European Food Safety Authority (EFSA) is charged with regulating pesticides, genetically modified (GM) foods, and food contaminants to protect public health. But some prominent EFSA regulators have conflicts of interest, holding positions in organisations that are funded by the same companies whose products they are supposed to regulate.

This report shows that over a period of many years, influential EFSA managers and regulators have been heavily involved with a US-based organisation called the International Life Sciences Institute (ILSI), which is funded by multinational pesticide, chemical, GM seed, and food companies.

Publicly funded regulators in the EFSA, as well as in US regulatory agencies, have developed a cosy relationship with ILSI. They collaborate with ILSI in workshops and conferences that work on redesigning the risk assessment processes under which ILSI member companies' products are evaluated for safety.

EFSA regulators also collaborate with ILSI affiliates in publishing papers in scientific journals. Unlike most published scientific research in the field of toxicology, ILSI papers do not report the outcomes of actual research. Instead, they propose changes to risk assessment based on the outcomes of ILSI workshops and projects, citing as their authority ILSI and other industry-generated publications.

ILSI cultivates an image of independent scientific inquiry and constructive engagement with government-funded regulators. But its proposals on risk assessment follow a trend of making safety testing procedures less rigorous and cheaper for industry – at the expense of public health and the environment.

ILSI proposals are often uncritically embraced by EFSA regulators. They make their way into influential EFSA policy Opinions and Guidances on the risk assessment of pesticides, chemicals, and GM foods. In effect, EFSA is allowing industry to help design the rules of risk assessment for its products.

The presence of ILSI and other industry-affiliated people on EFSA scientific panels, combined with evidence of industry influence on EFSA policy, fatally undermines the integrity of the pesticide and food safety regulatory process.

If public confidence in the regulatory procedures for pesticides, chemicals, and GM foods is to be restored, EFSA must cease participating in privileged access meetings and projects on risk assessment with the industry it is paid to regulate. In addition, EFSA must make a 'clean sweep' of ILSI and other industry influence from its management boards and scientific panels.

Introduction

Pesticide safety regulator Angelo Moretto has resigned from the European Food Safety Authority's Plant Protection Products and their Residues (PPR) Panel, which assesses the safety of pesticides,[1] after reportedly failing to declare a conflict of interest.

EFSA launched an investigation after it emerged that Moretto was an adviser to a consultancy company, Melete Srl. Melete was founded to support companies needing to comply with REACH, an EU regulation intended to improve the protection of health and the environment from adverse effects of chemicals.[2] Moretto owns 17% of the shares in Melete.[3]

As part of its investigation, EFSA reviewed Moretto's involvement in Opinions on pesticides issued by the PPR panel. (Opinions are written into legislation if the member states vote to approve them.) EFSA decided that as there had been no written contribution, the risk of a conflict of interest was negligible and it did not need to reopen the Opinions adopted.[4]

Judging from the only report to date on the Moretto case,[5] EFSA's investigation was inadequate. With regard to Moretto himself, it barely scratched the surface of his conflicts of interest. More importantly, EFSA has not extended its investigation beyond Moretto to address the conflicts of interest of other pesticide and food safety regulators.

Moretto is just one of several prominent EFSA officials with links to the International Life Sciences Institute (ILSI), an industry-funded group that is active in redesigning pesticide and food safety regulations in government agencies. So far, EFSA has largely overlooked the involvement of its officials in ILSI, even though ILSI represents the very industries that EFSA is charged with regulating.

This report examines Moretto's case more fully and uses it as a starting point to look at conflicts of interest of other EFSA officials. These include Alan Boobis, Milan Kováč, Diána Bánáti, and Theodorus Brock. It shows how ILSI is redesigning the regulation of toxic chemicals worldwide, making the risk assessment processes less rigorous and cheaper for industry. Finally, it considers the harmful impacts of ILSI and other industry interference in regulatory procedures.

Angelo Moretto

Moretto is involved in two projects of the International Life Sciences Institute (ILSI), an industry organisation based in Washington, DC, USA. ILSI says in response to criticism that it is not a lobby group and is a registered charity.[6] Whatever its technical description, ILSI is funded by multinational pesticide, agribusiness, and food firms, including ADM, BASF, Bayer, Cargill, DuPont, Kraft, Mars, Monsanto, and Unilever.[7] Its member companies have an interest in reducing the cost and rigour of pesticide and food safety testing – and a duty to their shareholders to do so.

ILSI has set up a body called the Health and Environmental Sciences Institute (ILSI HESI), which specializes in defining and redesigning risk assessment procedures for pesticides, chemicals, and foods. ILSI says HESI is recognized by the US government as a publicly supported non-profit organisation that is independent from ILSI. But ILSI HESI is funded by "industry members"[8] including BASF, Bayer, Dow, DuPont, Monsanto, and Syngenta.[9] [10]

Moretto has been involved in two ILSI HESI projects:[11]

- Agricultural Chemical Safety Assessment (ACSA), a public-private project in which industry and government scientists collaborated to develop "an improved approach to assessing the safety of crop protection chemicals" (pesticides).[12]
- Risk Assessment for the 21st Century (RISK21). Moretto is a member of the steering team of the RISK21 project on cumulative risk (the risk posed by multiple chemical exposures). RISK21 is directly financed by pesticide companies BASF, Bayer, Dow, DuPont, and Monsanto, as well as ExxonMobil and Coca-Cola.[13] The project brings together scientists from industry and government regulatory bodies – a private-public partnership. Industry is represented on the steering team by employees of Arysta Life Science, Dow, and Syngenta. The public side is represented by government regulators from the US Environmental Protection Agency (EPA), Health Canada, the European Commission, and Germany's BfR (Federal Institute for Risk Assessment). ILSI HESI claims that a balance is maintained between public and private interests: "Each project team has one co-chair from the public sector, and one co-chair from the private sector". But claims of balance are unconvincing when these pairings are more closely examined. The cumulative risk team consists of Moretto (the affiliation listed is his publicly funded academic position at the University of Milan, rather than his industry affiliations) and an ExxonMobil employee, Dick Phillips.[14] It could be said that this is not a 'public + private' pairing, but 'private + private'.

According to Moretto's EFSA declaration of interest, ILSI does not pay him a salary, but only reimburses expenses. However, in questions of conflicts of interest, EFSA needs to look beyond salaries. There are less direct

and less obvious ways in which a scientist seen as a 'safe pair of hands' might be rewarded by industry. Moretto's employment history includes paid consultancy roles to industry, including ILSI funders Dow and Syngenta, and three companies embroiled in pollution scandals.[15]

In January 2011, Moretto was a member of the EFSA's Pesticide Risk Assessment Peer Review (PRAPeR) Unit, responsible for the peer review of pesticides.[16] It is unclear whether he is still a member, since at the time of writing, the list of members had disappeared from EFSA's website.

Moretto has contributed to Opinions of the PPR Panel over many years. The extent of his influence cannot be evaluated by looking for written contributions, as EFSA has done. A thorough independent review of all Opinions to which he contributed should be conducted to consider whether their recommendations are in the interests of the public or of the pesticide industry.

Alan R. Boobis

Alan R. Boobis was vice-chair of the EFSA PPR Panel 2006–2009.[17] He subsequently moved to the Panel on Contaminants in the Food Chain (CONTAM).[18]

Boobis and Moretto, in their roles as PPR Panel members, contributed to an important EFSA Opinion on pesticide data requirements,[19] among many other Opinions. At the same time, Boobis was chair of the Board of Trustees and of the Executive Committee of ILSI HESI (until 2010),[20 21] and a Trustee of ILSI[22] and ILSI Europe. Since 2010 he has been a member of the board of directors at ILSI Europe.[23 24] ILSI Europe members include many food companies, among them Kraft, Nestlé, Premier Foods, and Kellogg.[25]

In his EFSA declaration of interests, Boobis listed his ILSI roles, adding that his involvement "has not involved any substance reviewed by EFSA".[26] But as a claim of 'no conflict of interest', this is irrelevant. ILSI's interests are not confined to any single substance: its member companies manufacture and promote thousands such substances. ILSI has a duty to its member companies to promote an industry-friendly climate within regulatory bodies and Boobis's activities could be said to fulfill this role.

Boobis's trusteeships at ILSI are unpaid.[27] But he is involved in at least one ILSI project for which he is paid – not by ILSI, but by its publicly funded partner, the EU. In this project on risk-benefit analysis of food and food chemicals, he carries out research funded by the EU and "coordinated by ILSI Europe".[28] This appears to be a project controlled by ILSI but funded by the taxpayer, an arrangement that is not in the public interest.

RISK21 and consultancies

Like Moretto, Boobis is involved in the ILSI RISK21 project, but he has an even more important role, as co-chair of the overall project. His affiliation is given on the ILSI website as his publicly funded academic position at Imperial College London. Following the ILSI line of 'public + private' pairings for each leadership role (see Angelo Moretto, above), the 'public' Boobis is paired with an overt representative of industry, Syngenta employee Tim Pastoor.[29]

Boobis describes the RISK21 project in his EFSA declaration of interests as a "risk assessment umbrella project with four sub-groups: dose-response, cumulative risk, exposure assessment and tiered testing strategies".[30] These are topics of crucial importance in protecting public health from the effects of chemicals. As detailed below, EFSA takes at face value ILSI's recommendations on these topics – despite the fact that they come courtesy of RISK21 funders BASF, Bayer, Dow, DuPont, ExxonMobil, Monsanto, and Syngenta.[31]

Boobis's career includes consultancy roles for the same companies whose products the EFSA paid him to regulate, including Endura, Sumitomo Chemical, and Proctor & Gamble (the last two are members of ILSI HESI[32]). He even played a role in deciding which research papers on food and chemical toxicology were published, in his former position as editor-in-chief of the scientific journal, *Food and Chemical Toxicology*.[33 34]

Diána Bánáti

In October 2010 French MEP José Bove held a press conference to announce that Diána Bánáti, chair of the EFSA management board, was also a member of the board of directors of ILSI Europe. The EFSA management board's considerable powers include setting EFSA's budget, approving the annual work programme, and appointing the members of the Scientific Committee and the Scientific Panels that give Opinions on pesticides, food safety, and genetically modified crops and foods to the EU Commission. In the wake of the scandal, Bánáti resigned from ILSI. But controversially, she kept her post at EFSA.[35 36]

Milan Kovác

Milan Kováč is another ILSI-linked member of the

EFSA management board. His positions at ILSI are:

- 2002–2011 (now): ILSI Europe – Member of the board of directors, non-industry member
- 2001–2011 (now): Member of the board of trustees of ILSI Global – Washington, USA, non-industry member from board of directors of ILSI Europe.[37]

Kováč is a member of the scientific advisory board of the European Food Information Council, an organisation that is largely funded by food companies. Members include Cargill, Cereal Partners, Coca-Cola, Danone, DSM Nutritional Products Europe Ltd., Ferrero, Kraft Foods, Mars, McDonald's, Nestlé, PepsiCo, Pfizer Animal Health, Südzucker, and Unilever.[38]

Theodorus Brock

Theodorus Brock is a member of the EFSA PPR Panel and a former member of the EFSA Working Group on Ecotoxicological Effects. He is a senior research scientist in ecotoxicology at Alterra, an institute connected to Wageningen University in the Netherlands. Alterra receives public funding from the Dutch government to carry out research to "scientifically underpin the environmental risk assessment procedure for pesticides". Brock helps design these studies. Since 1991 Brock has worked as a consultant to the chemical industry on toxicological risk assessment. His clients include Bayer, Cheminova, Dow Agrochemicals, BASF, Syngenta, Monsanto, Feinchemie Schwebda GMBH, and Makhteshim-Agan.[39]

Brock says that the funding he receives from these companies goes directly to Alterra. But this does not reassure, since Brock is an employee of Alterra.[40] In other words, the money that Brock earns in his work for the chemical industry goes to Alterra, which then pays Brock. In this context, Alterra could be seen as playing the role of a money-laundering facility.

In addition, this financial arrangement means that Brock's pesticide industry clients are funding an institute (Alterra) that helps design regulations for their pesticide products.

Since 1995 Brock has been an "active",[41] if unpaid, member of the Society of Environmental Toxicology and Chemistry (SETAC), a scientific society with extensive industry backing. He is a former president of SETAC Europe and former chair of the SETAC/EU Workshop on Linking Aquatic Exposure and Effects in the Registration Procedure of Plant Protection Products.

Brock describes SETAC in his EFSA declaration of interests as a public body. But its "partners" include chemical and petrochemical companies 3M, BP, DuPont, Eastman Chemical Company, ExxonMobil, Shell, S.C. Johnson & Son, Syngenta, and Unilever – as well as ILSI.[42]

EFSA Opinion teaches industry to bend regulations

EFSA has the reputation among some NGOs of being unduly biased towards industry. This view is supported by a 2007 PPR Panel Opinion[43] on pesticide assessment data requirements. The Opinion is examined here as an example of how pro-industry bias in pesticides regulation can endanger public health.

As then members of the PPR Panel, ILSI-affiliated regulators Boobis and Moretto were among the contributors to this Opinion. The Opinion is one of many that EFSA investigators reportedly decided was not compromised by Moretto's conflict of interest as it included no written contribution from him.[44]

Data requirements are crucial to pesticide risk assessment. They stipulate the tests that industry has to perform on a pesticide it is putting forward for approval. It is in the public's interest that these data requirements are rigorous, but industry has consistently lobbied to weaken them. Weak data requirements save industry time and money spent on testing, while allowing it to move products more quickly and cheaply to market.

The Opinion suggests ways in which industry can manipulate the toxicological data requirements of the current pesticide regulation, 91/414. These include negotiating away the need for a study, substituting a required study with another, and even submitting a "reasoned argument" about the effects of combined toxins instead of doing actual tests.

In detail, the Opinion recommends that industry should be allowed to:

- "submit a reasoned scientific argument as to why a particular study is not needed. Handling of such cases will generally be assisted by dialogue between the notifier [industry] and regulatory authority at an early stage in the approval process."[45]
- use "alternative methods" than those specified in the data requirements to address an aspect of the risk assessment[46]
- use "fewer but more informative studies"[47]
- address the problem of combined toxicity, where two or more active substances are co-formulated in

the same product", by "reasoned argument" rather than by actual tests[48]

- omit the prenatal developmental toxicity study in the rat under certain conditions[49]
- conflate one or more tests rather than doing individual tests, as a way of reducing the number of studies carried out[50]
- make certain histopathological examinations (microscopic analysis of tissue) in carcinogenicity studies optional, in the interests of "flexibility".[51]

In short, the Opinion encourages industry to negotiate away data requirements stipulated by a democratically established regulation. Taken together, these proposals follow a trend of making the data requirements less rigorous and cheaper for industry – at the expense of public health and the environment.

There is no suggestion that Moretto or Boobis were solely or even chiefly responsible for the views in this Opinion. Contributors include the entire PPR Panel.[52] The point is that the presence of industry-affiliated people on the Panel, combined with an industry-friendly result in the form of the Opinion, casts doubt on the integrity of the pesticide regulatory process.

The Opinion's proposals would add to the existing failures of the regulatory chronic toxicity testing protocol, which include:

- no testing at realistic exposure levels
- no dosing at critical developmental windows
- no testing of chemical mixtures
- kiling the animals before they have a chance to develop the disease caused by the dosing.[53]

How industry influences EFSA regulators

While the 2007 PPR Panel Opinion shows EFSA's pro-industry bias, it also shows how industry influences EFSA policies on pesticides.

The PPR Panel suggests that industry could jettison the 1-year dog study and the mouse carcinogenicity study that form part of the data requirements for pesticides assessment under current law. EFSA says the mouse carcinogenicity study "does not provide any additional contribution to risk assessment" on top of the same study done on a second rodent species, usually the rat.[54]

The PPR Panel cites as its authority for this argument a 2006 paper by ILSI HESI task force leader and then Syngenta employee, John E. Doe.[55] Moretto and Boobis are co-authors of this paper. Doe, like Moretto and Boobis, is involved in the ILSI HESI RISK21 project, as the industry representative of one of the teams working on risk assessment. He is paired with Doug Wolf of the US EPA.[56] EFSA does not mention ILSI's industry backing in its favourable citation.[57]

In his paper, Doe published the recommendations of an ILSI HESI task force he headed on toxicity testing for pesticide regulatory assessment.[58]

Doe's task force on pesticide regulatory assessment was one of several set up by ILSI HESI under its Agricultural Chemical Safety Assessment (ACSA) project. ACSA, like other ILSI projects, was a public-private project in which industry and government scientists collaborated to develop "an improved approach to assessing the safety of crop protection chemicals" – in other words, to redesign pesticide risk assessment.[59] [60] The Doe paper was published as part of this project.[61] Three 'sister' papers were also published in scientific journals in 2006 by other ILSI HESI task forces. All four papers were co-authored by ILSI and other industry scientists together with scientists from government regulatory bodies in the US and Europe. All proposed detailed changes in the way pesticides are tested for safety.[62] [63] [64]

Doe's co-authors on his toxicity testing paper include employees of Syngenta, Bayer, Monsanto, DuPont, and BASF, as well as affiliates of ILSI. The public sector is represented by employees of the European Commission and the US Environmental Protection Agency (EPA).[65]

Origins of the mouse carcinogenicity study argument

Doe gives as a source for his recommendation to jettison the mouse carcinogenicity study a paper on pharmaceuticals regulation by Van Oosterhout (1997). The paper was published in the controversial chemical/pharmaceutical industry-sponsored journal *Regulatory Toxicology and Pharmacology* (RTP). RTP was one of several industry-linked outfits that were investigated by a US Congressional Committee in 2008 over their role in the Food and Drug Administration (FDA) decision allowing the toxic chemical bisphenol A in infant formula and other foods.[66] [67] [68]

Van Oosterhout says in his study that regulators never act on mouse tumour findings, so there is no point in industry doing the test.[69]

Doe also cites another paper on pharmaceuticals regulation by Monro (1993), which concludes that tumours in mice are irrelevant to human risk assessment and that the mouse carcinogenicity test should be abandoned. But Monro's study was sponsored by the pharmaceutical company Pfizer.[70]

Industry links apart, there may be good scientific reasons to jettison the mouse carcinogenicity study. Van Oosterhout argues that mice are less sensitive than rats in carcinogenicity studies and add little to the data.[71] And given the age of the mouse carcinogenicity study, it is possible that independent toxicologists could come up with more sensitive, up-to-date, and relevant testing methodologies.

But both EFSA and the industry-affiliated authors it cites only seem interested in one half of the equation – throwing out the mouse study and, at best, having other tests stand in for it. They do not mention the other half – putting forward a more rigorous alternative. Both EFSA and industry put forward the animal welfare argument that getting rid of the mouse study would reduce the number of animals used in pesticide testing.[72] But the public may well conclude that another factor briefly mentioned by both parties – saving "resources" (money) – is the driving force.[73] [74]

Interestingly, neither EFSA nor industry mentions studies by independent scientists that argue for the specific usefulness of mice in research on cancer causes and treatments.[75] [76]

As well as throwing out the mouse carcinogenicity study, EFSA also recommends getting rid of the important multi-generation reproduction study, which is designed to find out if exposing animals to a pesticide affects their offspring. EFSA wants to substitute a less rigorous "extended one-generation study".[77] Again, EFSA cites ILSI HESI as its authority, as well as a paper by Cooper,[78] the leader of an ILSI HESI task force.[79]

What is needed is an open and transparent debate among independent scientists (who would be paid from public funds to do the job) regarding the best and most sensitive methods of testing for a required endpoint. What is unacceptable is for EFSA to argue for jettisoning studies in lockstep with industry interests.

ILSI's latest recommendations for redesigning risk assessment

ILSI-affiliated authors are prolific, generating a large number of published scientific papers each year. But unlike most published papers in the field of toxicology, ILSI-generated papers do not report actual laboratory research findings. Instead, they report the outcomes of ILSI workshops. These workshops invariably recommend changes to risk assessment procedures, citing as their authority other ILSI workshops and papers.

Below is an analysis of the recommendations of just two of these papers, selected at random, giving the ILSI and other corporate affiliations of some of the authors.

McGregor, D., A. Boobis, et al. 2010. Guidance for the classification of carcinogens under the Globally Harmonised System of Classification and Labelling of Chemicals (GHS). Crit Rev Toxicol 40(3): 245-285.

This paper recommends:

- Classifying carcinogens under the Globally Harmonised System of Classification and Labelling of Chemicals (GHS). Industry likes harmonization of chemicals risk assessments across the globe because it saves money and resources in testing. This is not dangerous in itself, but the paper uses the system to 'level down' the carcinogenicity risk assessment of one chemical by cherry-picking the most reassuring evaluation of its safety (the EU's), dismissing another evaluation (Japan's) that views it as more risky.
- Adopting carcinogenicity risk assessment methods developed by ILSI.
- Identifying the mode of action (MOA), the biochemical process by which an adverse effect is created. This is a dangerous distraction, as for many known toxic chemicals, the mode of action is still unknown. For example, it is known that the widely banned pesticide DDT causes eggshell thinning and decreased numbers of birds of prey and that it works by endocrine disruption, but the mechanism of action is still debated. It can take decades to find out a chemical's MOA. Delaying regulatory action on a chemical until a MOA is known suits industry but puts public health at risk. It is not yet clear that ILSI intends to insist on delaying action until an MOA is identified, but this is a likely outcome of its preoccupation. In addition, the emphasis on MOA gives industry room to negotiate away cumulative effects on the grounds that the different chemicals have different MOAs. This argument has already crept into EFSA views on risk assessment.[80] Its danger is that it ignores interaction between different MOAs and the problem of cumulative stress from chemicals with different MOAs.
- Establishing whether a MOA is relevant to humans. This gives industry and its allies the chance to dismiss worrying findings on the claimed grounds that they are not relevant to humans – as in the case of the German ministry BVL's response to Professor Andrés Carrasco's findings that glyphosate causes malformations in frog and chicken embryos.[81] [82] Industry also uses this argument to dismiss mouse carcinogenicity findings, as detailed above.[83]

McGregor's co-authors include current and former

representatives of ILSI (Boobis among them), petrochemical companies BP and ExxonMobil, chemical companies Solvay and Syngenta, chemical products company S.C. Johnson, and pharmaceutical company Nycomed.

Carmichael, N., M. Bausen, et al. 2011. Using mode of action information to improve regulatory decision-making: An ECETOC/ILSI RF/HESI workshop overview. Critical Reviews in Toxicology 41(3): 175–186.

This paper recommends "broader uptake and use of the MOA concept", citing ILSI workshops as its authority. The benefits to industry are made clear: "Setting up a repository of accepted MOAs and associated guidance concerning appropriate data to support specific MOAs for critical effects would facilitate categorization of chemicals and allow predictions of toxicity outcomes by read-across." This will lead to the industry-friendly outcome of "reduction of toxicity testing in animals" – saving industry time and money.

Favouring "read-across" predictions of toxicity over actual toxicological testing is potentially dangerous and operates against the public interest. In addition, Carmichael's paper, like McGregor's, puts forward MOA as a way of questioning the relevance of toxicological findings to humans.[84]

Carmichael is a former ILSI ACSA task force leader[85] and Bayer employee.[86] Co-authors of his paper include ILSI's Michelle Embry; former ILSI ACSA task force leader and former Syngenta employee John Doe; and employees of Syngenta, BASF, and AstraZeneca.[87]

It remains to be seen to what extent these and other ILSI recommendations will make their way into EFSA's regulatory policies. However, it is clear that through ILSI, industry is making strenuous efforts to influence EFSA policy.

ILSI database for regulators

As another tool in its 'redesigning risk assessment' box, ILSI is setting up a "Developmental Toxicity Database" for the use of "public health researchers and regulators".[88] While it may be tempting to assume that this is an act of charity on ILSI's part to help hard-pressed regulators, it should be seen in the context of ILSI's parallel development of the Crop Composition Database to assist regulators of genetically modified crops (see How ILSI designed EFSA's GM crop risk assessment process, below). Clearly, this initiative represents an industry attempt to define and control the risk assessment of developmental toxins by controlling the information that is put into the process.

EFSA praises ILSI proposals for redesigning pesticides regulation

There is no suggestion that EFSA tries to hide ILSI's industry links. On the contrary, the EFSA PPR Panel uses its Opinion to proudly promote ILSI HESI's "proposals for radical changes to data requirements" of pesticides regulation.[89] Equally, it sees nothing wrong with citing in support of these proposals the four ILSI sister papers[90] by ILSI HESI task force leaders Doe, Carmichael (an employee of Bayer[91]), Barton (US EPA[92]), and Cooper (US EPA[93]).

The PPR Panel praises ILSI's proposals as "emerging developments in scientific understanding" and examples of "the way in which scientific understanding on risk assessment for plant protection products is currently evolving".[94]

It would be more accurate to substitute for "evolving" the words, "being directed by industry", as these developments appear to have little to do with an emerging independent scientific consensus or with public health protection – but everything to do with industry's needs.

This Opinion is not unusual in its enthusiasm for ILSI proposals. Another PPR Panel Opinion, this time on assessment of cumulative and synergistic risks of pesticides, cites ILSI as its authority for the reassuring conclusion that pyrethroid pesticides are unlikely to have a synergistic toxic effect at low levels of exposure.[95]

Regulators at the EFSA and the World Health Organisation even held a conference supported by ILSI Europe in 2005 on risk assessment of genotoxic (damaging to DNA) and carcinogenic (cancer-causing) substances.[96] The following year, in 2006, EFSA held a colloquium on cumulative risk assessment of pesticides to human health – and cited in its summary report ILSI's "Useful frameworks and guidances … for determining mode of action". Attending the colloquium were ILSI affiliates Alan Boobis and Andras Szoradi, along with employees of Syngenta and Bayer. Another participant was a representative from Exponent,[97] a company that, according to one investigative report, "is known for its scientific research on behalf of corporate clients facing product liability concerns."[98] Notably absent were any representatives from NGOs or the general public.

The fact that EFSA sees its alliance with industry as normal and even desirable is a sign of how far Europe's pesticide regulation has shifted from its rightful alignment with the public interest.

ILSI collaborations with regulators condemned

ILSI's involvement with regulators in Europe, the US, and internationally has come under heavy criticism from independent scientists and NGOs.

2006: ILSI barred by WHO from setting standards on food and water

In January 2006 the World Health Organisation (WHO) decided that ILSI can no longer take part in WHO activities setting microbiological or chemical standards for food and water because of its funding sources. ILSI's status was downgraded following a letter to the WHO from the Natural Resources Defense Council, Environmental Working Group, United Steelworkers of America, and other groups, protesting against its role in setting standards.

Jennifer Sass, senior scientist at the US's National Resources Defense Council, wrote in the letter on behalf of the groups that ILSI "has a demonstrated history of putting the interests of its exclusively corporate membership ahead of science and health concerns… ILSI's special status with the WHO provides a back door to influence WHO activities."[99]

2007: US EPA scientifically weakened by partnership with ILSI

In 2007, Jennifer Sass of the National Resources Defense Council testified before a Congressional Committee that due to budget cuts, the US Environmental Protection Agency (EPA) was "spiralling into an increasingly weak scientific state" and was "increasingly reliant on data supplied by the very industries that it regulates". Sass's chief example of "a relationship that has demonstrably compromised the quality of EPA's scientific inquiry" was EPA's relationship with ILSI. Sass said that such partnerships had developed into little more than opportunities for the regulated industry to redesign EPA's scientific analysis and risk assessment.[100]

2010: US scientists condemn regulators' links with ILSI and RISK21

In 2010, the participation of US government regulators in an ILSI RISK21 workshop was condemned by the Natural Resources Defense Council and the Environmental Defense Fund. In a letter to scientific advisor to the US EPA Paul Anastas, Jennifer Sass of the NRDC wrote, "Because this is a meeting fully funded by industry and comprised largely of industry scientists on scientific topics for which the industry has a financial stake in the outcome, having regulators participate and even co-lead meeting planning and the meeting discussions is an obvious conflict and misuse of our publicly-funded scientists."

Sass noted that ILSI was one of a few "corporate-membership groups" which "have relied upon similar industry-driven workshops in which government officials have participated, and in some cases which government has financially supported, to challenge chemical regulations; to share their anti-regulatory views; and to give workshop outcomes – in line with their interests – a veneer of credibility and independence."

Sass said that industry has a right to hold its own meetings to discuss risk assessment but that public funds should not be used to send government regulators to such meetings. Also, regulators should not meet with industry in a forum unless the process is public and all stakeholders, including NGOs, are involved.[101]

2011: WHO collaborates once more with ILSI

In February 2011 in Paris, ILSI HESI held a workshop with the World Health Organisation (WHO) on the risk assessment of chemical mixtures. Pesticide Action Network (PAN) Europe wrote to the director of WHO, Dr Margaret Chan, protesting against the collaboration. Hans Muilerman of PAN Europe wrote: "The topic is right but the cooperation with ILSI HESI is very wrong… there is no reason to distinguish [ILSI HESI] from any other industry lobby club… Allowing ILSI HESI a cooperation with WHO/OECD is a grave mistake. It allows influence of industry in developing public risk assessment methodologies, which is unfair and simply wrong. Either you have a stakeholder meeting with a balanced representation of all powers, or you have a meeting of independent regulators."[102]

How ILSI designed EFSA's GM crop risk assessment process

ILSI has been influential in designing EFSA's risk assessment process for genetically engineered (GM) crops. This was highlighted by a report by the NGO TestBiotech,[103] which revealed close links between ILSI and the EFSA's GMO Panel.

Harry Kuiper, chair of the EFSA GMO Panel, has been a leading scientist at ILSI since 2003. Just before he joined the EFSA, he worked for an ILSI task force. A Monsanto employee, Kevin Glenn, heads this task force and all other members are representatives from large biotech corporations (Cargill, Monsanto, Renessen, Dupont/Pioneer, Bayer CropSciences, Syngenta, and Dow AgroSciences). Even after starting work at EFSA, Kuiper has remained active in ILSI. Other EFSA GMO Panel members have also worked for the ILSI task force.

TestBiotech says the collaboration between ILSI and the GMO Panel experts has had a marked effect on EFSA guidelines for the risk assessment of GM crops. A concept developed by ILSI, "comparative assessment",[104] was implemented as a starting point for EFSA's risk assessment.[105] Under comparative assessment, if no significant differences are found in the comparison of certain basic components, such as carbohydrates and protein, then the GM crop is said to be as safe as its non-GM counterpart and no further in-depth investigations of its safety, such as rigorous animal feeding trials, are required.

TestBiotech shows that the document published by EFSA to explain why animal feeding trials are not necessary was partly plagiarized from an ILSI paper.[106] [107] [108]

To help regulators follow its prescribed system of risk assessment for GM crops, ILSI set up the Crop Composition Database, a databank of industry tests that compare the composition of GM plants with those of plants derived from conventional breeding. ILSI presents this database as "an essential part of the safety assessment of new crop varieties" and as a "useful resource" for "regulatory scientists" in the field of GM crops.[109]

ILSI's term "comparative assessment" is a flagrant renaming of the widely discredited concept of "substantial equivalence," developed in the early 1990s by the Organization for Economic Cooperation and Development (OECD). Substantial equivalence has been much criticized by independent scientists as scientifically inadequate.[110] "Comparative assessment" avoids using the same controversial terminology but has the same meaning, as ILSI itself states in a 2004 paper:

> This comparative assessment process (also referred to as the concept of substantial equivalence) is a method of identifying similarities and differences between the newly developed food or feed crop and a conventional counterpart that has a history of safe use.[111]

The problem with the comparative assessment approach from the public health point of view is that you only find what you are looking for. Unexpected changes that occur in the plant as a result of the GM process will be missed. Such unexpected effects could be revealed by rigorous nutritional and toxicological testing on animals. But it appears that industry's aim was to encourage EFSA to set a policy that accepts a finding of no significant difference in the comparative assessment as justification for avoiding doing such rigorous testing.

Due to ILSI's influence, GM crops are less rigorously investigated than they would have been if EFSA had not based much of its safety assessment on the concept of "comparative assessment". EFSA must require GM companies to acknowledge the established scientific fact that GM and conventionally bred crops are different and that in-depth toxicological and nutritional studies, not superficial comparisons, are necessary.

ILSI has also taken control of the environmental risk assessment for GM crops. It has set up a body called the Center for Environmental Risk Assessment (CERA) to "develop and apply sound science to the environmental risk assessment of agricultural biotechnologies". CERA has its own "GM Crop Database" which claims to give environmental safety information about GM crops.[112]

ILSI's projects and databases on GM crops are direct parallels to its 'redesigning risk assessment' projects and Developmental Toxicity Database on chemicals.

Dangers of industry involvement in regulation of hazardous products

Some may argue that there is no danger in allowing industry to involve itself in the regulatory procedure because it is a rigorous scientific process that cannot be manipulated. But this would be naive in the extreme. Bias can creep into scientific inquiry in many ways, from the initial decisions of which question to ask and which endpoint to look for, to selection of methodology, choice of experimental animal and exposure route, length of study, and other factors.

The tendency to bias in industry-sponsored studies on risky products and technologies is well documented. The best known example is tobacco industry studies, which successfully delayed regulation for decades by manufacturing doubt and controversy about the effects of smoking and

passive smoking.[113] More recently, studies sponsored by the pharmaceutical and mobile phone industry have been shown to be more likely to portray their products in a favourable light than non-industry-funded studies.[114 115 116]

Fewer comparisons of industry vs. independent studies have been performed for chemicals (including pesticides), but in four such reviews the same relationship is found: industry sponsorship is more likely to find favourable results, while the independent literature finds both safety and risk.[117 118 119 120]

As the IBT fraud in the 1970s–1980s (which brought into question 15% of all pesticides in the US) and the Craven Labs fraud in the 1990s showed, industry tests can be biased. This is true whether or not they use Good Laboratory Practice (GLP), a set of rules instituted by regulators to try to combat industry fraud. GLP, in spite of frequent claims by industry and regulators, is a management tool and not a guarantee of 'good science'. But because regulatory agencies worldwide require GLP, only industry's GLP-compliant toxicity data is ever used in risk assessments – excluding more rigorous and up-to-date independent science.[121 122]

There are examples of industry pressure, fraud, and bias in pesticides approvals processes worldwide:

- In 2006 in the US, union leaders representing thousands of scientists and risk managers with the US Environmental Protection Agency (EPA) sent a letter to EPA Administrator Stephen Johnson objecting to imminent agency approval for more than 20 neurotoxic pesticides, which they said violated the precautionary principle mandated by the Food Quality Protection Act. In their letter, the union leaders warned Johnson about political pressure from industry to allow high tolerances of these pesticides.[123]
- During the public consultation on the proposed release of Bt brinjal (aubergine) in 2010 in India, the former managing director of Monsanto India, Tiruvadi Jagadisan, said that Monsanto broke regulatory rules and "used to fake scientific data" submitted to government regulatory agencies to get approval for its herbicides in India.[124]
- In December 2010, a leaked memo[125] revealed that the US EPA was aware that the neonicotinoid pesticide clothianidin poses risks to honeybees, yet it allowed Bayer to use the pesticide on corn, wheat and other staple food products.[126] In the face of similar regulatory inaction by the EU authorities, some member states have brought in their own bans and restrictions.[127]

Case study in industry bias and regulatory failure: bisphenol A

Pro-industry bias in regulatory procedures is exemplified by the case of the chemical bisphenol A (BPA), a plastics ingredient widely used in food packaging.

Hundreds of peer reviewed published studies show significant effects of BPA at low doses, with over 30 showing significant effects below the predicted "safe" dose. The evidence that BPA poses a danger to public health is strong. It has been found in human blood and tissues, including in human foetal blood, at levels higher than those causing adverse effects in mice. An epidemiological study shows that that BPA is related to ovarian disease in women.[128]

But industry studies on BPA have reached diametrically opposite conclusions. While 94 of 104 (90%) of government-funded published studies on bisphenol A reported significant effects at low doses, no industry-funded studies (0 of 11) report significant effects at the same doses. A 2005 review of studies on BPA found that source of funding is highly correlated with positive or negative findings.[129]

A 2009 review authored by 30 scientists blamed regulatory fixation on Good Laboratory Practice (GLP) for the BPA débacle. The scientists criticized the US FDA and the EFSA for deeming two industry-funded studies that adhered to GLP to be superior to hundreds of independent non-GLP studies funded by the US National Institutes of Health and similar agencies in other countries.[130]

The authors pointed out that there is simply no data from GLP studies on many of the toxic effects observed in independent studies on BPA, such as some adverse effects on the female reproductive system. This is because those effects have not yet made their way into the outdated regulatory testing system. In other words, the reason the effects are not found in GLP studies is not because the chemical is safe, but because those effects are not looked for. The authors added that there is a large literature on neurotoxic effects and behavioral abnormalities caused by low doses of BPA which are not capable of being detected by current GLP studies conducted for regulatory purposes because of their outdated methodologies.[131]

The authors argued that the chemical industry-sponsored GLP studies on which the agencies based their decisions are incapable of detecting low-dose endocrine-disrupting effects of BPA and other

hormonally active chemicals. They stated that the FDA and EFSA "mistakenly assumed that GLP yields valid and reliable scientific findings (i.e., 'good science')."

The authors stated that the main factors determining the reliability of scientific findings are independent replication and use of the most sensitive and up-to-date tests – neither of which is an expectation of GLP. They concluded, "We are not suggesting that GLP should be abandoned as a requirement for industry-funded studies. We object, however, to regulatory agencies implying that GLP indicates that industry-funded GLP research is somehow superior to NIH-funded studies that are not conducted using GLP."[132]

EFSA continues to rely for its risk assessment of BPA on the few industry studies adhering to GLP guidelines that found no adverse effects. Based on these studies, EFSA refuses to take decisive action restricting its use.[133] [134] The EU Commission announced in November 2010 that it would ban BPA from babies' bottles but would not extend the ban to materials such as the linings of food and drinks cans as there was no scientific evidence to support such a move.[135] [136]

The regulatory prejudice against open scientific literature and in favour of industry OECD- and GLP-standardized studies has forced the public to live with many more years of exposure to potentially dangerous levels of BPA.

Conclusions and recommendations

The independence of EFSA's risk assessment processes on pesticides and food safety has been seriously compromised by its close involvement with industry, chiefly represented by ILSI.

EFSA must make a 'clean sweep' of ILSI- and other industry-affiliated people from its boards and Panels. It should reform its conflicts of interest rules to exclude people with unpaid as well as paid roles in industry organisations.

EFSA Opinions and Guidances issued during the tenure of ILSI-connected people on the PPR, CONTAM, and GMO Panels must be reviewed for pro-industry bias by independent experts on toxicology and public health, as well as representatives of the general public. The independent experts and public representatives must be paid solely from public funds to do this work – a doubling-up of expense made necessary by EFSA's failure to ensure its independence.

It is not enough to identify specific written contributions to Opinions and Guidances by individual panel members, as EFSA did regarding Moretto. The reviewers should consider whether the recommendations in EFSA Opinions and Guidances are in the best interests of public health and the environment – or in the best interests of industry. Until this process is complete, the recommendations of EFSA Opinions and Guidances should not be adopted as EU regulations. Those that have already been adopted must be re-examined.

EFSA should ban its scientific panel members from working for industry while they are employed to work for the public and should pay them well enough to ensure that they do not need to seek industry funds. Also, rules should be implemented to banish the 'revolving door' syndrome, whereby someone passes straight from a job with industry to EFSA.

EFSA should not be taken in by industry-generated claims that suitable scientific expertise is only to be found in the industry sector and that industry interests are unavoidable. EFSA should recruit its scientific advisers from the ranks of toxicologists, ecotoxicologists, and public health experts in the public sector who have not received relevant industry funding.

Further, EFSA should favour scientists who are actively doing research in toxicology, embryology, epidemiology, ecology, and other fields directly relevant to public health and the environment. Many of these people are engaged in far more advanced and relevant scientific work than that practised by industry toxicologists, who still use the same outdated and insensitive methods developed almost a hundred years ago by the pharmaceutical industry.[137] [138] [139] Care should be taken to exclude people who seldom see the inside of a laboratory but who specialize in helping industry get its products onto the market and keep them there.

Industry is entitled to hold its own meetings, as is EFSA. But it is not acceptable for EFSA regulators to collaborate with industry people in forums and projects that exclude other stakeholders, such as the public and NGOs. EFSA could hold multi-stakeholder meetings that are open to public representatives, NGOs, and industry. This would ensure that the discourse between EFSA and all stakeholders, including industry, is transparent.

Until these measures are implemented, the public cannot have confidence in EFSA's regulatory processes.

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Herbicide tolerance and GM crops

Why the world should be Ready to Round Up glyphosate

EXECUTIVE SUMMARY & REPORT

June 2011

GM FREEZE
the campaign on GM food, crops and patents

GREENPEACE

Canada, 2007: Greenpeace activists created a 60 metre-wide question mark in a cropfield containing Monsanto's genetically engineered corn.

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Herbicide tolerance and GM crops

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Executive Summary

Glyphosate is the active ingredient in many herbicides sold throughout the world, including the well-known formulation, Roundup. Glyphosate-based herbicides are used widely for weed control because they are non-selective; glyphosate kills all vegetation.

Glyphosate has been promoted as 'safe'. However, mounting scientific evidence questions the safety of glyphosate and its most well known formulation, Roundup. **The evidence detailed in this report demonstrates that glyphosate-based products can have adverse impacts on human and animal health, and that a review of their safety for human and animal health is urgently needed.**

The widespread and increasingly intensive use of glyphosate in association with the use of GM (genetically modified, also called genetically engineered or GE) crops poses further risks to the environment and human health. GM crops specifically engineered to be tolerant to glyphosate are known as 'Roundup Ready' (RR). These RR varieties allow farmers to spray the herbicide over the top of the growing crop, killing virtually all weeds without affecting the crop. The use of glyphosate on GM RR crops such as soy, maize and cotton has increased dramatically in North and South America, where they are predominantly grown.

GM RR crops are marketed by the US agrochemical giant Monsanto, and are associated with its own formulation of glyphosate herbicide, Roundup. Monsanto's sales pitch to farmers promised, and still does, reduced labour and financial savings by simplifying and reducing the costs of weed control. The reality is turning out to be different, with increasing health, biodiversity and environmental concerns and the development of weed resistance.

Given the problems that are now evident, no new GM glyphosate-tolerant crops should be authorised. In broader terms, GM herbicide-tolerant crops have been developed for an industrial farming model. They are therefore intrinsically linked to unsustainable farming practices that damage the basic natural resources food production is based upon, and their cultivation should be banned.

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Glyphosate is present in soils, waters and our food as a result of its widespread use with GM Roundup Ready crops.

Exposure to glyphosate

People, plants and animals can be exposed to glyphosate and Roundup in many ways. Farmers, bystanders and other operators can be exposed during its application, and neighbouring natural habitats by drift from the area where it is being applied. Aerial application is used on some crops, such as on the vast monoculture plantations of GM RR soya in the Americas, which greatly increases the chances of accidental exposure of neighbouring populations or habitats.

Exposure to glyphosate and Roundup also occurs via their residues, frequently found in food and the environment. The Maximum Residue Levels (MRLs) in food for glyphosate and its breakdown product were agreed by the UN-based Codex Alimentarius Commission in 2006, but appear to be related more to the type of agricultural practices characteristic of each food crop rather than to safety thresholds for human health.

In light of the new scientific evidence on the health and environmental impacts of glyphosate it is essential to re-evaluate MRLs in order to align them with updated safety assessments.

In the environment, glyphosate can be held in the soil by binding to particles but, depending on soil chemistry, can also leach into groundwater. Glyphosate can also wash directly into drains and surface waters and it has been detected in both. Glyphosate and its degradation product have been detected in studies of drainage surface waters in Canada, the US and Denmark. These finding have implications for surface water quality and drinking water quality. Given the evidence that glyphosate can cause harm to health and the environment, the leaching of glyphosate has also serious implications for aquatic life.

Glyphosate is present in soils, waters and our food as a result of its use as a herbicide. Therefore, rigorous assessment of the safety of glyphosate to plant, humans and animals is of great importance.

Human health problems related to glyphosate

Independent scientific studies are underscoring the call for an urgent reassessment of glyphosate and its related products. These studies associate exposure to glyphosate with a number of negative effects on human and animal health, including long term or chronic effects:

- **Birth defects in the Argentinean state of Chaco**, where GM soya and rice crops are heavily sprayed with glyphosate, increased nearly fourfold over the years 2000 to 2009. Similar defects were also found in women from Paraguay exposed to glyphosate-based herbicides during pregnancy. These defects were compatible with those induced in laboratory experiments at much lower concentrations than normal commercial glyphosate concentrations.
- **Glyphosate is a suspected endocrine disruptor**. This means it could disrupt production of vital reproductive hormones, such as progesterone and oestrogen. Published studies demonstrate various endocrine effects in animals and human cells associated with glyphosate.
- Studies of illness patterns in human populations (epidemiological studies) have linked glyphosate exposure to **non-Hodgkin's lymphoma** (a type of blood cancer) whilst laboratory studies have confirmed that glyphosate and/or its associated products exhibit characteristics typical of cancer causing agents (i.e. genotoxicity or mutagenicity) in both humans and animals. Together, these studies suggest that glyphosate may contribute to cancer. Evidence that glyphosate **may also affect the nervous system** and may even be implicated in Parkinson's disease.

Scientific evidence highlighting these health effects must be taken very seriously. An urgent reassessment of the health impacts of glyphosate and its related products must take place.

Executive Summary (cont.)

Glyphosate affects biodiversity

Glyphosate can impact on biodiversity in a number of different ways and can have short and long term, as well as direct and indirect negative effects. Evidence is accumulating that glyphosate can have a damaging impact on aquatic organisms as a result of its normal use in agriculture or forestry. Several studies have suggested that, under close-to-field conditions, glyphosate-based products, including Roundup, have a direct toxic effect on the adults and tadpoles of a range of amphibian species. Despite these findings, Monsanto still claims that Roundup has '*no adverse effect on aquatic animals*' (Monsanto 2010a).

Many aquatic animals - from microscopic algae to fish and mussels - have been found to be affected by exposure to glyphosate and/or Roundup. The observed effects included: shorter life spans and reduced reproductive rates in rotifers (a type of freshwater invertebrate); changes in population structure in phyto- (or plant-) plankton; increased mortality in aquatic worms; and changes in liver cells in carp. A recent study found genotoxic effects in the red blood cells of European eels when exposed to Roundup for a short period. There is also a suggestion that glyphosate may affect the nervous system of aquatic animals in a manner similar to an organophosphate.

Glyphosate can also have a direct impact on non-target plants in the environments where it is used through spray drift or deliberate over spraying. This could lead to the loss of rare or endangered species or an overall reduction in diversity and numbers. Research carried out in the UK on the use of glyphosate on GM RR beet showed significant indirect effects of this form of weed control. These included reduced weed numbers in arable fields and reduced weed seed production both of which are potentially deleterious to species further up the food chain, including threatened bird species, if repeated over a number of years.

'…If GM herbicide-tolerant beet were to be grown and managed as in the FSEs [UK Farm Scale Evaluations 2000- 2003] this would result in adverse effects on arable weed populations, as defined and assessed by criteria specified in Directive 2001/18/EC, compared with conventionally managed beet. The effects on arable weeds would be likely to result in adverse effects on organisms at higher trophic levels (e.g. farmland birds), compared with conventionally managed beet'
(ACRE 2004)

It is apparent that glyphosate and its formulated commercial products (e.g. Roundup) can be harmful to species at many stages along the food chain, including the aquatic food chain. Regulators must ensure that usage of herbicides is safe for wildlife when it is used for purposes it has been approved for. Therefore, the safety of glyphosate to biodiversity urgently needs to be re-assessed.

Glyphosate impacts on the soil-plant system

The impact of glyphosate on soil biodiversity and the soil-plant system is of concern because of the effects observed with GM RR crops. Glyphosate enters the soil by being directly sprayed on it, via the roots of plants that have been sprayed, or from dead vegetation. Importantly, glyphosate affects the rhizosphere – the region of the soil surrounding the roots that is essential to the health and nutrient uptake of the plant. Surprisingly, the approvals processes for glyphosate and its formulated products around the world, including the EU, currently do not require exhaustive testing of its soil impacts.

Studies of earthworms exposed to glyphosate showed reduced growth rate, reduced cocoon hatching and behaviour to avoid treated areas. Earthworms are vital to soil health so any adverse effect on them is likely to affect soil health.

Independent researchers are now publishing studies showing that glyphosate has an impact on key functions of the rhizosphere. These include:

- Reduction in the uptake of essential micronutrients by crops
- Reduction in nitrogen fixation, resulting in reduced yields
- Increased vulnerability to plant diseases

Such changes can have a direct impact on the health and performance of crops. Plant diseases - such as take-all in cereals, damping off, root rot and sudden death syndrome in soya - are encouraged by the changes in soil biology and chemistry that glyphosate induces. These impacts are of concern to farmers and environmentalists and need to be addressed urgently.

GM Roundup Ready crops include oilseed rape or canola (pictured), soya, maize and cotton. Such crops do not contribute to sustainable agriculture practices.

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Glyphosate and the plague of resistant weeds

When glyphosate first appeared in the mid 1990s, weed resistance to herbicides as a result of GM RR crops was rarely discussed, although the phenomenon of weed resistance to herbicides was well known. Now, 15 years later, weed resistance to glyphosate is one of the most well documented effects and is a major environmental concern of the cultivation of GM RR crops.

Since the introduction of RR crops, there has been a dramatic increase in the number of weed species exhibiting glyphosate resistance. Glyphosate resistance has now been confirmed in over 20 species, with over 100 resistant strains identified, primarily in the Americas. Many scientists attribute this increase to the over reliance on glyphosate to control weeds in fields of GM RR soya, maize and cotton.

'No-tillage corn and soybean production has been widely accepted in the mid-Atlantic region, favouring establishment of horseweed. Within 3 years of using only glyphosate for weed control in continuous glyphosate-resistant soybeans, glyphosate failed to control horseweed in some fields. Seedlings originating from seed of one population collected in Delaware were grown in the greenhouse and exhibited 8- to 13-fold glyphosate resistance compared with a susceptible population'
(Van Gessel 2001)

Controlling glyphosate-resistant weeds in GM RR crops is now a major problem for farmers. Monsanto acknowledges this, and has published guidance on how to deal with the growing weed resistance problems in GM RR crops. Monsanto's recommended strategies include:

- the use of either stronger formulations of glyphosate or of mixtures of glyphosate and other herbicides, e.g. the notorious 2,4-D – one active ingredient of Agent Orange, the defoliant used by the US Army during the Vietnam; and
- producing GM seeds with several herbicide tolerant genes (gene stacking), which would allow other herbicides, in addition to glyphosate, to be sprayed over crops.

These strategies add to the amount of herbicides being used therefore increasing the overall toxic burden from GM RR crops and continue the industrial agriculture treadmill of herbicide usage and resistance. The development of more weeds with resistance to multiple herbicides seems probable. The widespread nature of weed resistance, and the additional herbicides required to control these weeds means that Monsanto's promise of cheaper and easier weed control with GM RR crops has not been delivered

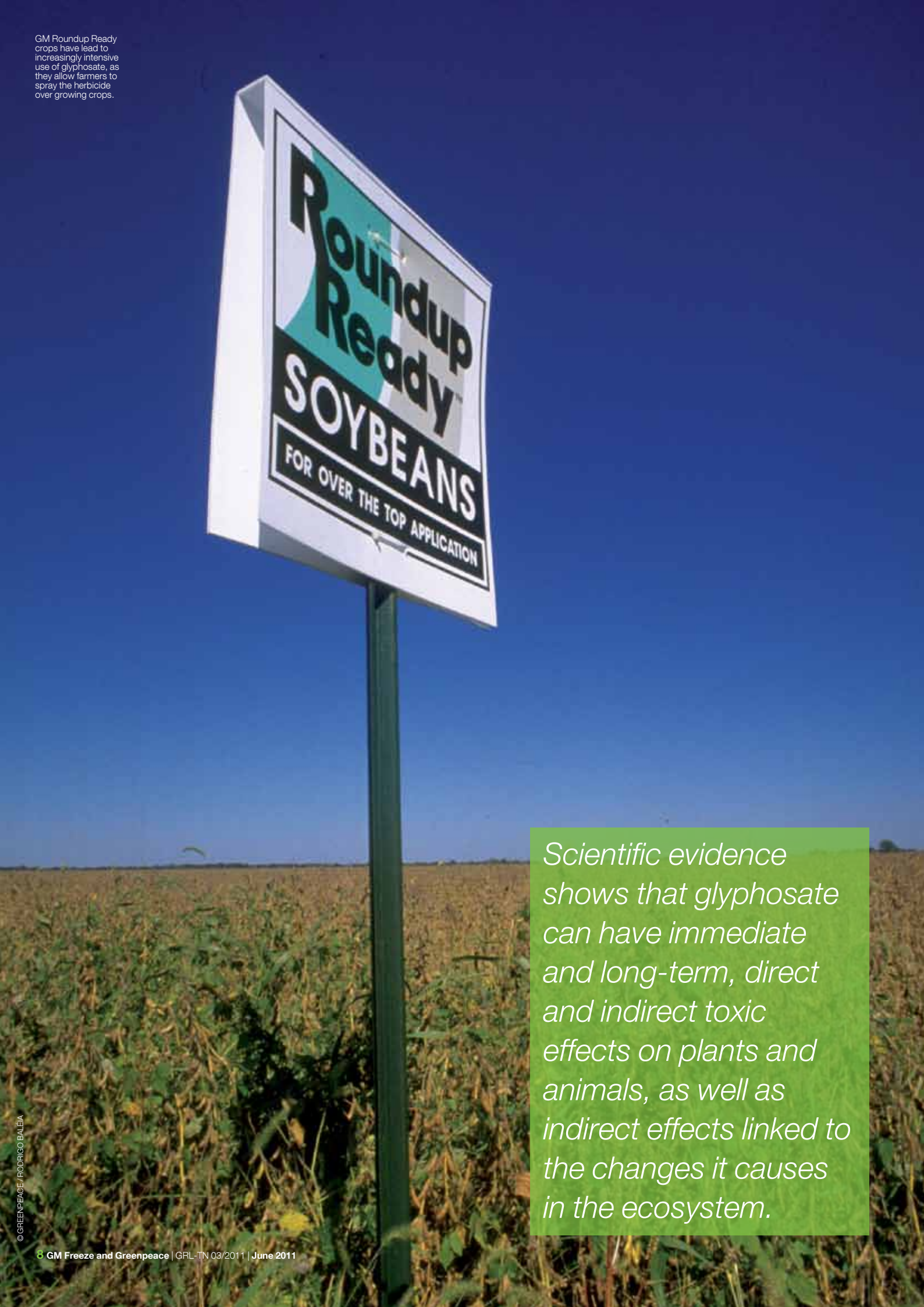
The toxicological profiles for mixtures of herbicides are not clear. However, **it is clear that GM RR crops have brought about an escalation in the pesticides 'arms race' with an increasing toxic burden on the environment and people.**

Conclusion

Recent studies demonstrate that glyphosate-based herbicides, such as Roundup, can have harmful effects to human health and the environment. Exposure of humans to glyphosate has been linked to various health effects including reproductive effects, cancer and neurological effects. Glyphosate interacts with soil chemistry and biology, resulting in a variety of impacts including reduced plant nutrition and increased vulnerability to plant disease. Glyphosate may also leach into surface and groundwaters, where they may damage wildlife and possibly end up in drinking water. Glyphosate and Roundup are far from benign herbicides and a review of their safety for human and animal health and for the environment is urgently needed.

GM RR crops have greatly increased glyphosate usage, especially in the Americas where they are primarily grown. Given the new evidence of glyphosate toxicity, this of great concern. The rise in glyphosate resistant weeds is associated with GM RR crops, and the escalation in the 'arms-race' against these resistant weeds fuels concerns that even more glyphosate will be used in the future with GM RR crops, in stronger formulations and possibly with additional herbicides. This facet of GM herbicide-tolerant crops should be enough to lead to a ban on their cultivation.

GM herbicide-tolerant crops, as epitomised by GM RR crops, are not part of sustainable agriculture practices. They are part of an industrial agriculture system that involves large-scale monocultures that depend on costly, polluting inputs such as herbicides. There is no doubt that there is an urgent need to find sustainable solutions to agriculture. As the recent UN/ World Bank global assessment of agriculture (IAASTD) recently stated, 'business as usual is no longer an option' (IAASTD 2009b). Sustainable solutions will not come from GM crops, and definitely not from GM herbicide-tolerant crops.



GM Roundup Ready crops have lead to increasingly intensive use of glyphosate, as they allow farmers to spray the herbicide over growing crops.

Scientific evidence shows that glyphosate can have immediate and long-term, direct and indirect toxic effects on plants and animals, as well as indirect effects linked to the changes it causes in the ecosystem.

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1] Introduction

Glyphosate - the active ingredient in many herbicides sold throughout the world - has always been promoted as 'safe'. But is it?

Mounting scientific evidence suggests that there can be adverse impacts on human and animal health, and the environment. The safety of glyphosate is in serious doubt.

The most well-known formulated herbicide based on glyphosate is 'Roundup', sold by the US-based agricultural biotechnology corporation Monsanto, the world's leading producer of glyphosate. Monsanto is also the leading producer of genetically modified (GM, also called genetically engineered, GE) seed, producing glyphosate-tolerant GM crops that are marketed as 'Roundup Ready' (RR). The glyphosate-tolerance of these crops subsequently leads to a widespread use of glyphosate-based products; thus, the close correlation between crop and herbicide is a major cause for concern.

This report examines the increasing evidence on the impacts of glyphosate-based products - and glyphosate's main breakdown product aminomethylphosphonic acid (AMPA) - on health, the environment, biodiversity and farmers. It also looks at the use of glyphosate or Roundup on GM RR crops: how its use in connection with these crops is resulting in widespread weed resistance; what that means for future herbicide usage; and the wider considerations about GM herbicide-tolerant (HT) crops.

This report comes at a time when the use of Roundup has increased dramatically around the world. At the same time there is a growing body of evidence indicating its harmful impacts.

1.1 Glyphosate: how does it work?

Glyphosate is a water-soluble, broad-spectrum, non-selective herbicide that is absorbed by the leaves and transported to all parts of the plant, including the roots. It is therefore capable of completely killing even deep-rooted plants, in contrast to other products - such as paraquat - which affect only the leafy part of the plant above ground. This property, combined with marketing campaigns promoting it as a 'safe' product, has made glyphosate a very popular herbicide.

A Monsanto employee discovered the herbicidal nature of the glyphosate molecule in 1970. Monsanto introduced the first commercial Roundup product (Monsanto 2005a), which uses glyphosate as the active ingredient, in 1974. It is claimed that Roundup is now used in 130 countries on 100 different crops (Monsanto 2005a).

The enzyme EPSPS (5-enolpyruvylshikimate-3-phosphate synthase) is present in all plants, fungi and bacteria. Glyphosate chelates (or binds) manganese, making it unavailable to the EPSPS. Because manganese is essential for EPSPS to work (Johal & Huber 2009), inhibiting it in this way subsequently affects an essential biochemical pathway in plants, the shikimate pathway, leading to a shortage of vital molecules for building proteins and causing the plant's death.

Because EPSPS is not found in animals, it is assumed that glyphosate is relatively harmless to mammals, insects, fish and birds. However, independent research shows that this is not the case. In addition glyphosate breaks down in the natural environment to form aminomethylphosphonic acid (AMPA), which is very similar in chemical structure to glyphosate. There is evidence that AMPA can also have impacts on animal and human health, and the environment.

On its own, glyphosate is not very effective as a herbicide. Therefore, it is marketed in formulated products mixed with other chemicals known as adjuvants or surfactants. These chemicals enable the herbicide to stick to foliage and allow the glyphosate molecule to penetrate the cuticle on the leaves and enter cells and the plant's circulatory systems. Glyphosate is then transported to all parts of the plant, including the tips of the roots.

So, when examining the impact of this herbicide on health and the environment, it is important to take AMPA and the adjuvants or surfactants into account. The impacts of these chemicals - singularly and in combination - are explored in this report.

1.2 GM crops: a perfect match for Roundup

Roundup is Monsanto's top-selling range of herbicides, and all products contain glyphosate as the active ingredient. There are many different formulations of the product sold under the same brand name around the world - for instance Roundup PowerMax and Roundup Weathermax, or under other brand names such as QuikPro[1].

Monsanto's patent on glyphosate ran out in 2000. However, Monsanto had already secured markets for their glyphosate by introducing GM seeds – soya, maize, cotton and canola - that are specifically engineered to be glyphosate tolerant. All Roundup Ready seeds are GM, as there are no conventional methods to produce herbicide tolerance to Roundup. These GM seeds have been marketed from the mid 1990s onwards[2] as Roundup Ready (RR). Because Monsanto does not guarantee crop performance with non-Roundup-brand herbicides, farmers are encouraged to use only Monsanto's Roundup on the GM crops rather than other brands of glyphosate herbicide (Monsanto 2011).

GM RR varieties allow farmers to spray the herbicide over the growing crop, killing virtually all weeds without affecting the crop itself. Monsanto's sales pitch to farmers promised - and still does - simplified weed control and reducing the number of spray passes required, subsequently reducing the costs of weed control (Monsanto 2009a). However, the reality is turning out to be different with increasing health (Chapters 2 and 3), biodiversity (Chapter 5) and environmental (Chapters 4 and 6) concerns and the development of weed resistance (Chapter 7).

GM RR crops are primarily grown in the Americas. In 2009, more than 90% of the soya crop planted in the US was GM RR (National Agricultural Statistics Service 2009). GM RR maize and cotton were also widely grown. While GM RR soya also dominates the soya crop in Argentina and Paraguay, adoption of the technology elsewhere in the world has been met with less enthusiasm. In Brazil, take-up of GM RR soya has been much slower, with 40% of the soybean crop being non-GM in 2009/10 (The Crop Site 2010). In Europe, no GM RR crops have so far been approved for cultivation.

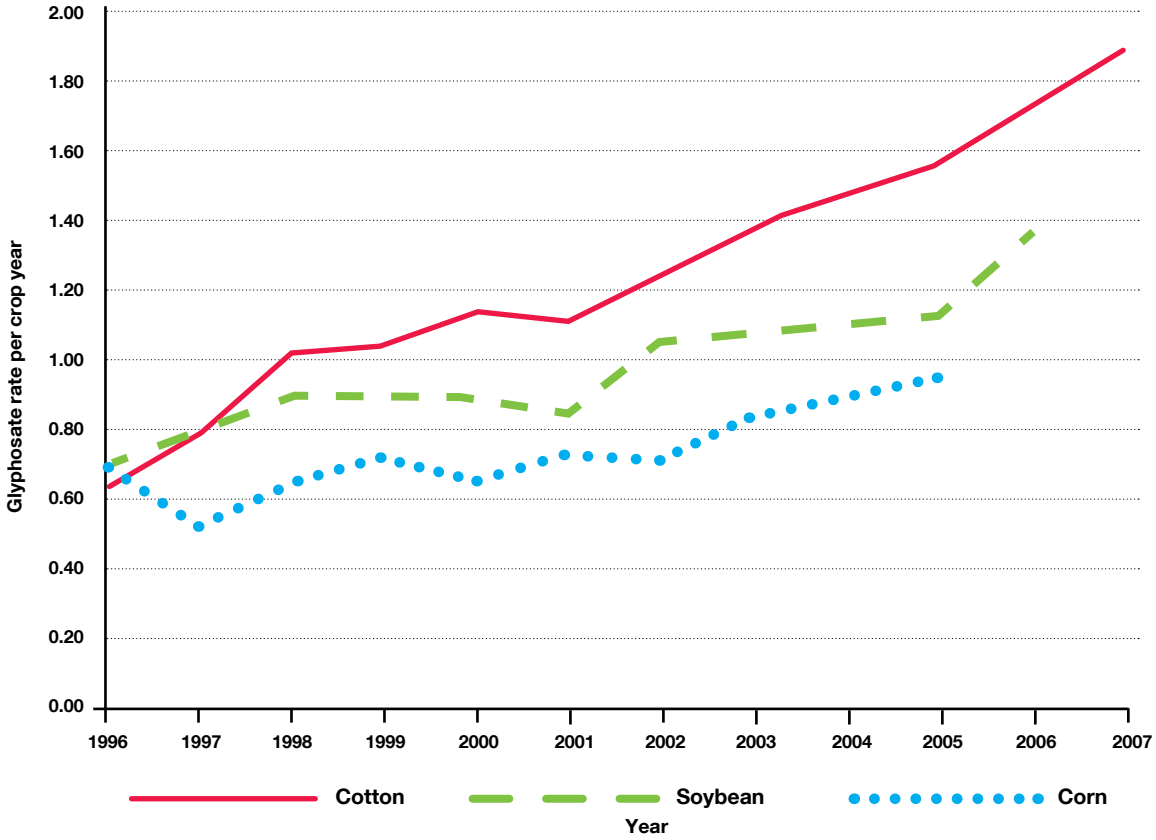

Fig. 1: Average glyphosate application rate per crop year for corn, soya and cotton in the US. Application rates of glyphosate-based herbicides have increased steadily since the introduction of glyphosate-tolerant RR cotton, soya and corn in the mid 1990s. Data are from US National Agricultural Statistic Service who define "rate per crop year" as the average one-time rate of application multiplied by the average number of applications. Redrawn from Benbrook (2009) with permission.

1 http://www.monsanto.com/products/Pages/agricultural-herbicides.aspx
2 http://www.cera-gmc.org/?action=gm_crop_database

Glyphosate is present in soils, waters and our food as a result of its widespread use with GM Roundup Ready crops.

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Since the introduction of GM RR seeds, the amount of glyphosate used in countries where these crops are grown has increased dramatically. In a series of reports, Charles Benbrook analysed USDA data charting the rise of glyphosate usage in the US since the introduction of GM RR crops (Fig. 1; Benbrook 2001; 2004; 2009). He noted a 39% rise for maize (1996-2005); nearly 200% for cotton (1996-2007) and nearly 100% for soybean (1996-2006). Peer-reviewed literature also notes considerable increases of glyphosate associated with the introduction of GM RR crops in the US (e.g. Duke, 2005; Cerdeira & Duke 2006). Similar trends have followed the introductions of GM RR soya in Argentina (Binimelis et al. 2009) and Brazil (Lucas 2006). It is apparent that the introduction of GM RR seeds has been instrumental in the increased use of glyphosate - much of it as part of Monsanto's Roundup range - in recent years.

Since the introduction of GM Roundup ready (RR) seeds, the amount of glyphosate used in countries where these crops are grown has increased dramatically.

1.3 Other uses of glyphosate

The potential markets for glyphosate extend beyond GM RR crops to many types of arable crops and many types of land management (see, e.g. Monsanto 2005a).

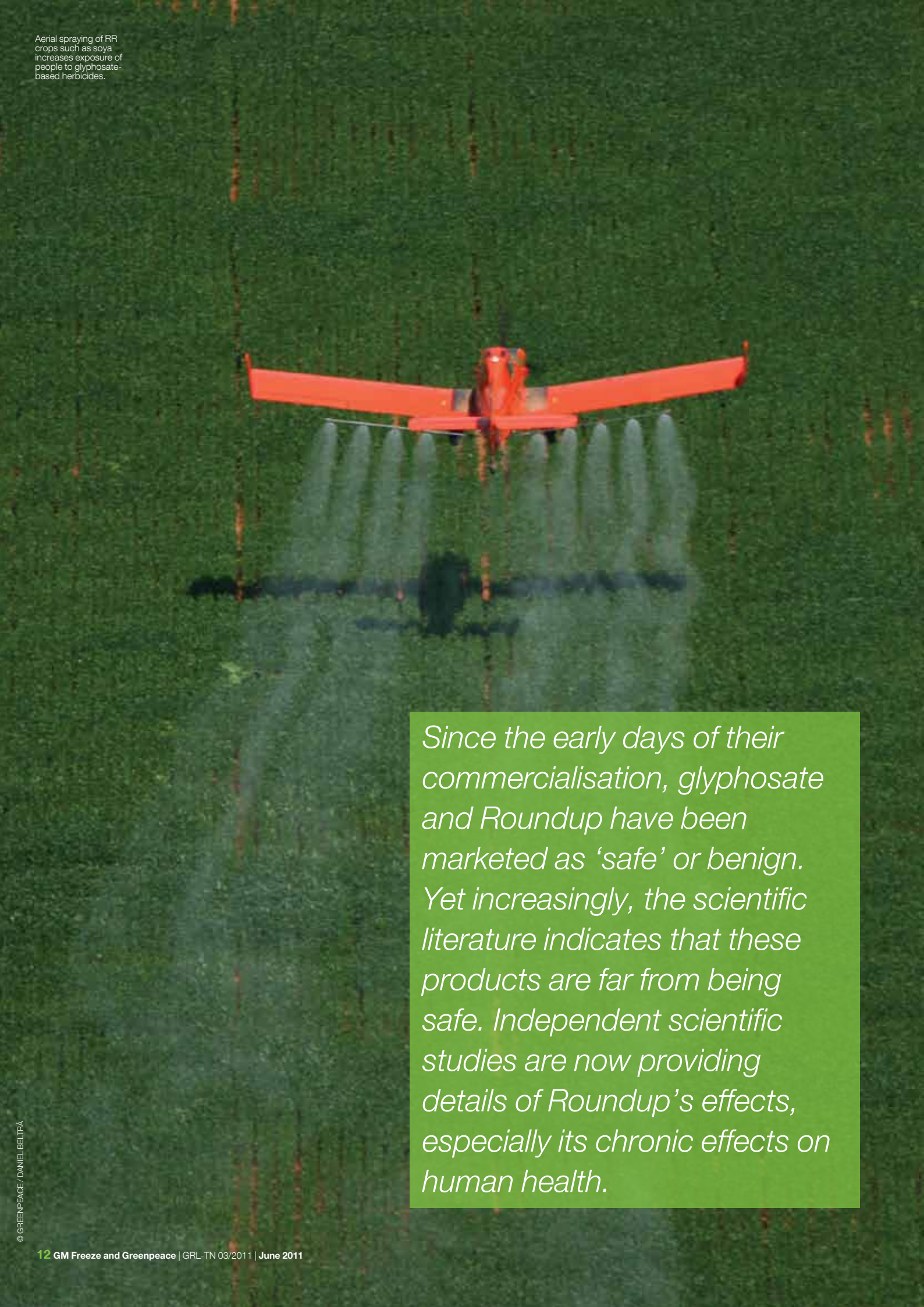
Increasingly, Monsanto is marketing GM insect-resistant crop varieties that also include glyphosate-tolerance (RR) genes[3]. In addition, crops with the GM RR gene and tolerance to other herbicides such as dicamba are being developed by biotech companies to deal with glyphosate-resistant weeds (see Chapter 7) (Behrens et al. 2007; Service 2007; Stride 2010).

1.4 Summary

Glyphosate is the active ingredient in many herbicides. It is generally sold as formulations that include other ingredients in order to increase its effectiveness by allowing it to adhere to plant leaves. The most well-known of these formulations is the Roundup range of herbicides sold by Monsanto. Although first marketed in 1974, glyphosate use increased drastically following the introduction of GM RR crops in the mid 1990s. Monsanto maintains a high market share of glyphosate sales by selling Roundup as a package with its GM glyphosate-resistant seeds.

The dramatic increase in the use of glyphosate has serious implications for health and the environment. These implications are described in the following chapters.

3 http://www.monsanto.com/products/Pages/cotton-seeds.aspx



Aerial spraying of RR crops such as soya increases exposure of people to glyphosate-based herbicides.

Since the early days of their commercialisation, glyphosate and Roundup have been marketed as 'safe' or benign. Yet increasingly, the scientific literature indicates that these products are far from being safe. Independent scientific studies are now providing details of Roundup's effects, especially its chronic effects on human health.

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2] Glyphosate impacts on human health

Glossary of terms

Axon the long fibre of a neuron.

Congenital present at birth.

Dendrites threadlike extensions of the cytoplasm of a neuron.

Dopamine a chemical produced by the brain, which functions as a neurotransmitter.

Free radicals electrically-charged reactive atoms or molecules in cells, which can damage other molecules within cells.

Globus pallidus part of the nucleus of the brain.

Implantation the attachment of the embryo to the lining of the uterus.

Lymphocytes vertebrate white blood cells.

Necrosis premature death of cells.

Mitochondria cell organelles responsible for energy production.

Mitochondrial transmembrane potential - difference in voltage across a mitochondrial membrane.

Mitochondrial energy energy generated by mitochondria in cells.

Ossification the process of creating bone.

Oxidative stress various pathologic changes seen in living organisms in response to excessive levels of free radicals in the environment.

Plasma the fluid portion of the blood.

RNA transcription the synthesis of RNA from a DNA template.

Serotonin a chemical produced by the brain, which functions as a neurotransmitter.

Steroidogenic acute regulatory (StAR) protein protein that regulates steroid hormone synthesis.

Seminal tubules tubes that carry sperm from the testes.

Substantia nigra movement centre in the brain.

2.1 Chronic effects

2.1.1 Reproductive

Birth defects in the Argentinean state of Chaco, where GM soy and rice crops are heavily sprayed with glyphosate, increased nearly fourfold over the years 2000 to 2009, according to a report released by the Chaco state government in April 2010 (Otaño et al. 2010). Paganelli et al. 2010 also reported 'several cases of malformations together with repeated spontaneous abortions were detected in the village of Ituzaingo' Cordoba, which is surrounded by GMO-based agriculture'. On its own, this information does not implicate glyphosate, for other pesticides are also used on the soy and rice fields. However, taken together with laboratory studies and other epidemiological information (patterns of illness in the human population), it raises concerns that can no longer be ignored.

'…Several cases of malformations together with repeated spontaneous abortions were detected in the village of Ituzaingo' Cordoba, which is surrounded by GMO-based agriculture'.
(Paganelli et al. 2010)

In Paraguay, 52 women who were exposed to glyphosate-based herbicides during pregnancy delivered offspring with congenital (i.e. present at birth) malformations. These birth defects showed striking similarities to those induced by glyphosate in laboratory experiments (Paganelli et al. 2010). However, they cannot yet be linked directly to glyphosate exposure.

The congenital malformations included microcephaly (small head), anencephaly, and cranial malformations. Anencephaly occurs when the neural tube fails to close during pregnancy, resulting in the absence of the majority of the brain, skull and scalp.

In 2009, Argentinean researchers lead by Professor Carrasco showed that even weak concentrations (down to 0.02%) of a commercial glyphosate formulation caused disruption to the development of the craniofacial skeleton of tadpole embryos (Fig 2). Other effects included shortening of the trunk, reduced head size and eye defects. The authors concluded that their results were 'compatible with the malformations observed in the offspring of women chronically exposed to glyphosate-based herbicides during pregnancy' (Paganelli et al. 2010). Although this study has recently been criticised by the agrochemical industry (Saltmiras et al. 2011), the study nonetheless raises concern regarding the impacts of glyphosate on reproduction.

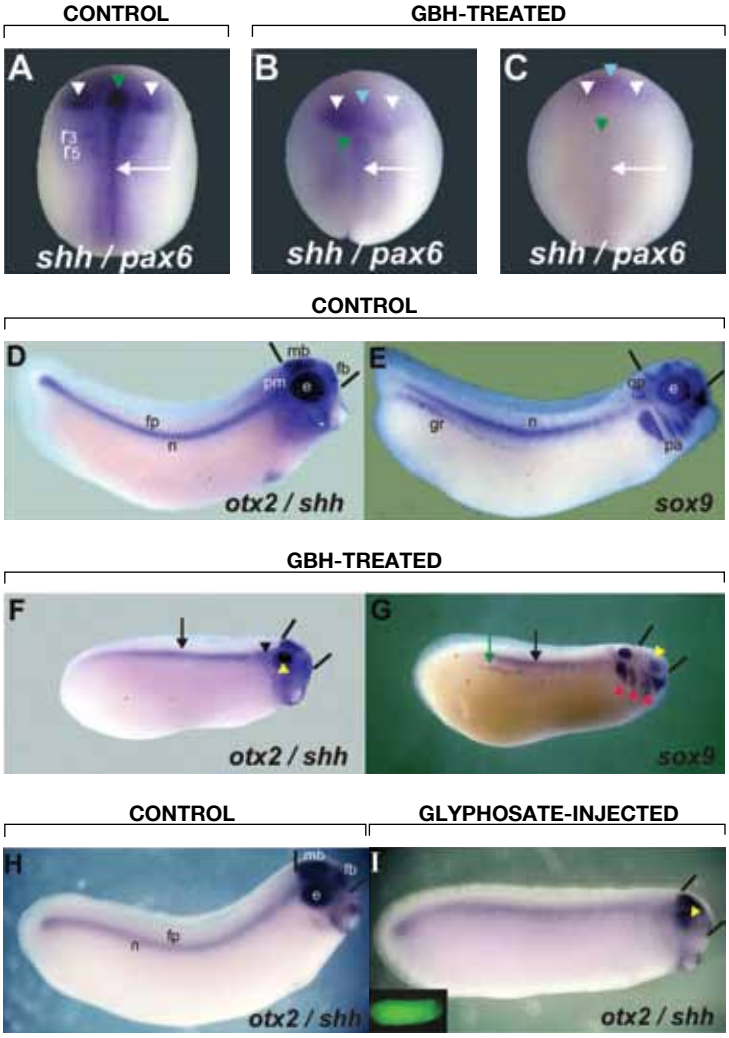

IMAGE PAGANELLI ET AL. 2010

Fig 2: Glyphosate-based herbicides (GBH), and glyphosate itself, interfere with early development in both frog and chicken embryos (Paganelli et al. 2010). Clear differences in frog embryos are seen here, with malformations present in those exposed to a 1/5,000 (0.02%) dilution of GBH but note, the last panel are injected with glyphosate.
Reproduced with permission from American Chemical Society. For full details, see Paganelli et al. (2010)

Previous studies also indicate the potential of glyphosate to disrupt reproduction. One study showed that applying glyphosate and Roundup at dilutions far below those used in agriculture severely affected human embryonic and placental cells, producing mitochondrial damage and two types of cell death, necrosis and programmed cell death, within 24 hours. Cell deaths occurred at concentrations corresponding to the level of residues in food expected from Roundup-treated GM crops (Benachour & Séralini 2009). The authors concluded that, if this occurred in the body, it would result in impacts on fertility, as well as carbohydrate metabolism, immune system function and water balance.

'Applying glyphosate and Roundup at dilutions far below those used in agriculture severely affected human embryonic and placental cells, producing mitochondrial damage and two types of cell, death necrosis and programmed cell death, within 24 hours.'

(Benachour & Séralini 2009)

Other studies demonstrate glyphosate and/or Roundup's endocrine disrupting effects:

- **Roundup disrupted the production of the female reproductive hormone progesterone in mouse cells by disrupting expression of the steroidogenic acute regulatory (StAR) protein** (Walsh et al. 2000).
- **Glyphosate at dilutions 100 times lower than agricultural rates inhibited activity of the enzyme aromatase, which is responsible for synthesis of another female reproductive hormone oestrogen.** Roundup itself had an even greater effect. This effect occurred once the glyphosate and Roundup had entered the cells, but prior to entry Roundup had the opposite effect causing 40% increase in aromatase activity (Richard et al. 2005). The authors concluded this might explain premature births and miscarriages observed in female farmers using glyphosate (Savitz et al. 1997; Arbuckle et al. 2001).
- **Hokanson et al also demonstrated a synergistic effect of glyphosate with oestrogen, with implications for pregnancy-induced hypertension and foetal growth retardation.** (Hokanson et al. 2007)
- **In 2007, Benachour et al. demonstrated that low levels of glyphosate inhibit aromatase in human embryonic cells resulting in reduced oestrogen production, with adjuvants in Roundup increasing the effect.** (Benachour et al. 2007)

- **Roundup, but not glyphosate, inhibited the conversion of androgens to oestrogen**. However glyphosate was anti-androgenic at levels 40 times lower than residues permitted in soybeans (Gasnier et al. 2010).
- **Pre-pubertal exposure to the product Roundup Transorb delayed puberty, altered the structure of seminal tubules in the testes of male rats, and reduced testosterone production** (Romano et al. 2010).

The implications of these effects on reproduction and the developing foetus are profound, with work by Mose et al. 2008 confirming that **glyphosate does cross the placenta**.

Finally, high-dose experiments on rats resulted in decreased total implantations and viable foetuses, reduced litter size, reduced foetal weight and pup weight, and reduced ossification of the breastbone (US EPA 1993, 2006; IPCS 1994).

2.1.2 Cancer

The Chaco report (Otaño et al. 2010) mentions a significant increase in cancer and particularly child cancer including leukaemia, lymphoma and brain tumours. Once again, while these could be caused by a number of factors including other pesticides, there is support from epidemiology and laboratory studies to indicate that glyphosate might be contributing to these cancers.

A number of epidemiological studies have linked exposure to glyphosate to **non-Hodgkin's lymphoma** (Norsdtrom et al. 1998; Hardell & Eriksson 1999; Hardell et al. 2002; McDuffie et al. 2001; De Roos et al. 2003; Eriksson et al. 2008;) and **multiple myeloma** (De Roos et al. 2005). Three studies of people exposed to the aerial spraying of illegal crops in Columbia have found **DNA damage** amongst those who had experienced acute effects from the spray (Mueckay & Malondao 2003; Paz-y-Mino et al. 2007; Bolognesi et al. 1997).

A number of laboratory studies have shown glyphosate, Roundup and/or the metabolite of glyphosate, AMPA, to be **genotoxic or mutagenic** in human cells, including liver (Mañas et al. 2009a; Gasnier et al. 2010; Mañas et al. 2009b), and lymphocytes (Lioi et al. 1998a; Bolognesi et al. 1997; Vigfusson & Vyse 1980). Numerous other studies have demonstrated genotoxicity or mutagenicity in mouse, bovine, fish, caiman, tadpole, fruit fly, sea urchin, onion and bacterial cells (Rank et al. 1993; Kale et al. 1995; Bolognesi et al. 1997; Clements et al. 1997; Peluso et al. 1998; Lioi et al. 1998b; Kaya et al. 2000; Grisolia 2002; Siviková & Dianovský 2006; Bellé et al. 2007; Cavaş & Könen 2007; Cavalcante et al. 2008; Guilherme et al. 2009; Mañas et al. 2009b; Mañas et al. 2009a; Poletta et al. 2009).

Other ways in which glyphosate may be contributing to cancer include:

- **its ability to deregulate cell division**, a hallmark of tumour cells, demonstrated to occur in sea urchin embryos at concentrations up to 4,000 times lower than normal sprayed concentrations (Marc et al. 2002, 2003, 2004);
- **its inhibition of RNA transcription**, demonstrated in sea urchin embryos at concentrations 25 times lower than normal sprayed concentrations (Marc et al. 2005); and
- **its ability to cause oxidative stress**, demonstrated for glyphosate and/or Roundup in human lymphocytes (Lioi et al 1998a; Pieniazek et al 2004) and skin cells (Gehin et al. 2005; 2006), as well as in bovine lymphocytes (Lioi et al. 1998b), bullfrog tadpoles (Costa et al. 2008), pregnant rats and their foetuses (Beuret et al. 2005), rat liver cells (El-Shenawy 2009), mouse kidney cells and liver DNA (Bolognesi et al. 1997), and in rice leaves (Ahsan et al. 2008).

2.1.3 Neurological

Glyphosate may affect the nervous system and may even be implicated in neurodegenerative diseases such as **Parkinson's disease**. Both Roundup and glyphosate were found to inhibit growth of 'neurite-like structures' (axons or dendrites), at concentrations lower than those measured in plasma and tissue of farmers exposed to Roundup (Axelrad et al. 2003). Two other studies on rats have demonstrated that glyphosate depletes **serotonin and dopamine** (Anadón et al. 2008); and caused a loss of mitochondrial transmembrane potential in rat brain cells, especially in the *substantia nigra* region of the brain (Astiz et al. 2009). The brain is very dependent on mitochondrial energy to maintain normal physiology, and **loss of mitochondrial function** is associated with many human neurodegenerative disorders. Damage in the *substantia nigra* is implicated in Parkinson's disease. Additionally, the central nervous system - and particularly the *substantia nigra* - is highly sensitive to free radical damage, which results from **oxidative stress**. A number of studies reported earlier show that glyphosate and Roundup cause oxidative stress in various different cells, including brain cells.

These laboratory findings are reflected in an epidemiological study and one reported clinical case. In a study of children born to pesticide applicators in Minnesota in the US, 43% of the children reported to have ADD/ADHD (Attention Deficit Hyperactivity Disorder) had parents who were exposed to glyphosate-containing herbicides (Garry et al. 2002). A 54-year-old man developed skin lesions six hours after he accidentally sprayed himself with a glyphosate herbicide, and one month later developed a 'symmetrical Parkinsonian syndrome'. Two years later, magnetic resonance imaging revealed effects in the *globus pallidus* and *substantia nigra* regions of the brain associated with Parkinson's disease (Barbosa et al. 2001).

2.2 Acute effects

A number of deaths have resulted from intentional ingestion (suicide), preceded by metabolic acidosis, respiratory and kidney failure, cardiac arrest, seizures, and coma (IPCS 1994; Chang & Chang 2009).

The most commonly reported acute effects from occupational and bystander exposures to glyphosate-based herbicides are those of the skin, eyes, respiratory, gastrointestinal and cardiac systems. They include:

- irritation, swelling, tingling or burning of the skin, dermatitis, photo-contact dermatitis;
- conjunctivitis, painful eyes, corneal injury, burning eyes, blurred vision, double vision, swelling of the eye and lid;
- oral and nasal discomfort, unpleasant taste, tingling and irritation of throat, sore throat, swollen tongue;
- burning in chest, cough;
- nausea, vomiting, headache, fever, diarrhoea, shakes and chills, tiredness, lethargy; and
- rapid heartbeat, raised blood pressure, dizziness, light-headedness, tingling in hands and feet; aching arms (IPCS 1994; Goldstein et al. 2002; Bradberry et al. 2004).

One recent epidemiology study in the US reported that exposure to glyphosate herbicides was associated with both asthma and rhinitis ('runny nose') (Slager et al. 2009).

Significant exposure to glyphosate herbicides has occurred in Ecuador and Columbia as a result of the aerial spraying campaign to eradicate coca in Columbia and along its border with Ecuador since 1997. Symptoms reported there include many of those reported above and, in addition, red eyes, skin rashes and blisters, skin infections, abdominal pain, gastrointestinal infections, respiratory infections, difficulty in breathing, numbness, insomnia, depression, debilitation, weeping eyes (Gallardo 2001; Oldham & Massey 2002; Paz-y-Miño et al. 2007).

2.3 Summary

Chronic effects related to glyphosate and its derivative products can be classified in the following categories: **reproductive** (birth defects), **cancer**, **neurological** (even implicated in causing Parkinson's disease), and **acute effects** linked with the direct use of the product by farmers or exposure of bystanders.

There is concern that birth defects experienced by women in Argentina and Paraguay may result from their exposure to glyphosate used on GM soya and rice crops. Other studies have demonstrated glyphosate's potential to disrupt reproduction by its ability to cause mitochondria damage, necrosis and cell death in human embryonic and placental cells; and to cause endocrine disruption, including disruption of progesterone and oestrogen production, and delayed male puberty.

Epidemiological studies have linked exposure to glyphosate with non-Hodgkin's lymphoma and multiple myeloma, as well as DNA damage among people who had experienced acute symptoms from glyphosate exposure. These findings are supported by laboratory studies that demonstrate that glyphosate can cause genotoxicity, mutagenicity, oxidative stress and dysregulation of cell division. Potential chronic neurological effects include Parkinson's disease and ADD/ADHD, while acute exposure symptoms include a wide range of effects on skin, eyes, respiratory, gastrointestinal and cardiac systems.

These effects must be taken very seriously and an urgent reassessment of the health impacts of glyphosate and its related products must now take place.

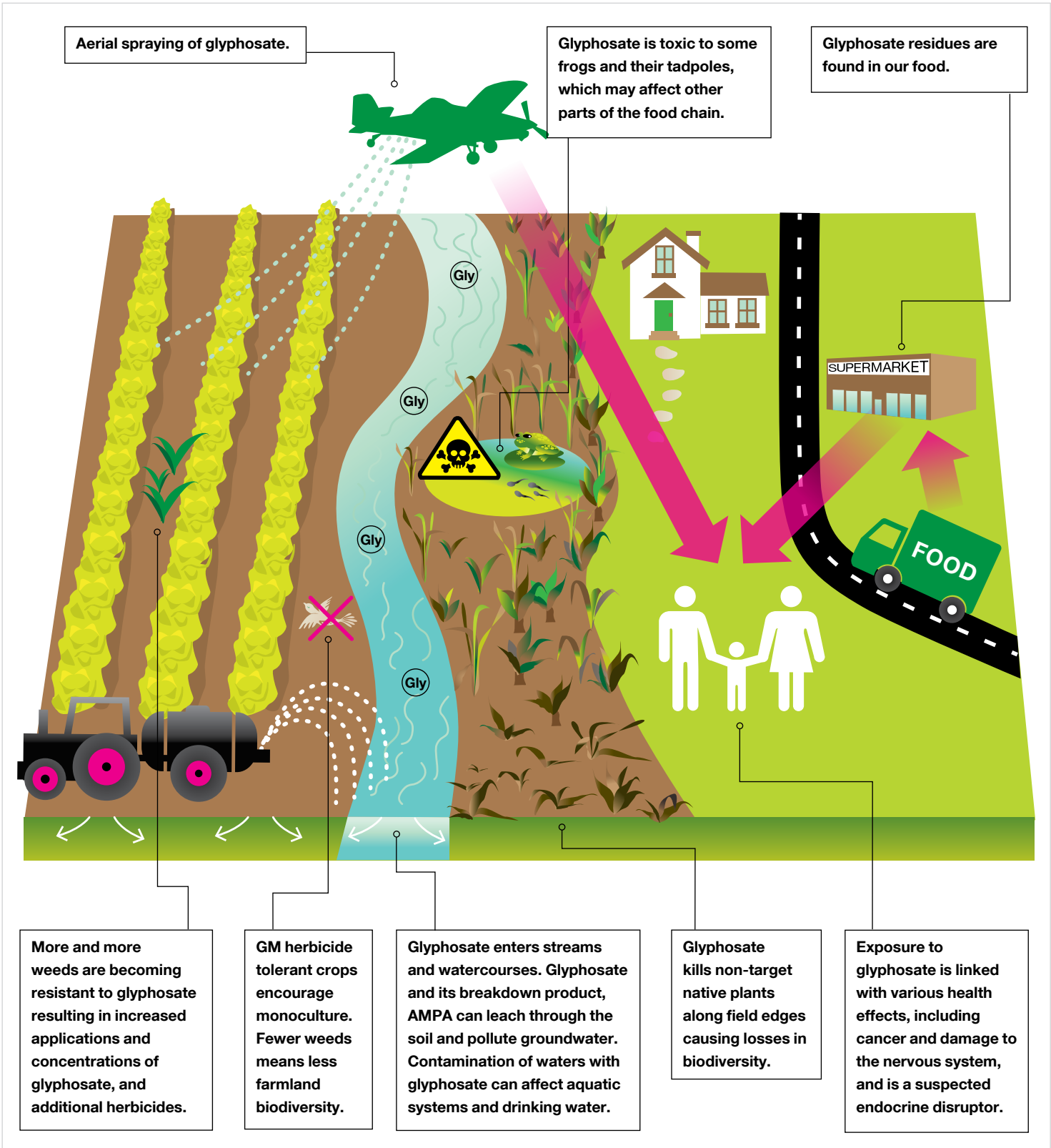

Fig 3: **Environmental and human health effects of glyphosate**

An urgent assessment of the health impacts of glyphosate and its related products must now take place.

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3] Glyphosate residues in food

The use of Roundup on food and feed crops means that residues of glyphosate and other chemicals used in the various formulations will be found in our food (Fig. 3). However, data on the presence of glyphosate and its breakdown product aminoglyphosate acid (AMPA) in food, feed and animal products from glyphosate sprayed crops are sparse.

Maximum Residue Levels (MRLs) are the maximum permitted concentration of pesticide residue in a food or animal feed. MRLs are primarily trading standards, but they are also intended to ensure that pesticide residues do not pose a risk for consumers. The current MRLs for residues of glyphosate in food were agreed by the United Nations Food and Agriculture Organisation's Codex Alimentarius (or food code) in 2006 and are listed in Table 1. The MRLs are for the combined levels of both the herbicide and its main breakdown product, AMPA.

Glyphosate is frequently used to desiccate cereal and oilseed rape crops immediately prior to harvesting. This results in residues in crops and processed products. The MRLs in Table 1 are generally higher for crops where glyphosate is applied directly than when it is used for weed control prior to sowing. That is, MRLs are higher for crops where glyphosate is used as a desiccant to dry grain prior to harvest (e.g. wheat and barley) or for crops where GM RR crops are commercially grown (e.g. soya, maize, cotton, rapeseed), than those for crops (e.g. pea and bean) where glyphosate is not sprayed on the crop itself, but may be used for clearing a field before planting. Thus, MRLs appear to be based upon the levels likely to be found in a specific product as a result of expected usage of glyphosate, rather than on safety concerns.

Table 1: Maximum Residue Levels (MRLs) for glyphosate in foods[4]

Commodity	MRL mg/kg
Animal products	
Poultry meat	0.05
Meat (from mammals other than marine mammals)	0.05
Edible offal of poultry	0.5
Edible offal of pigs	0.5
Edible offal mammalian (except pigs)	5.0
Eggs	0.05
Crops	
Banana	0.05
Beans (dry)	2.0
Sugar cane	2.0
Peas (dry)	5.0
Maize	5.0
Sunflower seed	7.0
Sugar cane molasses	10
Soya bean (dry)	20
Wheat bran unprocessed	20
Rape seed	20
Cereal grains	30
Cotton seed	40
Sorghum straw and fodder. Dry	50
Oat straw and fodder. Dry	100
Maize fodder. Dry	150
Bean fodder. Dry	200
Wheat straw and fodder Dry	300
Barley straw and fodder. Dry	400
Hay or fodder (dry) of grasses	500
Alfalfa fodder	500
Pea hay or pea fodder (dry)	500

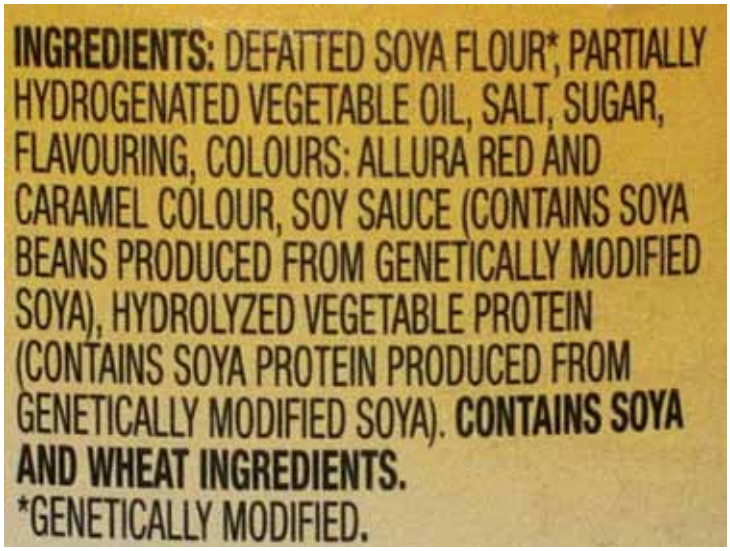
4 Source: UN FAO Codex Alimentarius. http://www.codexalimentarius.net/pestres/data/pesticides/details.html;jsessionid=7BA965F7D5BAA909CE2C7C2A6E3FAF97?d-16497-o=2&id=158&d-16497-s=3

Sampling of foodstuffs often detects glyphosate and/or AMPA.

- In Denmark, sampling of cereals in successive years in the late 1990s found glyphosate and/or its degradation product AMPA in more than half of the cereal samples. The average concentration of glyphosate in 46 samples from the 1999 harvest was 0.11 mg/kg compared with 0.08 mg/kg in 49 samples for the 1998 harvest (Granby & Vahl 2001).
- In the UK, sampling of food for glyphosate residues has largely concentrated on cereals, including bread and flour. Glyphosate has been regularly detected, and usually below the current MRL (Pesticides Residues Committee 2010, 2009, 2008 and 2007a). In 2006, the UK's Pesticide Residues Committee monitoring found a sample of wheat flour containing 0.8 mg/kg above the Codex MRL of 0.5 mg/kg (Pesticide Residues Committee 2007b).
- Residues of glyphosate in tofu and soya pieces were reported in the UK in 2006. Six out of eight samples of tofu/soya pieces originating from Brazil contained glyphosate with the highest level recoded being 1.1 mg/kg (Pesticide Residues Committee 2007a).
- In an EU survey of pesticide residue frequency, glyphosate was found in 9.54% of samples in 2007 (EFSA 2009).

WHO/FAO 2005 reported on feeding trials in pigs that were given feed containing 40, 120 and 400 mg/kg of glyphosate and AMPA. At the highest level (400 mg/kg), glyphosate residues in the liver were 0.72 (1.4 including AMPA) mg/kg and in kidneys, 9.1 (11) mg/kg. These residues are comparable with the MRL for edible offal from pigs of 0.5 mg/kg (Table 1). Despite this, no animal products have been sampled in the EU in recent years (EFSA 2009) nor in the US (USFDA 2008), meaning that exposure of consumers has not been monitored in recent times.

The levels found in cereals and animal products are below the current MRLs but indicate that consumers of cereal-based products are regularly exposed to glyphosate and AMPA residues. Importantly, the MRLs seem more dependent on the levels likely to be found in a specific product rather than on whether a specific residue level is safe or not.



CREDIT: PETE RILEY

Fig 4: **Food label displaying RR soya ingredients**

Summary

Despite the extensive use of products that contain glyphosate, there are limited data on residues in food and feed, including animal products such as offal, consumed by people and animals. However, there are data showing that glyphosate and AMPA are found in food destined for people at levels below the current MRLs.

The MRLs do not appear to be based on whether a specific residue level is safe or not but more on the levels likely to be found in a specific product as a result of agricultural practice, e.g. the use of glyphosate as a dessicant. As recent scientific studies (see Chapter 2) question the human safety of glyphosate-based products, the basis upon which these MRLs are made is called into question.

Along with a rigorous review of the environmental and the health impacts of glyphosate, a revision of the existing MRLs is also needed. In light of the new scientific evidence on glyphosate impacts it is essential to re-evaluate MRLs in order to ensure that they remain in line with updated safety assessments.

In light of new scientific evidence on glyphosate impacts, it is essential to re-evaluate maximum residue levels in order to ensure that they remain in line with updated safety assessments.

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"…Glyphosate, when applied in late autumn, can leach through the root zone at unacceptable concentrations in loamy soils"

(Kjær et al. 2003)

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4] Glyphosate in water

"From soil and plant applications of glyphosate herbicide, it is expected that a small amount of the applied glyphosate may enter surface waters through runoff or attached to soil particles that wash off treated field"
(Monsanto 2003)

Glyphosate is highly soluble in water and therefore has the capacity to be mobile in aquatic systems. In fact, glyphosate is far more soluble (in the range 10 000-15 700 mg/l at 25°C) than other herbicides, such as atrazine (in the range 20-35 mg/l) and isoproturon (in the range 70-72 mg/l), which are already known to leach from the soil to contaminate surface waters. However, as will be discussed further in Chapter 6, it is glyphosate's capacity to bind tightly to soil particles that prevents it from being highly mobile. Binding can immobilise it in the soil provided that there are sufficient suitable sites. This varies depending on the soil type and composition. Studies have found that binding of glyphosate is greater in soils with lower pH (i.e. more acidic) (Gimsing et al. 2004) and that phosphates (Simonsen et al. 2008) can compete for binding sites. All of this adds to the complexity of glyphosate's movements in the soil, and predictions of its leachability.

A report by the World Health Organisation (WHO 2005) confirmed that glyphosate is found in surface waters at levels between 0.5 µg/l and 1 µg/l and its environmental breakdown product, AMPA, was present at levels around 6 µg/l[5]. The levels of glyphosate exceed the maximum allowed for pesticides in drinking water under EU law (see below) and would require water companies to undertake expensive filtration before the water could be supplied to the public.

Glyphosate has often been detected during monitoring of surface waters and groundwater. A comprehensive study of streams in the midwest US examined the presence of herbicides, including glyphosate and AMPA, at different stages in the crop-growing cycle (Battaglin et al., 2005). Glyphosate was detected during every season up to a maximum concentration of 8.7 µg/l. This is over 80 times the EU maximum permitted concentration of 0.1 µg/l in drinking water (European Union Council 1998) but substantially below the US drinking water maximum concentration of 700 µg/l (US EPA 2009). Such a massive difference in permitted concentrations is hard to justify, especially given the growing body of evidence on the harm glyphosate can cause to health and aquatic life. AMPA was also detected above 0.1 µg/l in more than half of the samples taken through the year, most frequently after crops had emerged from the soil. The maximum concentration of AMPA recorded in this study was 3.67 µg/l.

Further evidence that glyphosate can enter surface waters comes from monitoring in Alberta, Canada, where it was found in 8 out of 13 sites and in 22% of samples taken in wetland and streams, with a peak concentration of 6.07 µg/l (Humphries et al. 2005). In Denmark, a major government-sponsored study on the leaching of pesticides was undertaken between 1999 and 2009. The conclusions of an interim report were that 'glyphosate, when applied in late autumn, can leach through the root zone at unacceptable concentrations in loamy soils' (Kjær et al. 2003). Glyphosate was detected to the depth of the drainage system and not in groundwater (Kjær et al. 2003, 2005). The final report (Rosenbom et al. 2010) declared that glyphosate and AMPA exhibited 'pronounced leaching'. A peer-reviewed paper based on the study stated 'both glyphosate and AMPA can leach through structured soils, they thereby pose a potential risk to the aquatic environment'.

5 In the Netherlands in 1988/89

The Danish study monitored pesticides leaching from different soil types, crops/agronomy and climates. Loamy soils (with roughly equal amounts of sand, silt and clay) were found to be more prone to leaching of glyphosate and AMPA than coarse sandy soils, where matrixes of aluminium and iron provide the right conditions for sorption and degradation. On loamy soils, autumn application resulted in detectable concentrations of glyphosate and AMPA in the drainage water in the upper metre of soil, often at concentrations exceeding the EU's maximum concentration for drinking water. The maximum concentrations of glyphosate recorded in drainage water at the two most vulnerable sites were found in 2009 (31 µg/l and 4.7 µg/l respectively). Average concentrations of glyphosate in drainage water following the first drainage after application were well above 0.1 µg/l for some crops, for instance maize in 2005 (4.04 µg/l) and peas in 2001 (0.54 µg/l), both following the application RoundUp. Detection of glyphosate and AMPA was mainly confined to drainage water although it was detected at three sites below the drainage system. At one site in the wet August of 2008, glyphosate was frequently detected in groundwater, with a maximum concentration of 0.67 µg/l.

The Danish results show that, in certain soil types with low sorption capacity, glyphosate can easily find its way into surface waters at concentrations that well exceed the EU drinking water maximum of 0.1 µg/l. In more exceptional circumstances, i.e. after heavy rain, it can also find its way into groundwater.

Standards for protecting aquatic life from glyphosate have not been widely set. None are agreed in the US or the EU, for example. In Canada, an interim standard of 0.65 µg/l was agreed upon as long ago as 1989 (Canadian Council for Environment Ministers, 1999) and work is presently in progress to establish a new one. US researchers investigating small water bodies in areas where glyphosate-based herbicides were used found levels up to 328 µg/l, well above the level set in Canada to protect freshwater aquatic life (Battaglin et al. 2008).

The amount of glyphosate entering watercourses is dependent on the weather immediately following its application. Heavy rain on low sorption soils is most likely to result in glyphosate washing into drainage systems.

Glyphosate can enter surface waters from land-based spraying either by becoming attached to soil particles, by leaching or by spray drift at concentrations that, in the EU, would have to be removed before waters entered the public supply. For example, small catchment studies in Sweden (Keuger 2005), France (Delmas 2004) and Greece (Papadopoulou-Mourkidou 2004) have confirmed that glyphosate can leach into drainage systems and surface waters. Losses amount to a small percentage of the glyphosate applied in the catchment but can exceed levels permitted in drinking water.

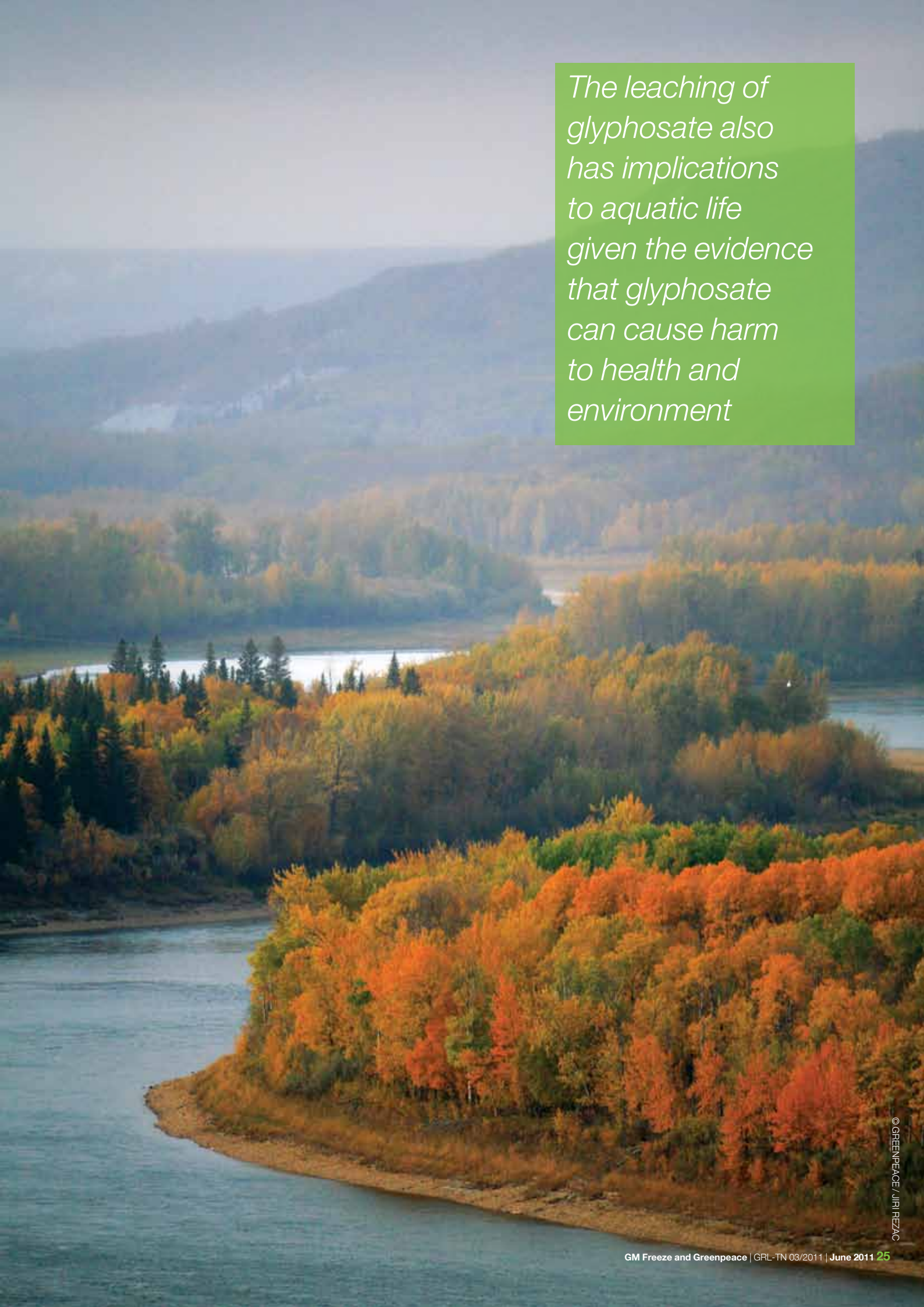
The use of glyphosate on paved surfaces in urban settings can also result in glyphosate quickly entering drainage water - and hence, surface waters - immediately after rainfall. A study in France showed that glyphosate can enter watercourses more readily from urban areas via the sewerage system than in rural environments due to applications on roads and railways. High levels were linked to rainfall events (Botta et al. 2009). Glyphosate is banned from use on hard surfaces in Denmark and by half of Swedish municipalities (Kristoffersen 2008).

Conclusion

Glyphosate is mobile in the root zone in soils with weak sorption capacity. This results in the presence of glyphosate and its degradation product, AMPA, in drainage water and surface waters. Groundwater has been polluted in similar soils after spraying followed by heavy rainfall. Run-off from the weed treatment of paved areas can also contribute to levels of glyphosate in watercourses.

These finding have implications for surface water quality and drinking water quality. The leaching of glyphosate also has implications to aquatic life given the evidence that glyphosate can cause harm to health and the environment (see Chapters 2 and 5).

The leaching of glyphosate also has implications to aquatic life given the evidence that glyphosate can cause harm to health and environment



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5] Glyphosate impacts on biodiversity

Although promoted as a benign herbicide, accumulated scientific evidence detailed in this chapter shows that glyphosate, and its formulated commercial products such as Roundup, can affect biodiversity.

Glyphosate can impact on plants and animals via:

- direct toxic effects of exposure to the spray;
- chronic effects caused by long-term exposure in the ecosystem; and
- indirect effects due to changes in the ecosystem.

5.1 Direct toxic effects

Since Roundup was first introduced in the 1970s, Monsanto has consistently claimed that glyphosate and Roundup are not likely to harm animals. It argues that, because glyphosate destroys an enzyme in plants that is not present in animals, it will not affect them.

For example, Monsanto says 'glyphosate-containing products labelled for forestry use have shown no adverse effect on aquatic animals' (Monsanto 2010a) and that these products present 'extremely low toxicity to mammals, birds and fish' (Monsanto 2010b).

However, there is now a significant body of evidence from the peer-reviewed scientific literature showing that these claims can no longer be supported where Roundup formulations are applied. The toxicity of glyphosate is strongly increased by the adjuvants and surfactants that it is mixed with in order for it to adhere to foliage and penetrate into plant cells, allowing it to then be transported (or translocated) to all parts of the plant. Approvals of products are based on separate assessments of glyphosate and the adjuvants and surfactants[6] but not the combined commercial product. At least 12 different adjuvants have been used in glyphosate-based formulations (Cox 2004). In most cases, the mixtures and ratios are commercially confidential.

5.1.1 Toxicity to amphibians

Declines in the numbers and the diversity of amphibian species across the world have been widely reported since the 1980s. It is estimated that one in three of species globally is threatened with extinction (Williams 2004). Causes such as habitat loss, habitat fragmentation, disease and environmental contamination have been put forward as contributing to this decline.

In the past, testing pesticides on amphibians, as part of the approval process, was rare. When it did occur, it was only over short time periods (Reylea 2005a). However, the global decline of amphibian numbers led researchers to focus on agro-chemicals as a potential cause of their decline. Glyphosate and Roundup formulations were selected for independent toxicity studies because of their widespread use.

The conclusions from several projects suggest that, under close-to-field-conditions, glyphosate-based products, including Roundup, have a direct toxic effect on the adults and tadpoles of a range of amphibian species:

- Roundup was found to have the potential to cause substantial mortality in many amphibian species in a controlled study of aquatic communities that included algae and tadpoles from five North American species of toads and frogs (Reylea 2005b).
- Three species of North American frog and toad tadpoles exposed to Roundup in artificial ponds exhibited very high mortality (96-100%) over three weeks, which the author suggests could lead to population decline in the wild (Reylea 2005c).
- Western chorus tadpoles exposed to the glyphosate product Roundup WeatherMax at 572 µg/l glyphosate acid equivalents (a.e.) resulted in 80% mortality, which the authors suggested resulted from a unique surfactant formulation. Exposure to WeatherMax or Roundup Original Max at 572 µg/l a.e. also lengthened the larval period for American toads (Williams & Semlitsch 2010).
- Frog tadpoles (*Rhinella arenarum*) exposed to concentrations used in commercial formulations showed decreases in the activities of AChE (acetylcholinerterase) (Lajmaonovich et al. 2010).

The findings of these studies suggest that glyphosate-based products harm amphibians at concentrations which occur as a result of their normal use in agriculture or forestry. This group of animals includes many species that are predators of pests in and around agro-ecosystems and forest ecosystems. Losses of the order reported above in wild populations could have significant impacts upon pest populations and a long-term impact on crop yield and quality.

6 Adjuvants have been categorised as extenders, wetting agents, sticking agents and fogging agents designed to enhance the activity or other properties of a pesticide mixture. Surfactants are formulants for reducing surface tension, thereby increasing the emulsifying, spreading, dispersibility or wetting properties of liquids or solids.

5.1.2 Aquatic toxicity

In the last few years, independent research on the toxicity of glyphosate and its formations has found that they are biologically active in aquatic systems at concentrations that could arise from routine applications. Many different aquatic organisms have been affected.

- Rotifer (*Brachionus calyciflorus*) (microscopic aquatic animals) exposed to different concentrations of glyphosate had longer embryonic developmental time, longer durations of juvenile and reproductive periods, shorter average lifespan, a reduced net reproductive rate and reductions in the intrinsic population growth rates (Vera et al. 2010).
- The parasitic horsehair worm (*Chordodes nobilii*) showed a number of responses, including reduced infective capacity of larvae and 50% mortality in adults, when exposed to glyphosate concentrations lower than expected in freshwater environments, and lower than specified in the relevant legislation, (Achiorno et al. 2008).
- Phytoplankton and periphyton[7] communities showed changes in the microbial population structures consistent with a direct toxicological effect of glyphosate (Pérez et al. 2007).
- A study of the combined effects of glyphosate with the trematode parasite (*Telogaster opisthorchis*) and the fish parasite (*Galaxias anomalus*) found that the glyphosate and the parasite acted synergistically on aquatic vertebrates at environmentally-relevant concentrations. Researchers suggested that glyphosate might increase the risk of disease in fish (Kelly et al. 2010).
- Disturbance in the marine microbial communities was caused by exposure to 1 µg/l Roundup concentration, a value typical of those reported in coastal waters during run-off events (Stachowski-Haberkorn et al. 2008).
- A freshwater mussel (*Lampsilis siliquoidea*) was found to be acutely sensitive to Roundup and its separate components. Researchers tested the specific active ingredient (technical-grade isopropylamine (IPA) salt of glyphosate), the surfactant (MON 0818) and the commercial product itself. MON 0818 was found to be the most toxic, but juvenile *Lampsilis siliquoidea* were found to be acutely sensitive to all three (Bringoff et al. 2007).
- Carp (*Cyprinus carpio*) exhibited changes to the internal appearance of liver cells and changes to mitochondria at Roundup concentrations between 2 and 40 times lower than used in practice (Szarek et al. 2000).

It is clear that glyphosate can be toxic to many aquatic organisms if it enters watercourses (see Chapter 4)**.**

5.2 Does glyphosate affect the nervous system?

Acetylcholinesterase (Ach) is an enzyme that breaks down acetylcholine, which transmits nervous impulses between nerves. Organophosphate and carbamate insecticides inhibit Ach formation, resulting in nervous impulses being maintained. Eventually, insects die - as do mammals and birds if they are exposed to high enough levels of these pesticides. Sub-acute levels are known to cause changes in birds and mammals in their temperature regulation, food consumption and reproduction (Grue et al. 1997).

Monsanto (1982) and some studies (e.g. Rom & Markowitz 2007) found that glyphosate has no Ach-inhibiting activity, despite the presence of phosphate in its molecule, meaning it is not classed as an organophosphate chemical. However, other studies report that glyphosate does suppress Ach activity in the brain, but not in muscles, of species examined (Lajmaonovich et al. 2010; Glusczak et al. 2006; Glusczak et al. 2007). The implications of these changes arising from exposure to glyphosate have yet to be fully investigated and this needs to be carried out within a review of glyphosate herbicides.

5.3 Impacts on non-target plants

As expected from its broad-spectrum use, glyphosate also impacts non-target wild plants in field margins or in water bodies. However, there are considerable cascading effects on farmland biodiversity. Glyphosate, in its formulated products such as Roundup, is a highly effective herbicide on all types of vegetation until weed resistance develops (see Chapter 7), and therefore has the capacity to cause major changes to the agro-ecosystem. These impacts include the loss of botanical diversity in the agro-ecosystem, including the loss of rare species growing in arable fields. In Iowa, US, glyphosate is classed as 'high risk' for off-target plants growing in soya and maize fields (i.e. those of botanical interest but not major weeds in the crops) (Iowa University State Extension 2003). Accidental drift from glyphosate in approved use has also been found to impact on rare plants in Australia (Matarczyk et al. 2002). Monsanto runs an 'endangered species initiative'[8] in the US, which specifies particular areas of land with sensitive species present. However, this does not automatically preclude the use of glyphosate sprayed from the air in the area outside the buffer zone surrounding the site.

7 Periphyton is the complex of algae and micro-organisms attached to underwater surfaces.
8 http://www.monsanto.com/ourcommitments/Pages/glyphosate-endangered-species-initiative.aspx

Impacts of GM herbicide-tolerant crops on weed abundance and the biodiversity food chain were studied during the Farm Scale Evaluations (FSE) in the UK between 2000 and 2003 (Heard et al. 2003a; Heard et al. 2003b; Roy et al. 2003). The only GM RR crop trialled was beet. The other GM herbicide-tolerant crops (oilseed rape and maize) were tolerant to a different herbicide, glufosinate ammonium. Equivalent data are not available for any GM RR crops elsewhere in the world.

The conclusions were clear:

'Based on the evidence provided by the FSE results published in October 2003, if [GM herbicide-tolerant RR] beet were to be grown and managed as in the FSEs this would result in adverse effects on arable weed populations, as defined and assessed by criteria specified in Directive 2001/18/EC, compared with conventionally managed beet. The effects on arable weeds would be likely to result in adverse effects on organisms at higher trophic levels (e.g. farmland birds), compared with conventionally managed beet'
(ACRE, 2004)

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Fig 5: Use of glyphosate-based herbicides on RR crops affects biodiversity. The use of glyphosate on RR beet reduces the numbers of weeds which form the base of the food chain needed to support farmland birds, such as the skylark (ACRE 2004).

The FSE research showed how weed seed production (seed rain) was reduced by the use of glyphosate on GM RR beet and warned that 'relatively small differences could eventually sum to produce a large effect if they were sustained over several crop rotations, say for 10 or more years' (Heard et al. 2003a).

Data on GM RR maize and oilseed rape were not included in the FSE reports, as only glufosinate ammonium-tolerant GM varieties of these crops were trialled. In the trials, glufosinate ammonium-tolerant GM oil seed rape demonstrated similar impacts on biodiversity to GM RR beet but the herbicide-tolerant GM maize apparently showed less adverse effects on weed abundances than the non-GM variety, but the trial was invalidated by the use of a herbicide, atrazine, that was subsequently banned. Retrospective analysis suggested that the removal of the atrazine from the analysis very much reduced any effects on weed abundance (Perry et al. 2004).

5.4 Summary

There is a growing body of scientific evidence that glyphosate is harmful to species at many stages along the food chain, including the aquatic food chain. Scientific evidence shows that glyphosate (and its formulated commercial products such as Roundup) can have immediate and long-term, direct and indirect toxic effects on plants and animals, as well as indirect effects linked to the changes it causes in the ecosystem.

This new evidence of glyphosate toxicity, together with the increase in glyphosate usage associated with GM RR crops (see Chapter 1) **is now of great concern. It is time that regulators examined the new evidence of harm in aquatic ecosystems that is now emerging from independent research on toxicity and mobility in soil and aquatic systems.**

6] Glyphosate impacts on the soil-plant system

Glyphosate enters the soil by being directly sprayed on it, via the roots of plants that have been sprayed, or from dead vegetation. Glyphosate is soluble in water and can be washed into the soil by rainfall or irrigation. In some soils, it can bind tightly to soil particles. This means it cannot be washed deeper into soil and is less likely to be degraded by soil microbes. In other soil types, it remains mobile in soil water and can be leached into drains and decomposed. Tightly-bound glyphosate can be displaced by other chemicals, such as phosphate, meaning it can become present in soil water again.

The interactions between the chemical, physical and biological components of the soil and glyphosate are complex (Kremer & Means 2009; Zablowicz & Reddy 2004). Given this complexity, the requirements for the risk assessment of glyphosate by regulators around the world are surprisingly limited. For instance, in the EU, applicants are only required to provide data on the persistence of glyphosate in the soil and the impact on earthworms and other functional groups of soil organisms. Detailed examination of the impact of glyphosate on the make-up and activity of soil microbial species including pathogens is not required (EU Commission, Directorate General for Health – DG SANCO 2002).

Glyphosate binds so tightly to soil particles that it is rendered inactive and hence unavailable to organisms. It is therefore claimed that glyphosate has limited biological availability in the soil (Monsanto 2005b; Geisy et al. 2000). However, several important interactions between glyphosate and soil microbes have been identified that impact on the function of plants (Kremer & Means 2009). These interactions are detailed in Fig. 6.

When glyphosate is available in the soil, it affects microbial communities leading to:

- Reduction in mineral uptake by crops;
- Increased microbial biomass and activity;
- Proliferation of phytopathogens in crops;
- Reduction in nitrogen fixation and nodulation, leading to increased demands for nitrogen fertiliser.

6.1 Availability of glyphosate in the soil

The impact that glyphosate will have on the soil ecosystem is largely dependent on whether it is bound to soil particles or unbound and free. Glyphosate molecules bind with particles present in the soil that have a high binding capacity - such as aluminium hydroxide and ferric oxides, minerals or organic matter - and subsequently become inert (Shushkova et al. 2009). The extent to which this happens varies from soil to soil, depending on its composition and on the presence of other chemicals and mineral nutrients. When glyphosate is not bound (or only loosely bound) to soil particles, it is available for microbes to break down and utilise as a source of energy and nutrients. It is when this happens that glyphosate starts to impact on the environment.

Soil chemistry can also play an important part in how much or how little glyphosate binds to the soil. Phosphate competes with glyphosate molecules for soil-binding sites. In experiments, soils to which a phosphate solution has been applied are found to have raised levels of glyphosate and AMPA in solution, thus making it mobile in the soil (Simonsen et al. 2008) and available for microbes to break down or leach through the soil.

The rhizosphere is the thin layer of soil immediately surrounding plant roots, an area that is extremely important for the uptake of nutrients into the plant. It is markedly different from the bulk soil (Chin-hua & Palada 2006; see Fig 6). Glyphosate appears to interfere with the biological and chemical processes in this important rhizosphere, unintentionally affecting plant growth and nutrition.

6.2 Activity and abundance of soil microbes

Molecules of glyphosate and its breakdown product AMPA, which are not bound to soil particles, are available for soil and rhizosphere microbes (also called micro-organisms) to utilise as a source of nutrients and energy, thus leading to increased microbial biomass and activity (Haney et al. 2000; Wardle & Parkinson 1990). Glyphosate can therefore affect the structure of the microbial community, increasing the abundance of some microbes and decreasing others.

The existence of the EPSPS enzyme in microbes and fungi means they can be affected by the presence of free glyphosate in the soil, and changes in microbial populations occur in the rhizosphere of GM RR crops depending on how susceptible they are to glyphosate. Some groups increase, such as manganese-oxidising bacteria, and some decrease, such as pseudomonads that act against fungal pathogens. Thus, important roles for microbes such as growth promotion and biological control can be disrupted (Kuklinsky-Sobral et al. 2005).

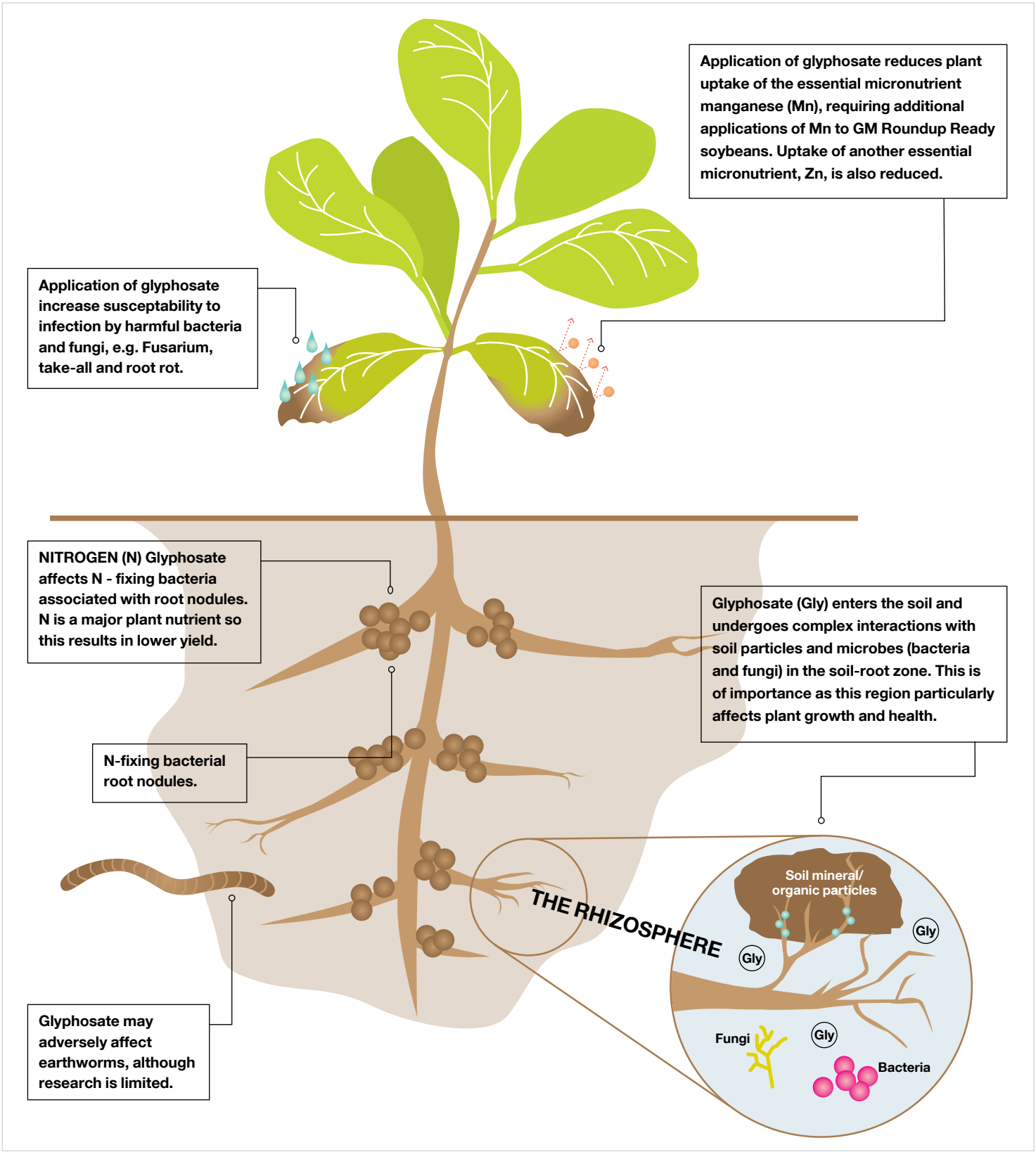

Fig 6: **Plant-soil interactions of glyphosate.**

A recent study on Monsanto's new variety of GM RR soya (RR2) found that glyphosate negatively impacted 'the complex interactions of microbial groups, biochemical activity and root growth that can have subsequent detrimental effects on plant growth and productivity' (Zobile et al. 2011b). The plant roots had higher numbers of *Fusarium* species and reduced numbers of manganese-reducing bacteria.

These imbalances in the soil and rhizosphere microbial community can affect soil and plant health. They may reduce the availability of plant nutrients, or cause increased vulnerability to disease.

6.3 Reduced nutrient uptake by plants

Research is beginning to uncover the complex relationship between glyphosate use and plant nutrients, such as manganese and zinc. Manganese is vital to plants, enabling photosynthesis, enzyme function, nitrate assimilation and the formation of vitamins (Ducic & Polle 2005). Zinc is vital in the structure and function of enzymes (Broadly et al. 2007).

Glyphosate has been shown to interact with micronutrients, such as manganese, in the rhizosphere and appears to reduce their availabilty to plants. These interactions possibly happen because glyphosate affects micro-organisms in the rhizosphere (see Chapter 5). Laboratory experiments with sunflowers show that after glyphosate application there was 'an impairment of the manganese-nutritional status, which was still detectable after a waiting time of up to 21 days' (Tesfamariam et al. 2009). This confirmed previous field observations and research suggesting that glyphosate affected microbes associated with the mobilisation of rhizosphere manganese. This then influences the mobility of manganese in the rhizosphere and hence reduces the amount that is available to the plant even when the element is plentiful in the soil (Kremer & Means 2009). Applications of manganese to GM RR soya are necessary to counteract this reduction in manganese uptake compared with the conventional varieties (Gordon 2007).

Studies on GM RR soya confirm these findings and suggest that other nutrients may also be affected by a reduced availability to the plant. Research in Brazil showed that the application of glyphosate 'interfered [with the] mineral nutrition of soybean and the total contents of [nitrogen, manganese, copper, zinc and iron]' (Serra et al. 2011). Recent research on Monsanto's GM RR soya 2 has shown that it also suffers from reduced macro-and micro-nutrient as a result of glyphosate applications (Zobiole et al. 2011a).

6.3.1 Nitrogen fixation impaired

It is known that nitrogen fixation and uptake is affected in GM RR soya. Conventional agriculture normally relies upon the addition of a nitrogen fertiliser to the soil. However, some crops - such as legumes (peas, beans etc.) - are able to utilise atmospheric nitrogen. They do this by forming symbiotic relationships with 'nitrogen-fixing' bacteria in the soil. The bacteria form characteristic nodules around the roots of the plants. There is evidence that the functioning of these nodules in GM soya plants is affected by the presence of glyphosate.

One study found that 'nodulation was always lower on GR [GM glyphosate-resistant] soybean with or without glyphosate compared with conventional varieties with non-glyphosate or no herbicide' (Kremer & Means 2009). The authors suggested that 'glyphosate and perhaps genetic modification in the GR plant may affect the numerous processes involved with nitrogen fixation symbiosis', which processes include nitrogenase activity and leghaemoglobin (an oxygen-carrying protein found in plants) content. This effect could have a significant impact on the long-term sustainability of the crop, which relies on fixation to provide 40% to 70% of the nitrates required by the crop (Kremer & Means 2009). In the longer term, this will lead to an increased dependency on the external addition of nitrates (Bohm et al. 2009), along with the all the environmental concerns associated with the use of nitrate fertilisers (Tillman 1999).

It is clear that GM RR crops, especially RR soya, suffer from a range of nutrient deficiencies induced by the application of glyphosate.

6.3.2. Glyphosate toxicity to earthworms

Independent research on the impact of glyphosate in earthworms is limited. However, there is evidence that repeated use can damage this vitally important group of species. Growth rates of one earthworm species were reduced in culture chambers for 100 days by a range of glyphosate concentrations (Springett & Gray 1992). Similar findings were found in a different species (Yasmin & D'Souza, 2007). Another study found a significant change in the hatching of earthworm cocoons exposed to glyphosate and that the earthworms actively avoided glyphosate-treated soil in the laboratory (Casabé et al. 2007). The conclusion was that the study 'showed deleterious effects of [glyphosate] … formulations when applied at the nominal concentrations recommended for soya crops'.

The repeated use of glyphosate on GM crops and in general weed control across a wide range of agro and forest ecosystems could possibly have long-term impacts on earthworm populations. Given the vital importance of earthworms in improving soils and in the food chain, there is an urgent need to assess the impact of long-term exposure.

6.4 Increased vulnerability to plant diseases

'The synergistic activity of glyphosate weed control in predisposing plants to infectious organisms has been observed for many diseases … and the extensive use of glyphosate in agriculture is a significant factor in the increased severity or 're-emergence' of diseases once considered efficiently managed'
(Johal & Huber 2009)

The impact of glyphosate on the ability of plants to fight off disease has now been extensively studied. Pathogenic (or harmful) fungal diseases have been found to worsen in the presence of glyphosate in 13 crops, including soybeans, wheat, cotton, sugar beet and canola. Diseases include take-all in cereals, damping off, root rot and sudden death syndrome in soybeans (Johal & Huber 2009).

Several plant diseases caused by *Fusarium* species (pathogenic fungi) are increased by glyphosate. The presence of the herbicide in the rhizosphere enables these fungi to become the dominant group (Kremer & Means 2009). Soil-dwelling *Fusarium* species cause a wide range of diseases in crop plants, ornamentals and grasses (Nelson et al. 1983). Therefore, any increase arising from the use of glyphosate could be significant in a wide range of different land uses, including GM RR crops.

Research on the impact of glyphosate on microbes inhabiting soil outside the rhizosphere is limited (Kremer & Means 2009). Other research found that numbers of the soil-borne pathogen (or disease) *Pythium ultimum* were significantly greater in root exudates from bean plants treated with glyphosate than those that were not (Kuklinsky-Sobral et al. 2005). Other *Pythium* species were not stimulated in this way.

The toxicity of glyphosate to soil microbes is highly variable and is thought to be dependent on the sensitivity of the microbe's EPSPS enzyme to glyphosate. For instance, five species of the ubiquitous family of soil bacteria *Pseudomonas* were found not to be sensitive to glyphosate, while the activity of one commonly-found member of the family, *Pseudomonas fluorescens*, was inhibited by glyphosate (Schullz, Krüper & Amrhein 1985). *Pseudomonas* species are thought to be important in the breakdown of glyphosate in the soil (Gimsing et al. 2004). Other microbes use glyphosate and AMPA as a source of phosphorus.

There are a number of possible explanations why GM RR soya treated with glyphosate should suffer from increased *Fusarium* activity compared with crops not sprayed with glyphosate (Powell & Swanton 2008):

- Stimulation of pathogenic fungi by glyphosate, either via the roots or by direct application to the soil.
- Glyphosate may inhibit of the production of antagonistic chemicals produced by the plant to protect itself (for example, Phytoalexins are produced by plants to protect them from harmful microbes).
- Glyphosate may inhibit the production of protective plant tissues such as lignin.
- Increased levels of pathogen inoculum on weeds if control in the GM RR crop is delayed.
- Enhanced stimulation of pathogens compared with microbes that are antagonistic to pathogens.

6.5 Case studies of glyphosate impacts on soil-plant system

6.5.1 Root rot in soybeans

The roots of soybean plants growing near giant ragweed plants (*Ambrosia trifida*) that had been treated with glyphosate in Indiana, US, were found to have black lesions on 90 to 95% of their roots, caused by the pathogenic fungus *Corynespora cassiicola*. By comparison, lesions were found on only 5-10% from plants growing next to non-treated ragweed. Yield losses from plants affected by glyphosate sprayed weeds were four times those of other soybean plants (Huber et al. 2005).

6.5.2 Citrus variegated chlorosis (CVC)

The symptoms of this disease are a yellowing of the leaves of citrus plants, similar to that caused by manganese and zinc deficiencies. Weed control in citrus plantations in Brazil involved the use of glyphosate. The method developed by the International Plant Nutrition Institute in Brazil was to stop using glyphosate for weed control around the trees and replace it with a mulch of grass cut from between the rows (Yamada & Castro 2005). This controlled weeds and restored manganese and zinc to sufficient levels in the soil. The removal of glyphosate also reduced the incidence of crown rot (*Phytophora* species).

6.5.3 Take-all in cereals

The take-all fungus, *Gaeumannomyces graminis* (*ascomycota*), is a major root-rot pathogen of cereals and grasses. Glyphosate is used extensively to clear weeds before cereals are sown, and it has been recognised for many years that take-all infection is increased following the use of the herbicide (Johal & Huber 2009). Take-all is also increased following applications of glyphosate associated with the cultivation of GM RR soya the preceding year in comparison with the use of other herbicides. It is thought that this increase in take all severity is thought to be associated with Mn-deficiency induced by glyphosate (Johal & Huber 2009).

6.6 Summary

When sprayed, glyphosate enters the soil either directly or indirectly. In the soil, the inter-relationships between glyphosate, AMPA, soil minerals and microbes are complex.

It is not known exactly how glyphosate influences soil processes, or soil health. However, **it is now clear that presence of glyphosate in the rhizosphere can affect the uptake of essential micronutrients from the soil, the fixing of nitrogen by root nodules and increase plant's vulnerability to diseases.**

7] Weed resistance and glyphosate - the failure of GM Roundup Ready technology

As with GM crops in general, GM herbicide-tolerant crops are primarily grown in North America, Brazil and Argentina (ISAAA 2011; see Chapter 1). Farmers who adopted these GM crops did so because the seeds were advertised (e.g. Monsanto 2009a) as allowing better and easier weed control that would make crop management much simpler, cheaper and less time intensive (see Chapter 1). Consequently, GM RR soya, maize and cotton have gained significant market shares in the Americas.

When they first appeared in the mid 1990s, weed resistance to herbicides as a result of GM RR crops was rarely discussed, although the phenomenon of weed resistance to herbicides was well known. Now, 15 years later, weed resistance to glyphosate is one of the most well documented effects and a 'major environmental concern' of the cultivation of GM RR crops (IAASTD 2009a).

7.1 A false dawn

For the first few years following their introduction in 1996, GM RR crops did indeed perform as the adverts had promised. Roundup was widely, and possibly indiscriminately, used on GM RR crops, as evidenced by the increase in glyphosate usage (see Chapter 1). Farmers soon became dependent on glyphosate as their main means of chemical weed control in fields of GM RR soya, maize and cotton. They were unaware - or possibly unconcerned - that weed resistance could occur on their farms. However, it was only a very short time before the first glyphosate resistant weed - horseweed (*Conyza canadensis*) - was confirmed in areas of soybean cultivation in 2000 (Zelaya et al. 2004).

US scientists have suggested that the rapid spread of glyphosate resistance in horseweed can be traced to the use of zero tillage in GM RR crops. Zero tillage is where the soil is not ploughed or tilled. It used as a soil and carbon conservation tool by both sustainable and industrial agricultural systems. In industrial agricultural systems, it is often associated with GM herbicide-tolerant crops where weed control is achieved by the use of herbicides.

'No-tillage corn (Zea mays L.) and soybean (Glycine max (L.) Merr.) production has been widely accepted in the mid-Atlantic region, favouring establishment of horseweed (Conyza canadensis (L.) Cronq). Within 3 years of using only glyphosate for weed control in continuous glyphosate-resistant soybeans, glyphosate failed to control horseweed in some fields. Seedlings originating from seed of one population collected in Delaware were grown in the greenhouse and exhibited 8 to 13-fold glyphosate resistance compared with a susceptible population.'
(Van Gessel 2001)

A survey of 1,200 farmers across six US States in 2005/06 found that only 3 out of 10 farmers thought that glyphosate-resistant weeds were a serious issue and a 'substantial number of farmers underestimated the potential for glyphosate resistant weed (GR) populations to evolve in an agro-ecosystem dominated by glyphosate as the weed control tactic' (Johnson et al. 2009). Other studies have confirmed that farmers do not start to manage for weed resistance until they have appeared in their fields (Beckie 2006):

'Part of the reason growers do not manage proactively is because most know other options are still available and expect companies to continue to provide new technology. Unfortunately, companies are not being as successful in discovering selective herbicides with new modes of action as they have been in the past.'
(Green 2008)

In Argentina, the first glyphosate resistant weed to be recorded was Johnsongrass (Sorghum halepense) in 2002 (Binimelis et al. 2009). However, early warnings were not heeded, and farmers who raised concerns in the Las Lijatas (northern Argentina) area were reassured.

'Little attention was paid to the uncontrolled clumps [of glyphosate-resistant Johnsongrass] and the farmer complained that no effective action was taken because they were misled by technical advisors who stated that the situation was not problematic. This year, upset by the increasing severity of the resistance problem, he decided to speak up and talk to the local press to raise awareness and speed up proper action.'
(Valverde & Gressel 2006)

This lack of attention to the early signs of weed resistance may have been important in deepening the problems of weed resistance in Argentina. Johnsongrass is 'one of the world's worst weeds' (Bryson 2000) and hence there is real concern about its sudden resurgence in GM RR soya.

'…The evolution of glyphosate-resistance in S. halepense [Johnsongrass] is a major threat to glyphosate-resistant soybean productivity in northern fields of Argentina.'
(Vila Aiud et al. 2008)

A glyphosate-resistant biotype (variety or strain) of Johnsongrass has also been found in Arkansas in 2005, once again in areas of GM RR soya cultivation (International Survey of Herbicide Resistant Weeds 2010).

The first reported case was confirmed in Rigid Ryegrass (*Lolium rigidia*) in Victoria, Australia in 1997 (Powles 1998). Since then the number of species and strains with glyphosate resistance has increased dramatically (Fig. 7). From zero in 1996, glyphosate resistance has now been confirmed in over 20 species and over 100 resistant strains have been identified (Table 2). Although these weeds occur in several continents, they primarily occur in the US and the Americas (Fig. 7), where GM RR crops are primarily grown (see Chapter 1). Weed scientists link this rapid growth to the expansion of GM RR crops and there is widespread concern about the agricultural and economic impacts this has and will be causing.'

'Because glyphosate is the herbicide most often used in no-till and minimum-till systems, GR [glyphosate resistant] volunteer crop plants and glyphosate-resistant or tolerant weeds will jeopardise the sustainability of those systems.'
(Mallory-Smith& Zapoila 2008)

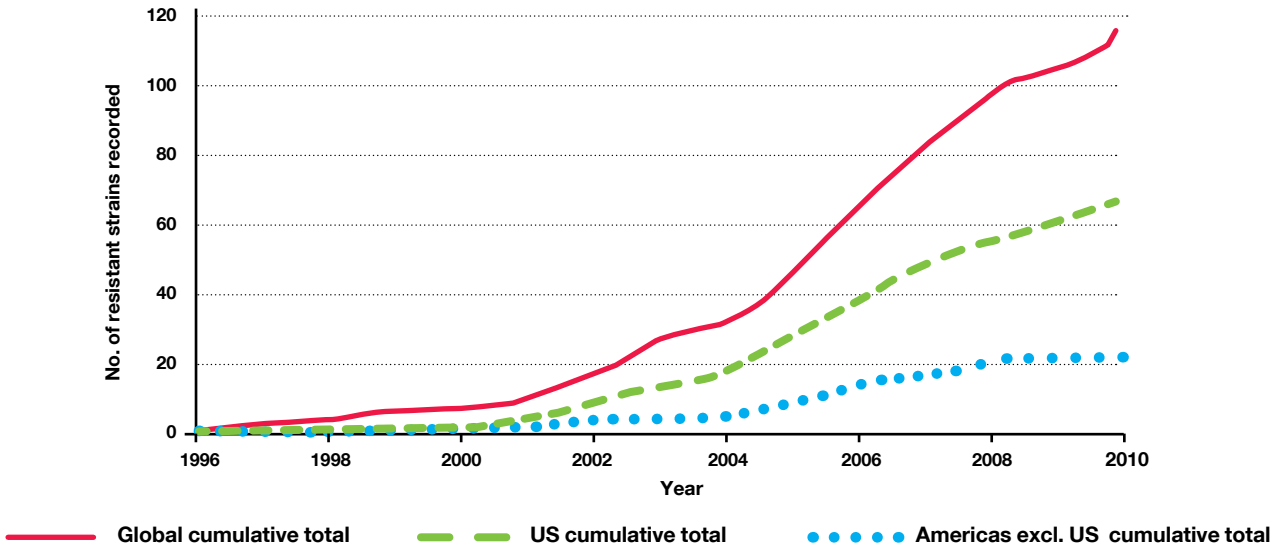

Fig 7: Increase in the occurrence of glyphosate resistant weeds over the past 15 years in the US, the Americas and globally. GM Roundup Ready (RR) crops (resistant to glyphosate) were first introduced in the mid 1990s and grown principally in the US and elsewhere in the Americas (South America and Canada). The occurrence of glyphosate-resistant weed strains follows the pattern of GM RR cultivation with the highest frequency occurring in the Americas, notably the US, and increasing in the years since the introduction of GM RR crops. Based on data from the International Survey of herbicide Resistant Weeds www.weedscience.org.

Table 2: Infestation levels of glyphosate-resistant weed species around the world[9]

Glyphosate-resistant weed	Country	Number of locations where resistance confirmed[10]	Estimated maximum total area infested (all locations) (ha)	Crops affected	Year glyphosate resistance first detected
Palmer amaranth *Amaranthus palmeri*	US	11	2 030 000	Maize, cotton and soya	2005
Common water hemp *Amaranthus rudis*	US	7	413 000	Maize and soya	2005
Common ragweed *Ambrosia artemisiifolia*	US	7	4 960	Soya	2004
Giant ragweed *Ambrosia trifida*	US, Canada	12	9 780	Soya, cotton and maize	2004
Australian Fingergrass *Chloris truncata*	Australia	1	4.05	Cropland	2010
Hairy Fleabane *Conyza bonariensis*	US, Colombia, Brazil, Spain, South Africa, Israel, Australia	9	8 620	Roadsides, fruit and orchards, maize, wheat, soya	2003
Sumatran fleabain *Conza sumatrensis*	Spain	1	20.2	Orchards	2009
Horseweed/Marestail *Conyza canadensis*	US, Brazil, Spain, China, Czech Rep	23	3 340 000	Soya, maize, cotton, rice, fruit, orchards, road side, railway, nursery	2000
Sourgrass *Digitaria insularis*	Paraguay, Brazil	5	81 400	Soya, orchards	2006
Junglerice *Echinochloa colona*	Australia	2	607	Cropland	2007
Goosegrass *Eleusine indica*	Colombia, Malaysia	3	208	Cropland, coffee, cotton	1997
Wild poinsettia *Euphorbia heterophylla*	Brazil	1	202	Soya	2006
Italian ryegrass *Lolium multiflorium*	Chile, Brazil, US, Spain, Argentina	11	8 680	Cropland, orchards, fruit, cotton, soya,barley, wheat	2001
Rigid ryegrass *Lolium rigidia*	Italy, Spain, France, South Africa, Australia, US	14	10 400	Orchard and vineyards, asparagus, cereals, wheat, almonds, cropland, sorghum	1996
Perennial ryegrass *Lolium perennes*	Argentina	1	20.2	Barley, cropland, soya, wheat	2008
Ragweed Parthenium *Parthenium hysterophorus*	Colombia	1	40.4	Fruit	2004
Kochia *Kochia scoparia*	US	2	4 050	Maize, cotton, cropland and soya	2007
Buckhorn Plantain *Plantago lanceolata*	South Africa	1	20.2	Orchards and vineyards	2003
Johnsongrass *Sorghum halepense*	US, Argentina	4	40 500	Soya	2005
Liverseedgrass *Urochloa panicoides*	Australia	1	20.2	Sorghum, wheat	2008
Blue grass *Poa annua*	US	1	4.04	Turf	2010
Total global area glypohosate resistant weeds (2010)			**5 960 000**		

9 Data from the International Survey of Herbicide Resistant Weeds (www.weedscience.org). It does not include glyphosate resistant volunteer crops, which are also common in RR crops.
10 Represents the number of locations where the resistant biotypes are found. The number of infestations at each location range from one to 100 000.

The confirmation of glyphosate resistance in more species in the near future seems highly probable. Twenty-one other weeds in Argentina have been listed as 'just barely controlled by glyphosate' and 'might be the next to upgrade to full resistance by another evolutionary step' (Valverde & Gressel 2006). These include field bindweed (*Convolvulus arvensis*), curled dock (*Rumex crispus*) and morning glory (*Impomoea purpurea*).

It is very clear that weed resistance to glyphosate is an increasing problem across the globe and most prominently where GM RR crops are widely grown. The ramifications of this increased weed resistance are that extreme measures are recommended by Monsanto to prolong the effectiveness of GM RR crops.

'…More worrisome are glyphosate-resistant populations of far more economically damaging weed species [than Lolium].'
(Powles 2008)

7.2 Monsanto's Reaction to reports of resistant weeds

Monsanto is highly aware of the growing resistance problem in GM RR crops but appears reluctant to take on liability for the extra costs currently being borne by farmers.

'Growers must be aware of and proactively manage for glyphosate-resistant weeds in planning their weed control program. When a weed is known to be resistant to glyphosate, then a resistant population of that weed is by definition no longer controlled with labelled rates of glyphosate. Roundup agricultural herbicide warranties will not cover the failure to control glyphosate-resistant weed populations.'
(Monsanto, undated)

Monsanto has published guidance on how to deal with the growing weed resistance problems in GM RR crops (Monsanto 2011) and has already begun developing prevention strategies based on the use of combinations of herbicides and timing of applications.

- The first strategy is **the use of either stronger formulations of glyphosate**[11] **or of tank mixtures of glyphosate and other herbicides.** For instance, 2,4-D – one of the active ingredients of Agent Orange, the defoliant used by the US Army during the Vietnam War – is recommended for burning down weeds prior to sowing marestail (Monsanto 2008).
- The second strategy is **to produce seeds with several herbicide tolerant genes (gene stacking) by crossing different GM herbicide-tolerant varieties** so that different herbicides can be applied to the growing crop in rotation or in tank mixes. This will ensure that weeds that are resistant to glyphosate will be killed by other herbicides (see, for example, Monsanto 2009). For instance, Monsanto has recently announced an agreement with the chemical and biotechnology company BASF to develop crops stacked with glyphosate and dicamba tolerant genes (Monsanto 2010c; see also Behrens et al. 2007; Service 2007). Less is known about the toxicity of dicamba but there are concerns it may be toxic to aquatic organisms[12].
- The third strategy is **to use herbicides that remain active in the soil (residual herbicides or residuals)**, which kill seedling weeds as soon as they germinate.

It is clear from these strategies that weed resistance is a serious problem for the continued efficiency of GM RR crops, and tackling the problem requires extreme measures. Currently, no cost estimates are available for the increased amount of farmer expenditure on weed control as a result of weed resistance, but they are likely to be considerable. These extreme measures may have environmental and possibly health implications.

'Most of the documented cases of evolved GR [glyphosate resistant] weeds in the past six years have been in GR crops.'
(Duke and Powles 2008)

11 For example, 'Roundup Weather MAX'. See http://www.monsanto.com/products/Pages/roundup-weathermax-herbicide.aspx
12 Pesticide Action Network. See http://www.pesticideinfo.org/Detail_Chemical.jsp?Rec_Id=PC32871

Farmers are having to resort to stronger formulations of glyphosate or herbicide mixtures to cope with weeds resistant to glyphosate. This has resulted in an escalation of the pesticides 'arms race', with an increasing toxic burden on the environment.

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7.3 False solutions create more problems

The strategy of applying tank mixes pre and post-emergence and residual herbicides will add to the amounts being used and to the overall toxic burden on the environment from GM RR crops.

This strategy could also create new problems if herbicides are overused, leading to the evolution of weeds with resistance to several herbicides. The problem of multiple weed resistance is already well established in the US soya and corn belts. Several weeds that have developed glyphosate resistance are also resistant to other herbicides. In soya crops one strain of common waterhemp (*Amaranthus rudis*) already has resistance to sulphonylureas (e.g. thifensulfuron-methyl), triazines (e.g. atrazine) and glyphosate. Another has resistance to sulphonylureas (e.g. cloransulam-methyl), triazines (e.g. atrazine) and diphenyl ethers (e.g. Lactofen). Twelve other strains have double-resistance. In all there are already seven biotypes in soya crops with multiple resistances that include a resistance to glyphosate. In maize, there are three multi-resistant biotypes including glyphosate. Many of these problem weeds are common to both crops (International Survey of Herbicide Resistant Weeds 2010).

Options for using tank mixes of herbicides or soil residuals to cope with weed resistance are already limited in both crops by the numerous (over 20) weed species that already have resistance to one or more active ingredients.

The future strategy for dealing with glyphosate-resistant weeds involves the use of a wide range of active ingredients in mixtures or singly with a cocktail of adjuvants used in each formulated product. The toxicology of such mixtures is unclear, as approval processes tend to focus on the individual products rather than any additive and/or synergistic effects. Nor can the development of more weeds with multiple resistances in the future be ruled out. Sustainable solutions will not come from the continual adherence to the crop monocultures reliant on chemical weed control that GM RR crops epitomise.

7.4 Conclusion

The rapid evolution of weeds that are resistant to glyphosate is a result of farmers becoming over-reliant on one herbicide for weed control. This is particularly associated with GM RR crops. Now that resistance to glyphosate is widespread in weeds within GM RR soy, maize and cotton crops, farmers have to resort to using mixtures of herbicides.

Thus, the promise of reduced herbicide use and cheaper and easier weed controls has not been delivered. However, it is clear that GM RR crops have brought about an escalation in the pesticides 'arms race', with an increasing toxic burden on the environment involving significant uncertainty about the overall safety of glyphosate for people and biodiversity.

8] Conclusions

There are many problems with GM crops, fundamentally their tendency to produce unexpected and unpredictable effects. This is related to the process by which they are created, the forcible insertion of gene(s) into a plant genome. No GM crops should be cultivated in the environment, nor enter the food chain.

In this report, the focus is on one GM trait, that of herbicide resistance - in particular, it looks at the close association between Roundup Ready crops and the herbicide glyphosate. The evidence presented in the report demonstrates that glyphosate-based herbicides, such as Roundup, can have harmful effects on human health and the environment.

Exposure of humans to glyphosate has been linked to various health effects, including reproductive effects, cancer and neurological effects. Glyphosate interacts with soil chemistry and biology, resulting in a variety of impacts including reduced plant nutrition and increase vulnerability to plant diseases. Glyphosate may also leach into surface and groundwater, where it may damage wildlife and possibly end up in drinking water.

Thus, glyphosate and Roundup are far from benign herbicides. A review of their safety for human and animal health and for the environment is urgently needed.

GM RR crops have greatly increased glyphosate usage, especially in the Americas where they are primarily grown. Given the new evidence of glyphosate toxicity, this is of great concern. The rise in glyphosate-resistant weeds is associated with GM RR crops, and the escalation in the 'arms-race' against these resistant weeds fuels concerns that even more glyphosate, in stronger formulations and possibly with additional herbicides, will be used on GM RR crops in the future. Similar problems would be highly likely to arise if other GM herbicide-resistant crops are widely cultivated and farmers become dependent on a single herbicide, e.g. GM crops resistant to glufosinate ammonium, marketed as 'Liberty Link'. This facet of GM herbicide-tolerant crops should be enough to lead to a ban on their cultivation.

GM herbicide-tolerant crops, as epitomised by GM RR crops, are not part of a sustainable agriculture system. As with all GM crops they have been developed for, and are economically profitable within, an industrial agriculture system that involves large-scale monocultures that depend on costly, polluting inputs such as herbicides, synthetic fertilisers and fossil fuels.

In contrast, ecological farming both relies on and protects nature by taking advantage of nature's goods and services, such as biodiversity, nutrient cycling, soil regeneration and natural enemies of pests, and by integrating these natural goods into agro-ecological systems.

The widespread and increasingly intensive use of glyphosate in association with the use of GM RR crops, poses risks to the environment and human health. Given the problems that are now evident, no new GM glyphosate-tolerant crops should be authorised. As part of broader considerations of the way forward for agriculture, no GM herbicide-tolerant crop can form part of a sustainable agriculture model, and the cultivation of all such crops should be banned.

GM herbicide-tolerant crops, as epitomised by GM RR crops, are not part of a sustainable agriculture system…In contrast, modern agro-ecological farming practices both relies on and protects nature by taking advantage of nature's goods and services.

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No GM herbicide-tolerant crop can form part of a sustainable agriculture model, and the cultivation of all such crops should be banned

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GLYPHOSATE: DESTRUCTOR OF HUMAN HEALTH AND BIODIVERSITY

Another Silent Killer

Compiled by Rosemary Mason MB ChB FRCA with information from a global network of independent scientists, toxicologists, beekeepers, environmentalists, Governments, Industry and Regulators

An increase in the incidence of Type 2 diabetes, obesity and autism has been reported in Scotland. Similar increases have been seen globally. The herbicide glyphosate was introduced in 1974 and its use is accelerating. The manufacturers claim it to be safe, but none of the Regulatory Agencies are monitoring glyphosate levels in groundwater. By courtesy of independent researchers around the world we present evidence that glyphosate interferes with many metabolic processes in plants, animals and humans, and glyphosate residues have been found in all three. Glyphosate is an endocrine-disruptor (as are many herbicides) it damages DNA and it is a driver of mutations that lead to cancer. We present graphs from the US which correlate glyphosate application and the percentage of GE soy and corn crops to the incidence and prevalence of various diseases in those on a Western diet. The Pearson's correlation coefficients are very strong and highly significant for obesity, diabetes, autism, thyroid cancer, liver cancer, deaths from Parkinson's, Senile Dementia and Alzheimer's, inflammatory bowel disease and acute kidney failure. We present Cancer Research UK graphs of upward trends in cancer incidences between 1975 and 2009, which are in line with the US graphs. Other consequences are gastrointestinal disorders, heart disease, depression, infertility, birth defect s and other cancers. The data for the amount of non-agricultural use of glyphosate in the UK appear to be confidential. Parts of South Wales, in former mining areas, Japanese knotweed and Himalayan Balsam abound. The local Council does not hold glyphosate records. Instead it contracts out to a commercial organisation to supply industry approved vegetation management techniques. A quote from the contractor: "The glyphosate we use called round up has a hazard free label." The level of glyphosate in a river draining from areas of Japanese knotweed was 190 parts per trillion (ppt) and local tap water was 30 ppt. These were of the order of concentrations found in a study in 2013 which showed that breast cancer cell proliferation is accelerated by glyphosate in extremely low concentrations: *"potential biological levels at part per trillion (ppt) to part per billion (ppb)."*

Summary

Glyphosate, the most widely used herbicide, is destroying human and animal health as a result of disruption of gut bacteria.Two key problems caused by glyphosate in the diet are nutritional deficiencies, especially minerals and essential amino-acids, and systemic toxicity.

We present graphs from the US which correlate glyphosate application and the percentage of GE soy and corn crops to the incidence and prevalence of various diseases in those on a Western diet. The Pearson's correlation coefficients are very strong and highly significant for obesity, diabetes, autism, thyroid cancer, liver cancer, deaths from Parkinson's, Senile Dementia and Alzheimer's, inflammatory bowel disease and acute kidney failure. We present Cancer Research UK graphs of upward trends in cancer incidences between 1975 and 2009, which are in line with the US graphs. Other consequences are gastrointestinal disorders, heart disease, depression, infertility, birth defects and other cancers. The data for the amount of non-agricultural use of glyphosate in the UK appear to be confidential. Parts of South Wales, in former mining areas, invasive plants such as Japanese knotweed and Himalayan Balsam abound. The local Council does not hold annual records of glyphosate application to these invasive weeds. It has a contract with a commercial organisation to supply industry-approved vegetation management techniques. A quote from the contractor: "*The glyphosate we use called round up has a hazard free label".*

Monsanto Corporation has been repeatedly convicted in Law Courts around the world for not telling the truth about the safety of its best-selling weed-killer, Roundup®. In 2010, in a document on glyphosate use in Europe, Monsanto continues to promote the myth. It is described as "*environmentally benign*"…"*has an excellent safety profile to operators, the public and the environment"…"uses to benefit mankind and the environment."*
The level of glyphosate in one Welsh river draining from areas of Japanese knotweed spraying was 190 parts per trillion (ppt) and local tap water was 30 ppt. These were of the order of concentrations found in a study in 2013 which showed that breast cancer cell proliferation is accelerated by glyphosate in extremely low concentrations: "*The present study used pure glyphosate substance at log intervals from 10^{-12} to 10^{-6} M. These concentrations are in a crucial range which correlated to the potential biological levels at part per trillion (ppt) to part per billion (ppb) which have been reported in epidemiological studies."* In the UK the incidence of breast cancer almost doubled between 1975 and 2010.

Glyphosate sales in Europe are increasing because industry is continually finding new uses. It is recommended throughout the crop cycle, including as a drying agent 7-10 days before harvest. This leaves glyphosate residues on crops which enter the food chain of animals and humans. On non-agricultural land it is sprayed "*around structures on farms, amenity and industrial areas and on railways.*" In urban areas it is sprayed on vegetation on streets, pavements and major highways. Japanese Knotweed, Bracken and Rhododendron and are amongst many invasive weeds for which Roundup® is promoted. It is *"approved for weed control in forestry and aquatic areas*". In the US its use has increased dramatically on GE crops because of super-weeds. Massive amounts of GM soya is being imported into Europe for animal feed and some foods, and Regulators have been allowing the industry to increase the Maximum Residue Limits for glyphosate in food and feed in imports.

Independent scientists have measured glyphosate in soil, air and rainwater. During flooding events, run-off is particularly high after urban use. The effects of pesticides are manifest at water catchment areas. However, levels of glyphosate and the neonicotinoid insecticides are not monitored in surface water, groundwater or drinking water by the US Geological Survey

National Water Quality Assessment Program, under the European Water Frame Directive, or by the UK Environment Agency.

Regulators and Industry have only tested the 'active' ingredient glyphosate. The commercial formulations contain an untested adjuvant which is toxic to human cells. The work of independent scientists has been rejected or suppressed by Industry, Regulators or Rapporteur Member States. Industry data are hidden on the grounds of commercial confidentiality. When scientists have exposed the dangers of GMOs many have been vilified or have lost their jobs.

Glyphosate and aminomethylphosphonic acid (AMPA) residues were found in soy bean plants, leaves and grains; higher levels were found when glyphosate was sprayed several times during the crop year. In 2013, glyphosate and AMPA residues were found in the urine of more than one third of urban dwellers in 18 countries in Europe. Glyphosate must be in our food and/or drinking water. Regulators have increased the Maximum Residue Levels in food and feedstuffs of glyphosate, neonicotinoid insecticides and many other pesticides.

GMO crops were approved by the European Food Safety Authority (EFSA) after 90-day feeding studies on rats by Monsanto. Séralini's team at CRIIGEN argued that 90 days was too short to evaluate chronic toxicity of glyphosate and GM crops. His team did a 2-year study and found Roundup®-tolerant maize and Roundup® provoked chronic hormone and sex dependent pathologies. Female mortality was 2-3 times increased mostly due to large mammary tumours and disabled pituitary. Males had liver congestions, necrosis, severe kidney nephropathies and large palpable tumours. Tumours started to occur in male rats at 4 months, one month beyond the time for which GMs were tested. When the paper was published in October 2012, industry and GMO scientists cried "*fraud!"* However, EFSA has eventually agreed on 2-year feeding studies for new GMOs. Here is a 12-minute YouTube made by Séralini's team over the 2-year period of testing in rats.
http://www.youtube.com/watch?v=Njd0RugGjAg&feature=player_embedded

Evidence was published in 2013 (a combined study from Australia and the US) that pigs fed a GM diet had abnormal organs, compared with those on a non-GM diet. GM-fed females had on average a 25% heavier uterus than non-GM-fed females and the level of severe inflammation in stomachs was markedly higher in pigs fed on the GM diet. This confirmed the experiences of some farmers that mortality was higher in sows on GM feed compared with non-GM. Sows had digestive problems, some died and the piglets had diarrhea. Reproductive problems were manifested by abortions, deformities in new born pigs and smaller litters. They required more antibiotics. Studies of the effects on pathogens in farm animals showed that glyphosate destroys beneficial bacteria and allows harmful ones, such as salmonella and clostridium, to flourish. This could account for outbreaks of food poisoning in humans that continue to occur. In the search for the causes of serious diseases of entire herds of animals in northern Germany, especially cattle, glyphosate has repeatedly been detected in the urine, faeces, milk and feed of the animals.

Glyphosate causes environmental damage to earthworms, songbirds, small mammals and bees. Glyphosate, an endocrine-disrupting herbicide, and the systemic neonicotinoid insecticides, cause immune suppression in insects and mammals. Both are highly toxic to aquatic organisms, amphibians, bees and fish.

US Kid's Health Report October 2012[1]. A Generation in Jeopardy: How pesticides are undermining our children's health & intelligence p 26

"*Our current system of industrial agriculture and pest control relies on chemical inputs sold by a handful of corporations. These multinational corporations wield tremendous control over the system, from setting research agendas to financing, crop selection and inputs throughout the production and distribution chain. Not surprisingly, these same corporations also hold significant sway in the policy arena, investing millions of dollars every year to influence voters, lawmakers and regulators at both the state and federal level to protect the market for pesticides. The result is agriculture, food and pest control systems that serve the interests of these corporations well. It does not, however, serve farmers, who have lost day-to-day control of their operations and are putting themselves and their families in harm's way. Farmworker interests are not served, as workers are continuously exposed to chemicals known to harm human health. And the health of children across the country is compromised by exposure to pesticides used to control pests in agriculture and where they live, learn and play. In short, the system is broken*".

The above statement from Pesticides Action Network North America applies equally well to the UK. The British Government played its part in suppressing the dangers of GM Crops. In 1998 Prime Minister Tony Blair received a phone call from the White House. A Senior GM Scientist Dr Arpad Pusztai working in Scotland had shown that rats fed GM potato had sustained immune damage. Dr Pusztai's Department at the Rowett Research Institute in Scotland was closed down, Dr Pusztai was suspended, he was silenced and he was banned from working on GMO. Likewise, in 2012, the Science Media Centre did its best to discredit Prof Gilles-Eric Séralini when his 2-year feeding study in rats showed tumours, liver and kidney damage. The Science Media Centre and the Department of Health played down the advice of the Royal College of Obstetricians and Gynaecologists for pregnant patients to avoid exposure to pesticides, some of the most toxic of which are marketed for home and garden use. GM Roundup® Ready crops are lethal to human health and the environment, yet the Defra, Science and Environment Ministers are trying to force them on an unwilling public.

As well as working closely with the Agrochemical Corporations, the British Government's Strategy for UK Life Sciences[2] is dependent on funding from the Pharmaceutical Corporations and the Pesticides Industry. Syngenta's parent company is AstraZeneca. Syngenta and AstraZeneca are represented on the UK Advisory Committee on Pesticides and the Committee on Toxicity of Chemicals in Foods, Consumer Products and the Environment. The founder of Syngenta is the Chairman of Cancer Research UK (CRUK). CRUK is giving money (£450 million/year) to the Government's Strategy for UK Life Sciences and AstraZeneca is providing 22 compounds to academic research to develop medicines. AstraZeneca manufactures six different anti-cancer drugs mainly aimed at breast and prostate cancer. The Corporation has links in Asia, including Hospitals in China, Japan, Korea, and collaborators in Russia. AstraZeneca's Oncology Website[3] has the following prediction: "*Cancer claims over 7 million lives every year and the number continues to rise. Deaths are estimated to reach 12 million by 2030.*

[1] http://www.panna.org/publication/generation-in-jeopardy

[2] https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/32457/11-1429-strategy-for-uk-life-sciences.pdf

[3] http://www.astrazeneca.co.uk/medicines/oncology

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This document has been compiled by Rosemary Mason MB ChB FRCA with information from a global network of independent scientists, toxicologists, beekeepers, environmentalists, as well as the UK, US and Australian Governments, the Pesticides Industry and Regulators.

With grateful thanks to Anthony Samsel, Dr Stephanie Seneff and Dr Nancy Swanson; however, the responsibility for the contents of this paper lies with the author.

02/09/2013

Part 1 Medical Agencies in Scotland highlight epidemics of obesity, diabetes and autism in 2013

- Ms Judson, Scottish Director of Diabetes UK, was quoted as saying: "*Since 2006 the incidence of diabetes had increased by 25.6% and the consequences of diabetes such as blindness and the need for amputation were also increasing in younger age groups*." She said people as young as 13 have been diagnosed with Type 2 diabetes[4].

- A similar warning about obesity had come from Dr Andrew Fraser representing the Royal College of Physicians of Edinburgh on 10th March 2013[5].

- On June 12/13th 2013, an autism conference was held in Edinburgh[6]. Dr Martha Herbert, an expert on autism from Harvard Medical School, was an invited speaker. Dr Herbert believes the culprit is an environmental toxin in autistic children that interferes with nutrient absorption. "*We need to get them built up again, getting the gut micro-flora sorted out*". The US has had an even more dramatic (and earlier) rate of increase than in Scotland (261% for boys and 385% for girls between 1997 and 2008)[7].

Samsel and Seneff have reviewed independent evidence against glyphosate
In a Review, Samsel & Seneff argue that Glyphosate, a widely used herbicide, is associated with most of the diseases and conditions associated with a Western diet, including gastrointestinal disorders, obesity, depression, autism, infertility, cancer and Alzheimer's disease. It is claimed by industry supporters that: "*Glyphosate is not poisonous to mammals- it inhibits EPSP (5-enolpyruvylshikimate-3 phosphate) synthase an enzyme that mammals lack because we obtain aromatic amino acids in our diet"*. However, we can only absorb nutrients by courtesy of the bacteria in our gut. Glyphosate disrupts our gut bacteria, without which we could not live. It is a strong chelator of essential minerals, such as cobalt, zinc, manganese, calcium, molybdenum and sulphate. In addition it kills off beneficial gut bacteria and allows toxic bacteria such as *Clostridium difficile* to flourish[8]. Two key problems caused by glyphosate in the diet are nutritional deficiencies, especially minerals and essential amino-acids, and systemic toxicity.

Glyphosate residues are increasingly found in humans and animals
Samsel & Seneff's paper has some complicated metabolic concepts, so we have provided links to 3 videos. In the first Dr Stephanie Seneff is interviewed by Jeffrey M. Smith, the Executive Director of the Institute for Responsible Technology and bestselling author of *Genetic Roulette* and *Seeds of Deception.* The whole interview takes about an hour, but it has been also split up into shorter sections in which obesity, diabetes and autism are discussed

[4] http://www.thetimes.co.uk/tto/health/news/article3799473.ece

[5] http://www.scotsman.com/news/health/doctors-warn-obesity-is-lifestyle-choice-for-scots-1-2828840

[6] http://www.scotsman.com/lifestyle/autism-unlocking-a-generation-1-2944710

[7] 87222060-CDC-Autism-Study-March-2012.pdf

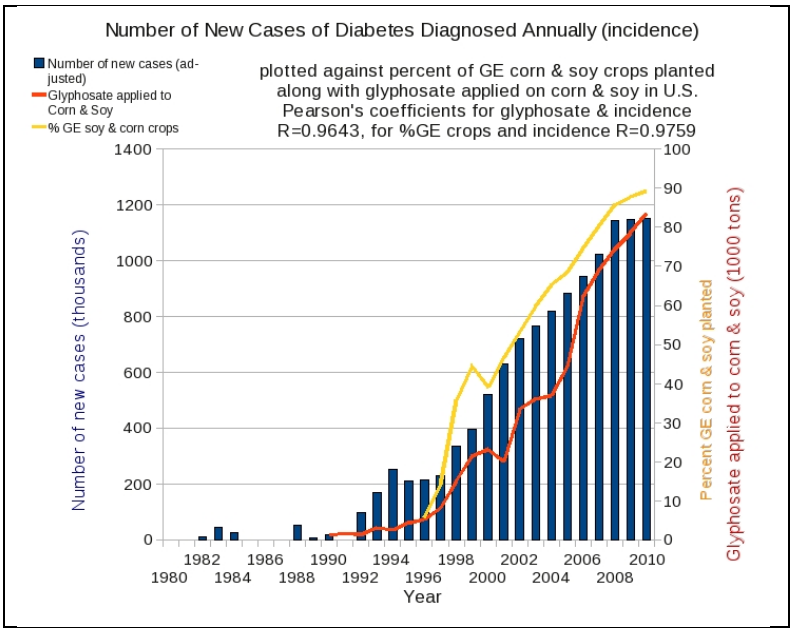
[8] http://www.nationofchange.org/new-study-finds-roundup-could-be-linked-severe-health-issues-1367071482

separately[9]. The second interview, conducted by Zen Honeycutt[10] for Moms Across America, is in two parts. In Part 1 Anthony Samsel explains the implications of children eating GM foods with glyphosate residues: for example, impaired learning abilities, decreased IQ, autism, allergies and asthma. In Part 2[11] he explains the mechanisms of action of glyphosate in the causation of different diseases. There are 160 crops/fruit/vegetables containing glyphosate residues. Gut bacteria form a protective layer over our cell walls; glyphosate disruption causes a leaky gut resulting in inflammatory bowel diseases. Disrupted aromatase impairs immune function. Glyphosate allows toxins through the blood-brain barrier. It disrupts the Cytochrome P450 enzymes in the liver and kidney which provides the mechanism for detoxification of environmental toxins.

Incidence of diabetes, obesity and autism in the US plotted against % GE corn and soy crops planted along with glyphosate applied to corn and soy

The following graphs for the United States are reproduced by kind permission of Dr Nancy Swanson from Genetically Modified Organisms and the Deterioration of Health in the United States[12] (see original doc for references, raw data and statistics).

The incidence of the three diseases has been plotted against the % of GE corn and soy and the glyphosate applied.



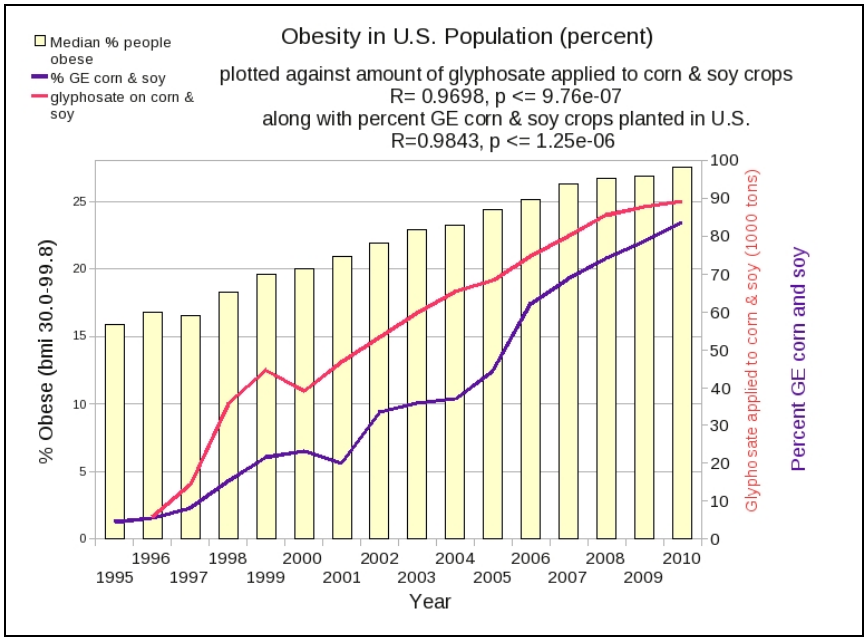
Graph 1 US data for % GE corn and soy crops planted and glyphosate applied plotted against the number of new cases of diabetes (adjusted) diagnosed annually. Crop and glyphosate data from the United States Department of Agriculture; diabetes data from U.S. Centers for Disease Control (CDC).

[9] http://www.youtube.com/watch?v=h_AHLDXF5aw&feature=player_embedded
http://www.youtube.com/watch?v=3rIHhdYCUVw diabetes
http://www.youtube.com/watch?v=JB4GFyjewHQ obesity
http://www.youtube.com/watch?v=JB4GFyjewHQ autism

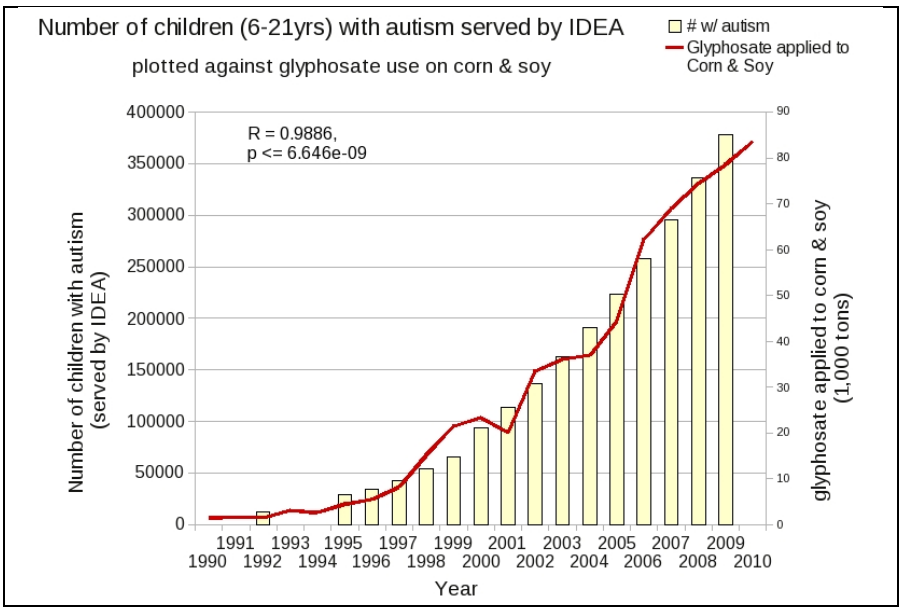
[10] http://www.momsacrossamerica.com/glyphosate_and_autism_asthma_copd_diabetes_and_more
[11] http://www.youtube.com/watch?v=nVjntXhDrx8

[12] http://sustainablepulse.com/wp-content/uploads/GMO-health.pdf

The incidence of Type 2 diabetes, obesity[13] and autism[14] has undergone similar increases in England and Wales[15]. According to Department of the Environment, Food and Rural Affairs, the total area of crops treated with glyphosate in the UK[16] is 1,835,306 ha. However, we have no idea how much is used for the domestic or commercial markets, for forestry, amenity or aquatic areas or to keep towns and cities clear of invasive weeds.



Graph 2 US data for % GE corn and soy crops planted and glyphosate applied to corn & soy plotted against % of U.S. population who are obese (BMI 30.0-99.8). Crop and glyphosate data from the USDA; obesity data from U.S. CDC. By kind permission of Dr Nancy Swanson.



[13] http://news.sky.com/story/1127385/obesity-warning-for-british-children

[14] http://www.telegraph.co.uk/health/9160322/Number-of-children-with-autism-soars-by-more-than-50-per-cent-in-five-years.html

[15] http://www.walesonline.co.uk/news/health/tackling-epidemic-diabetes-wales-4715622

[16] http://pusstats.csl.gov.uk/

Graph 3 Number of children with autism plotted against glyphosate use on GE corn and soy. Autism data were obtained from the U.S. Department of Education, which keeps track of school age children receiving services under the Individuals with Disabilities Education Act (IDEA). This plot is shown using data from USDE for the number of autistic children receiving services. By kind permission of Dr Nancy Swanson.

In 1970, the incidence of autism in the US was 1:10,000. In 2007 it was 1:150. In 2009 it was 1:100. In 2013 it is 1:50 and by 2025 it will be 1:2, i.e. 50%.

Part 2 Evidence from industry of massive increases in glyphosate use in Europe, the US and Latin America

Glyphosate is now used to dry crops before harvest as well as for weed control
Pre-harvest application of glyphosate to wheat and barley in the UK was suggested as early as 1980, but its routine use as a drying agent 7-10 days before harvest began in 2006.
Monsanto's document: The agronomic benefits of glyphosate in Europe [2010][17]
Page 3: "*Since its discovery in the early 1970's the unique herbicidal active ingredient glyphosate 'has become the world's most widely used herbicide because it is efficacious, economical and environmentally benign.' These properties have enabled a plethora of uses which continue to expand to this day providing excellent weed control both in agricultural and non-crop uses to benefit mankind and the environment*. Glyphosate has an "*excellent safety profile to operators, the public and the environment*". The document outlined at least 16 use areas (p3) from vegetation control on land throughout agricultural production, on GM Roundup® Ready Crops and on non-agricultural land "*around structures on farms, amenity and industrial areas and on railways*" (p 4). In 2004 it was used on 13% wheat area. By 2006 it became used more routinely for weed control or pre-harvest treatment (at least 40% cereal and 80% oilseed rape, p 21). This increases glyphosate residues in animal and human food.

Monsanto's recommendations for the use of Roundup® in UK towns and cities
Streets and pavements[18], Japanese knotweed[19], Bracken[20], Rhododendron[21] are amongst many weeds for which Roundup® is promoted. "*It is approved for weed control in amenity, industrial, forestry and aquatic areas*". "*Roundup Pro Biactive and ProBiactive 450 can be used at any time of the year as long as weeds are green and actively growing*". Monsanto advises re-spraying if die-back is not observed at 6 weeks. However, repeated spraying of weeds with Roundup® results in 'super-weeds' since weeds become resistant. NEW RULES 2012: Streets and pavements[9]. *"From 2012 new rules from the regulator, Chemical Regulations Directorate (CRD) prohibits blanket spraying of any herbicide on non-porous hard surfaces. Targeted treatment of weeds must be undertaken on roads, pavements, concrete and paved areas and drains must not be oversprayed."* Did the CRD find toxic levels of glyphosate in water?

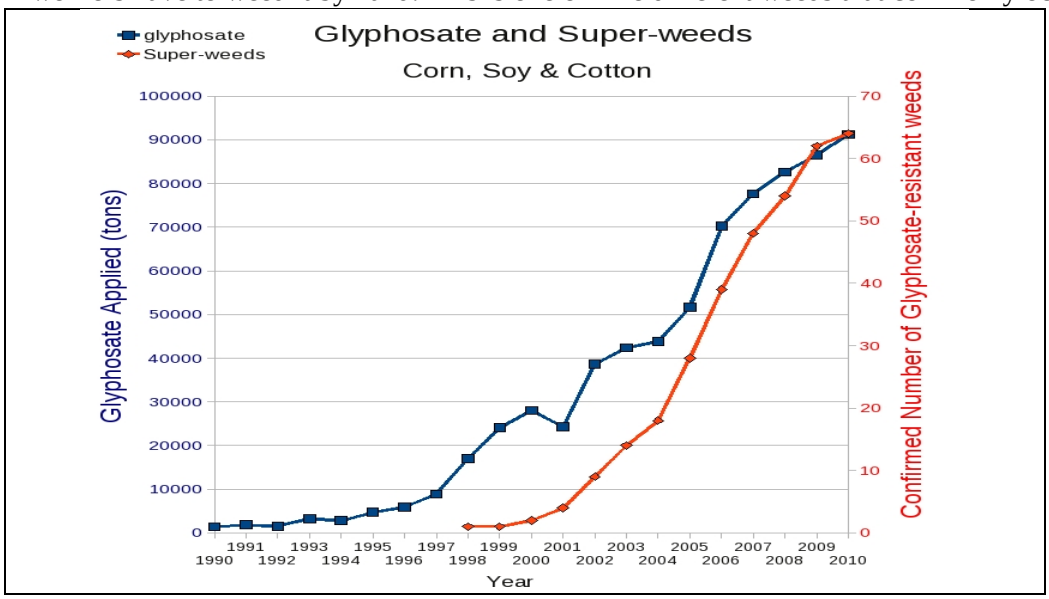
[17] http://www.monsanto.com/products/Documents/glyphosate-background-materials/Agronomic%20benefits%20of%20glyphosate%20in%20Europe.pdf

[18] http://www.monsanto-ag.co.uk/content.output/165/165/Roundup/Amenity/Streets%20and%20Pavements.mspx
[19] http://www.monsanto-ag.co.uk/content.output/170/170/Roundup/Difficult%20Weeds/Japanese%20Knotweed.mspx
[20] http://www.monsanto-ag.co.uk/content.output/171/171/Roundup/Difficult%20Weeds/Bracken.mspx
[21] http://www.monsanto-ag.co.uk/content.output/174/174/Roundup/Difficult%20Weeds/Rhododendron.mspx

In the US, Benton County's 3-year control of river weeds; is it linked to birth defects?
Washington State has a Noxious Weed Control Board and glyphosate is the main herbicide recommended for noxious weed eradication. Benton County Herbicide treatment started in the Yakima River in 2010 and continued for 3 years without monitoring glyphosate levels in water[22]. Three Washington Counties (Yakima, Benton and Franklin) sharing the same irrigation water for agriculture, reported a high number of pregnancies resulting in a fatal birth defect, anencephaly[23]. The cause was a mystery to state health officials[24].

Since the introduction of GM seeds in 1996 the amount of glyphosate used on crops in the US has increased almost 10-fold; 27 million pounds to 250 million pounds in 2009[25]
Industry and lobbyists claim that GM crops reduce the amount of pesticides and that '*super-weeds*' are a myth. The photograph and Graph 4 below and prove them to be wrong.

Northern Indiana. Giant Ragweed (3 m) resistant to glyphosate.
Farm workers have to weed it by hand. This is one of nine different weeds that commonly occur.



[22] http://agr.wa.gov/plantsinsects/weeds/npdespermits/docs/IPMFreshwaterEmergentNoxiousQuarantineListedWeeds.pdf

[23] http://farmwars.info/?p=11137

[24] http://abcnews.go.com/Health/washington-state-health-officials-stumped-high-rate-birth/story?id=19687592

[25] http://water.usgs.gov/nawqa/pnsp/usage/maps/show_map.php?year=2009&map=GLYPHOSATE&hilo=L

Graph 4 Glyphosate and Super-weeds: Glyphosate applied to Corn, Soy and Cotton crops in the U.S. and the number of confirmed glyphosate-resistant weeds. Glyphosate data from USDA; super-weed data from Charles Benbrook. By kind permission of Dr Nancy Swanson.

Impacts of genetically engineered crops on pesticide use in the US – the first sixteen years[26]. Charles Benbrook showed that: "*Herbicide-resistant crop technology has led to a 239 million kilogram (527 million pound) increase in herbicide use in the United States between 1996 and 2011*"… "*The spread of glyphosate-resistant weeds in herbicide-resistant weed management systems has brought about substantial increases in the number and volume of herbicides applied. If new genetically engineered forms of corn and soybeans tolerant of 2,4-D are approved, the volume of 2,4-D sprayed could drive herbicide usage upward by another approximate 50%.*

Monsanto found guilty in courts around the world for false claims about Roundup®
Glyphosate is not environmentally benign. Monsanto Corporation has been repeatedly convicted in Law Courts around the world for not telling the truth about the safety of its best-selling weed-killer, Roundup®. Despite being found guilty every time Monsanto continues to promote the myth.

- 1996 The Attorney General of the State of New York, Consumer Frauds and Protection Bureau, Environmental Protection Bureau. False advertising by Monsanto regarding the safety of Roundup® herbicide (glyphosate)[27].
- 2001 French environmental groups had brought the case on the basis that glyphosate, Roundup®'s main ingredient, is classed as "*dangerous for the environment*" by the European Union. France's highest court confirmed an earlier judgment that Monsanto had falsely advertised its herbicide as "*biodegradable*" and claimed it "*left the soil clean*."
- 2004 Brazil. "*To affirm in advertising that transgenic soy seeds were beneficial to the environment, has cost to the multinational Monsanto American Agrochemicals fined $250,000 by the Federal Regional Court of Brazil. Monsanto used misleading advertising to promote the soybeans, in year 2004, encouraging consumption of GM seeds when even they were prohibited in Brazil. And they not only encouraged their consumption, but also claimed that these seeds were highly beneficial to the environment. This consideration took into account to the Court of Justice headquartered in the Porto Alegre City*"[28].
- 2007/2008 "*In the latest ruling, France's Supreme Court upheld two earlier convictions against Monsanto by the Lyon criminal court in 2007, and the Lyon court of appeal in 2008, the AFP news agency reports*."
- "*In Brazil, Monsanto has been convicted by a court for false advertising claims that GM soy and the herbicide glyphosate, as used in the 'no-till with herbicides' model of cultivation, are beneficial to the environment. This is not the first time Monsanto has been convicted by a court for false advertising over claims that its glyphosate-based herbicides are safe and environmentally friendly. Court rulings against Monsanto's misleading advertising of glyphosate herbicides as safe for human health and the environment date back to the 1990s*"[29].

[26] http://www.enveurope.com/content/24/1/24

[27] http://www.mindfully.org/Pesticide/Monsanto-v-AGNYnov96.htm

[28] http://cimalatinamerica.blogspot.co.uk/2012/08/brazil-brazilian-court-convicts-monsanto.html

[29] http://bit.ly/OZ9icp

Monsanto's Mission Statement for its projects in Latin America (2012 website)
"*Monsanto is committed to helping improve lives – especially the lives of farmers in small rural communities around the world*." Pablo Vaquero, Monsanto Latin America South corporate affairs director, said: "*Today, we are helping to change the lives of many individuals in remote and forgotten communities where opportunities are scarce. We are convinced that by helping with training and education, as a company, we are able to add value to people and their communities.*"
'Projects have been implemented in 14 provinces in Argentina (Buenos Aires, Santa Fe, Córdoba, La Pampa, San Luis, Santiago del Estero, Entre Ríos, Corrientes, Formosa, Misiones, Salta, Tucumán, Jujuy and Chaco) and one in the Republic of Paraguay. Many farmers and people know about Monsanto Company because of the Roundup® Ready trait, which is a trait that gives in-plant tolerance to Roundup® agricultural herbicides. The trait was introduced to the market in 1996 and brought a whole new element to farmers. In 1996, farmers could now plant soybeans, spray the soybeans with Roundup®, and poof- the weeds were gone and the soybeans were still as healthy as they were before they sprayed the field'.

The same rural communities in which glyphosate was regularly sprayed on Roundup® Ready Soya had increased incidence of birth defects, miscarriages, infertility, cancers, DNA damage, neurological development problems in children and allergies[30]
"For nearly 10 years, the residents of rural and periurban areas, where agricultural activities are carried out based on the current model of agro-industrial production, have been demanding to the political authorities, the courts of justice, and also protesting before the general public, because they feel that the health of their communities is being environmentally affected, mainly through sprayings of agrochemicals used for different types of agricultural crops, but also for the handling and storage of these chemicals in populated areas, the waste disposal, as well as the collection of grains soaked with chemicals within the towns. The towns specified in the Monsanto Latin America website above: " *are only some of the places where the increased number of cancer cases, birth defects, reproductive and endocrine disorders, have been suffered and detected ever since systematic pesticide spraying has become commonplace"…*
In these towns GM corn and Roundup® Ready Soy required increasing amounts of glyphosate to be sprayed because of glyphosate-resistant weeds.

- In 1996, the sprayings started at less than 2 liters/hectare
- By 2010 some areas are sprayed with 10 liters/hectare, and almost 20 liters/hectare in other areas (five to 10 times the amount of glyphosate over 14 years).

Prof Andrès Carrasco and his team in Buenos Aires showed that glyphosate caused malformations in amphibian and chicken embryos, confirming the effects on humans
Paganelli, A. *et al.* Glyphosate-Based Herbicides Produce Teratogenic Effects on Vertebrates by Impairing Retinoic Acid Signaling *Chem. Res. Toxicol.*, 2010, 23 (10), 1586–1595
DOI: 10.1021/tx1001749[31]
Reports of neural defects and craniofacial malformations from regions where glyphosate-based herbicides (GBH) are used led them to undertake an embryological approach to explore the effects of low doses of glyphosate in development. Treated embryos were highly abnormal with marked alterations in cephalic and neural crest development and shortening

[30] INGLES-Report-from-the-1st-National-Meeting-Of-Physicians-In-The-Crop-Sprayed-Towns.pdf :Faculty of Medical Sciences, National University of Cordoba, Argentina, August 27th & 28th 2010

[31] http://pubs.acs.org/doi/abs/10.1021/tx1001749

of the anterior-posterior (A-P) axis. It was shown that the effects were due to the glyphosate itself, rather than the additive.

Evidence of *in vitro* genotoxicity of glyphosate metabolite in humans
Mañas F *et al*. Genotoxicity of AMPA, the environmental metabolite of glyphosate, assessed by the Comet assay and cytogenetic tests. *Ecotoxicol Environ Saf.* 2009 72 (3):834-7. doi: 10.1016/j.ecoenv.2008.09.019[32]. AMPA was found to be genotoxic in all tests.

Lawyer Dr Graciela Gomez gained small victories on behalf of the rural communities
On 21/08/2012, judgement was announced in a court case in Argentina against GM soy producers and glyphosate. Sofica Gatica, who initiated her complaints in 2001, had two children with birth defects (one of whom died at birth without kidneys) and she made the first health survey in the neighbourhood of Ituzaingo, near Cordoba. "*Five hours after the initial time of the announcement, the verdict was in: one farmer was absolved due to lack of evidence, but the other farmer and the aviator were found guilty. Well, actually, conditional jail. This means they can very much get out of doing any time, although they will be obliged to do social work."* The Argentine government continues to allow GM Soya to be grown.

A baby with a neural tube defect; this is a meningo-myelocoele. More extensive defects can occur. Hospital de Posadas, Misiones, Argentina. Photograph by kind permission of Dr Graciela Gomez.

Julieta, who died aged 7 months from multiple abnormalities in 2010 Bandera Santiago del Estero Photograph by kind permission of Dr Graciela Gomez

[32] http://www.ncbi.nlm.nih.gov/pubmed/19013644

In 2013 birth defects are still occurring in rural Argentina
Dr Medardo Vasquez is a neonatal specialist at the Children's Hospital in Cordoba. "*I see new-born infants, many of who are malformed. I have to tell parents that their children are dying because of these agricultural methods. In some areas in Argentina the primary cause of death for children less than one year old are malformations*." Fritz Kreiss: News Report Sunday 17 March 2013[33].

Fabian Tomasi aeroaplicador (aerial pesticide applicator) Entre Rios Argentina.

Photograph by kind permission of Dr Graciela Gomez.

In 2012 Bayer expanded its domestic market in 2012 to promote home usage of neonicotinoid insecticides and a concentrated form of glyphosate[34]
"Last season Bayer Garden introduced new packaging designed to create a 'family' feel across its products. The aim was to make sure gardeners would know the product they were about to purchase was manufactured by a company they already knew and trusted through favourite products, including Provado Ultimate Bug Killer, Bio Slug & Snail Killer and Super Strength Glyphosate. The company also returned to the television, running a high profile advertising campaign that focused on its unique Simple Soluble Sachets. (Adjuvant: Ethoxylated hydrogenated tallow alkylamines).

Bayer's description of how imidacloprid kills termite colonies by immune suppression[35]

- Imidacloprid binds to the nicotinergic acetylcholine receptors, which leads to paralysis and eventual death.
- When termites stop grooming the naturally-occurring fungi in the soil kill the termites. Premise® 200sc makes fungi 10,000 times more dangerous to termites. Nature assists Premise® in giving unsurpassed control.
- In Denmark imidacloprid preparations are sold in Garden Centres for killing ants.
- For termites and ants, substitute the word 'honeybees'. That is why *Varroa destructor* and other pathogens weaken bees; by suppressing the immune system[36].
- Glyphosate[37] also suppresses the immune system. It acts synergistically with parasites to reduce fish survival at environmentally relevant concentrations.
- Atrazine[38] also causes immune suppression in amphibians at levels below the US EPA threshold for drinking water.

[33] http://www.nationofchange.org/argentina-s-bad-seeds-1363532747

[34] http://www.gardenforum.co.uk/tradeforum/peoplenews/?artid=2382
[35] http://www.research.bayer.com/en/20/-termites.pdfx
[36] http://www.stmconnect.com/toc/jeit/2013v1n1/page3-12.pdf
[37] http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2664.2010.01791.x/full
[38] http://www.pnas.org/content/99/15/9900.full

Shift in pest management on crops worldwide

Over the last 20 years, a shift in pest management worldwide has taken place without anyone realizing. The industry has moved away from reactive to prophylactic. Now many fungicides, pesticides and herbicides are applied to the seeds before sowing. Application of the chemical before pest damage has occurred often involves routine, calendar-based spraying and pre-emptive treatments[39]. It is like humans taking permanent antibiotics.

Multiple pesticides found in pollen collected by bees in the US

Pettis JS, Lichtenberg EM, Andree M, Stitzinger J, Rose R, *et al.* Crop Pollination Exposes Honey Bees to Pesticides Which Alters Their Susceptibility to the Gut Pathogen Nosema ceranae. PLoS ONE 2013, 8(7): e70182[40]. The project was funded by the US Department of Agriculture and the National Honey Board.

"We collected pollen from bee hives in seven major crops to determine 1) what types of pesticides bees are exposed to when rented for pollination of various crops and 2) how field-relevant pesticide blends affect bees' susceptibility to the gut parasite Nosema ceranae. Our samples represent pollen collected by foragers for use by the colony, and do not necessarily indicate foragers' roles as pollinators. In blueberry, cranberry, cucumber, pumpkin and watermelon bees collected pollen almost exclusively from weeds and wildflowers during our sampling. Thus more attention must be paid to how honey bees are exposed to pesticides outside of the field in which they are placed. We detected 35 different pesticides in the sampled pollen, and found high fungicide loads. Our results highlight a need for research on sub-lethal effects of fungicides and other chemicals that bees placed in an agricultural setting are exposed to". Two herbicides were measured, but not glyphosate. Carfentrazone-ethyl: estimated use in 2009, 0.09 million pounds; pendimethalin: estimated use in 2009, 14 million pounds; glyphosate: estimated use in 2009, 250 million pounds and increasing dramatically.

We asked Lord Smith Chairman of the UK Environment Agency to measure glyphosate and the neonicotinoid insecticides in ground water[41]

We sent him evidence that:

- Contamination of groundwater is destroying human health
- Environment Agency's own data was used in a British Geological Survey Report 2012[42]. On page 35: "*Glyphosate is now the most widely used herbicide in the world, with dramatic increases in agricultural use since the introduction of (GM) glyphosate resistant crops. Microbial degradation produces aminomethyl phosphonic acid (AMPA) (Kolpin et al., 2000) and it has been anticipated that AMPA may be problematic. The high water solubility of both the parent and the metabolite has meant that their analysis has been difficult… …Similarly for parent compounds which have non-agricultural applications, there will be routes to groundwater which would not be identified, such as routes which do not pass through the soil zone. Kolpin (2006) showed AMPA to be detected in wastewater-impacted surface waters about four times as frequently as the parent.*"
- We pointed out that the BGS Report was unpublished.

[39] http://ento.psu.edu/publications/are-neonicotinoids-killing-bees
[40] http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0070182
[41] Personal communications from 09/04/2013 to 13/05/2013
[42] http://nora.nerc.ac.uk/14557/1/OR11013.pdf

- A study in a German University of glyphosate residues in an urban population found significant contamination in all urine samples with 5 to 20 times above the legal limit for drinking water. They authors concluded it must be coming from food[43].
- Syngenta and Monsanto had initiated a new practice; desiccation of crops with glyphosate (or another herbicide) to dry them. This has resulted in glyphosate residues on crops, which then enter the food chain of animals and humans.

According to Dr Kennedy, the Gas Chromatography Mass Spectrometry (GCMS) scan cannot measure glyphosate

Dr Jo Kennedy replied on Lord Smith's behalf on 1st May 2013. With regard to glyphosate, she replied: "*The GCMS scan is not able to measure glyphosate, and glyphosate is not part of the routine suite of substances monitored for nationally across our network. The main reason for this is that glyphosate analysis is relatively costly and it was felt that the additional costs of analysis could not be justified. If local glyphosate problems have been identified in groundwater the Environment Agency can carry out operational monitoring at a local level.*"

Why is the herbicide glyphosate not monitored in ground or drinking water in the US?

In the US in 2009 total sales of glyphosate were estimated to be 250 millions of pounds of active ingredient[44]. Glyphosate and its metabolite AMPA are not monitored in groundwater, but atrazine and 2, 4-D are. The usage of glyphosate was 3.6 times greater than atrazine (70 million pounds)[45] and 4 times greater than 2, 4-D, the less toxic half of Agent Orange (62 million pounds)[46]. Sometimes cheaper forms of 2, 4-D are contaminated with dioxins.

California set limits (1997) for glyphosate in drinking water[47]

Summary: A Public Health Goal (PHG) of 1,000 ppb is developed for glyphosate in drinking water. California's and U.S. Environmental Protection Agency's Maximum Contaminant Levels (MCLs) are 700 ppb based on systemic toxicity (renal tubular dilation) in a three generation rat reproduction study with an NOAEL of 10 mg/kg-day. ***"****There are only a few published health effects studies on glyphosate in the past few years. The majority of the available studies on glyphosate were conducted by the Monsanto Company for the registration of glyphosate as a pesticide".*

The United States Geological Survey (USGS) established a National Water Quality Assessment Program (NAWQA) for measuring pesticides in groundwater in 1991. It did not include glyphosate or the neonicotinoid insecticides

In 2008, a 10-year study (1993-2003) of pesticides in ground-water and drinking water[48] was published. In a press statement the author said: "*Despite sustained use of many popular pesticides and the introduction of new ones, results did not indicate increasing detection rates or concentrations in shallow drinking water resources over the 10 years studied*" In

[43] Brändli, D., Reinacher, S. Herbicides found in human urine. *Ithaka Journal* 1/2012: 270- 272. http://www.ithaka-journal.net/druckversionen/e052012-herbicides-urine.pdf

[44] http://water.usgs.gov/nawqa/pnsp/usage/maps/show_map.php?year=2009&map=GLYPHOSATE&hilo=L
[45] http://water.usgs.gov/nawqa/pnsp/usage/maps/show_map.php?year=2009&map=ATRAZINE&hilo=L
[46] http://water.usgs.gov/nawqa/pnsp/usage/maps/show_map.php?year=2009&map=24D&hilo=L

[47] http://oehha.ca.gov/water/phg/pdf/glypho_c.pdf

[48] Bexfield, Laura M. (2008) Decadal-scale changes of pesticides in ground water of the United States, 1993-2003: *Journal of Environmental Quality* 37: S226-S239

2009 Trends in pesticides concentrations in corn-belt streams[49] was published. The authors made a similar statement in their press release: "*The declines in pesticide concentrations closely followed the declines in their annual applications, indicating that reduced pesticide use is an effective and reliable strategy for reducing pesticides contamination in streams.*"

The USGS Pesticide National Synthesis Data [50] of pesticides measured in water was published. It did not include glyphosate or the neonicotinoid insecticides

In 2013 a further Report was published[51]. This was an update on: "*a previously published water-quality dataset of 44 commonly used pesticides and 8 pesticide degradates suitable for national assessment of trends in pesticide concentrations in streams of the United States*". *Samples analysed at the USGS National Water Quality Laboratory by the GCMS analytical method were the most extensive in time and space and, consequently, were selected for trend analysis*". The UK Environment Agency had claimed that the GCMS cannot measure glyphosate. Is that why the USGS is not measuring them?

We had raised the absence of water data on neonicotinoid insecticides with Robert R Gilliom [Chief, Pesticide National Synthesis] in April 2011[52]. GMOs have neonicotinoid insecticides applied to the seed and are genetically modified to be Roundup® Ready (or other herbicide-tolerant). Glyphosate is the most used herbicide in the US and its use is increasing.

Estimation of Annual Agricultural Pesticide Use US 1992-2009[53]

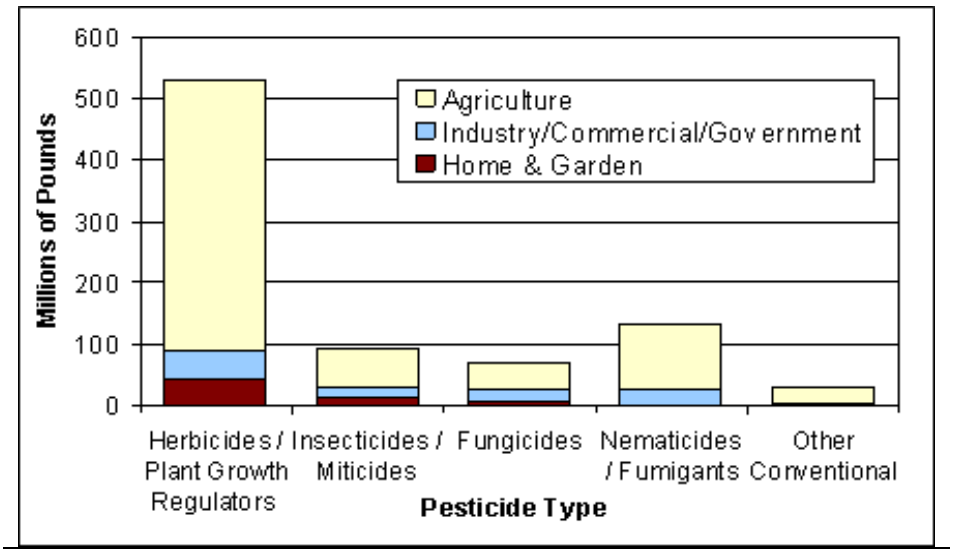


Fig 1 Amount of Conventional Pesticide Active Ingredient Used in the United States By Pesticide Type and Market Sector, 2007 Estimates US EPA

In the Foreward to this document, William H. Werkheiser USGS Associate Director for Water stated: "*The U.S. Geological Survey (USGS) is committed to providing the Nation with*

[49] Sullivan, D.J., Vecchia, A.V., Lorenz, D.L., Gilliom, R.J., and Martin, J.D. (2009) Trends in pesticide concentrations in corn-belt streams, 1996-2006: *U.S. Geological Survey.*

[50] Martin JD. Sources and preparation of data for assessing trends in concentrations of pesticides in streams of the United States, 1992-2006. U.S. Geological Survey Scientific Investigations Report 2009-55062.

[51] http://pubs.usgs.gov./ds/655/ Martin, JD, Eberle M, Nakagaki N. Sources and Preparation of Data for Assessing Trends in Concentrations of Pesticides in Streams of the United States, 1992-2010. Data Series 655.

[52] Personal communication.

[53] http://pubs.usgs.gov/sir/2013/5009/

reliable scientific information…Information on the Nation's water resources is critical to ensuring long-term availability of water that is safe for drinking and recreation and is suitable for industry, irrigation, and fish and wildlife."
The map for glyphosate shows that the agricultural usage went from less than 20 million pounds in 1992 to 250 million pounds in 2009.[54] This excluded the use in the following sectors: home/garden/industry/commercial/government/market. In 2007 the non-agricultural sector accounted for more than 20% of the total amount of pesticides used.[55]
Is it a coincidence that pesticides whose sales dominate global markets are not being monitored in ground, surface or drinking water by any Environmental Protection Agency anywhere? They are not being measured in Europe[56] or in the US[57] or by the Australian Pesticides and Veterinary Medicines Authority (APVMA). Why are all these killers of weeds being used? What has happened to farming?

All pesticide problems are manifest at water catchment areas
The American Bird Conservancy (ABC) commissioned world-renowned environmental toxicologist Dr Pierre Mineau and Cynthia Palmer an environmental lawyer and Pesticides Program Manager for ABC to conduct research on the effects of neonicotinoid insecticides on birds. The Report: Neonicotinoids and Birds: The Impact of the Nation's Most Widely Used Insecticides on Birds[58] was published in March 2013.
Dr Mineau, the UK Environment Agency and the European Water Frame Directive are in unanimous agreement about the approaches to pesticide assessment: "*Many of the problems facing our water environments are best understood and tackled at a catchment level."*
Page 8 of ABC: "*This suggests that we should be looking at possible links between neonicotinoid insecticides* (or any other pesticide) *and birds, not on a farm scale, but in the context of whole watersheds and regions. Impacts from the neonicotinoids may very well be further afield than the arable area on which they are used, and many of those impacts may be mediated through the aquatic environment."*
Mineau and Palmer have called for a ban on the use of the neonicotinoid insecticides as seed treatments and for the suspension of all applications pending an independent review of the products' effects on birds, terrestrial and aquatic invertebrates, and other wildlife.
"It is astonishing that EPA would allow a pesticide to be used in hundreds of products without ever requiring the registrant to develop the tools needed to diagnose poisoned wildlife. It would be relatively simple to create a binding assay for the neural receptor which is affected by this class of insecticides," said Dr Mineau.
Page 64 of ABC: *"It is clear that we are witnessing contamination of the aquatic environment at levels that will affect aquatic food chains. This has a clear potential to affect consumers of those aquatic resources, be they birds, fish or amphibians."*

Measurement of glyphosate in watersheds
Coupe *et al*. studied glyphosate and its major degradation product, aminomethylphosphonic acid (AMPA) levels in four agricultural basins[59]. Three were in the Midwest US where the

[54] http://water.usgs.gov/nawqa/pnsp/usage/maps/show_map.php?year=2009&map=GLYPHOSATE&hilo=L
[55] http://epa.gov/pesticides/pestsales/07pestsales/usage2007_2.htm

[56] http://ec.europa.eu/environment/water/water-dangersub/pdf/com_2011_876.pdf

[57] http://pubs.usgs.gov./ds/655/
[58] http://www.abcbirds.org/abcprograms/policy/toxins/Neonic_FINAL.pdf
[59] Coupe, R.H. *et al*. Fate and transport of glyphosate and aminomethylphosphonic acid in surface waters of agricultural basins. *Pest Manag Sci* 2012; **68**: 16–30. http://www.ncbi.nlm.nih.gov/pubmed/21128261

intensity of use was greatest because of GM corn, soybeans and cotton, and one was from the vineyards of Eastern France. Paul Capel USGS chemist and an author of the study said that, despite the 8-fold increase in use of glyphosate between 1992 and 2007, details of the fate of the chemicals on a watershed scale were lacking[60]. *"In these studies, Glyphosate was frequently detected in surface waters, rain and air in areas where it is heavily used in the basin. The consistent occurrence of glyphosate in streams and air indicates its transport from its point of use into the broader environment. The degradation product of glyphosate, aminomethylphosphonic acid (AMPA), which has a longer environmental lifetime, was also frequently detected in streams and rain".* They concluded that: *"The watersheds most at risk for the offsite transport of glyphosate are those with high application rates, rainfall that results in overland runoff and a flow route that does not include transport through the soil…" In Mississippi and Eastern France, where the use is almost continuous, glyphosate and AMPA were detected in almost every sample…"*

Glyphosate is in the air and comes down in rainfall, as well as being in the rivers
Two-thirds to 100% of air and rainfall samples tested in Mississippi and Iowa in 2007–2008 contained glyphosate[61]. *"This is the first report on the ambient levels of glyphosate, the most widely used herbicide in the United States, and its major degradation product, aminomethylphosphonic acid (AMPA), in air and rain. The concentrations of glyphosate ranged from <0.01 to 9.1 ng/m^3 and from <0.1 to 2.5 µg/L in air and rain samples, respectively."*

Pesticides in surface drinking-water supplies of the northern Great Plains[62]
Human health anomalies have been associated with pesticide exposure (including impaired cognitive abilities in children, an increased incidence of human birth malformations and cryptorchidism in male children). Of two insecticides and 27 herbicides that were detected in reservoir water, consistent detection of a subset of 7 herbicides suggested that atmospheric deposition, either directly or in rain, was the principal pathway from fields to the reservoirs. Highest concentrations and numbers of herbicides in drinking water were associated with a 133-mm rainfall over 15 days towards the end of the spring herbicide application. Drinking water contained 3-15 herbicides.

In storms, glyphosate from urban drainage systems contributes 60% of the load[63]
Contributions of agricultural and urban uses to the glyphosate contamination of surface water were studied in a small catchment area in Switzerland (25 km^2). "*The concentrations at peak discharge during storm events were elevated throughout the year with maximum concentrations of 4.15 µg L^{-1}… Extrapolations from agricultural loss rates and from concentrations found in the urban drainage system showed that more than half of the load during selected rain events originates from urban areas. The inputs from the effluent of the*

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[60] http://www.usgs.gov/newsroom/article.asp?ID=2909#.Uh_aEuNIxY8
[61] Feng-chih Chang, Matt F. Simcik, Paul D. Capel Occurrence and fate of the herbicide glyphosate and its degradate aminomethylphosphonic acid in the atmosphere *Environmental Toxicology and Chemistry* 30, (3), 548–555, March 2011 http://www.sciencedirect.com/science/article/pii/S0045653513008837

[62] http://www.ncbi.nlm.nih.gov/pubmed/17687445
[63] Hanke I, Wittmer I, Bischofberger S, Stamm C and Singer H, Relevance of urban glyphosate use for surface water quality. *Chemosphere* ***81****:422–429 (2010).*
http://www.sciencedirect.com/science/article/pii/S0045653510007411

wastewater treatment plant, the overflow of the combined sewer system and of the separate sewer system summed up to 60% of the total load". This confirms the study by Coupe *et al*. that the watersheds most at risk for the offsite transport of glyphosate are: '*flow routes that do not include transport through soil*'. That suggests that urban populations are more at risk from run-off from roads and from spraying of noxious weeds in, or close to, streams.

Data confirm that glyphosate is capable of reaching groundwater
Sanchís, J. *et al.* Determination of glyphosate in groundwater samples using an ultrasensitive immunoassay and confirmation by on-line solid-phase extraction followed by liquid chromatography coupled to tandem mass spectrometry. *Anal Bioanal Chem*. 2012 402 (7):2335-45. doi: 10.1007/s00216-011-5541-y.[64]
"This is one of the few works related to the analysis of glyphosate in real groundwater samples and the presented data confirm that, although it has low mobility in soils, glyphosate is capable of reaching groundwater."

Part 3 Pesticide Regulatory Agencies

Why did the EU authorise Glyphosate?
The Rapporteur Member State (RMS) for glyphosate is Germany. It was discovered that Draft Assessment Report (DAR) studies had found teratogenicity in mammals. Several malformations were found in rabbits and rats according to the industry's own teratogenicity studies submitted for the 2002 EU approval of the active ingredient glyphosate. The original industry studies are claimed to be commercially confidential. However, the said industry data were compiled from the 1998 Draft Assessment Report by the German Government. (Germany will remain in this rôle for the next review of glyphosate in 2015.) Malformations include extra ribs, distortions affecting thoracic ribs, heart malformations, kidney agenesia, unossified sternebrae, reduced ossification of cranial centers and sacrocaudal vertebral arches, and also skeletal variations and major visceral malformations, which were unspecified in the DAR.

Independent scientists pointed this out and, in the light of the embryo research from Argentina where families in rural communities exposed to GM soya and glyphosate had children with birth defects, asked for new risk assessments[65]
"The publication of a study in 2010, showing that a glyphosate herbicide formulation and glyphosate alone caused malformations in the embryos of Xenopus laevis and chickens through disruption of the retinoic acid signalling pathway, caused scientific and regulatory controversy. Debate centred on the effects of the production and consumption of genetically modified Roundup Ready® soy, which is engineered to tolerate applications of glyphosate herbicide. The study, along with others indicating teratogenic and reproductive effects from glyphosate herbicide exposure, was rebutted by the German Federal Office for Consumer Protection and Food Safety, BVL, as well as in industry-sponsored papers. These rebuttals relied partly on unpublished industry-sponsored studies commissioned for regulatory purposes, which, it was claimed, showed that glyphosate is not a teratogen or reproductive toxin. However, examination of the German authorities' draft assessment report on the industry studies, which underlies glyphosate's EU authorisation, revealed further evidence of

[64] http://www.ncbi.nlm.nih.gov/pubmed/22101424
[65] Antoniou, M. *et al.* Teratogenic Effects of Glyphosate-Based Herbicides: Divergence of Regulatory Decisions from Scientific Evidence *J Environ Anal Toxicol* 2012, S:4
http://dx.doi.org/10.4172/2161-0525.S4-006

glyphosate's teratogenicity. Many of the malformations found were of the type defined in the scientific literature as associated with retinoic acid teratogenesis. Nevertheless, the German and EU authorities minimized these findings in their assessment and set a potentially unsafe acceptable daily intake (ADI) level for glyphosate. This paper reviews the evidence on the teratogenicity and reproductive toxicity of glyphosate herbicides and concludes that a new and transparent risk assessment needs to be conducted. The new risk assessment must take into account all the data on the toxicity of glyphosate and its commercial formulations, including data generated by independent scientists and published in the peer-reviewed scientific literature, as well as the industry-sponsored studies."

Agencies and Industry have only tested the 'active' ingredient glyphosate. The commercial formulations contain an untested adjuvant which is toxic to human cells[66]

The health and environmental agencies and pesticide companies assess the long-term effects on mammals of glyphosate alone, and not the full formulation. But the commercial formulations of these pesticides as they are sold and used contain added ingredients (adjuvants). These are often classified confidential and described as 'inerts'. However, they help to stabilize the chemical compound glyphosate and help it to penetrate plants, in the manner of corrosive detergents. The formulated herbicides (including Roundup®) can affect all living cells, especially human cells. This danger is overlooked because glyphosate and Roundup® are treated as the same by industry and regulators on long-term studies.
The authors studied nine formulations and demonstrated that all formulations are more toxic than glyphosate alone. Among them, POE-15 appears to be the most toxic principle against human cells, even if others are not excluded.

Why did EFSA Reasoned Opinion Group grant 100-fold increase in Maximum Residue Limits (MRLs) of glyphosate in foods?

Monsanto Europe asked the European Food Safety Authority (EFSA) to raise the import tolerance for glyphosate in lentils "*in order to accommodate the authorised desiccation use of glyphosate in lentils in the US and Canada*" from 0.1 mg/kg to 10 mg/kg (i.e. 100 times). This was approved on 13th January 2012[67]. A Joint FAO/WHO meeting on Pesticide Residues in 1994 had granted elevated Maximum Residue Limits (MRLs) for glyphosate on soya (from 5 mg/kg to 20 mg/kg) and soya bean fodder (from 20 mg/kg to 200 mg/kg)[68].

Complaint on 16/05/2012 to the European Commission about increase of MRLs

Michael Flüh replied on behalf of the European Commission[69] on 6th July 2012. "*As regards the toxicity of glyphosate and the maximum residue levels established in EU legislation, we refer again to our strict approval system in the EU. EU-MRLs are established based on a thorough assessment carried out by Member States and subsequently set by EFSA and are set at levels that ensure consumer safety based on the worst-case dietary habits across the EU*".

The Industry hosted a secret meeting on 26/06/2012 to get GM into the UK[70]

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[66] Ethoxylated adjuvants of glyphosate-based herbicides are active principles of human cell toxicity. Toxicology 2013. http://dx.doi.org/10.1016/j.tox.2012.09.006

[67] http://www.efsa.europa.eu/en/search/doc/2550.pdf

[68] http://www.fao.org/fileadmin/templates/agphome/documents/Pests_Pesticides/JMPR/Evaluation94/glyphos.pdf

[69] Personal communication.

[70] http://tinyurl.com/9jbce4g , http://tinyurl.com/8ahylza , http://tinyurl.com/92rrajn

Monsanto, Syngenta, Bayer and BASF and their industry body, the Agricultural Biotechnology Council (ABC) are setting the agenda for UK agricultural research with a view to bringing GM crops into the UK and exporting them overseas. Two Ministers and two MPs met with scientists from Defra, the John Innes Centre, Rothamsted Research and the National Farmers Union. They had a round table discussion including how to overcome the negative public opinion that currently prevents the UK achieving these outcomes and a strategy to attain them.

Further evidence of glyphosate residues in humans
Urine tests were performed in 182 volunteers from cities in 18 countries in Europe to measure glyphosate and aminomethylphosphonic acid (AMPA, a metabolite of glyphosate). On average, 44 % and 36 % of the urine samples analysed were found to contain quantifiable levels of glyphosate and AMPA respectively[71].

Glyphosate and AMPA residues in soy bean plants, leaves and grains
Arregui, M.C. *et al*. Monitoring glyphosate residues in transgenic glyphosate-resistant soybean. *Pest Manag. Sci.* 2004 Feb; 60 (2):163-6[72].
The objective of this work was to monitor glyphosate and AMPA residues in soybean plants and grains in field crops in Santa Fe Province, Argentina. Five sites were monitored in 1997, 1998 and 1999. Individual soybean plants were sampled from emergence to harvest, dried and ground. Analysis consisted in residue extraction with organic solvents and buffers, agitation, centrifugation, clean-up and HPLC with UV detection. In soybean leaves and stems, glyphosate residues ranged from 1.9 to 4.4 mg kg^{-1} and from 0.1 to 1.8 mg kg^{-1} in grains. Higher concentrations were detected when glyphosate was sprayed several times during the crop cycle, and when treatments approached the flowering stage. AMPA residues were also detected in leaves and in grains, indicating metabolism of the herbicide.

GMO food and animal feeds with glyphosate residues are coming into Europe
The industry and lobbyists claim that GM reduces the amount of pesticides that need to be sprayed during the year. The photograph on page 12 shows that weeds become resistant to glyphosate, so more and more has to be applied. This paper shows that GM fails to increase maize yields in mid-West US but increases the use of herbicides. Between 1996 and 2011, overall herbicide use on GMOs in the US increased by 239 million kilograms[73].

Endocrine Disrupting Chemicals (EDC) – 2012
An assessment of the State of Science of Endocrine Disruptors was prepared for the United Nations Environment Program and the World Health Organization by a group of approximately 50 experts[74].
The authors outlined evidence of 1) a high incidence, and increasing trends, of many endocrine-related disorders in humans; 2) observations of endocrine-related effects in wildlife populations; 3) identification of chemicals with endocrine disrupting properties linked to disease outcomes in laboratory studies.
Endocrine-related disorders in humans are manifest by:

- Increases in low semen quality in young men (up to 40%)
- Incidence of genital malformations has increased over time

[71] http://www.foeeurope.org/weed-killer-glyphosate-found-human-urine-across-Europe-130613
[72] http://www.ncbi.nlm.nih.gov/pubmed/7797819
[73] Heinemann JA et al. Sustainability and innovation in staple crop production in the US Midwest. International Journal of Agricultural Sustainability, 2013 http://dx.doi.org/10.1080/14735903.2013.806408
[74] http://unep.org/pdf/9789241505031_eng.pdf

- Adverse pregnancy outcomes and birth defects has increased in many countries
- Neurobehavioural disorders related to thyroid dysfunction has increased
- Endocrine-related cancers (breast, endometrial, ovary, prostate, testicular and thyroid cancers) have been increasing over the past 40‑50 years
- Earlier onset of breast development in young girls which leads to breast cancer
- The prevalence of obesity and type 2 diabetes is increasing. The WHO estimates that 1.5 billion adults worldwide are overweight or obese and that the number with type 2 diabetes increased from 153 million to 347 million between 1980 and 2008

The conclusion was: "*It is essential to evaluate associations between EDC exposures and health outcomes by further developing methods for which proof of concept is currently under development.*" An Editorial in the Lancet[75] concluded: "*there is currently no widely agreed system for assessing the strength of associations between exposure to chemicals (including EDCs) and adverse health outcomes*."

Were there too many cooks? Or was it reluctance amongst scientists to point fingers?
The herbicide atrazine was considered. It was banned in Europe in 2004, but is still widely used throughout the world. In 2009 it was the second most commonly applied herbicide in the US. Recommendations should have been made for it to be banned on multiple counts.

- On p 169: '*these data indicate that atrazine has convincing effects on the immune system, and further investigation is warranted.'*
- On p 196, the extent of atrazine's current use in the USA is highlighted
- Hayes *et al* have written extensively about atrazine as an endocrine-disruptor in amphibians[76,77] and it has been cited as a possible contributor to the massive global declines in amphibian populations[78].
- Birth defects in humans. Atrazine has been associated with a major anomaly in babies, gastroschisis. Gastroschisis is a congenital defect in the abdominal wall, through which the abdominal contents freely protrude. A case-controlled study of agricultural-related chemical exposure concluded: *"Maternal exposure to surface water atrazine is associated with fetal gastroschisis, particularly in spring conceptions"*[79].
- In the UK in Northfleet in Kent, nine babies within 12 years (from 1999-2012) had been born in the same street with gastroschisis[80]. *"Southern Water acknowledged that atrazine had been found in 2008, but said tap water came from a variety of sources and any pollutant would be heavily diluted".* An update on the Water Frame Directive on groundwater status in the UK had been presented to Defra's Pesticides Forum in

[75] Endocrine-disrupting chemicals: how much of a health threat?
[76] Hayes, T.B. *et al.* Hermaphroditic, demasculinized frogs after exposure to the herbicide atrazine at low ecologically relevant doses. *PNAS* 2002 99 (8) 5476-5480
[77] Hayes, T.B *et al.* Atrazine induces complete feminization and chemical castration in male African clawed frogs (*Xenopus laevis*) PNAS 2010, 107 (10): 4612-4617
doi: 10.1073/pnas.0909519107

[78] Hayes TB, Falso P, Gallipeau S, Stice M The cause of global amphibian declines: a developmental endocrinologist's perspective. *Journal of Experimental Biology,* 2010, 213(6):921-933.
[79] Waller SA, Paul K, Peterson SE, *et al.* Agricultural-related chemical exposures, season of conception, and risk of gastroschisis in Washington State. *Am J Obstet Gynecol* 2010,202: 241.e1-6.

[80] http://www.dailymail.co.uk/news/article-2142106/One-street-Nine-babies-born-horrific-rare-deformity-And-troubling-question--mothers-poisoned-weedkiller.html

2008[81]. It showed that atrazine and/or its two breakdown products were found at more than 25% of monitoring sites and were present in quantities in excess of 0.1µg/l. An investigation into the cases was carried out by the Kent Public Health Department. The Report, published on 05/03/2012[82], did not find evidence of higher rates of gastroschisis than could be considered normal in the Waterdales Road area. Syngenta said: "*There is no proven link between atrazine and these defects. Atrazine does not cause developmental abnormalities."* However, an unpublished Report on Emerging contaminants in groundwater 2011 was compiled from Environment Agency Data by the British Geological Survey and the Natural Environment Research Council.[83] Appendix 2, p 93 Summary of non-licences pesticides, atrazine was found at 1039 monitoring sites in the UK (maximum concentration: 13.04 µg/l: EU legal limit <0.1 µg/l).

- Atrazine-Induced Aromatase Expression Is SF-1 Dependent: Implications for Reproductive Cancers in Humans[84].
- In 2009, atrazine was the second most commonly applied herbicide in the US (70 million pounds)[85]. Glyphosate is the commonest herbicide in the US and is widely applied throughout the world.
- "*In the US in 2012, in a settlement between plaintiffs and the manufacturer of the endocrine disrupting herbicide atrazine, Syngenta will pay $105 million to settle a nearly 8-year-old lawsuit and could help reimburse community water systems (CWS) in 45 states that have had to filter the toxic chemical from its drinking water. It will provide financial recoveries for costs that have been borne for decades by more than 1,887 CWSs that provide drinking water more than one in six Americans across at least 45 states[86]. On October 23, 2012, Judge Phil Gilbert in the United States District Court for the Southern District of Illinois approved the $105 million nationwide atrazine settlement. After an extensive notification effort that included two first-class letters, an email and direct phone contact, 1,085 class members filed claims seeking a portion of the $105 million settlement fund. These class members will receive payments based on evidence of: (1) the levels of atrazine in the water; (2) how often atrazine had been found in the water; (3) how long ago atrazine had been found in the water; and (4) the population served. Generally, the more water processed by a system or the frequency of high concentrations of atrazine, the more money they received. The following map shows the location of each water system receiving funds and the magnitude of their recovery[87].*

[81] Jo Kennedy Pesticides_Forum_Oct_2008_WFD.pdf
[82] Investigation into gastro~ cases final amended.pdf
[83] http://nora.nerc.ac.uk/14557/1/OR11013.pdf

[84] WuQiang Fan *et al.* Atrazine-Induced Aromatase Expression Is SF-1 Dependent: Implications for Endocrine Disruption in Wildlife and Reproductive Cancers in Humans *Environ Health Perspect*. 2007 May; 115(5): 720–727. doi: 10.1289/ehp.9758

[85] http://water.usgs.gov/nawqa/pnsp/usage/maps/show_map.php?year=2009&map=ATRAZINE&hilo=L

[86] http://www.atrazinesettlement.com/utility/GetFile/c3e918bf-742a-41fa-8af6-0637bcf0b253
[87] http://www.atrazinesettlement.com/

Glyphosate - the missing endocrine-disruptor
Glyphosate is the most widely used herbicide in the world. It was introduced in 1974. Industry claims it to be safe. Is that why it wasn't even considered by experts in the State of Science as a candidate for the increasing burden of diseases of those on a Western diet?

Part 4 Other Independent Research on glyphosate and glyphosate-based herbicides, including Roundup®

Independent scientists have shown that glyphosate is an endocrine disruptor
Gasnier, C. *et al*, Glyphosate-based herbicides are toxic and endocrine disruptors in human cell lines. *Toxicology* doi:10.1016/j.tox.2009.06.006[88].
"All parameters were disrupted at sub-agricultural doses with all formulations within 24h. These effects were more dependent on the formulation than on the glyphosate concentration. First, we observed a human cell endocrine disruption from 0.5 ppm on the androgen receptor in MDA-MB453-kb2 cells for the most active formulation (R400), then from 2 ppm the transcriptional activities on both estrogen receptors were also inhibited on HepG2. Aromatase transcription and activity were disrupted from 10 ppm. Cytotoxic effects started at 10 ppm with Alamar Blue assay (the most sensitive), and DNA damages at 5 ppm. A real cell impact of glyphosate-based herbicides residues in food, feed or in the environment has thus to be considered, and their classifications as carcinogens/mutagens/reprotoxics is discussed.

Glyphosate is associated with most of the diseases and conditions associated with a Western diet[89].
"Here, we show how interference with Cytochrome P450 (CYP) enzymes acts synergistically with disruption of the biosynthesis of aromatic amino acids by gut bacteria, as well as impairment in serum sulfate transport. Consequences are most of the diseases and conditions associated with a Western diet, which include gastrointestinal disorders, obesity, diabetes, heart disease, depression, autism, infertility, cancer and Alzheimer's disease. We explain the documented effects of glyphosate and its ability to induce disease, and we show that glyphosate is the' textbook' example of exogenous semiotic entropy: the disruption of homeostasis by environmental toxins."
There is a link to Stephanie Seneff being interviewed by Jeffrey Smith[90].

Birth defects in frog & chicken embryos and in humans[91]
Genetically-Engineered Corn and Roundup®-Ready Soya were introduced into the rural towns of Argentina and Paraguay in 1996. The devastation of human and animal health and biodiversity is described in this chapter: *"In South America, the incorporation of genetically modified organisms (GMO) engineered to be resistant to pesticides changed the agricultural*

[88] http://www.ncbi.nlm.nih.gov/pubmed/19539684
[89] Samsel, A., Seneff, S. Glyphosate's Suppression of Cytochrome P450 Enzymes and Amino Acid Biosynthesis by the Gut Microbiome: Pathways to Modern Diseases. *Entropy* **2013**, *15*, 1-x manuscripts; doi:10.3390/ e140x000x http://www.nationofchange.org/new-study-finds-roundup-could-be-linked-severe-health-issues-1367071482

[90] Stephanie Seneff: video interview with Jeffrey Smith: http://www.youtube.com/watch?v=h_AHLDXF5aw&feature=player_embedded
[91] Lopez, S.L. *et al* GMO Pesticides Used in South American GMO-Based Agriculture: A Review of Their Effects on Humans and Animal Models. In *Advances in Molecular Toxicology*, Vol. 6, 201 published by Elsevier: ISSN 1872-0854

model into one dependent on the massive use of agrochemicals. Different pesticides are used in response to the demands of the global consuming market to control weeds, herbivorous arthropods, and crop diseases. Here, we review their effects on humans and animal models, in terms of genotoxicity, teratogenicity, and cell damage. We also stress the importance of biomarkers for medical surveillance of populations at risk.

European Commission is challenged about its continued registration of Roundup®[92]
"The European Commission has previously ignored or dismissed many other findings from the independent scientific literature showing that Roundup® and glyphosate cause endocrine disruption, damage to DNA, reproductive and developmental toxicity, neurotoxicity, and cancer, as well as birth defects. Many of these effects are found at very low doses, comparable to levels of pesticide residues found in food and the environment."...
"This issue is of particular concern now that Monsanto and other producers of genetically modified seed are trying to get their glyphosate-tolerant crops approved for cultivation in Europe. If the EU Commission gives its approval, this will lead to a massive increase in the amount of glyphosate sprayed in the fields of EU member states, as has already happened in North and South America. Consequently, people's exposure to glyphosate will increase."
The review of glyphosate was due to take place in 2012. Soon after the Commission was notified of the latest research showing that glyphosate and Roundup® caused birth defects, it quietly passed a directive delaying the review of glyphosate and 38 other dangerous pesticides until 2015.

Prof Gilles-Eric Séralini and colleagues at CRIIGEN in Caen had already questioned the adequacy of Monsanto's testing both for glyphosate and GM crops[93].
"*The 90-day-long tests are insufficient to evaluate chronic toxicity, and the signs highlighted in the kidneys and livers could be the onset of chronic diseases. However, no minimal length for the tests is yet obligatory for any of the GMOs cultivated on a large scale, and this is socially unacceptable in terms of consumer health protection. We are suggesting that the studies should be improved and prolonged, as well as being made compulsory, and that the sexual hormones should be assessed too, and moreover, reproductive and multigenerational studies ought to be conducted too."*

Seralini's 2-year feeding study provoked chronic hormone and sex dependent pathologies in rats; males developed tumours at 4 months and females at 7 months
Séralini, G-E *et al*. Long term toxicity of a Roundup® herbicide and a Roundup®-tolerant genetically modified maize. *Food Chem Toxicol.* November 2012, 50: 4221‑4231[94]
"*The health effects of a Roundup®-tolerant genetically modified maize (from 11% in the diet), cultivated with or without Roundup®, and Roundup® alone (from 0.1 ppb in water), were studied 2 years in rats. In females, all treated groups died 2 ‑3 times more than controls, and more rapidly. This difference was visible in 3 male groups fed GMOs. All results were hormone and sex dependent, and the pathological profiles were comparable. Females developed large mammary tumors almost always more often than and before controls, the pituitary was the second most disabled organ; the sex hormonal balance was modified by*

[92] Antoniou M, Habib M, Howard CV, *et al.* Roundup and birth defects: Is the public being kept in the dark? Earth Open Source. June 2011. http://bit.ly/IP2FWH

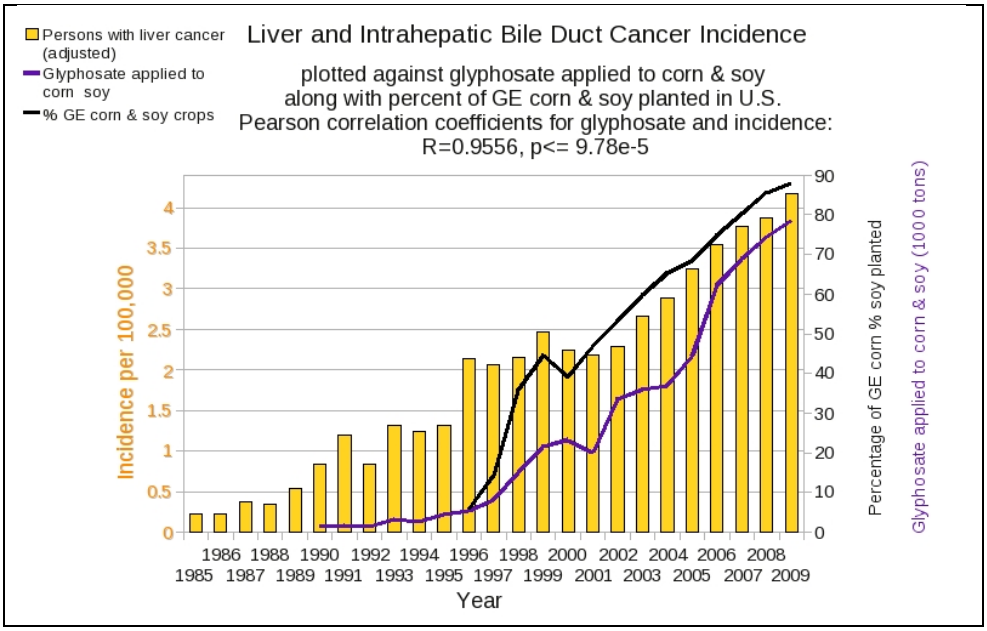
[93] Séralini, G-E. *et al*. Genetically modified crops safety assessments: present limits and possible improvements *Environmental Sciences Europe* 2011, 23:10 doi:10.1186/2190-4715-23-10.
[94] http://dx.doi.org/10.1016/j.fct.2012.08.005

GMO and Roundup® treatments. In treated males, liver congestions and necrosis were 2.5 - 5.5 times higher. This pathology was confirmed by optic and transmission electron microscopy. Marked and severe kidney nephropathies were also generally 1.3 -2.3 greater. Males presented 4 times more large palpable tumors (kidney) than controls which occurred up to 600 days earlier. Biochemistry data confirmed very significant kidney chronic deficiencies; for all treatments and both sexes, 76% of the altered parameters were kidney related. These results can be explained by the non- linear endocrine-disrupting effects of Roundup®, but also by the overexpression of the transgene in the GMO and its metabolic consequences."

Highlights:

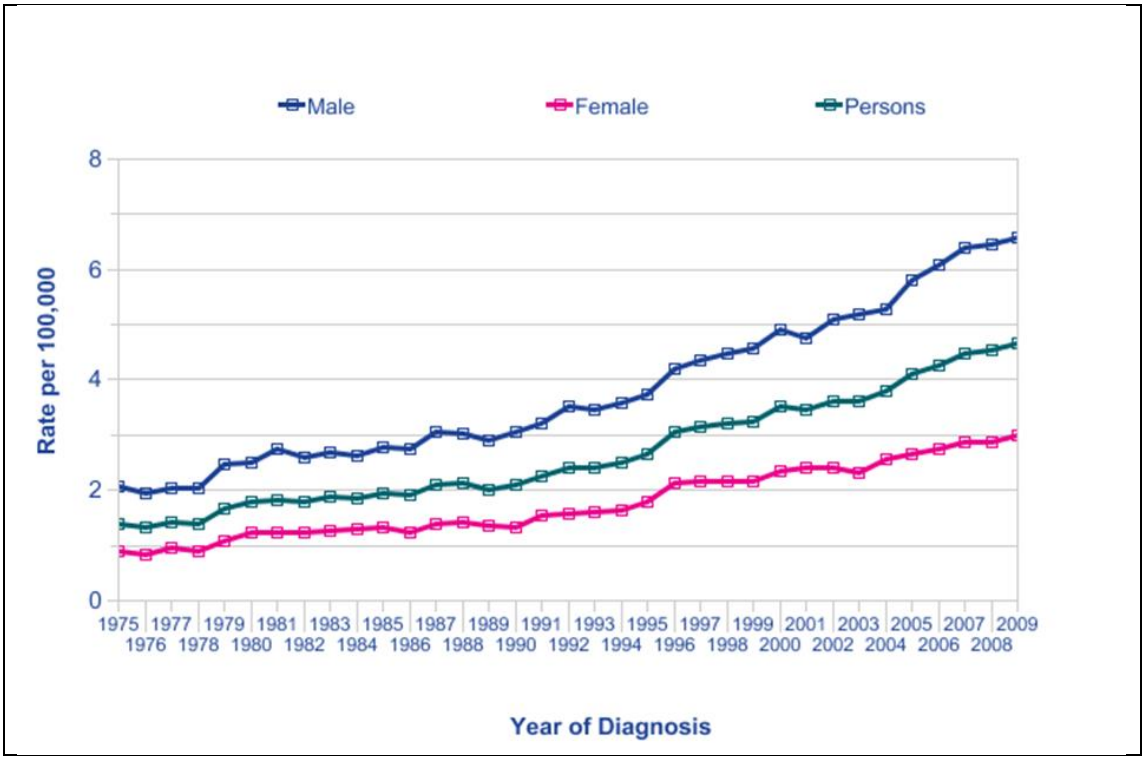
- A Roundup®-tolerant maize and Roundup® provoked chronic hormone and sex dependent pathologies.
- Female mortality was 2-3 times increased mostly due to large mammary tumours and disabled pituitary.
- Males had liver congestions, necrosis, severe kidney nephropathies and large palpable tumours.
- This may be due to an endocrine disruption linked to Roundup® and a new metabolism due to the transgene.
- GMOs and formulated pesticides must be evaluated by long term studies to measure toxic effects.

Watch the 12 minute You Tube video explaining the whole 2-year experiment by Séralini's team in the CRIIGEN laboratory[95].

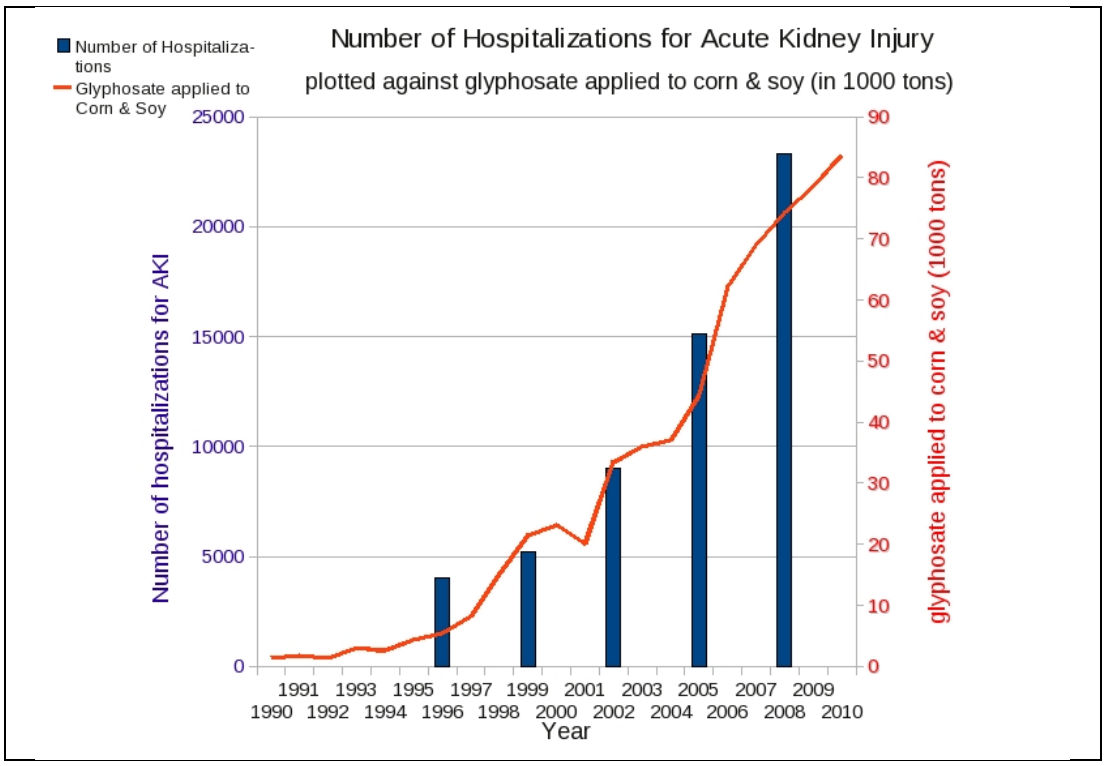


Graph 5 Persons with liver and bile duct cancer plotted against glyphosate applied to corn and soy and % GE corn & soy planted in the US By kind permission of Dr Nancy Swanson. Data from USDA and US CDC

[95] http://www.youtube.com/watch?v=Njd0RugGjAg&feature=player_embedded



Graph 6 Cancer Research UK (CRUK) Liver Cancer: European Age-Standardised Incidence Rates, male and females, Great Britain, 1975-2009[96]



Graph 7 Number of Hospitalizations in the US for Acute Kidney Injury (a sudden, temporary, and sometimes fatal loss of kidney function) plotted against glyphosate applied to corn & soy. Data from USDA and US CDC

[96] http://www.cancerresearchuk.org/cancer-info/cancerstats/types/liver/incidence/#trends

Acute kidney injury (AKI) (See Graph 7 for US increases since 1990)
A new guideline report issued on Wednesday (28/08/2013) from the National Institute for Health and Care Excellence (Nice) says AKI (a sudden loss of kidney function) costs the NHS between £434m and £620m a year – more than it spends on breast, lung and skin cancer combined[97]. Between 262,000 and 1 million people admitted to hospital as an emergency in a year will have AKI, of which just under a quarter will die. Dr Mark Thomas, chair of the new guideline development group and nephrologist at the Heart of England NHS Foundation Trust, said: "*AKI has been something of a Cinderella condition in the past both within healthcare and in the public perception, yet it kills more people than any of the common cancers.*" He said AKI "*is clearly one of the major patient safety issues for the NHS. It affects the vulnerable and leads to thousands of unnecessary deaths because of failings in care.*" Professor Donal O'Donoghue, the government's national clinical director for kidney care from 2007 to earlier this year, has said 32 people die needlessly every day from AKI. He said AKI represented a "*human tragedy*".

EFSA's new assessment of GM crops[98]
The European Food Safety Authority (EFSA) has finally issued new guidelines for two-year whole food feeding studies to assess the risk of long-term toxicity and carcinogenicity from GM foods.

Non-Hodgkin's Lymphoma & Hairy Cell Leukemia
Two Swedish studies suggested that herbicides, particularly glyphosate, were associated with the above conditions.
Lennart Hardell, Mikael Eriksson, Marie Nordstrom: Exposure to pesticides as risk factor for non-Hodgkin's lymphoma and hairy cell leukemia: pooled analysis of two Swedish case-control studies. *Leuk Lymphoma*. 2002 May; 43(5):1043-9[99]
Increased risk for non-Hodgkin's lymphoma (NHL) following exposure to certain pesticides has previously been reported. Among herbicides, significant associations were found for glyphosate (OR 3.04, CI 95% 1.08-8.52) and 4-chloro-2-methyl phenoxyacetic acid (MCPA) (OR 2.62, CI 95% 1.40-4.88). For several categories of pesticides the highest risk was found for exposure during the latest decades before diagnosis
Eriksson M, Hardell L, Carlberg M, Akerman M. Pesticide exposure as risk factor for non-Hodgkin lymphoma including histopathological subgroup analysis[100]. *Int J.Cancer*. 2008, 123:1657-1663. In this category the dominating agent was glyphosate, which was reported by 29 cases and 18 controls, which produced OR (Odds Ratio) 2.02 (95% CI 1.10–3.71)

Glyphosate induces human breast cancer cells growth via estrogen receptors
Thongprakaisang S, Thiantanawat A, Rangkadilok N, Suriyo T, Satayavivad J. Glyphosate induces human breast cancer cells growth via estrogen receptors. *Food Chem Toxicol.* 2013, 59C: 129-136. doi: 10.1016/j.fct.2013.05.057[101]
The study found that breast cancer cell proliferation is accelerated by glyphosate in extremely low concentrations. "*The present study used pure glyphosate substance at log intervals from*

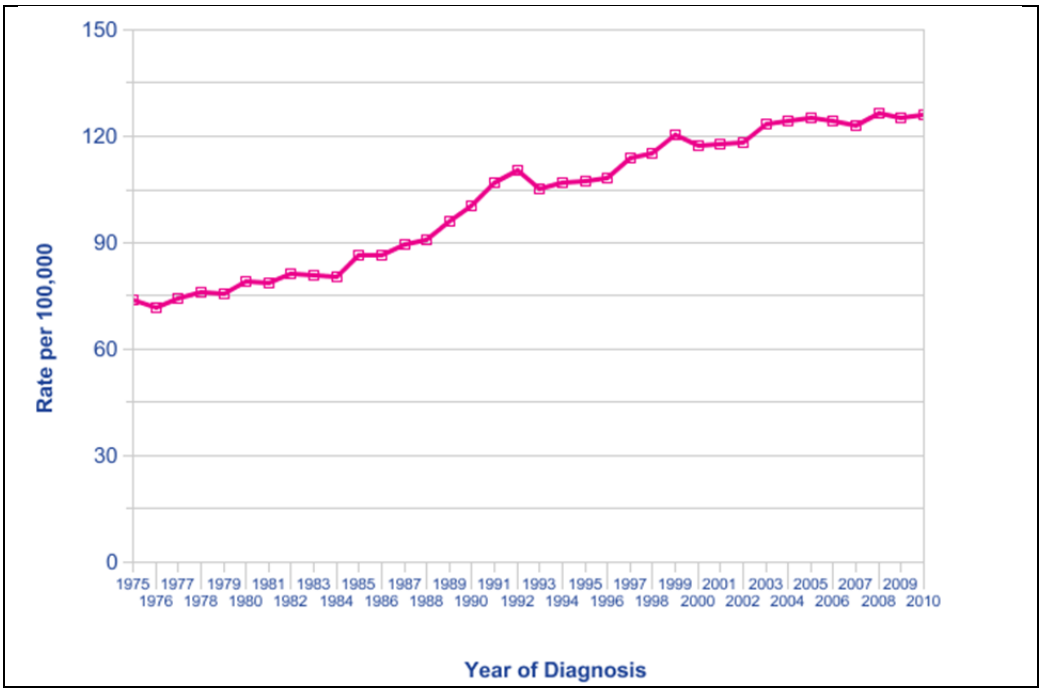
[97].http://www.theguardian.com/society/2013/aug/28/kidney-care-lives-nice

[98] http://www.efsa.europa.eu/en/efsajournal/pub/3347.htm

[99] http://www.ncbi.nlm.nih.gov/pubmed/12148884
[100] http://onlinelibrary.wiley.com/doi/10.1002/ijc.23589/full

[101] http://www.ncbi.nlm.nih.gov/pubmed/23756170

10^{-12} to 10^{-6} M. These concentrations are in a crucial range which correlated to the potential biological levels at part per trillion (ppt) to part per billion (ppb) which have been reported in epidemiological studies."



Graph 8 Cancer Research UK Breast Cancer (C50), European Age-Standardised Incidence Rates, Females, Great Britain, 1975-2010[102]

Effects on male reproduction

Clair, É., Mesnage, R., Travert, C., Séralini, G-É. A glyphosate-based herbicide induces necrosis and apoptosis in mature rat testicular cells *in vitro*, and testosterone decrease at lower levels. *Toxicology in Vitro* **26** (2) 269-279 2012.[103]

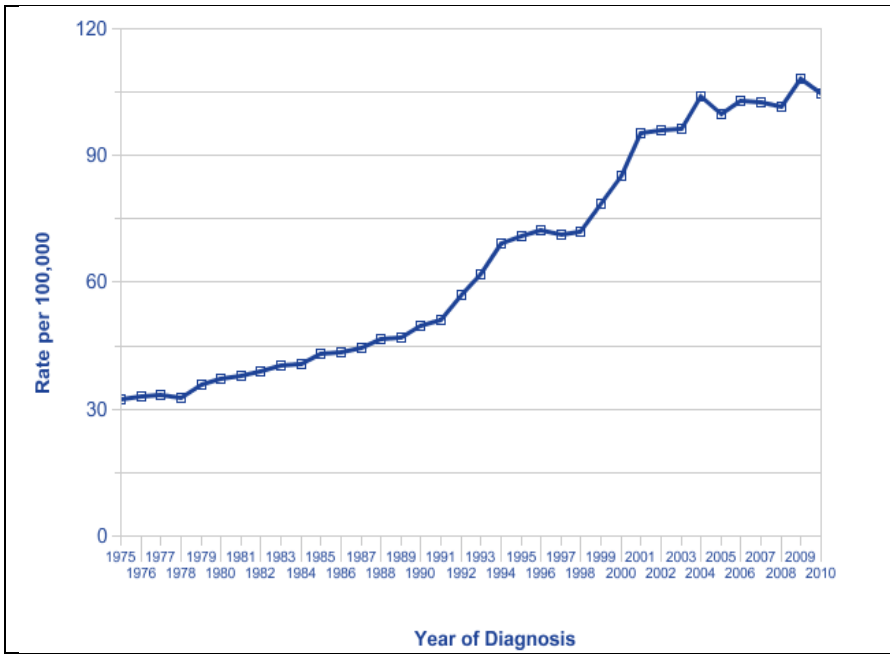
de Liz Oliveira Cavalli VL *et al.* Roundup® Disrupted Male Reproductive Functions By Triggering Calcium-Mediated Cell Death In Rat Testis And Sertoli Cells[104].

Yousef, M.I. *et al.* Toxic effects of carbofuran and glyphosate on semen characteristics in rabbits. *J Environ Sci Health B.* 1995 Jul; 30(4):513-34[105].

The present study was undertaken to investigate the effect of chronic treatment with two sublethal doses of Carbofuran (carbamate insecticide) and Glyphosate (organophosphorus herbicide) on body weight and semen characteristics in mature male New Zealand white rabbits. Pesticide treatment resulted in a decline in body weight, libido, ejaculate volume, sperm concentration, semen initial fructose and semen osmolality. This was accompanied with increases in the abnormal and dead sperm and semen methylene blue reduction time. The hazardous effect of these pesticides on semen quality continued during the recovery period, and was dose-dependent. These effects on sperm quality may be due to the direct cytotoxic effects of these pesticides on spermatogenesis and/or indirectly via hypothalami-pituitary-testis axis which control the reproductive efficiency.

[102] http://www.cancerresearchuk.org/cancer-info/cancerstats/types/breast/incidence/#trends
[103] http://www.ncbi.nlm.nih.gov/pubmed/22200534
[104] http://www.sciencedirect.com/science/article/pii/S0891584913003262
[105] http://www.ncbi.nlm.nih.gov/pubmed/7797819

What is causing the steep rise in prostate cancer in men in Great Britain?



Graph 9 CRUK incidence figures for Prostate Cancer 1975-2010. European Age standardised incidence rates per 100,000 Population, males, Great Britain[106]

Hsing, A.V., Chokkalingam, A.P. Prostate cancer epidemiology *Frontiers in Bioscience* 2006, 11: 1388-1413[107]. In examining the epidemiology of prostate cancer, the authors presented evidence for further areas of promising research: defects in DNA repair pathway, the role of inflammation markers and biological pathways related to dietary factors.

Effects on pathogens in farm animals: evidence that glyphosate destroys beneficial bacteria and allows harmful ones, such as salmonella, and clostridium, to flourish
Clair, E. *et al*. Effects of Roundup® and Glyphosate on Three Food Microorganisms: *Geotrichum candidum*, *Lactococcus lactis subsp. cremoris* and *Lactobacillus delbrueckii subsp. bulgaricus*. *Curr Microbiol.* Epub 2012 Feb 24.[108]
Shehata, A.A. *et al.* The Effect of Glyphosate on Potential Pathogens and Beneficial Members of Poultry Microbiota *In Vitro*. *Current Microbiology* 2013, 66 (4): 350-358[109]
Krüger, M. *et al*. Glyphosate suppresses the antagonistic effect of Enterococcus spp. on *Clostridium botulinum*. *Anaerobe* 2013, Feb 6[110].
In the search for the causes of serious diseases of entire herds of animals in northern Germany, especially cattle, glyphosate has repeatedly been detected in the urine, faeces, milk and feed of the animals[111]*. Even more alarming, glyphosate was detected in the urine of the farmers.* This could explain why the incidence of food poisoning is not decreasing in humans.

[106] http://www.cancerresearchuk.org/cancer-info/cancerstats/types/prostate/incidence/uk-prostate-cancer-incidence-statistics#trends
[107] http://dceg.cancer.gov/files/hsing1113882006.pdf
[108] http://link.springer.com/article/10.1007/s00284-012-0098-3

[109] http://link.springer.com/article/10.1007/s00284-012-0277-2

[110] https://www.ncbi.nlm.nih.gov/m/pubmed/23396248/?i=4&from=/15071029/related
[111] http://www.ithaka-journal.net/druckversionen/e052012-herbicides-urine.pdf

Evidence of GMO harm in pig study[112]

Judy A. Carman, Howard R. Vlieger, Larry J. Ver Steeg *et al*. A long-term toxicology study on pigs fed a combined genetically modified (GM) soy and GM maize diet. *Journal of Organic Systems* 2013 8(1) 38-54.

This was a combined study between the US and Australia. GM-fed females had on average a 25% heavier uterus than non-GM-fed females, a possible indicator of disease that requires further investigation. Also, the level of severe inflammation in stomachs was markedly higher in pigs fed on the GM diet. The research results were striking and statistically significant. Lead researcher Dr Judy Carman, adjunct associate professor at Flinders University, Adelaide, Australia, said: "Our findings are noteworthy for several reasons.

- First, we found these results in real on-farm conditions, not in a laboratory, but with the added benefit of strict scientific controls that are not normally present on farms.
- Second, we used pigs. Pigs with these health problems end up in our food supply. We eat them.
- Third, pigs have a similar digestive system to people, so we need to investigate if people are also getting digestive problems from eating GM crops.
- Fourth, we found these adverse effects when we fed the animals a mixture of crops containing three GM genes and the GM proteins that these genes produce. Yet no food regulator anywhere in the world requires a safety assessment for the possible toxic effects of mixtures. Regulators simply assume that they can't happen".

"*Our results provide clear evidence that regulators need to safety assess GM crops containing mixtures of GM genes, regardless of whether those genes occur in the one GM plant or in a mixture of GM plants eaten in the same meal, even if regulators have already assessed GM plants containing single GM genes in the mixture*."

Confirmation of 'changeover' studies

The new study lends scientific credibility to anecdotal evidence from farmers and veterinarians, who have for some years reported reproductive and digestive problems in pigs fed on a diet containing GM soy and corn. Iowa-based farmer and crop and livestock advisor Howard Vlieger, one of the coordinators of the study, said: "*For as long as GM crops have been in the feed supply, we have seen increasing digestive and reproductive problems in animals. Now it is scientifically documented. In my experience, farmers have found increased production costs and escalating antibiotic use when feeding GM crops. In some operations, the livestock death loss is high, and there are unexplained problems including spontaneous abortions, deformities of new-born animals, and an overall listlessness and lack of contentment in the animals."*

A Danish farming newspaper Effektivt Landbrug devoted a sizeable part of its 13th April 2012 edition to the discoveries by pig farmer lb Borup Pedersen that GM soy has a damaging effect both on his animals and on his farming profitability. In the previous 2 years, the farm had experienced piglet diarrhoea and 35 sows had died of stomach problems. In the previous 9 months he had had 13 malformed, but live-born, piglets.

[112] http://www.organic-systems.org/journal/81/8106.pdf

Photograph by kind permission of Ib Borup Pedersen

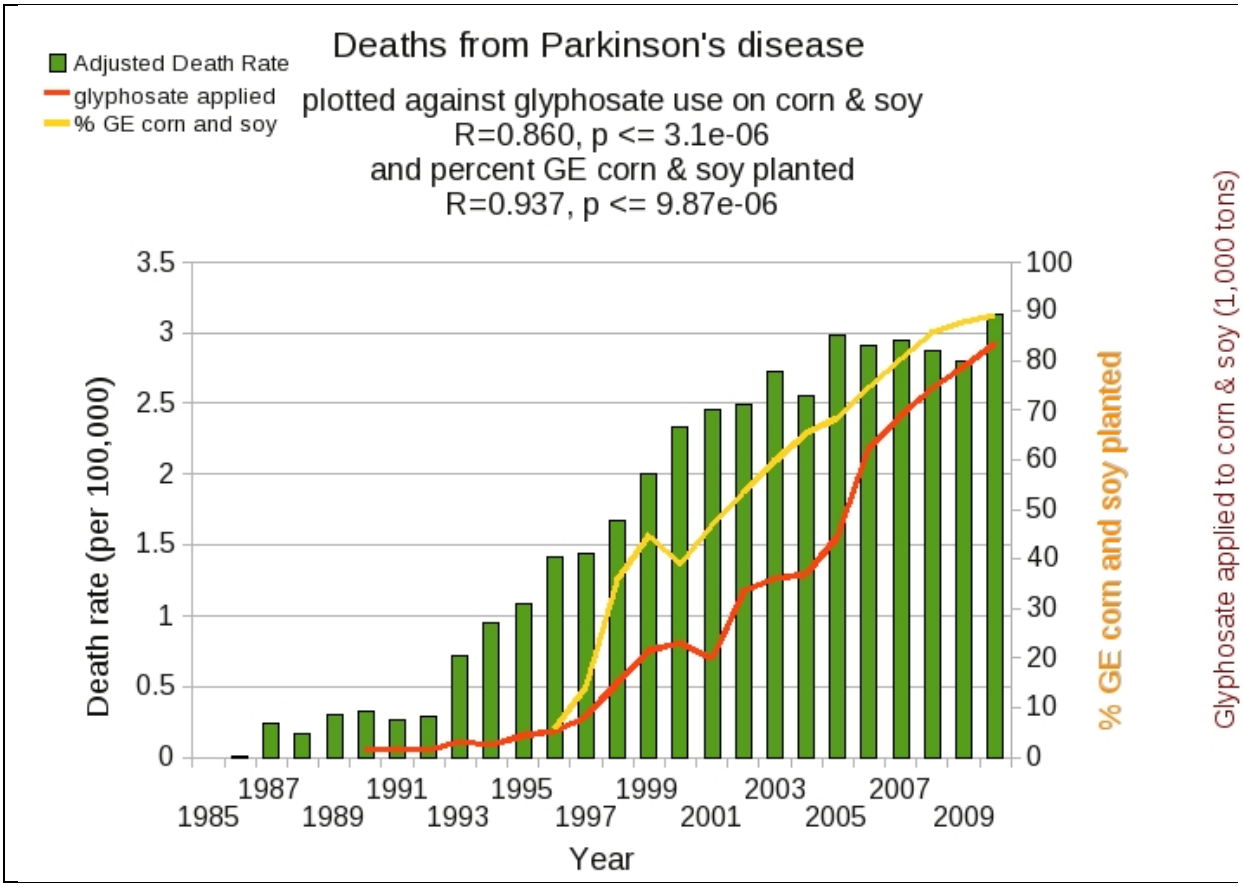
A deformed piglet; Siamese twins

Another colleague had had similar experiences. In April 2011 Mr Pedersen changed to GM-free soya, without telling his stockman. Within days the stockman noticed that the piglet diarrhoea had stopped.

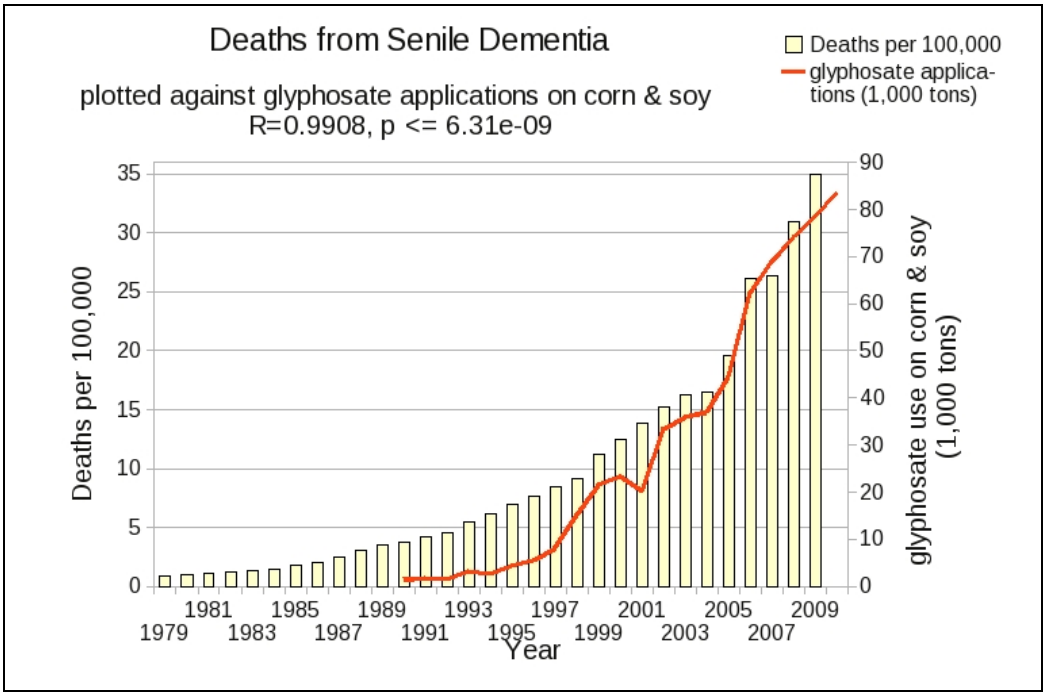
A Russian study found that feeding hamsters GMO soy resulted in complete sterility after two or three generations.
A joint study was carried out by the National Association for Gene Security and the Institute of Ecological and Evolutional Problems. One group of hamsters acted as a control; one was fed non-GM soya, one was fed with some GMO and the fourth one with an increased amount of GMO. "*When they selected new pairs from their cubs, their growth rate was slower and reached their sexual maturity slowly. We failed to get cubs from these pairs, which were fed with GM foodstuffs. It was proved that these pairs lost their ability to give birth to their cubs." Dr. Alexei Surov said*[113].

Associations with neurodegenerative disorders in humans
Ya-xing Gui *et al.* Glyphosate induced cell death through apoptotic and autophagic mechanisms. *Neurotoxicology and Teratology* 2012, 34 (3): 344–349[114]
Herbicides have been recognized as the main environmental factor associated with human neurodegenerative disorders such as Parkinson's disease (PD). Previous studies indicated that the exposure to glyphosate, a widely used herbicide, is possibly linked to Parkinsonism, however the underlying mechanism remains unclear. We investigated the neurotoxic effects of glyphosate in differentiated PC12 cells and discovered that it inhibited viability of differentiated PC12 cells in dose-and time-dependent manners. Furthermore, the results showed that glyphosate induced cell death via autophagy pathways in addition to activating apoptotic pathways. Interestingly, deactivation of Beclin-1 gene attenuated both apoptosis and autophagy in glyphosate treated differentiated PC12 cells, suggesting that Beclin-1 gene is involved in the crosstalk between the two mechanisms.

[113] http://voiceofrussia.com/2010/04/16/6524765.html/
[114] http://www.sciencedirect.com/science/journal/08920362
http://www.activistpost.com/2012/04/roundup-herbicide-linked-to-parkinsons.htm



Graph 10 Adjusted Death Rate from Parkinson's disease. Data from USDA and CDC. By kind permission of Dr Nancy Swanson



Graph 11 Deaths per 100,000 from Senile Dementia plotted against glyphosate applications on corn and soy. Data from USDA and CDC. By kind permission of Dr Nancy Swanson

Environmental damage: Effects on earthworms, songbirds, small mammals and bees
Springett, J.A, Gray R.A.J. Effect of repeated low doses of biocides on the earthworm *Aporrectodea caliginosa* in laboratory culture. *Soil Biol. Biochem*. 1992, 24(12): 1739-1744. *Repeated applications of glyphosate significantly affected the growth and survival of earthworms.*
Santillo DJ, Brown PW, Leslie DM. Response of songbirds to glyphosate-induced habitat changes on clearcuts. *J Wildlife Manage.* 1989, 53: 64–71. The authors investigated the use of glyphosate on intensively managed pine forests in Maine. Follow up for 1-3 years found a reduction in the complexity of vegetation and a reduction in the number of bird species.
Santillo DJ *et al*. Responses of small mammals and habitat to glyphosate application on clearcut. *J Wildlife Manage*. 1989, 53 (1): 164-172. The authors investigated the use of glyphosate on intensively managed pine forests in Maine. At 1-3 years there fewer small mammals; insectivores and herbivores were reduced because they were dependent on insect and plant communities which had been destroyed by glyphosate.
Foulk, K.E.; Reeves, C. Identifying the role of glyphosate-containing herbicides on honeybee mortality rates and colony collapse disorder[115].
The results of this study indicate that the mortality rate of bees that were fed glyphosate-supplemented diets, both pure glyphosate and Roundup QuikPro®, were significantly greater than that of hives without glyphosate supplemented diets (p < 0.001).

Genotoxic effects of glyphosate in fish and amphibians
de Castilhos, G.N, Cestari, M.M. Genotoxic effects of the herbicide Roundup(®) in the fish *Corydoras paleatus* (Jenyns 1842) after short-term, environmentally low concentration exposure. *Environ Monit Assess.* 2013, 185 (4):3201-7. doi: 10.1007/s10661-012-2783-x[116]. "*We conclude that for the low concentration used in this research, the herbicide shows potential genotoxic effects. Future research will be important in evaluating the effects of this substance, whose presence in the environment is ever-increasing".*
Relyea, R.A. The lethal impacts of Roundup® and predatory stress on six species of North American tadpoles. *Arch. Environ.Contam. Toxicol.* 2005, 48: 351-357[117]. "*The decline in amphibians across the globe has sparked a search for the causes, and recent evidence suggests a connection with pesticides."* Relyea found that the survival in tadpoles was greatly reduced with glyphosate at lower doses than in previous studies and that any additional predatory stress made Roundup® twice as lethal.

Glyphosate causes immune suppression in fish
Kelly, D.W. *et al*. Synergistic effects of glyphosate formulation and parasite infection on fish malformations and survival. *Journal of Applied Ecology* 2010, 47: 498–504[118].
This is the first study to show that parasites and glyphosate can act synergistically on aquatic vertebrates at environmentally relevant concentrations, and that glyphosate might increase the risk of disease in fish. Our results have important implications when identifying risks to aquatic communities and suggest that threshold levels of glyphosate currently set by regulatory authorities do not adequately protect freshwater systems.

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115 http://k12science.missouristate.edu/Junior_Academy/MJAS%20Docs/State%202009/Papers%202009/HS_ENV/Foulk_Kayla_HS.pdf

116 http://link.springer.com/article/10.1007%2Fs10661-012-2783-x

117 http://training.fws.gov/EC/Resources/pesticides/Aquatic%20Effects/Relyea2005.pdf

118 http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2664.2010.01791.x/pdf

The use of pesticides around the world has produced biological deserts

Here is a description of a 600 acre farm in Ohio with GMO corn on which Craig Childs[119] spent a long weekend and found virtually nothing. "*I listened and heard nothing, no bird, no click of insect. There were no bees. The air, the ground, seemed vacant…It felt like another planet entirely," he said, a world denuded.*

Robert Krulwich's blog commented on Craig Child's description[120]: "*Yet, 100 years ago, these same fields, these prairies, were home to 300 species of plants, 60 mammals, 300 birds, hundreds and hundreds of insects. This soil was the richest, the loamiest in the state. And now, in these patches, there is almost literally nothing but one kind of living thing. We've erased everything else. There's something strange about a farm that intentionally creates a biological desert to produce food for one species: us. It's efficient, yes. But it's so efficient that the ants are missing, the bees are missing, and even the birds stay away. Something's not right here. Our cornfields are too quiet.*" In the UK in 2012, on a warm August evening, in a garden surrounded by arable crops, no moths came to the candles[121]. There was not a single insect. Few people have noticed, or care much about their loss. But flying insects are the visible manifestation of a massive iceberg of trillions of invertebrates working away unseen in soil and water. The neonicotinoid insecticides attack the nervous system receptors of all invertebrates. These are the small things that run the world. Destroy these and you ultimately destroy life itself, at least as a planet fit for humans.

A major pollution incident on the River Kennet, a chalk stream in the UK

George Monbiot wrote an article on August 5th 2013: "*Neonicotinoids are the new DDT killing the natural world.*" In it he exposed the Government's cooperation with the Pesticides Industry. "*UK is collaborating in peddling the corporate line that neonicotinoid pesticides are safe to use*."[122] He was enraged by a pollution incident that had destroyed 15 miles of pristine chalk stream. The pollution incident, which was discovered on 1st July 2013, was with chlorpyrifos an organophosphate, one of a group of pesticides that had, in theory, been banned in 1982[123]. By 11th July it had wiped out insect and fresh water shrimp populations in the River Kennet that are food for fish, birds and amphibians. The river was beginning to stink[124]. An Environment Agency spokesman described chlorpyrifos as "*a common agricultural pesticide.*" A former MP said it should be banned.

Why are the organophosphates chlorpyrifos and dimethoate still being registered?

Two organophosphates are still being authorised in the UK. In 2009, the total agricultural area treated with chlorpyrifos was 277,593 ha and in 2010 dimethoate 48,264 ha[125]. Defra had always denied a link between organophosphate used as sheep dip in the 1980s and

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[119] Craig Childs Apocalyptic Planet

[120] http://www.npr.org/blogs/krulwich/2012/11/29/166156242/cornstalks-everywhere-but-nothing-else-not-even-a-bee

[121] Personal observations

[122] http://www.theguardian.com/environment/georgemonbiot/2013/aug/05/neonicotinoids-ddt-pesticides-nature

[123] http://www.newburytoday.co.uk/2013/kennet-pollution-hunt-for-culprit

[124] http://www.gazetteandherald.co.uk/news/towns/marlboroughheadlines/10541095.Effects_of_pollution_on_River_Kennet_beginning_to_come_clear/

[125] http://pusstats.csl.gov.uk/.

neurological problems in farmers. However, a new independent study contradicted the Defra findings. Mackenzie Ross, S.J. *et al.* Neurobehavioural problems following low level exposure to organophosphate pesticides: A systematic & meta-analytic review. *Clinical Reviews in Toxicology*; 2012[126]. These findings have implications for working practice for farm-workers and for other occupational groups exposed to organophosphates such as Aviation Workers and Gulf War Veterans.

Prenatal exposure to chlorpyrifos has effects on neurodevelopment aged 3 and aged 7
In the US is has been proved in several prospective studies that pre-natal exposure to chlorpyrifos causes neurodevelopmental problems. *It has long been associated with delayed neurocognitive development and most recently with decrements in working memory at age 7*.
Rauh, V. A. *et al*. Impact of Prenatal Chlorpyrifos Exposure on Neurodevelopment in the First 3 Years of Life Among Inner-City Children *Pediatrics* 2006, 118 (6) e1845-e1859 http://doi: 10.1542/peds.2006-0338[127].
Rauh, V *et al.* Seven-Year Neurodevelopmental Scores and Prenatal Exposure to Chlorpyrifos, a Common Agricultural Pesticide. *Environ Health Perspect.* 2011, 119:1196-1201 http://dx.doi.org/10.1289/ehp.1003160[128]. *We report evidence of deficits in Working Memory Index and Full-Scale IQ as a function of prenatal CPF exposure at 7 years of age. These findings are important in light of continued widespread use of CPF in agricultural settings and possible longer-term educational implications of early cognitive deficits.*
Lovasi GS *et al.* Chlorpyrifos exposure and urban residential environment characteristics as determinants of early childhood neurodevelopment *Am J Public Health.* 2011, 101 (1): 63-70. doi: 10.2105/AJPH.2009.168419[129]
Horton, M.K. *et al.* Does the home environment and the sex of the child modify the adverse effects of prenatal exposure to chlorpyrifos on child working memory? *Neurotoxicology and Teratology* 34, (5) 2012, 534–541[130]

Human Health Effects of Developmental Exposure to Chemicals in Our Environment
Epigenetics is the study of gene changes caused by environmental exposure to chemicals in the environment. The Faroes Statement 2007[131]: "*The periods of embryonic, foetal and infant development are remarkably susceptible to environmental hazards. Toxic exposures to chemical pollutants during these windows of increased susceptibility can cause disease and disability in infants, children and across the entire span of human life".*
The Policy Statement from the American Academy of Pediatrics about Pesticide Exposure in Children from the COUNCIL ON ENVIRONMENTAL HEALTH[132] "*This statement presents the position of the American Academy of Pediatrics on pesticides. Pesticides are a collective term for chemicals intended to kill unwanted insects, plants, molds, and rodents. Children encounter pesticides daily and have unique susceptibilities to their potential toxicity. Acute poisoning risks are clear, and understanding of chronic health implications from both acute and chronic exposure are emerging. Epidemiologic evidence demonstrates associations between early life exposure to pesticides and pediatric cancers, decreased cognitive function, and behavioral problems*."

[126] http://www.ncbi.nlm.nih.gov/pubmed/23163581
[127] http://www.ipminstitute.org/Fed_Agency_Resources/rauh_chlorpyrifos_pediatrics.pdf

[128] http://ehp.niehs.nih.gov/1003160/
[129] http://ajph.aphapublications.org/doi/abs/10.2105/AJPH.2009.168419?journalCode=ajph
[130] http://dx.doi.org/10.1016/j.ntt.2012.07.004
[131] http://www.ncbi.nlm.nih.gov/pubmed/18226057
[132] http://pediatrics.aappublications.org/content/130/6/e1757

In addition, the Royal College of Obstetricians and Gynaecologists has issued advice to the pregnant patient about avoiding exposure to pesticides[133].

These statements are dismissed out of hand by the Pesticides Industry

Carol J. Burns *et al*. Pesticide Exposure and Neurodevelopmental Outcomes: Review of the Epidemiologic and Animal Studies. *Journal of Toxicology and Environmental Health*, Part B: Critical Reviews 2013, 16:3-4, 127-283, DOI: 10.1080/10937404.2013.783383[134]
After 158 pages of Tables, Abbreviations and Statistical Analyses: *"In conclusion, epidemiologic evidence for causality between exposure to specific pesticides during critical periods of brain development and neurobehavioral outcomes is not compelling."*
The Review was funded by the Crop Protection Association. Carol Burns is employed by Dow. The remainder: "*are or have previously been employed by Exponent, Inc., a research and scientific consultant firm with clients from industry (including crop protection) and government".*

- Dow is a manufacturer of chlorpyrifos (see above) which has been linked to neurodevelopmental problems.
- Dow was also the first manufacturer of the herbicide 2,4-D in 1947. In 1986 it was associated with a six-fold increase of Non-Hodgkin's Lymphoma (NHL) among farmers exposed to herbicides more than 20 days per year. This was found to be consistent with the six-fold excess risk associated with exposure to either phenoxyacetic acids or chlorophenols in a Swedish study[135].

There are many weed killer products sold in the UK that contain 2,4-D and dicamba. They can be purchased on-line for amenity turf and pitch turf for professional use. It is the third most commonly used herbicide in the US[136]. In Australia (July 2013) cheap generic 2, 4-D is being imported that has been found to contain high levels of dioxins, but APVMA does not monitor for dioxins[137]. In the 1970s and 1980s, men were employed by the Agriculture Protection Board to spray noxious weeds. In Kimberley alone 320 men died and now their partners and children are getting sick. Nigel Sinclair's father and uncle died, and now he, at 31, has terminal cancer.

Relationships between Syngenta, AstraZeneca and Defra/Fera

In 1997, Dr Peter Campbell went straight from being the Head of Ecotoxicology Branch at the Pesticides Safety Directorate in York into the post of Head of Ecological Sciences at Syngenta[138]. In 2009 Syngenta and BBSRC gave £1 million to fund Warwick University and Rothamsted Research *"to help to improve honeybee health"*[139]. (Rothamsted had lost funding for its Bee Unit in 2006). Syngenta funded scientific assistants at Exeter University in 2012. Syngenta pioneered Operation Bumblebee in the UK and in 2010 announced expansion of

[133] Royal College of Obstetricians and Gynaecologists : May 2013 Chemical Exposures in Pregnancy.pdf
[134] http://dx.doi.org/10.1080/10937404.2013.783383

[135] Hoar, S.K. *et al*. Agricultural Herbicide Use and Risk of Lymphoma and Soft-Tissue Sarcoma. *JAMA* 1986;256:1141-1147 http://occupationalcancer.ca/wp-content/uploads/2012/05/Hoar-1986-Agricultural-herbicide-use-and-risk-of-lymphoma-and-STS.pdf

[136] http://water.usgs.gov/nawqa/pnsp/usage/maps/show_map.php?year=2009&map=24D&hilo=L

[137] http://mobile.abc.net.au/news/2013-07-22/four-corners-dangerous-dioxins/4833848
[138] http://uk.linkedin.com/pub/peter-campbell/4/283/6ba
[139] http://www.bbsrc.ac.uk/news/archive/2009/091001-pr-1million-award-honeybee-decline.aspx

programmes across Europe; up to €1 million over 5 years[140]. Programmes included *"What Operation Bumblebee can do for your golf course?"*
Syngenta had representatives on the Advisory Committee on Pesticides (ACP), the Committee on Toxicity of Chemicals in Foods, Consumer Products and the Environment (COT), on the Panel to choose the Pollinator Initiative Projects and on the Government's Foresight Future of Farming Report[141]. Syngenta's parent company AstraZeneca had two representatives on COT.
Defra's Pesticides Forum Annual Report 2011 concluded: *"The work of the UK Pesticides Forum in 2011 confirms that the use of pesticides is **not** adversely impacting on the health of UK citizens or the environment. This is testimony to the effectiveness of both statutory and voluntary controls."*

Syngenta commissioned a paper from Dr Helen Thompson, Fera Chief Bee Scientist
An assessment of key evidence about Neonicotinoids and bees March 2013[142]
The UK voted against the EU ban on neonicotinoids because it was waiting for '*new research on bumblebees to be completed by Fera'*.
Effects of neonicotinoid seed treatments on bumble bee colonies under field conditions was published by Dr Helen Thompson *et al*. Fera, York[143].
A letter from Defra Minister Owen Paterson to Syngenta (April 2013) was released to the *Observer* under freedom of information rules. He told the chemicals company Syngenta that he was *'extremely disappointed*' by the European Commission's proposed ban. He said that *'the UK has been very active*' in opposing it and *'our efforts will continue and intensify in the coming days'*[144].
On June 4 2013, EFSA rejected the study by Thompson *et al.* 2013 as weak. It said it "*does not change the conclusions of the risk assessment*" of January 2013[145].
Dr Helen Thompson left Fera to join Syngenta[146] on 1 September 2013.

Why is the Government determined to get GM crops into Britain?
Syngenta applied to EFSA GMO Panel for GM Roundup®-tolerant maize[147]: *"The UK Competent Authority and Syngenta applied for placing on the market of a GM, herbicide tolerant (glyphosate) maize GA21 for food and feed uses, import, processing and cultivation."* It was adopted by the Panel on GMO on 16 December 2011. The GMO Panel claimed that there were no effects on human or animal health or the environment. However, in the main document, the Panel admitted to the problems of reduction in farmland biodiversity, selection of weed communities and selection of glyphosate-resistant weeds and

[140] http://www.bbsrc.ac.uk/news/archive/2009/091001-pr-1million-award-honeybee-decline.aspx
[141] http://www.bis.gov.uk/assets/foresight/docs/food-and-farming/11-546-future-of-food-and-farming-report.pdf
[142] http://www.defra.gov.uk/publications/files/pb13937-neonicotinoid-bees-20130326.pdf
[143] http://www.fera.defra.gov.uk/scienceResearch/scienceCapabilities/chemicalsEnvironment/documents/reportPS2371Mar13.pdf
[144] http://www.guardian.co.uk/environment/interactive/2013/apr/29/environment-secretary-letter-syngenta-insecticide-ban.
[145] http://www.efsa.europa.eu/en/efsajournal/pub/3242.htm
[146] http://www.theguardian.com/environment/2013/jul/26/government-bee-scientist-pesticide-firm
[147] http://www.efsa.europa.eu/en/efsajournal/pub/2480.htm

destruction of food webs and the ecological functions they provide. Nevertheless, it was approved by the Panel, which covered itself by saying "*The magnitude of these potential adverse environmental effects will depend on a series of factors including the specific herbicide and cultivation management applied at farm level, the crop rotation...etc*. and recommended "*case-specific monitoring"*. However, the Chairman of the Panel, who had been involved in every case of risk assessment of GE crops since the start of EFSA, did not declare his conflict of interest.
Monsanto and the Competent Authority of the Netherlands applied to EFSA GMO Panel for herbicide-tolerant GM soybean. It was adopted June 2012[148]. "*If subjected to appropriate management measures, the cultivation of soybean 40-3-2 is unlikely to have environmental effects any more adverse than those associated with conventional soybean cultivation*".

Prof Maurice Moloney was appointed Director and Chief Executive of Rothamsted Research on 15/04/2010[149]. "*Previously, he was the head of the Cell Biology Group at Calgene Inc., where he developed the first transgenic oilseed plants using Canola as the model. This resulted in a landmark patent in plant biotechnology and eventually became the basis of RoundUp® Ready and Liberty Link® Canola, which now commands 85% of the Canola acreage in Canada, a market of more than $100 MM per annum*."
Prof Jonathan Jones[150] was Head of the Sainsbury Laboratory between 1994 and 1997. He then returned to the post in 2003. In 1997 he left to start two companies: Mendel Biotechnology (MBT) to carry out genomics experiments and Norfolk Plant Sciences Ltd to combine health-promoting traits and disease-resistance traits in potatoes and tomatoes. Monsanto is an investor and collaborator in MBT and in the 2008 Annual Report, Monsanto's Vice President Stephen Padgette is listed as on the Advisory Board. Prof Jones admitted in *The Observer* in 2010 that MBT had contracts with Monsanto, Bayer and BP, but that "*he had never tried to hide them".* In Plant Science News, 16/10/2011: "Leading plant researchers' call for science-based GM regulation", both he and Prof Maurice Moloney, Director of Rothamsted Research, forgot to declare their "*multinational*" connections.

Prof Jonathan Jones believes glyphosate to be harmless to mammals
January 2012 I had emailed Prof Jones about Monsanto's GM corn not being sold in France.

Dear Rosemary
Glyphosate is not poisonous to mammals- it inhibits EPSP synthase, an enzyme that mammals lack because we obtain aromatic amino acids in our diet. Roundup the herbicide contains surfactants- basically soaps- the consumption of which is ill advised. Roundup is considerably less damaging to the environment than the herbicides it replaced, such as those made by American Cyanamid (now bankrupt).
France has elected to reject the judgement of the European Court that it has no right to block planting of an approved insect resistant maize variety containing MON810. Fortunately Spain and Portugal have not been so stupid and their farmers plant 100k hectares of GM maize which requires less insecticides to control corn borer.
If the cost of deregulation of useful and benign GM traits were lower, there would be more competition for the MNCs from small companies and the public sector.
Regards Jonathan"

[148] http://www.efsa.europa.eu/en/efsajournal/pub/2753.htm
[149] http://www.rothamsted.ac.uk/PersonDetails-Who=1086.html
[150] http://www.tsl.ac.uk/profile/jonathan-jones.asp

Why is the pesticides industry investing so much money in human health?
Syngenta's parent company is AstraZeneca. AstraZeneca manufactures six different anti-cancer drugs mainly aimed at breast and prostate cancer. The Corporation has links in Asia, including Hospitals in China, Japan, Korea, and collaborators in Russia. AstraZeneca's Oncology Website[151] has the following portentous prediction: "*Cancer claims over 7 million lives every year and the number continues to rise. Deaths are estimated to reach 12 million by 2030*."
Michael Pragnell MA MBA was the founder of Syngenta and CEO of Syngenta AG based in Switzerland (from its public listing in 2000 to the end of 2007). He was appointed a Trustee of Cancer Research UK (CRUK) in March 2010 and Chairman in November 2010. CRUK is donating money (£450 million/year) to the Government's Strategy for UK Life Sciences[152] and AstraZeneca is providing 22 compounds to academic research to develop medicines.

Signatures of mutational processes in human cancer: Genetic map of cancer mutations
A study of mutations from 7,042 cancers by the Sanger Institute revealed that 21 distinct mutational signatures that alone, or in combination, drive 30 different types of cancer[153]. Mutations of DNA may be due to "*chemicals in the environment or faults that arise during aging.*" "*The work has shed light on how the body's natural defences might inadvertently drive a range of cancers. When cells are infected by viruses, they can switch on genes that produce a family of enzymes. These enzymes destroy viruses by mutating their DNA, but the onslaught may cause collateral damage." "It's speculation, but it may be that in killing the virus, many mutations are scattered in the genome of the cell itself, and that cell can then go on to become a cancer,*" said Prof Mike Stratton. "*The findings are expected to drive research into the causes of mutations behind each cancer. One way to do this is to expose human cells to suspected carcinogens in the environment to see if they produce similar patterns of mutations"*[154].

Pesticides are the obvious choice, since they are ubiquitous and are designed to kill
But few scientists dare to mention them for fear of being vilified by industry, losing their jobs, or threats of withdrawal of funding from their Universities. Prof Nic Jones, Chief Scientist at Cancer Research UK (whose Chairman is Michael Pragnell of Syngenta) was silent on the subject of pesticides. He could only suggest smoking and overexposure to UV rays as possible causes of faults in DNA that can lead to cancer[155]. CRUK website on Pesticides and Cancer denies links to pesticides: "*For now, the evidence is not strong enough to give us any clear answers. But for individual pesticides, the evidence was either too weak to come to a conclusion, or only strong enough to suggest a "possible" effect. The scientific evidence on pesticides and cancer is still uncertain and more research is needed in this area*[156].

[151] http://www.astrazeneca.co.uk/medicines/oncology
[152] https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/32457/11-1429-strategy-for-uk-life-sciences.pdf

[153] http://www.nature.com/nature/journal/vaop/ncurrent/full/nature12477.html
[154] http://www.theguardian.com/science/2013/aug/14/genetic-map-cancer-mutation-disease

[155] http://www.theguardian.com/science/2013/aug/14/genetic-map-cancer-mutation-disease
[156] http://www.cancerresearchuk.org/cancer-info/healthyliving/cancercontroversies/pesticides/

Many independent scientists over the years have been subjected to outrageous treatment when they have suggested inconvenient truths about GMO science[157].

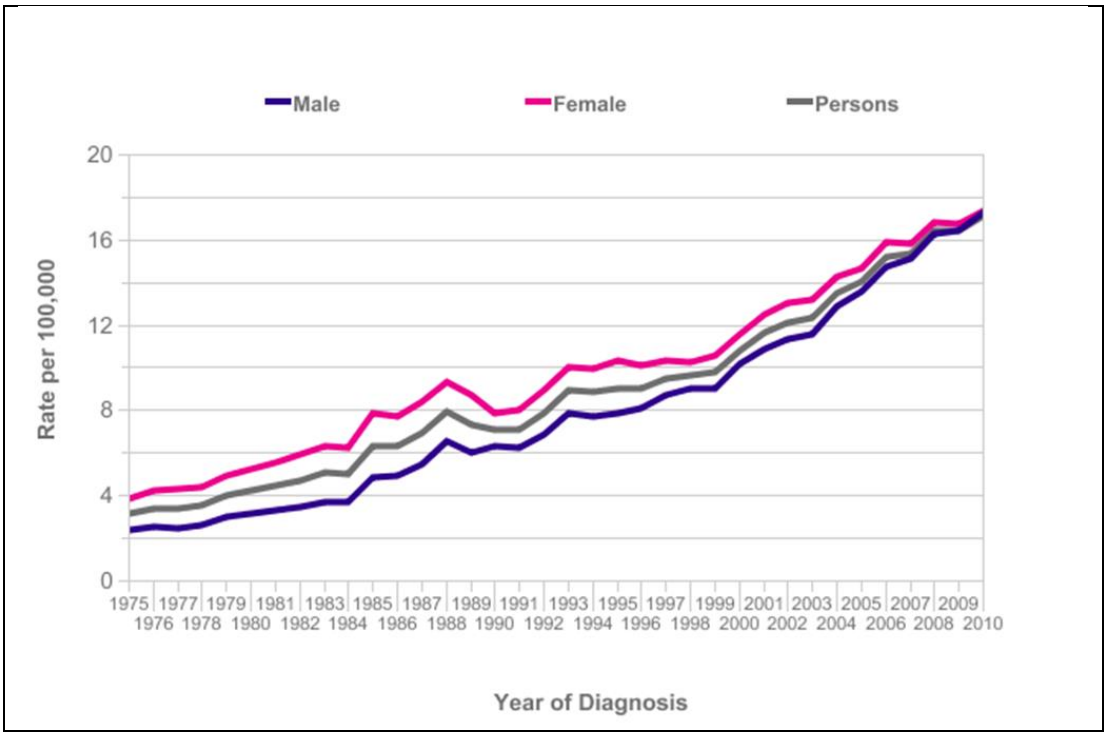
Cancer Research UK: Chairman, founder of Syngenta: 21/08/2013 Death rates from malignant melanoma in men higher than in women. Sunburn can damage DNA

"Death rates from malignant melanoma – the most serious type of skin cancer – are 70 per cent higher in men than women, despite similar numbers being diagnosed with the disease each year – according to the latest figures from Cancer Research UK, today (Wednesday). Each year in the UK, 3.4 men per 100,000 compared with 2.0 women die from malignant melanoma. But incidence rates are similar with 17.2 men per 100,000 diagnosed compared with 17.3 women.

This means that, of the 6,200 men who develop melanoma each year, 1,300 die from the disease, while 900 of the 6,600 women who develop it die.

And the gap is predicted to widen in the future, with death rates from malignant melanoma on the increase in men but remaining stable for women.

Since the early 70s, death rates in men have increased by 185 per cent compared to a rise of only 55 per cent in women. The key risk factors for melanoma include excessive exposure to UV from sunlight or sunbeds, pale skin colour and a high number of moles, and a family or personal history of the disease. Sunburn is a clear sign that the DNA in your skin cells has been damaged and, over time, this can lead to skin cancer".



Graph 12 Malignant Melanoma: Age standardised incidence rates per 100,000 Population by sex, Great Britain. Prepared by Cancer Research UK[158]

Evidence that pesticides can damage DNA

There is plenty of independent science that demonstrates that pesticides can damage DNA

[157] http://www.gmfreecymru.org.uk/open_letters/Open_letter26Jan2011.html The GM science community is its own worst enemy. Open Letter to Sir Paul Nurse, President of the Royal Society.

[158] http://info.cancerresearchuk.org/cancerstats/faqs/#

Simoniello, M.F. *et al.* DNA damage in workers occupationally exposed to pesticide mixtures. *J Appl Toxicol.* 2008, 28 (8): 957-65. doi: 10.1002/jat.1361[159].
"*Pesticides are used in agriculture to protect crops but represent at the same time a potential risk to farmers and environment. The aim of this work is the evaluation of 54 subjects occupationally exposed to pesticides and 30 subjects as a control group using the quantification of DNA damage level by means of the alkaline Comet assay and the evaluation of repair processes. Damage index Comet assay (DICA) and damage index repair assay (DIRA) were studied in 27 pesticide applicator workers, 27 non-pesticide applicators and controls. Our results show that both exposed groups revealed significant increase in DICA when compared with controls (P < 0.0001), as well as in DIRA (P < 0.0001). However, the spraying group exhibited a marginally significant difference in DICA (P = 0.05) when years of exposure are considered and a significant difference (P < 0.05) when the personal protective equipment used by individuals was taken as a comparison factor. The influence of confounding factors on the genotoxic effects of occupational exposure to pesticides was investigated and no significant differences were observed considering age, gender, smoking and alcohol consumption in relation to DICA and DIRA. Since DNA damage is an important step in events leading from carcinogen exposure to cancer disease, our study highlights the potential health risk associated with agrochemical exposure in developing countries with vast cultivated areas, such as Argentina*".

Danieli Benedetti *et al.* Genetic damage in soybean workers exposed to pesticides: Evaluation with the comet and buccal micronucleus cytome assays. *Mutation Research/Genetic Toxicology and Environmental Mutagenesis* 2013, 752 (1‐2): 28‐33[160]
"*Soybean cultivation is widespread in the State of Rio Grande do Sul (RS, Brazil), especially in the city of Espumoso. Soybean workers in this region are increasingly exposed to a wide combination of chemical agents present in formulations of fungicides, herbicides, and insecticides. In the present study, the comet assay in peripheral leukocytes and the buccal micronucleus (MN) cytome assay (BMCyt) in exfoliated buccal cells were used to assess the effects of exposures to pesticides in soybean farm workers from Espumoso. A total of 127 individuals, 81 exposed and 46 non-exposed controls were evaluated. Comet assay and BMCyt (micronuclei and nuclear buds) data revealed DNA damage in soybean workers. Cell death was also observed (condensed chromatin, karyorhectic, and karyolitic cells). Inhibition of non-specific choline esterase (BchE) was not observed in the workers. The trace element contents of buccal samples were analyzed by Particle-Induced X-ray Emission (PIXE). Higher concentrations of Mg, Al, Si, P, S, and Cl were observed in cells from workers. No associations with use of personal protective equipment, gender, or mode of application of pesticides were observed. Our findings indicate the advisability of monitoring genetic toxicity in soybean farm workers exposed to pesticides*".

Glyphosate and the additives in Roundup® are toxic to human cells
Marc, J., Mulner-Lorillon, O., Bellé, R. Glyphosate-based pesticides affect cell cycle regulation[161]. *Biol Cell.* 2004, 96 (3): 245-9 *Cell-cycle dysregulation is a hallmark of tumor cells and human cancers. Failure in the cell-cycle checkpoints leads to genomic instability and subsequent development of cancers from the initial affected cell. All the tested products,*

[159] http://www.ncbi.nlm.nih.gov/pubmed/18636400

[160] http://www.sciencedirect.com/science/article/pii/S138357181300003X

[161] http://www.ncbi.nlm.nih.gov/pubmed/15182708

Amega, Cargly, Cosmic, and Roundup Biovert induced cell cycle dysfunction. The threshold *concentration for induction of cell cycle dysfunction was evaluated for each product and suggests high risk by inhalation for people in the vicinity of the pesticide handling sprayed at 500 to 4000 times higher dose than the cell-cycle adverse concentration*.

Marc, J., Bellé, R. Formulated Glyphosate Activates the DNA-Response Checkpoint of the Cell Cycle Leading to the Prevention of G2/M Transition *Toxicological Sciences* 2004, 82 (2): 436-442.[162] "*At a concentration that efficiently impeded the cell cycle, formulated glyphosate inhibited the synthesis of DNA occurring in S phase of the cell cycle. The extent of the inhibition of DNA synthesis by formulated glyphosate was correlated with the effect on the cell cycle."*

Koller, V.J. *et al*. Cytotoxic and DNA-damaging properties of glyphosate and Roundup in human-derived buccal epithelial cells[163]. *Arch. Toxicol.* 2012, 86 (5): 805-13 doi: 10.1007/s00204-012-0804-8

"*Recent findings indicate that glyphosate exposure may cause DNA damage and cancer in humans. Since we found genotoxic effects after short exposure to concentrations that correspond to a 450-fold dilution of spraying used in agriculture, our findings indicate that inhalation may cause DNA damage in exposed individuals*".

Sophie Richard, Safa Moslemi, Herbert Sipahutar, Nora Benachour, Gilles-Eric Séralini. Differential Effects of Glyphosate and Roundup on Human Placental Cells and Aromatase *Environ Health Perspect*. 2005, 113 (6): 716–720[164] *Here we show that glyphosate is toxic to human placental JEG3 cells within 18 hr with concentrations lower than those found with agricultural use, and this effect increases with concentration and time or in the presence of Roundup adjuvants. Surprisingly, Roundup is always more toxic than its active ingredient. We tested the effects of glyphosate and Roundup at lower nontoxic concentrations on aromatase, the enzyme responsible for estrogen synthesis. The glyphosate-based herbicide disrupts aromatase activity and mRNA levels and interacts with the active site of the purified enzyme, but the effects of glyphosate are facilitated by the Roundup formulation in microsomes or in cell culture.*

Martini, C.N. *et al.* A commercial formulation of glyphosate inhibits proliferation and differentiation to adipocytes and induces apoptosis in 3T3-L1 fibroblasts. *Toxicol In Vitro.* 2012, 26 (6): 1007-13. doi: 10.1016/j.tiv.2012.04.017[165]. *According to our results, a glyphosate-based herbicide inhibits proliferation and differentiation in this mammalian cell line and induces apoptosis suggesting GF-mediated cellular damage. Thus, GF is a potential risk factor for human health and the environment.*

US National Cancer Institute Agricultural Health Study[166]

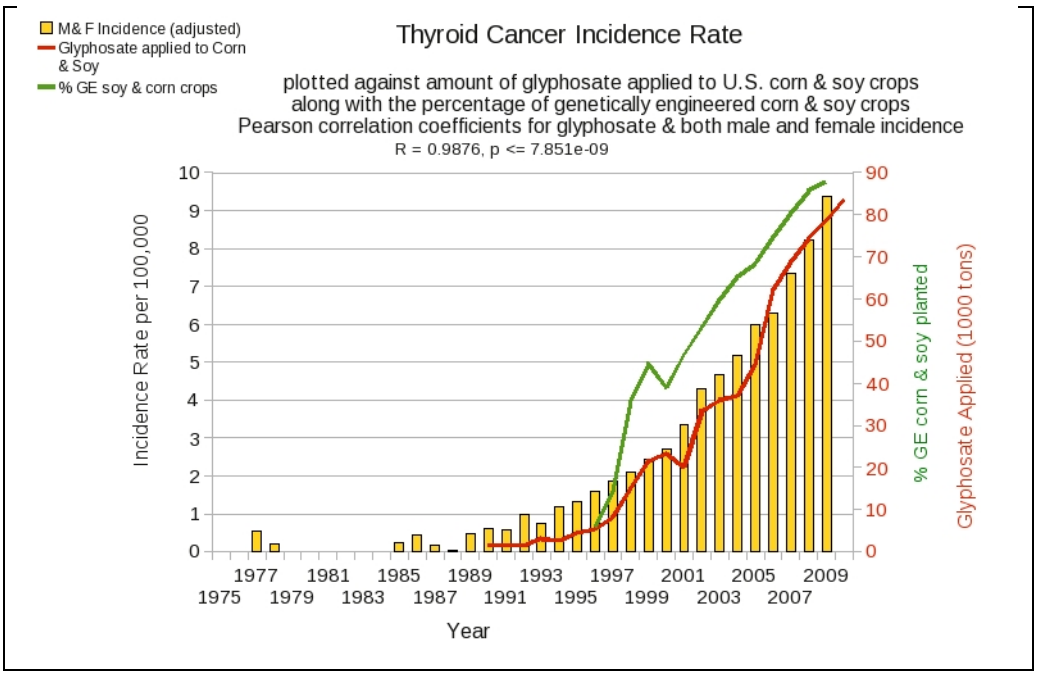
A prospective study of agricultural workers. The AHS cohort includes 90,000 men and women who live in Iowa or North Carolina who were recruited between 1993 and 1997. *What are some of the cancer trends among farmers? For example, farming communities have higher rates of leukemia, non-Hodgkin's lymphoma, multiple myeloma, and soft tissue sarcoma, as well as cancers of the skin, lip, stomach, brain, and prostate".* Scientific studies have suggested that pesticide exposure may increase the risk of developing Parkinson's disease.

[162] http://toxsci.oxfordjournals.org/content/82/2/436.full.pdf
[163] http://www.ncbi.nlm.nih.gov/pubmed/22331240

[164] 10.1289/ehp.7728
[165] http://www.ncbi.nlm.nih.gov/pubmed/22546541
[166] http://www.cancer.gov/cancertopics/factsheet/Risk/ahs

All pesticide exposure is now associated with cancer risk, not just farmers
Alavanja, M.C.R., Ross, M.K., Bonner, M.R. Increased Cancer Burden Among Pesticide Applicators and Others Due to Pesticide Exposure. *CA Cancer J Clin* 2013 63 (2): 120–142[167]. "*There is substantial evidence that the pesticides used in agricultural, commercial, and home and garden applications are associated with excess cancer risk…Rather than wait for human carcinogens to be identified, several European countries, including Sweden, Denmark, the Netherlands, and others, have initiated pesticide use reduction policies that have resulted in substantially diminished pesticide use overall"…*but not the British Government, nor that of the United States. In both countries the Industry has persuaded governments that they should adopt chemically-based systems of Agriculture '*in order to feed the world'*. These are chemicals of mass destruction, to which all humans are now exposed in the home and farm environment, in groundwater and drinking water.

Thyroid cancer rates are increasing in Scotland
"*In 1986, there were 1.8 cases of thyroid cancer per 100,000 Population. But since then, the rate has risen sharply to 3.1 - which translates into hundreds of extra tumours being discovered. There were a record 202 cases in Scotland in 2007*"[168].
Reynolds, R.M. *et al.* Changing trends in incidence and mortality of thyroid cancer in Scotland *Clinical Endocrinology* 2005, 62: 156-62[169].
Thyroid cancer was three times more common in females than in males and was more common in older than younger age groups. Between 1960 and 2000, the annual EASR of thyroid cancer increased from 1.76 to 3.54 per 100,000 for females (P < 0.001) and from 0.83 to 1.25 per 100,000 in males (P < 0.001). The overall thyroid cancer increase between 1975 and 2000 was primarily caused by an increase in papillary thyroid cancer, particularly over the most recent decade.



[167] http://onlinelibrary.wiley.com/doi/10.3322/caac.21170/full

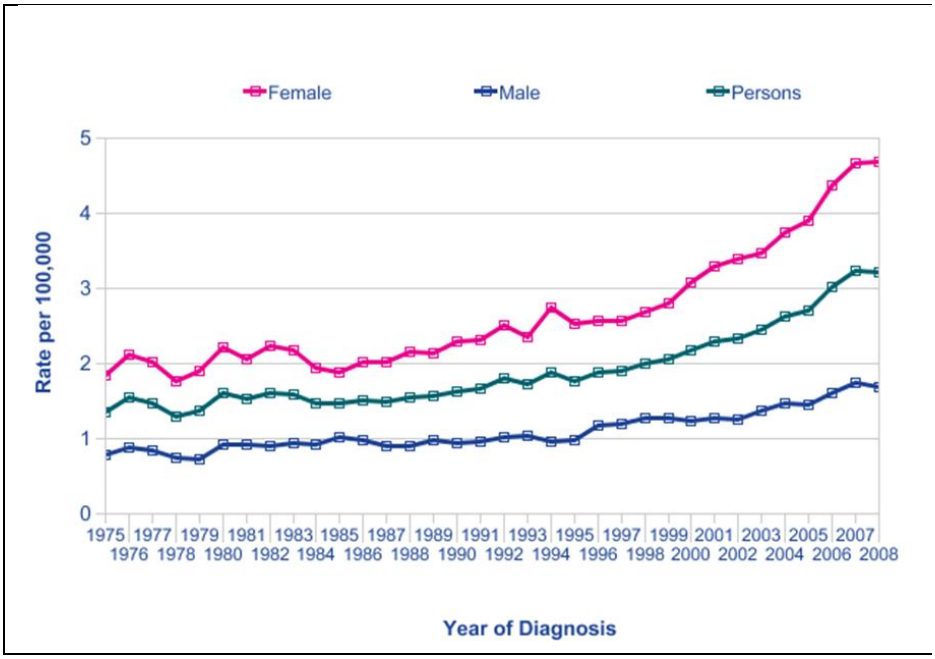
[168] http://www.dailyrecord.co.uk/news/health/campaigners-demand-probe-into-rise-in-scots-1101255
[169] http://www.ncbi.nlm.nih.gov/pubmed/15670190

Graph 13 Incidence of thyroid cancer (adjusted) related to glyphosate applied to corn & soy crops and % GE soy & corn crops in the US. Data from USDA and CDC. Graph reproduced by kind permission of Dr Nancy Swanson.

US Annual percentage changes for cancer of the thyroid between 1975 and 2010[170]

Sex	Period	Trend
Female	1975-1981	-1.6
	1981-1996	+2.5*
	1996-2010	+6.6*
Male	1975-1980	-4.6
	1980-1997	+1.8*
	1997-2010	+5.5*

Statistically significant*



Graph 14 CRUK statistics: Thyroid cancer (C73), European Age-Standardised Incidence Rates, Great Britain, 1975-2008[171]

Strong correlation was shown between cancer of the thyroid and glyphosate use on GE corn and soy crops, and that thyroid cancer affects women more than men. Many scientific studies have shown links between thyroid disruption and neurological diseases. "*Thyroid hormones are critical for development of the fetal and neonatal brain, as well as for many other aspects of pregnancy and fetal growth. Hypothyroidism in either the mother or fetus frequently results in fetal disease; in humans, this includes a high incidence of mental retardation.... numerous studies with rats, sheep and humans have reinforced this concept...*"[172] According to de Cock *et al*[173], "*Perinatal exposure to Endocrine Disrupting Chemicals appears to be associated with the occurrence of ASD [autism spectrum disorder] as well as ADHD*

[170] http://seer.cancer.gov/statfacts/html/thyro.html
[171] http://www.cancerresearchuk.org/cancer-info/cancerstats/types/thyroid/incidence/
[172] http://www.vivo.colostate.edu/hbooks/pathphys/endocrine/thyroid/thyroid_preg.html
[173] http://www.ncbi.nlm.nih.gov/pubmed/22458970

[Attention Deficit Hyperactivity Disorder]. Disruption of thyroid hormone function ... may offer an explanation for the observed relations...." MacSweeney *et al.* reported, "*that the mothers of 104 schizophrenic patients had: (1) a significantly higher incidence of thyroid disease than a carefully matched control group; (2) significantly more abortions, still-births and greater infant mortality. The findings and possible relevance of thyroid disease to schizophrenia are discussed*[174]."

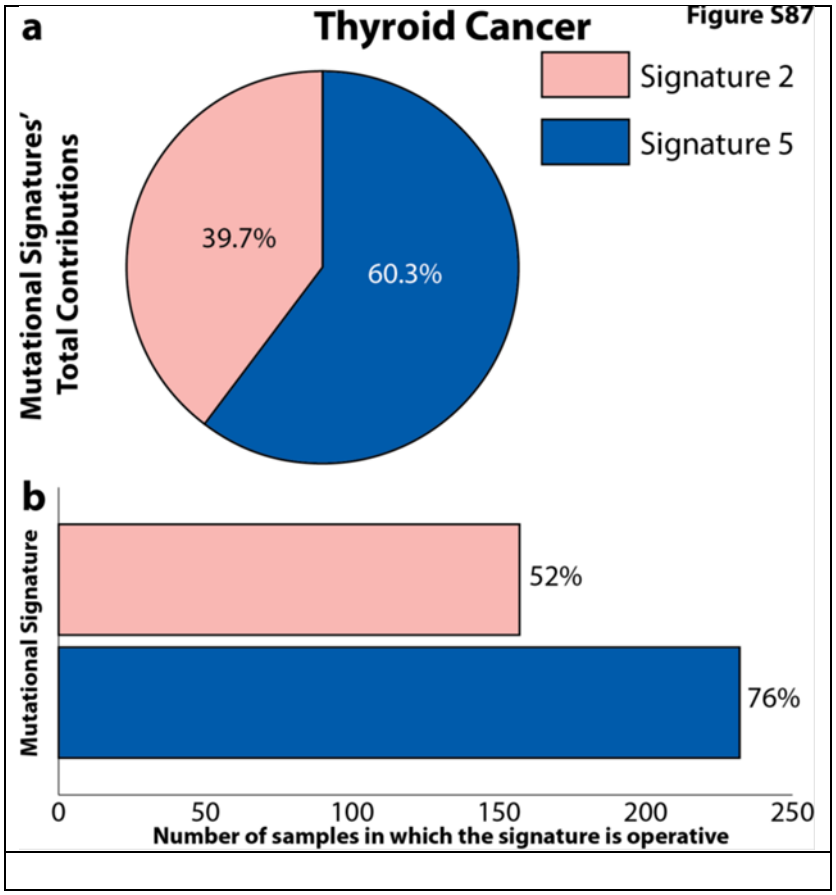


Fig 2: Summary of the contributions of the signatures of mutational processes operative in thyroid cancer[175] Supplementary Figure 87 from Alexandrov, L.B. *et al.*

World Health Cancer Statistic 2008 Cancer mortality and morbidity

"*Cancer is a leading cause of death and accounted for 7.6 million deaths (around 13% of all deaths) in 2008*[176]*. Lung, breast, colorectal, stomach, and prostate cancers cause the majority of cancer deaths. Important risk factors for cancer include tobacco use, unhealthy diet, physical inactivity and the harmful use of alcohol.**

The WHO Regions for Europe and the Americas had the highest incidence of all types of cancer combined for both sexes. High income countries had approximately ten times the rate

174 http://journals.cambridge.org/action/displayAbstract;jsessionid=3F7D8DD133AA9E1021A46FA46E03F054.journals?fromPage=online&aid=4985600

175 http://www.nature.com/nature/journal/vaop/ncurrent/extref/nature12477-s1.pdf

176 http://www.who.int/gho/ncd/mortality_morbidity/cancer_text/en/

of prostate cancer incidence of the lower middle income countries. For breast cancer, incidence rates rose rapidly with level of country income. High income countries had more than three times the rate of low income countries. Similarly, colorectal cancer incidence rates also rose by level of country income. High income countries had considerably higher colorectal cancer incidence rates than any other income group. This was nearly five times higher than the rate in low income countries"

*There is no mention of pesticides. Is the WHO is protecting the pesticides industry too?

Part 5 Have we reached a point of no return?

Only One Chance: How Environmental Pollution Impairs Brain Development[177]
Prof Philippe Grandjean, Professor of Environmental Health, Harvard University and University of Southern Denmark.
"*Today, one out of every six children suffers from some form of neurodevelopmental abnormality. The causes are mostly unknown. Some environmental chemicals are known to cause brain damage and many more are suspected of it, but few have been tested for such effects. The brain's development is uniquely sensitive to toxic chemicals, and even small deficits may negatively impact our academic achievements, economic success, risk of delinquency, and quality of life. Chemicals such as lead, mercury, polychlorinated biphenyls (PCBs), arsenic, and certain solvents and pesticides pose an insidious threat to the development of the next generation's brains*"[178]
Prof Philippe Grandjean's new book gives a courageous account of how, over the years, industrial chemicals have damaged children's brains and how each industry has fought to protect its products. The Pesticides Industry is no different. But this time we have a major disaster.

Can a collapse of global civilisation be avoided?
Professor Paul Erhlich has written about this in increasing urgent terms.
Ehrlich PR, Ehrlich AH. Can a collapse of global civilization be avoided? *Proc R Soc B* 2013, 280: 20122845[179]. Ehrlich PR The MAHB, the Culture Gap, and Some Really Inconvenient Truths. *PLoS Biol* 2010, 8(4): e1000330. doi:10.1371/journal.pbio.1000330[180]
Here are some pertinent phrases from these papers:

- *There have been increasing signs of great toxic peril for humanity and its life-support systems, with a growing threat from the release of hormone-disrupting chemicals that could even be shifting the human sex ratio and reducing sperm counts*
- *destroying fables such as 'growth can continue forever if it's in service industries', or 'technological innovation will save us'*
- *reduction of the worship of 'free' markets*
- *Unfortunately, awareness among scientists that humanity is in deep trouble has not been accompanied by popular awareness and pressure to counter the political and economic influences implicated in the current crisis*
- *Without significant pressure from the public demanding action, we fear there is little chance of changing course fast enough to forestall disaster*

[177] Only one chance: How environmental pollution impairs brain development – and how to protect the brains of the next generation" Oxford University Press
[178] www.chemicalbraindrain.info
[179] http://dx.doi.org/10.1098/rspb.2012.2845
[180] http://www.plosbiology.org/article/info%3Adoi%2F10.1371%2Fjournal.pbio.1000330

- *This will require developing mechanisms to force big corporations (including those in big agriculture and big pharma) to bear social responsibilities like the real individuals whose rights they legally want to assume*

Permanent People's Tribunal (PPT) Corporate Account Verdict[181]

The PPT Session was held in Bangalore, India between December 3 and 6, 2011. In accordance with the program (Attachment 2), witnesses, technical witnesses and survivors made oral presentation of specific cases and submitted supporting documents. As established in its Statute, the Tribunal notified the legal representatives of the transnational corporations headquartered in Germany (Bayer and BASF), Switzerland (Syngenta) and the United States (Monsanto, DuPont, Dow Chemical Company).

FINDINGS

The Tribunal makes the following declaration of responsibility for the six indicted TNCs and three Governments in particular and further also declares the responsibilities of all States, international organizations, UN Specialist Agencies, all other institutions of global governance.

CONCERNING THE INDICTED SIX CORPORATIONS (BASF, BAYER, DOW CHEMICAL, DUPONT, MONSANTO, SYNGENTA)

- The Tribunal finds on all evidence presented before it, the six TNCs prima *facie* responsible for gross, widespread and systematic violations of the right to health and life, economic, social and cultural rights, as well as of civil and political rights, and women and children's rights.

- The Tribunal further finds that their systematic acts of corporate governance have caused avoidable catastrophic risks, increasing the prospects of extinction of biodiversity, including species whose continued existence is necessary for reproduction of human life.

Annex 1

Synoptic list of the cases which have more specifically been submitted to the PPT

Defendants: Monsanto, Dow, Dupont (USA), Bayer, BASF (Germany), Syngenta (Switzerland) Pages 33-37 consist of 40 cases brought against the Corporations.

[181] Corporate account verdict.pdf http://www.internazionaleleliobasso.it/?lang=en

Postscript on chemical weapons and pesticides

Questions and Answers for the British and American Governments

- **Q:** Who 'wields tremendous control' over the British and American Governments[182]?
- **A:** The Agrochemical Corporations.
- **Q:** With regards to pesticide regulations, who controls human health and biodiversity?
- **A:** The Agrochemical Corporations.
- **Q:** Who has manufactured the chemical weapons used in Syria and Vietnam?
- **A:** The Agrochemical Corporations. The factories in Germany that made chemical weapons during the war were turned into factories to make pesticides.
- **Q:** What is the difference between chemical weapons and pesticides?
- **A:** For some pesticides the mode of action is identical.
- **Q:** What chemical did John Kerry reveal was used in Syria?
- **A:** Sarin; a potent organophosphate compound which kills by inhibiting anticholinesterase
- **Q:** What is chlorpyrifos?
- **A:** Chlorpyrifos, an organophosphate insecticide, is also an inhibitor of anticholinesterase. This is an enzyme vital to the nervous systems of animals and humans. Symptoms of acute chlorpyrifos poisoning in adults include headache, nausea, dizziness, muscle twitching, weakness, increased sweating and salivation, and occur when cholinesterase activity has been reduced by about 50%. Unconsciousness, convulsions, and death can result with sufficient exposure.
- **Q:** If it poisons insects, what does it do to the human fetal brain when it is the same size as that of an insect brain?
- **A:** *"Prenatal exposure to chlorpyrifos (CPF), an organophosphorus insecticide, has long been associated with delayed neurocognitive development and most recently with decrements in working memory at age 7"*[183]. *"We report evidence of deficits in Working Memory Index and Full-Scale IQ as a function of prenatal CPF exposure at 7 years of age. These findings are important in light of continued widespread use of CPF in agricultural settings and possible longer-term educational implications of early cognitive deficits"*[184].
- **Q:** In that case is there any difference between chemical weapons and pesticides?
- **A:** Chemical weapons kill fast: the effects are obvious for anyone to see.
  The effect of pesticides on humans and the environment is extremely subtle.
  Pesticides are silent destroyers: by the time the patterns are obvious, it is too late.
  People are being used as guinea pigs.

- **Statement:** John Kerry, in justification of the bombing of Syria by the US on 30/08/2013: "*History will judge us harshly if we turn a blind eye to use of weapons of mass destruction".*
- **Q:** Has John Kerry forgotten the Vietnam War, after which he gave evidence to Congress about US War Crimes?

[182] http://www.panna.org/publication/generation-in-jeopardy

[183] http://dx.doi.org/10.1016/j.ntt.2012.07.004

[184] http://dx.doi.org/10.1289/ehp.1003160

- **A:** *In the course of 10 years, American forces sprayed nearly 20 million gallons of the chemical (a dioxin, Agent Orange) in Vietnam, Laos and parts of Cambodia in an effort to deprive guerrilla fighters of cover by destroying plants and trees where they could find refuge*[185]
  Among the illnesses contracted by people exposed to the dioxin are non-Hodgkin's lymphoma, several varieties of cancer, type 2 diabetes, soft tissue sarcoma, birth defects in children, spina bifida and reproductive abnormalities, to name a few.
  The U.S. government, however, has dismissed these figures as unreliable and inflated.

.

Earlier this month (July 2013) the Association for Victims of Agent Orange in Ho Chi Minh City has filed its fourth lawsuit against Monsanto & Dow, the American chemical companies that produced Agent Orange.

- *South Korea's highest court on Friday upheld a ruling, ordering two U.S. Agent Orange makers to compensate 39 Vietnam War veterans in one of the country's most prominent lawsuits*[186].
- *The Supreme Court (SC) recognised the epidemiological correlation between the toxic defoliant and skin diseases for the first time, saying the 39 victims should receive a total of 466 million won ($415,000) from Dow Chemical and Monsanto.*
  U.S. forces widely sprayed Agent Orange, which contained the lethal chemical dioxin, in Vietnam during the conflict to deprive enemy guerrillas of forest cover and destroy food crops. Veterans in South Korea estimate the number of Korean victims of the chemicals at about 150,000. Many insisted they were suffering from various ailments associated with exposure to the powerful herbicide. Vietnam says millions of its people have died or suffered from direct or second-generation disabilities as a result of the use of Agent Orange.
- *Washington has never accepted responsibility for the Vietnamese government's claim.*

[185] http://www.dailymail.co.uk/news/article-2401378/Agent-Orange-Vietnamese-children-suffering-effects-herbicide-sprayed-US-Army-40-years-ago.html
[186] http://www.thehindu.com/todays-paper/tp-international/dow-monsanto-ordered-to-pay-agent-orange-victims/article4913976.ece

Roundup and birth defects

Is the public being kept in the dark?

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Mohamed Ezz El-Din Mostafa Habib
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About Earth Open Source

Earth Open Source uses open source collaboration to engage individuals, farmers, communities, corporations, universities, and governments in programmes to achieve breakthrough advances that help nourish humanity, increase equity, support food security, and preserve the Earth.

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Summary

Concerns about the best-selling herbicide Roundup® are running at an all-time high. Scientific research published in 2010 showed that Roundup and the chemical on which it is based, glyphosate, cause birth defects in frog and chicken embryos at dilutions much lower than those used in agricultural and garden spraying. The EU Commission dismissed these findings, based on a rebuttal provided by the German Federal Office for Consumer Protection and Food Safety, BVL. BVL cited unpublished industry studies to back its claim that glyphosate was safe.

The Commission has previously ignored or dismissed many other findings from the independent scientific literature showing that Roundup and glyphosate cause endocrine disruption, damage to DNA, reproductive and developmental toxicity, neurotoxicity, and cancer, as well as birth defects. Many of these effects are found at very low doses, comparable to levels of pesticide residues found in food and the environment.

This issue is of particular concern now that Monsanto and other producers of genetically modified seed are trying to get their glyphosate-tolerant crops approved for cultivation in Europe. If the EU Commission gives its approval, this will lead to a massive increase in the amount of glyphosate sprayed in the fields of EU member states, as has already happened in North and South America. Consequently, people's exposure to glyphosate will increase.

All these concerns could be addressed by an objective review of Roundup and glyphosate in line with the more stringent new EU pesticide regulation due to come into force in June 2011. Just such a review was due to take place in 2012. However, shortly after the Commission was notified of the latest research showing that glyphosate and Roundup cause birth defects, it quietly passed a directive delaying the review of glyphosate and 38 other dangerous pesticides until 2015. This delay is being challenged in a lawsuit brought against the Commission by Pesticides Action Network Europe and Greenpeace.

Delaying the review of glyphosate until 2015 is serious enough. But in reality, the Commission's slowness in preparing the new data requirements for the incoming regulation mean that glyphosate may well not be re-assessed in the light of up-to-date science until 2030. The beneficiary will be the pesticide industry; the victim will be public health.

The need for a review of glyphosate is particularly urgent in the light of the shortcomings of the existing review of the pesticide, on which its current approval rests. In this report, we examine the industry studies and regulatory documents that led to this approval. We show that industry and regulators knew as long ago as the 1980s and 1990s that glyphosate causes malformations – but that this information was not made public. We demonstrate how EU regulators reasoned their way from clear evidence of glyphosate's teratogenicity in industry's own studies (the same studies that BVL claimed show the safety of glyphosate) to a conclusion that minimized these findings in the EU Commission's final review report.

The German government and its agencies played a central role in this process. As the "rapporteur" member state for glyphosate, Germany was responsible for liaising between industry and the EU Commission and reporting the findings of industry studies. We show how Germany played down findings of serious harm in industry studies on glyphosate. It irresponsibly proposed a high "safe" exposure level for the public that ignored important data on glyphosate's teratogenic effects. This level was accepted by the Commission and is now in force.

Taken together, the industry studies and regulatory documents on which the current approval of glyphosate rests reveal that:

- Industry (including Monsanto) has known since the 1980s that glyphosate causes malformations in experimental animals at high doses
- Industry has known since 1993 that these effects could also occur at lower and mid doses
- The German government has known since at least 1998 that glyphosate causes malformations

- The EU Commission's expert scientific review panel knew in 1999 that glyphosate causes malformations
- The EU Commission has known since 2002 that glyphosate causes malformations. This was the year its DG SANCO division published its final review report, laying out the basis for the current approval of glyphosate.

The public, in contrast, has been kept in the dark by industry and regulators about the ability of glyphosate and Roundup to cause malformations. In addition, the work of independent scientists who have drawn attention to the herbicide's teratogenic effects has been ignored, denigrated, or dismissed. These actions on the part of industry and regulators have endangered public health. They have also contributed to the growing division between independent and industry science, which in turn erodes public trust in the regulatory process.

This report provides a comprehensive review of the peer-reviewed scientific literature, documenting the serious health hazards posed by glyphosate and Roundup herbicide formulations. On the basis of this evidence, we call on the Commission to cancel its delay in reviewing glyphosate and to arrange an objective review of the pesticide. The review must take into account the full range of independent scientific literature, as demanded by the new pesticides regulation, and should be started as soon as the new data requirements are in place this year. In the meantime, the Commission should use its powers to withdraw glyphosate and Roundup from the market.

1. Roundup link with birth defects – study

Research published in August 2010 showed that the best-selling herbicide Roundup[1] causes malformations in frog and chicken embryos at doses much lower than those used in agricultural spraying.[2] The malformations found were mostly of the craniofacial and neural crest type, which affect the skull, face, midline, and developing brain and spinal cord.

The research team was led by Professor Andrés Carrasco, lead researcher of the Argentine government research body CONICET. Carrasco was prompted to carry out the study by reports of high rates of birth defects in areas of Argentina dedicated to growing genetically modified Roundup Ready (GM RR) soy.[3] The birth defects seen in humans were of a similar type to those found in Carrasco's study.

GM RR soy is designed to be sprayed with Roundup herbicide, based on the chemical glyphosate. The Roundup Ready gene allows the crop to be sprayed with Roundup herbicide, which kills weeds but allows the crop to survive.

It is also important to note that GM RR soy and other crops are *tolerant* rather than *resistant* to Roundup and glyphosate: that is, they absorb the herbicide and survive. As a result, GM RR crops are a reservoir of potentially high levels of glyphosate, which will then be ingested by animals or people who eat the crops.

The spread of GM RR varieties has led to massive increases in the amount of glyphosate sprayed in soy-producing areas.[4] [5] [6] In Brazil, nearly 90,000 tons of glyphosate-based pesticides in 71 different commercial formulations were sold in 2009.[7] In Argentina, over half the cultivated land is given over to GM soy, which is sprayed with 200 million litres of glyphosate herbicide each year.[8] Spraying is often carried out from the air, causing major problems of drift.

Carrasco said, "From the ecotoxicological point of view, what is happening in Argentina is a massive experiment."[9] It is a cautionary tale of what could happen in any country that adopts glyphosate-tolerant GM crops on a large scale.

1.1. Why should Europeans worry?

The maximum residue limit (MRL) allowed for glyphosate in food and feed products in the EU is 20 mg/kg. Soybeans have been found to contain glyphosate residues at levels up to 17mg/kg.[10] Carrasco found malformations in frog and chicken embryos injected with 2.03 mg/kg glyphosate – ten times lower than the MRL. While an injected dose is not the same as eating food containing glyphosate residues, no attempt has been made to properly investigate how much glyphosate people and animals are ingesting.[11]

Each year, the EU imports around 35 million tons of soy and derivatives,[12] most of which is used for animal feed and biofuels. A loophole in the EU's GM labelling laws allows meat, dairy and eggs produced with GM animal feed to be sold without a GM label. So the GM soy, and residues of the glyphosate with which it is treated, go into the food chain through animal feed and remain hidden from European consumers.

Europeans are also exposed to Roundup in the form of sprays. In Europe, marketing claims that Roundup is safe and readily biodegradable have helped expand its use beyond farmers' fields. Municipal authorities use it for weed control on roadsides and in school grounds, parks, and other public areas. Home gardeners can easily buy it in supermarkets and garden centres.

Given the widespread use of the herbicide and industry plans to introduce glyphosate-tolerant GM crops into Europe, the safety questions over Roundup must be answered objectively and in accordance with the most up-to-date scientific knowledge. However, an opposite process appears to be in train: industry and regulators are minimising concerns in what seems to be an effort to keep the pesticide on the market.

2. EU regulators respond to birth defects study

In September 2010, Carrasco's research was sent to John Dalli, the EU Commissioner for Health and Consumer Policy. The following month, Greek Green MEP Michail Tremopoulos asked Dalli in a parliamentary question what action the Commission planned to take on Monsanto's application for cultivation in the EU of its NK603 glyphosate-tolerant GM maize.

The European Food Safety Authority (EFSA) has already given the go-ahead to NK603. If the Commission gives its approval, NK603 will be the first GM herbicide-tolerant plant to be grown commercially in the EU[13] – and the first to enable the intensive glyphosate spraying that has come under fire in Argentina.[14]

2.1. Glyphosate approval could be reconsidered – Dalli

Dalli's answer to Tremopoulos did not exactly promise action, but it did suggest a willingness to re-assess glyphosate on the basis of the new evidence. Dalli said that the existing approval of glyphosate could be reconsidered and, "depending on the seriousness and urgency of the matter," it could be restricted or even banned. Dalli said he would also consider reviewing the current maximum residue levels (MRLs) allowed in soy.[15]

Dalli said a programme was under discussion for re-examining those pesticides for which the EU approval was soon to expire – "and this programme includes glyphosate".[16] Pesticides approved for use in the EU are reviewed every ten years. Glyphosate was last reviewed in 2002,[17] so the next review would normally be expected in 2012.[18] But Dalli's response to Tremopoulos suggested that in light of the new evidence, more immediate action could be taken.[19]

Dalli asked the German government to examine Carrasco's study and report back on whether it reflected real-life exposure levels. Germany was given this task because it is the "rapporteur" member state for glyphosate, responsible for liaising between the industry applicants for the pesticide's approval, member states, and the EU Commission.

2.2. No reason for concern – Dalli

MEP Tremopoulos followed up with another parliamentary question to Dalli in December,[20] asking if the EU would carry out a new risk assessment of glyphosate, based on the latest scientific evidence. But Dalli had heard back from the German government and was reassured that there was no need. Dalli reported the German authorities' verdict on Carrasco's study:

- The study had been performed under "highly artificial" conditions that did not reflect the real-life use of glyphosate in agriculture or its effects on mammals
- There is a "comprehensive and reliable toxicological database for glyphosate" and the findings of these studies do not throw into doubt its existing approval
- There was no need to ban or restrict the use of the substance.[21]

As discussed below, the basis for these conclusions by the German regulators is highly questionable.

2.3. EU Commission flouts EU law

The glyphosate question has arisen at a crucial moment in EU pesticides regulation. The old Directive 91/414[22] is in the process of being replaced by the new Regulation 1107/2009,[23] which comes into force in June 2011. The new law contains stringent requirements to protect public health and the environment. It has the potential to set the gold standard for pesticide safety assessments internationally, bringing the system more into line with public health interests.

The new pesticide regulation 1107/2009 makes clear that the European Parliament and Council will no longer rely for pesticides approvals on industry-generated "grey literature"[24] and studies that are hidden from the public under commercial confidentiality rules. It states that the "scientific peer-reviewed open literature" must be taken into account from now on in assessing pesticides.[25]

The regulation also solves the problem of old and outdated studies dominating pesticides approvals dossiers. It states that studies from

the open literature published within the last ten years before submission of the dossier must be included in the assessment.[26]

But the EU Commission appears to be doing everything in its power to flout the intent of the new regulation. It is putting massive energy and resources into prolonging the approval of pesticides under the old, less stringent rule, instead of what it should be doing – working on the evaluation of pesticides under the new Regulation 1107/2009. If the Commission gets its way, glyphosate and other dangerous pesticides will avoid the scrutiny of the new regulation for many years.

2.4. Commission delays glyphosate review – until 2015

As it turned out, the Commission did not bring the glyphosate review forward, or even stick to the expected date of 2012. In an astonishing move, it delayed the review of glyphosate until 2015.[27] It then rushed through a new directive, setting the delay into law, on November 10, 2010 – two days before Dalli told Tremopoulos that action might be taken soon on glyphosate.[28] It is unclear whether Dalli misled Tremopoulos, or was unaware of the new directive.

The entire decision-making process on the delay was done behind closed doors with a limited group of national representatives (mainly from the agricultural ministries of member states) and set into law without notifying stakeholders. This process is called "comitology" and is much criticized for being non-transparent, confusing (even to legal experts) and undemocratic.[29]

2.5. Commission too busy to review glyphosate

The German government body dealing with the glyphosate review is BVL, the Federal Office for Consumer Protection and Food Safety. In December 2010, Friends of the Earth Germany (BUND) asked BVL the reason for the delay in the review. BVL replied that the EU Commission and other authorities (including food safety watchdog, the European Food Safety Authority, EFSA) had too heavy a workload and had not finalized the rules for renewing the approval of certain pesticides, including glyphosate.

BVL added that the delay is not confined to glyphosate but also applies to other pesticides.[30] In fact, the list of 39 pesticides for which the review will be delayed includes the highly toxic 2,4-D and diquat.[31]

If BVL meant this statement to reassure, it was mistaken. The fact that not just one but 39 pesticides will get a free regulatory ride for an extra three years is a political scandal. If BVL's explanation is taken at face value, public health is being put at risk because of bureaucratic inefficiency. The beneficiary is the pesticide industry.

The Commission's delay in reviewing the 39 pesticides is being challenged in a lawsuit brought by Pesticides Action Network Europe and Greenpeace.[32]

2.6. Why the delay matters

The delay will have far-reaching consequences because it means glyphosate will be reviewed under the data requirements of the old pesticide Directive 91/414 rather than the new Regulation 1107/2009. The old directive is much less effective than the new regulation because it has lax and outdated data requirements. Data requirements instruct industry which effects to study and which testing methods to use.

The data requirements of the old Directive 91/414 are based on outdated protocols designed decades ago.[33] They ignore new scientific insights and developments. Effects likely to be missed include endocrine disruption, effects on development, effects of added ingredients (adjuvants), effects of combinations of chemicals, and effects on bees. Also likely to be missed are effects found in independent peer reviewed scientific literature, as the old directive does not explicitly say that such studies must be included in industry's dossier. In short, the most rigorous and advanced science is ignored under the data requirements of the old Directive 91/414.

According to Danish MEP Dan Jørgensen, the Commission has been working on the new data requirements for Regulation 1107/2009 since 2002 and has still not completed them.[34] They are scheduled for publication on June 14, 2011.[35]

Once they are published, industry needs at least two years to do the new tests on glyphosate and to liaise with the rapporteur, Germany, and the Commission over its dossier. Industry has to deliver its new dossier for glyphosate by 31 May 2012,[36] and the EU Commission will give its delayed decision in 2015.[37]

Because the Commission has taken so long to prepare the new data requirements, industry will not have enough time to do the tests on glyphosate under the new data requirements. So glyphosate and the 38 other pesticides will be reviewed in 2015 under the old, lax data requirements. Commissioner Dalli confirmed this in a reply to a Parliamentary question from MEP Jørgensen.[38]

The Commission has the option to tighten the 2015 glyphosate review by forcing industry to include studies from the open peer-reviewed scientific literature in its dossier. The new regulation, which stipulates that such literature should be considered, will be in place. Also, EFSA has already published its Guidance on the use of science for the regulation,[39] giving industry time to collect the independent studies before its 2012 dossier submission deadline. However, it is not yet clear whether the Commission has the political will to make industry comply with this aspect of the new regulation.

2.7. The real delay – until 2030?

The EU Commission's delay in reviewing glyphosate and the 38 other pesticides until 2015 is serious enough. But the situation is far worse than it appears. Because glyphosate will go through its 2015 review on the basis of old, lax data requirements, it will likely be approved. The approval period is 15 years. As a result, glyphosate will not in effect face a review under the new, more stringent data requirements until 2030.[40] By then, public policy on glyphosate will be based on evidence generated using research protocols that are decades out of date.[41] It will exclude all evidence from independent studies unless the Commission insists that this be included.

2.8. What's keeping the Commission so busy

A Commission source who spoke on condition of anonymity confirmed that the real cause of the delay in the review of glyphosate and the 38 other pesticides is a process called Resubmission.[42] This was instituted in 2008 after the Commission rejected a number of industry pesticide applications on the grounds that the dossiers were incomplete. Industry disagreed and threatened the Commission with lawsuits. The Commission reached a compromise with industry, offering it a second chance to deliver more complete dossiers while allowing the pesticides to stay on the market for an additional 3–4 years. Resubmission is a fast-track procedure with a limited dossier.

According to Pesticides Action Network Europe, the loophole "turned into a big hole" when industry submitted applications for more than 80 substances, including some "dirty" pesticides that had been regarded as having no chance of approval.[43] PAN said that companies jumped on the train of this fast-track procedure, hoping for a mild evaluation or to put pressure on Commission through member states if their farmers were interested in getting a banned substance back.

The Commission has been bogged down in Resubmission applications ever since. Industry has benefited because the Commission is directing all its resources into prolonging the approval of pesticides under the weak old rule – and ignoring the demands of the new, more stringent regulation.

3. EU regulators "disappear" birth defects

The regulators' response to Carrasco's study suggests that they are in no hurry to take on board the findings of independent science. At Commissioner Dalli's request, the German Federal Office for Consumer Protection and Food Safety, BVL, produced a written response to the study.[44] This was not published but was only sent to the EU Commission.

BVL's statement is anonymous. Though common with such items of grey literature, this

operates against the public interest as no one can be held accountable a decision that could significantly affect public health. There is no way of knowing whether the people who wrote it are even qualified scientists, let alone if they have industry interests.

BVL's conclusion can be summarised as: no action is needed on glyphosate. It tries to isolate Carrasco's study, implying that it is the only one to find problems. BVL cites Germany's 1998 draft assessment report (DAR) on glyphosate, which it says showed "no evidence of teratogenicity" (ability to cause malformations/birth defects).[45]

The DAR is a crucial document underlying glyphosate's current EU approval. It is Germany's summary and report on the dossier of studies submitted by industry in support of glyphosate's approval. Based on this DAR, along with EU member states' comments and a peer review of the dossier by the EU Commission's ECCO scientific panel, the EU Commission's health and consumer division DG SANCO approved glyphosate for 10 years in 2002. DG SANCO's final review report on glyphosate acknowledges developmental abnormalities found in the industry studies but dismisses their importance by saying that they are confined to "maternally toxic doses" (see Section 3.1, below).[46]

BVL's response to Carrasco was followed by a response from industry. Employees of Monsanto and Dow, two major manufacturers of glyphosate herbicides, published a letter in the same journal that published Carrasco's original study.[47] The Monsanto/Dow letter was published back-to-back with Carrasco's response.[48]

Monsanto/Dow take the same line as BVL, claiming:

> Glyphosate does not cause adverse reproductive effects in adult animals or birth defects in offspring of these adults exposed to glyphosate, even at very high doses.[49]

But both BVL's and Monsanto/Dow's claims are misleading, as we show below.

3.1. Industry's own studies show that glyphosate causes malformations

Germany's DAR concludes from the industry dossier of studies, "Glyphosate does not cause teratogenicity". But Germany immediately goes on to qualify its conclusion, saying that higher doses of glyphosate caused "reduced ossification and a higher incidence of skeletal and/or visceral [internal organ] anomalies" in rats and rabbit foetuses.[50] In reality, at odds with Germany's reassuring conclusion, the details of the DAR contain convincing evidence of glyphosate's teratogenicity.

Germany adds that in the industry studies, glyphosate given at high doses reduced the number of viable foetuses produced by rats and rabbits.[51] Decreased numbers of viable foetuses are often consistent with increased incidence of malformations, as many mal-developed foetuses are spontaneously aborted.

The skeletal "anomalies" found in these early industry studies are consistent with Carrasco's findings. But Germany dismisses them on the claimed grounds that the doses at which the effects were found were so high as to be toxic to the mothers (maternally toxic doses).

Germany here makes an assumption common among regulatory authorities – that foetal abnormalities found at maternally toxic doses are irrelevant to human risk assessment. The reasoning is that poisoning of the mother with any substance can affect the development of the foetus and lead to birth defects and therefore such malformations may not be a direct effect of the chemical in question on the foetus. So malformations in foetuses found at dose levels that are considered toxic to the mother are dismissed as irrelevant and the substance under examination is not classed as a developmental toxin or teratogen.

But this assumption is debated in the independent scientific literature. Paumgartten (2010) says that in cases of maternal toxicity, it is not possible to know whether an effect on the embryo is only due to maternal poisoning or due to a direct action of the chemical at doses that also adversely affect the mother. In the latter case, the chemical would be a developmental toxin.[52]

Even industry is actively discussing the relationship between maternal toxicity and birth defects. It was the subject of a recent workshop held by the industry-funded group, the

International Life Sciences Institute.[53]

As yet there is no scientific consensus around the issue. The confusion is made worse by the poor design of standard industry chronic toxicity tests, which use so few animals that unrealistically high doses of the chemical have to be used in an attempt to obtain statistical significance in non-lethal effects.[54] In fact, the doses for chronic two-year toxicity tests are derived from, and are only slightly below, the acute poisoning dose. So poisoning effects are common in such tests, which often miss more subtle effects.[55]

Thus, virtually all chronic tests commissioned by industry have an escape clause: "Perhaps the dose was so high it poisoned the animals." This escape clause is frequently used by the rapporteur Germany in its DAR on glyphosate.

Germany's dismissal of the malformations found in industry studies on grounds of maternal toxicity is thrown into doubt by the findings of an independent study. Dallegrave (2007) examined the reproductive effects of Roundup on male and female offspring of Wistar rats treated with 50, 150 or 450 mg/kg of Roundup during pregnancy and lactation. The study found that these doses of Roundup did not induce maternal toxicity but did induce adverse reproductive effects on male offspring. Findings include a decrease in sperm number and daily sperm production during adulthood, an increase in the percentage of abnormal sperms, a dose-related decrease in the serum testosterone level at puberty, and signs of sperm cell degeneration during both periods. The study showed that Roundup is a reproductive toxin at non-maternally toxic doses.[56]

Even if we confine the argument to evidence generated by industry studies, Germany's argument that glyphosate's teratogenicity is confined to high, maternally toxic doses is untrue. The industry studies also found malformations at lower doses. This is made clear by Germany's own summaries of the industry studies in the DAR and by the comments of the UK's Pesticides Safety Directorate (PSD).

Our edited versions of Germany's summaries of industry studies are presented below, along with the UK PSD's comments and our own.

How are pesticides assessed for risk in the EU?

Risk assessment of pesticides in the EU is a long and complex process:

- Industry submits a dossier of studies in support of its application for approval of a pesticide. The studies should fulfil the data requirements of the regulation in force.
- The rapporteur member state reviews the industry dossier and compiles a draft assessment report (DAR).
- The EU member states are invited to comment on the industry dossier and DAR.
- A scientific panel of the EU Commission – formerly the ECCO Panel, now EFSA's Panel on Plant Protection Products and their Residues (PPR Panel) – reviews the industry dossier and DAR, and writes an Opinion.
- The EU Commission's Health and Consumer Protection Directorate General (DG SANCO) compiles a review report, summarising the evidence on the pesticide.
- A committee made up of representatives of DG SANCO and the member states, known as the Standing Committee on the Food Chain and Animal Health (SCFCAH) – Phytopharmaceuticals, meets to discuss the pesticide.
- DG SANCO makes a proposal at a meeting of the SCFCAH to approve, reject, or conditionally approve the pesticide for certain uses.
- If a large majority of SCFCAH members reject DG SANCO's proposal, DG SANCO can change it or find a compromise.
- The SCFCAH votes on whether to accept DG SANCO's proposal.
- In the event that a qualified majority vote is not achieved, the proposal passes to the European Council for a final decision.

The documents on which the current EU approval of glyphosate is based, including Germany's 1998 DAR on glyphosate and comments of member states, are not readily available to the public or seemingly even to the EU Commission's regulators, DG SANCO. DG SANCO told the authors of this report that it was unable to supply the DAR and referred the request to the German government office BVL, which only supplied it after a delay of several weeks. Even then, BVL withheld part of the DAR. In contrast, DG SANCO's 2002 review report on glyphosate is publicly available.

Suresh (1993)

Submitter company: Feinchemie[57]

Germany's summary: This study on the teratogenicity of glyphosate in rabbits found that the total number of foetuses with major visceral anomalies was high in all treatment groups, including the low-dose level of 20 mg/kg, and was significantly increased at the 500 mg/kg (highest dose) level. The percentage of foetuses with dilated heart was significantly elevated at all dose levels. Skeletal variations, anomalies and malformations were found but there was no clear dose-response pattern. There was a dose-related increase in the occurrence of an extra 13th rib in all the glyphosate-treated groups and in the highest dose group this was statistically significant.

The NOEL (no observable effect level, the highest dose tested that did not produce an adverse effect) for maternal toxicity was 20 mg/kg bw/d [body weight]/day, based on the fact that possibly treatment-related deaths occurred in the higher dose groups. With regard to visceral malformations, the study's author concluded that the NOEL was less than the lowest dose of 20 mg/kg bw/d.[58]

UK's comment: "The increased incidences of abnormalities … are of concern, particularly the heart effects which are also reported in other rabbit studies with glyphosate… The interpretation of this finding must rely on comparison with historical control data. If the typical incidence [of malformations] is approximately 5 fetuses per group then there is no concern. However if this is a very rare finding in control animals and the concurrent controls for this study are typical then there are concerns regarding the potential fetotoxicity of this source of glyphosate."[59]

Our comment: With regard to this study, even industry is telling Germany that glyphosate is toxic at 20 mg/kg bw/d, if not lower. Germany however explains away the findings on the grounds that the actual number of foetuses with dilated heart was small, that there was no increase in foetuses with heart dilation in the mid-dose over the low-dose group, that almost no other soft organ malformations occurred, and that the consequences of this heart malformation are "equivocal". Together, those arguments lead them to conclude that the low dose of 20 mg/kg bw/d and even the mid dose of 100 mg/kg bw/d were NOELs.

An objective evaluation of this study would conclude that the low dose of 20 mg/kg bw/d is not the NOEL, or, as it is usually called today, the NOAEL (no observed adverse effect level). In this study, 20 mg/kg is the LOAEL – the lowest level at which an adverse effect was found. Statistically significant teratogenic effects were found at this dose. As no NOEL was found in this study, Germany should have demanded that further tests be done to establish the NOEL, with the highest dose set at 20 mg/kg bw/d and lower doses added to try to establish a true NOEL.

Germany's comment that the number of foetuses with abnormalities was small merely identifies a shortcoming of industry studies. Larger numbers of test subjects are always preferable. If the number of animals used in the study is small, any effect will only be seen in small numbers of animals.

Germany's dismissal of the heart malformations on the grounds that no other types of soft organ malformations were found is not consistent with the current state of knowledge in developmental biology. Many toxic agents target a specific organ (known as "organ specific" effects) or have one specific effect. In light of this, Germany has no basis for arguing that the heart malformations are not important because malformations were not observed in other tissues. Also, Germany's argument that the heart dilation malformation has unknown consequences and can therefore be dismissed is scientifically and clinically indefensible.

Germany's expectation of a proportional dose-response pattern in skeletal malformations is also not supported by current knowledge of developmental biology. There is no evidence in the scientific literature demonstrating that toxicity must always be proportional to dose, increasing as the dose increases. Toxicologists now recognize that dose-response relationships can be complex, especially when the endocrine system is involved. Toxic effects can be found at low doses but not at higher doses, and different toxic effects can be found at different doses.[60 61 62 63]

Industry toxicologists ignore these scientifically established facts. They only test unrealistically

high doses and extrapolate effects to low doses, wrongly assuming a linear dose-response relationship. They also wrongly assume that there is a threshold dose below which there is no toxicity. In short, they fail to gather data from almost every area of the dose-response graph.

Germany has wrongly dismissed the hard data in this study, which clearly indicate the toxicity of glyphosate.

Germany repeatedly tries to explain away the finding of malformations in industry studies by referring to historical control data instead of focusing on comparison of the experimental and control groups within the study under consideration. When a study shows clear differences between experimental and control groups, instead of concluding that the study demonstrates the toxicity of glyphosate, Germany compares the experimental group to control data from other sources. Such control data will have wide variability, the range of which will overlap with the values reported for the glyphosate-treated groups in the study under consideration. Based on this overlap, Germany concludes that there is no evidence of toxicity, since the experimental results are within the range of normal variability. This conclusion is not valid, because the variability within the control data gathered by Germany is artificially large, due to the fact that the studies from which those data are drawn have been done under a range of conditions.

Germany's practices might be overlooked if the effects found were marginal and if other studies with similar findings did not exist. But neither condition applies to these industry studies on glyphosate, which consistently show malformations. Significantly, the independent studies cited in this report do not rely on "historical control data" to explain away findings.

It is clear from the UK's PSD's comment on the teratogenicity studies that it had not seen the historical control data and so was not prepared to discount the possibility that glyphosate was teratogenic and toxic to foetuses.[64]

Brooker et al., 1991

Submitter companies: Monsanto/Cheminova[65]

Germany's summary: This study looked at the effects of glyphosate on pregnancy in rabbits, at doses of 50, 150, and 450 mg/kg bw/d. It found a significant increase in embryonic deaths in all the glyphosate-treated groups compared with controls. However, a comparison with historical control data showed that the incidence in the control group was untypically low. Also, a clear dose-response relationship was not shown. On the other hand, an increase in late embryonic deaths at the top dose level (450 mg/kg bw/day) was also found in another study on rabbits.

There was concern about the more frequent occurrence of foetuses with heart malformations in the high dose group, but the incidence was in the range of historical background data. However, anomalies of the heart have been described in other rabbit teratogenicity studies with glyphosate, too. Thus, a possible effect on the occurrence of visceral anomalies remains equivocal.[66]

UK's comment: "The increased levels of embryonic death/post-implantational loss at all dose levels are of concern, as are the reports of heart defects… a more robust argument should be presented before these findings can be dismissed."[67]

Our comment: Again, Germany uses historical control data and an inappropriate model for toxicity dose-response to explain away malformations of the heart in a glyphosate-exposed group. Again, by taking this position, Germany appears to be acting against the public interest by ignoring or dismissing findings of glyphosate-induced teratogenicity and foetotoxicity.

Bhide and Patil (1989)

Submitter companies: Barclay/Luxan[68]

Germany's summary: This study examined teratological effects of glyphosate in rabbits at doses of 125, 250, and 500 mg/kg bw/d. At the high dose, two females aborted. There was no evidence of foetotoxic and teratogenic effects up to and including the mid-dose group. But the high-dose group had a decreased number of viable foetuses per litter and the number of non-viable implants (non-development and death of embryo) increased. The number of visceral and skeletal

malformations was increased in the high-dose group.[69]

The study's authors do not mention whether a statistical analysis was performed.

UK's comment: "Another study with equivocal evidence of heart defects."[70]

Our comment: The data shows that dose-dependent increases in lung and kidney malformations were found *across all glyphosate-exposed groups*. Increased heart malformations were found in all exposed groups. Increased skeletal (rudimentary 14th rib) malformations were found in the mid-dose and high-dose groups.

Germany incorrectly claims that the teratogenic NOAEL is the mid dose of 250 mg/kg bw/d. In reality, there are evident increases in most of the defects, even at the lowest dose of 125 mg/kg bw/d. The authors of this study do not provide an analysis of statistical significance and groups of only 15 animals were used, making statistical significance difficult to establish. But it is more accurate to say the mid dose, possibly even the low 125 mg/kg dose, is the LOAEL. Testing the effects of lower, realistic doses requires far larger animal groups if an increase in toxicity compared with the unexposed control group is to be reliably detected.[71 72]

At the very least, this study should have been repeated with a larger sample size and lower doses. Effects should have been examined thoroughly by allowing full gestation and pup development.

Anonym. (1981)

Submitter company: Alkaloida[73]

Germany's summary: This oral feeding study examined teratological effects of glyphosate in rats and rabbits. Vital details were either not recorded or poorly described, so the study was only considered as supplementary information. No malformations were recorded, but there were more foetal deaths at the two upper dose levels (50.7 and 255.3 mg/kg bw/d).[74] It is difficult to understand why an increase in foetal deaths would occur at doses far below those at which foetal effects were found in the gavage [force-feeding via stomach tube] studies. Thus it is doubtful whether this effect is related to glyphosate.[75]

UK's comment: "Though this study is questioned [by the rapporteur, Germany] for showing evidence of fetotoxicity at lower doses than other studies, the study by Brooker (see above) may also indicate fetotoxicity at 50 mg/kg bw/d."[76]

Our comment: Germany here again appears to show a bias towards considering low-dose findings as non-treatment-related and irrelevant – seemingly because it cannot accept that oral feeding may result in different exposures and effects than gavage. But the UK's PSD points out that another study supports this study's findings.

Tasker, E.J. and Rodwell, D.E. (1980)

Submitter companies: Monsanto and Cheminova[77]

Germany's summary: This teratogenicity study in rats found a higher number of foetuses with malformations at the highest dose level (3500 mg/kg bw/d), but this was within the range of historical control data and was not considered to be due to glyphosate treatment. Specifically, there were more foetuses with unossified sternebrae (bones of the sternum/breastbone) in the high-dose group. While this effect was considered to be due to the glyphosate treatment, it is "rather a developmental variation than a malformation."[78]

UK's comment: The UK PSD does not comment on this study.

Our comments: Germany once again resorts to historical control data in order to conclude that there is lack of evidence of teratogenicity. Given the findings of malformations from glyphosate treatment in several other studies, this is unjustifiable.

Germany's decision to redefine unossified sternebrae as a "variation" rather than a malformation is scientifically unjustifiable and at odds with other authorities. Unossified sternebrae in the rat are clearly defined as a skeletal deformity in *The Handbook of Skeletal Toxicology*.[79]

3.2. Glyphosate's "pattern" of teratogenicity dimissed by EU expert panel

The UK PSD's overall conclusion supports the teratogenicity of glyphosate: "Taken in isolation, none of the findings in these rabbit teratology studies would be clearly of concern. *However, overall there is an indication of a pattern*."[80]

The PSD ended by asking Germany to make

available the historical control data. It is unclear whether the PSD ever saw this data or, if it did, how it responded. Certainly, the data has not been placed in the public domain for scrutiny by independent scientists.

The teratogenicity question then passed to the EU Commission's ECCO scientific review panel. The panel noted "the incidence of heart malformations", but dismissed them on the grounds that they were "within the range of the historical control data".[81] It is unclear whether the ECCO Panel saw the historical control data or merely accepted Germany's conclusion. No details are given of the previous studies from which the historical control data were derived or how the figures were analyzed. The experimental animal species, experimental design, identity of the researchers and laboratories, and purity of the substance tested, are unknown. There are significant variations between different formulations of glyphosate: glyphosate produced in the 1970s will not be the same as formulations produced in later decades. But none of these variables can be checked because the historical control data does not appear to be in the public domain.

The historical control data that enabled the ECCO Panel to dismiss glyphosate's teratogenicity must be added to the large pile of grey literature supporting pesticide approvals that cannot be evaluated by the public or independent experts.

The use of historical rather than concurrent controls adds variables to an experiment that aims to control variables, obscures the teratogenic effects of glyphosate, and biases any conclusion. This is why the use of historical control data is controversial.[82 83] The practice should not be allowed in evaluating animal toxicological and other studies for pesticide approvals.

Valid control groups for an experiment are animals of the same strain and age, in the same environment, which are studied at the same time as the exposed (experimental) animals. In addition, the manner in which the animals are examined and evaluated, and the data recorded, must be the same. "Historical control data" fail to meet these criteria. It appears that they are being used as a smokescreen to hide glyphosate's teratogenic effects.

Clearly, only after findings emerged showing glyphosate's teratogenicity did Germany and the ECCO Panel introduce the artifice of historical control data as a way of calling into question the scientifically-proper controls. In this way, the differences between exposed and unexposed animals were buried in the variability within the historical control data.

If such practices were uncovered in an independent scientific study, they could be considered scientific fraud. In this case, we do not even know who perpetrated this act, which has placed public health at risk.

Taking all these industry studies together, there is enough evidence to require regulators to apply the precautionary principle and withdraw glyphosate from the market.

3.3. Industry and regulators failed to disclose glyphosate's teratogenicity

The evidence discussed above shows how EU regulators reasoned their way from evidence of glyphosate's teratogenicity in industry's own studies to a dismissal of these effects in DG SANCO's 2002 final review report.[84]

Taken together, the industry studies and regulatory documents on which the current approval of glyphosate rests reveal that:

- Industry (including Monsanto) has known since the 1980s that glyphosate causes malformations in experimental animals at high doses
- Industry has known since 1993 that these effects could also occur at low and mid doses
- The German government has known that glyphosate causes malformations since at least 1998, the year it submitted its DAR on glyphosate to the EU Commission
- The EU Commission's expert scientific review panel has known since 1999 that glyphosate causes malformations
- The EU Commission has known since 2002 that glyphosate causes malformations. This was the year its DG SANCO division published its final review report, laying out the basis for the current approval of glyphosate.

The public, on the other hand, has been kept

in the dark by industry and regulators about the ability of glyphosate and Roundup to cause malformations. In addition, the work of independent scientists who have drawn attention to the herbicide's teratogenic effects has been ignored, dismissed, or denigrated.

3.4. Germany set misleading "safe" level for glyphosate

The central purpose of any pesticide risk assessment is to establish the Acceptable Daily Intake (ADI), a level of exposure that is deemed safe for humans over a long period. The ADI is calculated from the industry tests in the dossier. The level that should be used to set the ADI is the highest dose at which no adverse effect is observed (NOAEL), which is also lower than the lowest dose that is toxic (LOAEL). This level should be selected from "the most appropriate study in the most sensitive species", as the glyphosate rapporteur Germany notes.[85]

Germany set the ADI for glyphosate at 0.3 mg/kg bw/d.[86] This ADI was accepted by the European Commission in its final review report.[87]

However, we argue that this is incorrect. Germany indulges in some creative manipulation of data to arrive at this level. It begins by excluding certain studies from the ADI process:

- Germany excludes mid-term studies on the grounds that only long-term studies should be used to set safe chronic exposure levels.[88] This enables it to avoid using the rabbit teratogenicity studies, which were mid-term.
- Germany claims that the most sensitive species for chronic exposure is the rat. This gives it another reason to exclude the inconvenient rabbit teratogenicity studies, which found significant adverse effects at lower doses than the rat studies.

Based on this biased selection of data, Germany cites as its starting point for working out the ADI a LOAEL of 60 mg/kg bw/d from a two-year rat study by Suresh (1996), which found significant toxicity at that level.[89] This is said to be the lowest dose at which toxicity was observed. Germany then identifies the highest NOAEL below that level: 31 mg/kg bw/d, in a study by Lankas (1981). It implies that this is the figure from which it calculates its ADI (though also, confusingly, denies that it bases the ADI on any single study).[90] The ADI is derived by dividing this figure by 100, to allow a safety margin. Applying this 100-fold safety factor, Germany arrives at an ADI of 0.3 mg/kg bw/d.

However, we argue that Germany should have begun the ADI process using the LOAEL of 20 mg/kg from the 1993 Suresh rabbit teratogenicity study, which is *three times lower than Germany's chosen LOAEL of 60 mg/kg bw/d*.[91 92]

To sum up the difference between these two studies:

- The study Germany uses to set the ADI: Suresh's 1996 chronic toxicity study on rats found statistically significant toxicity at 60 mg/kg bw/d (the LOAEL).
- The study Germany ignores in setting the ADI: Suresh's 1993 teratogenicity study on rabbits found statistically significant toxicity at 20 mg/kg bw/d (the LOAEL).

Germany relegates the inconvenient 1993 Suresh study to setting the acceptable operator (applicators') exposure level (AOEL). It argues that it is a mid-term rather than long-term experiment and therefore more suitable to setting an applicators' exposure level.[93]

We believe that Germany's reasoning would not stand up to independent scientific scrutiny. Germany's failure to take into consideration the worrying rabbit teratogenicity studies means that its ADI ignores the problem of the teratogenic effects of glyphosate – as shown even in weak industry studies.

In our view, the Suresh 1993 LOAEL of 20 mg/kg bw/d should be the starting point for the ADI and for the applicators' AOEL. The 1993 Suresh study from which this LOAEL is derived found no NOAEL (no observed adverse effect level). In other words, even the lowest dose produced adverse effects.[94 95] So Germany should have insisted on further tests to establish the NOAEL, using 20 mg/kg as the highest dose.

If this LOAEL of 20 mg/kg were used, then, following the same procedure as Germany, the highest NOAEL below this dose from Germany's approved list of studies is 10 mg/kg.[96] Applying the 100-fold safety factor, this would give a more

objectively accurate ADI of 0.1 mg/kg bw/d, one-third of the ADI suggested by Germany.

Interestingly, one of the industry applicants, Feinchemie, suggests a far lower ADI than Germany or us: 0.05 mg/kg bw/d. This is five times lower than the ADI suggested by Germany and accepted by the Commission. Feinchemie bases its suggested ADI on its 2-year rat study, which found a NOAEL of 5.5 mg/kg bw/d.[97]

Feinchemie's suggested ADI is consistent with the NOAEL of the 1996 Suresh study, which Germany used to derive the LOAEL but ignored to set the ADI. The NOAEL of that study was 6.3 mg/kg bw/d, which would give an ADI of 0.06 mg/kg bw/d, close to Feinchemie's proposed ADI of 0.05 mg/kg bw/d.

It is ironic that industry asked for stricter – and more scientifically justifiable – safety standards than the rapporteur, Germany. In contrast with Feinchemie's proposed low ADI, however, Monsanto asked for an ADI of 1.75 mg/kg bw/d, the highest of all the industry-suggested ADIs.[98]

3.5. What the ADI should be – according to independent studies

If a manufacturer of glyphosate says the ADI should be five times lower than the one suggested by Germany and accepted by the Commission, what do independent studies say it should be?

Two high-quality mammalian toxicity studies show that glyphosate's LOAEL should be even lower than that proposed by Feinchemie (which in turn was lower than that proposed by Germany):

- A study on rats showed that a Roundup formulation was a potent endocrine disruptor and caused disturbances in reproductive development when the exposure was performed during the puberty period. Adverse effects, including delayed puberty and reduced testosterone production, were found at all dose levels, including the LOAEL of 5 mg/kg. The dose-response relationship was clear.[99] One of the critical failures of regulatory toxicity tests is to ignore important developmental windows such as puberty. This study helps to fill that knowledge gap.
- A 75-day study on rats showed that Glyphosate-Biocarb (a Brazilian formulation) caused damage to liver cells in a dose-response manner, including at the LOAEL of 4.87 mg/kg. According to the authors, the findings suggest that the damage to liver cells was "irreversible".[100]

Both studies use a species (rats) and an exposure route (oral) approved by EU regulators and industry.

No dose below these two LOAELs was tested in these studies, so the true NOAEL is lower – by how much, no one knows. But the NOAEL could reasonably be assumed to be 2.5 mg/kg bw/d. Applying the usual 100-fold safety margin results in a scientifically defensible ADI of 0.025 mg/kg bw/d. This is over ten times lower than the Germany's ADI, which is currently in force. The MRL (safe level in food) should be correspondingly revised downward.

Of course, all assumptions need to be tested, and not even independent science has explored the full picture of Roundup and glyphosate's toxicity. Studies should be carried out immediately to determine the true NOAEL and ADI for glyphosate and Roundup, using the most comprehensive, up-to-date scientific knowledge. These studies would involve:

- testing for more effects
- using lower, more realistic doses that will allow accurate determination of the NOAEL
- using larger numbers of animals to ensure sufficient statistical power to reliably detect effects from realistic doses
- dosing during vulnerable developmental windows
- extending study time-frames to allow mid- and long-term effects to show up, instead of killing the test animals before disease has a chance to develop. Industry test animals are killed at the human equivalent of about 60 years old, so many effects of the chemical tested are missed.[101]

In addition, research should be done that determines glyphosate levels in food and feed imported into the EU. Finally, based on independent (not industry) data from North and South America, an assessment should be carried out of the increase in glyphosate use, and therefore exposure, that would be expected to occur if glyphosate-tolerant GM crops were allowed to be grown in the EU.

This science-based assessment of glyphosate and Roundup will allow the EU to establish a credible policy that protects EU citizens. Until that assessment is complete, the EU should apply the precautionary principle and withdraw glyphosate herbicides from sale in the EU.

3.6. Does current risk assessment protect the public?

The current system of pesticide risk assessment in the EU is not transparent or easy to understand. Those who make the effort to study it will see that it is open to manipulation and abuse. In risk assessment, it is the details that count. The conclusions that are drawn depend heavily on how data is selected – what is included and what is left out. This is clear from the above discussion of the approach Germany used in justifying its incorrect conclusion that glyphosate does not have teratogenic or foetotoxic effects. Particularly revealing was Germany's exclusion of the rabbit teratogenicity studies in setting the ADI for glyphosate.

Industry also has room for manoeuvre in discussions of how toxins behave in the human body. For example, industry uses broad arguments to claim that toxins are broken down in the liver, or do not cross the placental barrier in pregnant women. Even cases of clear harm can be minimized. An anonymous scientist critic said, "There are many tricks that are used. If all insects in a field are killed for a full year, this is not a problem, because they will come back next year. A regulator told me that with the current system of risk assessment you could get any chemical approved, including DDT."

Even the underlying assumption of risk assessment, that there is a "safe" level below which a toxic pesticide is not toxic, is questionable. Many compounds accumulate in the body. Some toxins, particularly endocrine disrupting chemicals, are more potent at low doses than higher doses. People and species vary in their susceptibility to toxins and individuals at different stages in development and maturation and at different stages of biological cycles. Even the latest independent science has only begun to explore the true effects of chemicals on vulnerable groups such as developing foetuses, infants and children, the elderly, and immune-compromised people.

In addition, the industry tests carried out for risk assessments mostly look for a narrow range of gross effects. These include tissue and structural changes, such as malformations and tumours, which tend to occur at the high doses that industry tests use. But these tests often miss functional changes (effects on how the body's organs and systems function), which tend to be seen at lower doses and more closely reflect effects from real-life human exposures. These functional changes are important because they can lead to more severe and difficult-to-reverse disease conditions. In other words, they perform a signalling role in predicting serious health problems. Independent scientific literature, which is not tied to OECD test designs, has been more effective than industry science in finding these functional effects – but it has hitherto been virtually ignored in pesticide risk assessments.

Other aspects that have not been adequately examined in existing risk assessments are the impact of the individual's existing body burden of toxins and synergistic effects that are not seen when the compounds are tested in isolation.

For these reasons and more, some scientists and policy-makers advocate reforming the risk assessment of pesticides – for example, by increasing the use of hazard analysis. Hazard analysis stipulates that if a pesticide has certain hazardous qualities, it should automatically be rejected ("hazard cut-off"). This differs from the current risk assessment approach, which assumes that even when a hazard exists, the risk can be managed. The new pesticide regulation 1107/2009 contains some "hazard cut-off" criteria. For example, a pesticide cannot be approved if it is carcinogenic, mutagenic, a reproductive toxin, persistent in the environment, bioaccumulative, or an endocrine disruptor (apart from specific uses, such as in closed systems).

These are positive developments. But industry, together with the German Federal Institute for Risk Assessment (BfR), which is involved in the registration of pesticides in Germany, is lobbying to prevent the new system of hazard analysis and

cut-off criteria gaining a foothold in Europe and to keep the existing system of risk assessment.[102 103] For the sake of public health, it is vital that they do not succeed.

4. The problem of industry bias in testing

Regulatory approvals of pesticides are based almost exclusively on industry's own studies. The conflicts of interest inherent in this system were pointed out by Andrés Carrasco in his original research study. The German government agency BVL replied to this criticism by defending the reliability of industry studies. BVL says industry studies on other substances have sometimes found developmental effects and "it is not likely that developmental effects would have not been reported for glyphosate but for other substances". BVL adds that many different companies provided their own toxicological data from tests they had commissioned from different laboratories, and all found "absence of teratogenicity".

It is interesting that the BVL makes this bold and categorical statement, despite the fact that industry studies in the dossier that the BVL reviewed did find evidence of teratogenicity.

Even if the industry tests had shown no malformations, this would not be proof of glyphosate's safety. Every time industry studies are compared with those from the independent scientific literature, the same verdict is reached: industry tests are biased towards conclusions of safety. The best known example is tobacco industry studies, which successfully delayed regulation for decades by manufacturing doubt and controversy about the effects of smoking and passive smoking.[104] More recently, studies sponsored by the pharmaceutical and mobile phone industry have been shown to be more likely to portray their products in a favourable light than non-industry-funded studies.[105 106 107] A review of studies on genetically modified crops and foods showed that the existence of either financial or professional conflict of interest was associated with study outcomes that cast products in a favorable light.[108]

Fewer comparisons of industry vs. independent studies have been performed for chemicals (including pesticides), but in four such reviews the same relationship is found: industry sponsorship is more likely to find favorable results, while the independent literature finds both safety and risk.[109 110 111 112]

The Monsanto/Dow employees follow BVL in defending industry studies. In their response to Carrasco, they write: "Multiple high quality toxicological studies and expert review panels consistently agree glyphosate is not a teratogen or reproductive toxicant." They say the industry-funded studies that Carrasco calls untrustworthy "have been exhaustively reviewed by multiple government scientific regulators, often comprised of academic expert scientists and all of which have strongly supported the conclusions put forth in those studies."[113] Monsanto/Dow names the "Regulatory authorities and independent experts who have documented this position" as WHO/FAO, US EPA, the European Commission, and Williams (2000).

But Monsanto/Dow's cited authorities for its position do not stand up to scrutiny:

- The European Commission's 2002 review of glyphosate claims that developmental effects are confined to "maternally toxic doses". But this claim is examined and discredited above.
- The WHO report on glyphosate (1994)[114] mainly cites industry studies. For example, 180 studies were generated by Monsanto, of which over 150 were not published or subjected to peer review. Other unpublished technical reports provided as references in the same document include 17 reports from Agrichem, five from Luxan BV, and five from Rhone Poulenc – all producers and/or marketers of pesticides.[115]
- Williams co-authored his paper on glyphosate's safety with Ian C. Munro.[116] Munro is executive vice president of the chemical industry consulting firm Cantox,[117] which states that its mission is "protect client interests while helping our clients achieve milestones and bring

products to market".[118] The Williams paper was published in the controversial chemical industry-sponsored journal Regulatory Toxicology and Pharmacology (RTP). RTP was one of several industry-linked organizations that were investigated by a US Congressional Committee in 2008 over their role in the FDA's decision allowing the toxic chemical bisphenol A in infant formula and other foods.[119] [120] [121] All this would matter less if Williams had cited credible sources in his claims for glyphosate's reproductive and developmental safety. But he cites unpublished industry studies, such as Schroeder (1981), Reyna (1990), and Tasker (1980). As these studies are from the industry dossier submitted for glyphosate's approval, it is strange that Williams fails to mention the other studies from the same dossier that we examine above – Suresh (1993), Brooker (1991), and Bhide and Patil (1989) – which found that glyphosate was teratogenic.

In sum, Monsanto/Dow relies for its claims of glyphosate's safety on carefully selected industry sources and cooperative regulators who only consider industry studies.

4.1. Good Laboratory Practice: A shield for industry?

In its response to Carrasco, Monsanto/Dow praises the "high quality" industry tests that it claims show the safety of glyphosate on the grounds that they were conducted under Good Laboratory Practice (GLP) rules.

GLP specifies the organisational process and the conditions under which industry studies for the regulatory purposes are planned, performed, monitored, recorded and reported. GLP is a management system. It is not a hallmark – much less a guarantee – of "good science".

GLP was initiated by the US Food and Drug Administration in 1978 in an attempt to end the serious problem of fraud in industry testing of pesticides, chemicals, and pharmaceutical drugs for regulatory assessment.[122] In 1983, the US Environmental Protection Agency (EPA) established similar guidelines for pesticide toxicology studies and in 1989, extended them to cover studies submitted for pesticide approvals.[123]

The move to GLP standards was prompted by a high-profile case of fraud involving a company called Industrial Bio-Test Laboratories (IBT), which brought into question 15% of the pesticides approved for use in the US.[124] [125] However, the implementation of GLP failed to prevent a second major case of fraud, this time at Craven Labs, which was discovered in the 1990s.[126]

Interestingly, both the IBT and Craven Labs fraud cases involved toxicological and residue tests of Roundup for regulatory purposes by laboratories under contract to Monsanto. Monsanto says it later repeated the tests under GLP rules,[127] though this is hardly reassuring given that the Craven Labs fraud occurred after GLP rules were in place.[128] Clearly, GLP neither prevents fraud, nor assures high quality science.

The GLP guidelines are set by the OECD (Organisation for Economic Cooperation and Development), a body dedicated not to public health but to promoting international trade and economic development. OECD guidelines prescribe the choice of experimental animal, number of animals, exposure times, and doses.[129] The aim was to establish a set of standardized tests that would be acceptable in all WTO member countries (WTO having come to an agreement with OECD). This facilitates international trade because all countries involved agree to the same testing requirements.[130] [131]

Though the aims of GLP were laudable, they have been used to create a regulatory system that excludes open peer reviewed scientific literature. One critic called GLP a "shield" that industry uses to protect itself from inconvenient findings in the independent scientific literature.[132] Regulatory bodies across the world – including the EU Commission's DG SANCO and the European Food Safety Authority (EFSA) – collude in this process by designating industry's GLP-compliant toxicity studies as the highest quality data. They rely almost exclusively on these industry-sponsored studies for pesticide and chemical assessments, rejecting studies from the open peer reviewed scientific literature because they are not conducted under GLP rules.[133] [134]

Thus, Monsanto/Dow is able to dismiss

Carrasco's research and other independent studies showing harm from glyphosate/Roundup by saying that the testing systems are "unvalidated" and the studies "inappropriate and irrelevant for human health risk assessment purposes".[135] In other words, they are not GLP.

The tyranny of GLP over regulatory processes has been heavily criticised in a paper co-authored by 30 scientists. The authors point out that GLP "specifies nothing about the quality of the research design, the skills of the technicians, the sensitivity of the assays, or whether the methods employed are current or out-of-date".[136] Indeed, the dismissive attitude of the EU Commission – and of pesticide regulators worldwide – to high-quality independent studies that find harm from pesticides raises the question: why do governments fund scientific research if they ignore its findings in almost every risk assessment?

Another review criticizes GLP toxicity studies for using outdated protocols, some of which "have failed to modernise for nearly 100 years": "Very high doses are used (to assure statistical significance, due to insensitivity of the assays), but such near-poisoning levels may have little to do with what happens to organisms that are exposed to real world doses... and which go untested.... Test animals are killed before old age, masking most developing diseases. In short, GLP tests use protocols that cannot find toxicity."[137]

Government pesticide and chemical regulators use data from industry OECD-compliant tests to determine the claimed safe level or NOAEL (no observed adverse effect level, the level at which the effect being looked for is not found). But Tweedale (2011) compared the NOAELs from industry and independent tests on dozens of chemicals and found that in every case, independent studies detected important toxic effects at levels well below those that industry studies claimed to be safe. Yet regulators ignore the independent data and take note only of the industry data because they comply with OECD GLP criteria.[138]

In addition, OECD tests set rigid and scientifically incorrect criteria regarding dose-response in toxicological tests. These criteria fail to take into account the fact that endocrine disrupting and other effects are often stronger at low dose than at high dose. Their assumption that there is a safe dose below which no significant toxicity occurs has been challenged by findings in the independent scientific literature.[139]

OECD has still not come to terms with low-dose effects or complex dose-response relationships. One critical scientist who spoke on condition of anonymity said, "It will probably take OECD 10–15 years to come up with a complete set of tests to take endocrine disruption into account – which by then will be outdated again. On endocrine disruption, only a few standardized tests are available at the moment and there is no overall strategy to decide which substances should be subjected to which tests."[140 141 142]

The EU Commission said in 2009 that it expects its range of tests on endocrine disrupting effects of pesticides to be ready in 2013.[143] The US Environmental Protection Agency is ahead of the EU Commission and OECD and already has a strategy and a list of substances for endocrine disruption screening. These include glyphosate.[144 145 146]

Even if we take Monsanto/Dow's elevation of GLP studies at face value, its argument does not stand up, as many of the studies in the industry dossier on glyphosate are not GLP. They are so old that they pre-date the introduction of GLP. The industry studies cited by Williams to back his claim that glyphosate is not a reproductive toxin include non-GLP studies by Schroeder (1981) and Tasker (1980).[147]

4.2. EFSA undermines democratic decision to end tyranny of GLP

Science has separated into two diverging pathways – industry GLP science, which is often used to claim safety for a risky product, and independent science, which is usually not conducted according to GLP rules, and which often shows harm. The new EU pesticide regulation has the potential to end the tyranny of GLP by insisting on the use of peer-reviewed independent scientific studies in pesticide assessments.

However, the new regulation obliges industry to do its own scientific literature search in preparing a pesticide dossier. The risk inherent

in giving industry control of the search could be removed by forcing it to do a complete and non-selective search. But the European Food Safety Authority (EFSA) has undermined the intent of the new democratically established regulation by issuing a Guidance on the use of peer-reviewed science in pesticide assessment.[148] The Guidance actively encourages industry to select only those studies it finds convenient to include in the dossier, through the following means.

Industry evaluates reliability of studies

The Guidance advises industry how to evaluate the reliability of, and thus how to select, studies for possible inclusion in its dossier. The first source that EFSA recommends industry to consult is a paper by a BASF employee, Klimisch (1997),[149] published in the industry-sponsored journal Regulatory Toxicology and Pharmacology.[150] Klimisch gives a list of "categories of reliability" by which to assess the suitability of a scientific study for inclusion in the regulatory dossier. His most reliable category 1 ("reliable without restriction"), consists of studies conducted according to GLP rules. Klimisch relegates independent studies, which do not follow GLP/OECD rules, to categories 2 and 3, "reliable with restrictions" and "not reliable", respectively.[151]

Industry can carry out selective searches

EFSA's Guidance encourages industry to choose search terms that would provide only a narrow-focused search of the literature by, for example, specifying the type of test design.[152] This works against the public interest, as a search for "mutagenicity AND GLP" would find industry-generated studies but exclude independent studies. If an independent study found mutagenicity by a non-GLP test, it would not turn up in the search.

Industry defines what is a "relevant" study

EFSA's Guidance encourages industry to select out studies on the basis that they are not "relevant" to human risk assessment. EFSA defines "relevant" species for toxicological studies as mammals, preferably rats, mice, and dogs. This would exclude studies such as Carrasco's, which was on frogs and chickens – even though the developmental mechanisms in humans are similar.[153]

EFSA defines "relevant" exposure routes as oral, dermal, or inhalation.[154] This would exclude many independent studies, which use injection or culture as the exposure route. Among the research findings excluded through this definition would be Carrasco's study and much of the research on glyphosate and Roundup conducted by Professor Gilles-Eric Séralini's team. However, the question of relevance of different exposure routes is by no means settled, and EFSA's exclusion of certain exposure routes as irrelevant is premature at best (see Section 6, below).

Through its Guidance, EFSA has given industry licence to dismiss independent scientific studies – and regulators an excuse to continue to ignore them in risk assessments of pesticides.

4.3. Case study in the misuse of GLP: bisphenol A

The problem of the tyranny of GLP over regulators is exemplified by the case of the chemical bisphenol A (BPA), a plastics ingredient widely used in food packaging.

Hundreds of peer reviewed, published – and non-GLP – studies show significant effects of BPA at low doses, with over 30 showing significant effects below the predicted "safe" dose. The evidence that BPA poses a danger to public health is strong. It has been found in human blood and tissues, including in human foetal blood, at levels higher than those causing adverse effects in mice. An epidemiological study shows that that BPA is related to ovarian disease in women.[155]

But industry studies on BPA have reached diametrically opposite conclusions. While 94 of 104 (90%) government-funded published studies on bisphenol A reported significant effects at low doses, no industry-funded studies (0 of 11) report significant effects at the same doses. A 2005 review of studies on BPA found that source of funding is highly correlated with positive or negative findings.[156]

A 2009 review blamed regulatory fixation on GLP for the BPA débacle. The authors criticized the US Food and Drug Administration and

the European Food Safety Authority (EFSA) for deeming two industry-funded studies that adhered to GLP to be superior to hundreds of independent non-GLP studies funded by the US National Institutes of Health (NIH) and similar agencies in other countries.[157]
The authors stated:

> It is of great concern that the US and EU regulatory communities are willing to accept these industry-funded, antiquated, and flawed studies as proof of the safety of BPA while rejecting as invalid for regulatory purposes the findings from a very large number of academic and government investigators using 21st-century scientific approaches. The basis for these decisions by US and EU regulatory agencies should be thoroughly investigated.[158]

The authors pointed out that there is simply no data from GLP studies on many of the toxic effects observed in independent studies on BPA, such as some adverse effects on the female reproductive system. This is because those effects have not yet made their way into the outdated regulatory testing system. In other words, the reason the effects are not found in GLP studies is not because the chemical is safe, but because those effects are not looked for. The authors added that there is a large literature on neurotoxic effects and behavioral abnormalities caused by low doses of BPA which are not capable of being detected by current GLP studies conducted for regulatory purposes because of their outdated methodologies.

The authors argued that the chemical industry-sponsored GLP studies on which the agencies based their decisions are incapable of detecting low-dose endocrine-disrupting effects of BPA and other hormonally active chemicals. They stated that the FDA and EFSA "mistakenly assumed that GLP yields valid and reliable scientific findings (i.e., 'good science')."[159]

The authors stated that the main factors determining the reliability of scientific findings are independent replication and use of the most sensitive and up-to-date tests – neither of which is an expectation of GLP. They concluded:

> We are not suggesting that GLP should be abandoned as a requirement for industry-funded studies. We object, however, to regulatory agencies implying that GLP indicates that industry-funded GLP research is somehow superior to NIH-funded studies that are not conducted using GLP.[160]

The EFSA continues to rely for its risk assessment of BPA on the few industry studies adhering to Good Laboratory Practice (GLP) guidelines that found no adverse effects. Based on these studies, EFSA refuses to take decisive action restricting its use.[161] [162] The EU Commission announced in November 2010 that it would ban BPA from babies' bottles but would not extend the ban to materials such as the linings of food and drinks cans as there was no scientific evidence to support such a move.[163] [164]

The regulatory prejudice against open scientific literature and in favour of OECD- and GLP-standardized studies has forced the public to live with many more years of exposure to potentially dangerous levels of BPA.

The case of bisphenol A parallels that of glyphosate. Many studies from the independent scientific literature indicate that glyphosate and Roundup cause harm to human and animal health and the environment at low, realistic doses. Yet EFSA and the Commission continue to rely on a few outdated and flawed industry studies as proof of the herbicide's safety.

5. Evidence of teratogenicity in independent studies

In its response to Carrasco's findings of malformations in frog and chicken embryos exposed to glyphosate and Roundup, the German government agency BVL says: "There is a huge and reliable database for developmental toxicity of glyphosate and no evidence of teratogenicity has been obtained."[165] It is fair to assume that BVL's "huge and reliable database" stretches beyond the industry studies to include the independent scientific literature. This interpretation is confirmed by the fact that BVL cites Dallegrave's studies (2003, 2007) on the reproductive and

developmental toxicity of Roundup on rats, which BVL claims showed "no craniofacial [of the skull and face] malformations".

But this is untrue. The 2003 Dallegrave study cited by BVL does show craniofacial malformations from Roundup. Dallegrave found that sublethal oral doses of Roundup cause craniofacial ossification defects, loss of caudal vertebrae, and misshapen atlas and other cervical and thoracic vertebrae in rats. The author did not use the word "craniofacial" but described the nature of the malformations, which included the craniofacial type: "incomplete skull ossification and enlarged fontanel". The effects were statistically significant and dose-dependent, strengthening the conclusion that they were caused by the glyphosate formulations.[166]

Another study, not cited by BVL, found that glyphosate formulations cause craniofacial and mouth deformities, eye abnormalities and bent, curved tails in tadpoles.[167]

Both these studies are part of what BVL calls the "huge and reliable database" on glyphosate. Both show evidence of teratogenicity.[168] Therefore, BVL must publicly retract its claims of "no craniofacial malformations" in Dallegrave's 2003 study and of "no evidence of teratogenicity" in the scientific literature. In dismissing these findings, BVL and the EU Commission are ignoring data that is publicly available in the peer-reviewed literature.

5.1. How Carrasco's findings built on previous studies

Carrasco built on the findings of Dallegrave in that he identified the mechanism for the teratogenic activity of Roundup/glyphosate. Such malformations in humans and animals are known to be linked with an excess of retinoic acid (RA), an oxidized form of vitamin A.[169] [170] [171] [172] [173] [174] [175] [176] The link between RA and malformations is the reason why pregnant women are advised not to take vitamin A supplements. Carrasco found that glyphosate increased RA activity in frog embryos and that this was the mechanism through which the malformations occurred.[177]

Carrasco says that the malformations of the vertebrae found by Dallegrave may represent teratogenic effects on late embryonic development. His experiments did not extend the observations to the same late stage of development as Dallegrave's. However, the malformations he found are compatible with those found by Dallegrave.[178]

5.2. Epidemiological evidence on glyphosate and birth defects

In response to Carrasco's study, BVL claims: "There is no epidemiological evidence in humans that glyphosate (herbicides) might be teratogenic" and "There is no clear-cut link to a hypothetic increase in malformations in regions with extensive use of plant protection products [pesticides, including herbicides] in South America."

It is true that the authorities in South America have not carried out systematic epidemiological studies in areas where glyphosate spraying is widespread. Even so, enough evidence exists to show that the rapid escalation in the rates of birth defects coinciding with the expansion of GM soy and glyphosate spraying is far from "hypothetic":

- Amnesty International reported that since Carrasco's research findings were announced, "Activists, lawyers and health workers ... have started to conduct their own studies, registering cases of foetal malformations and increased cancer rates in local hospitals."[179]
- An epidemiological study in Paraguay found that women who were exposed during pregnancy to herbicides were more likely then unexposed women to deliver offspring with birth defects of a similar type to those that Carrasco found in his experiments.[180] BVL dismisses this study on the grounds that it is small and does not mention glyphosate. BVL fails to mention that the study was carried out in an area of Paraguay (Itapua) devoted to GM soy monocultures sprayed with glyphosate and agrochemical mixtures. Itapua was home to Silvino Talavera, an 11-year-old boy who died in 2003 from agrochemical poisoning after being sprayed. Glyphosate was one of three agrochemicals found in his blood.[181] These were the facts that gave rise to public demand

for the epidemiological study that BVL so lightly dismisses.

- A report commissioned by the provincial government of Chaco, Argentina, analyzed health statistics in the town of La Leonesa and other areas where soy and rice crops are heavily sprayed. The report found that the rate of birth defects increased nearly fourfold over the entire state of Chaco in only a decade, coinciding with the expansion of the agricultural frontier into the province and the corresponding rise in agrochemical use. The report mentioned glyphosate as one of several agrochemicals that were causing problems. It noted that complaints from sprayed residents centred on "transgenic crops, which require aerial and ground spraying (dusting) with agrochemicals".[182]
- BVL dismisses newspaper reports of birth defects and other severe health problems in sprayed areas by saying "To our knowledge, there is no scientific confirmation of these reports so far". BVL fails to mention that some of these newspaper reports mention local epidemiological studies conducted by doctors and scientists showing an escalation in birth defects.[183] [184] Carrasco also refers to clinical observations in his study.[185] The fact that these small studies have not been translated into English or published in a scientific journal is no excuse for BVL to pretend that they do not exist. This is particularly true as BVL's report on Carrasco's study relies for its assurances of glyphosate's safety on unpublished, non-peer-reviewed industry studies.
- In March 2010, just months after the release of Carrasco's findings, a court in Santa Fe province in Argentina banned the spraying of glyphosate and other agrochemicals near populated areas. The court found that farmers "have been indiscriminately using agrochemicals such as glyphosate, applied in open violation of existing laws [causing] severe damage to the environment and to the health and quality of life of the residents". While the decision is limited to the area around San Jorge, other courts are likely to follow suit if residents seek similar court action.[186]
- An epidemiological study in Ontario, Canada found high levels of premature births and miscarriages in female members of farming families that used pesticides, including glyphosate.[187]

None of these cases provides unequivocal evidence that glyphosate is the culprit in causing the harm, since other agrochemicals are used in the areas concerned. This is especially so since the spread of glyphosate-resistant weeds accompanying the spread of GM Roundup Ready crops has forced farmers to use other agrochemicals, such as 2,4-D, in addition to glyphosate.[188] [189] [190] [191] [192] [193]

However, this type of uncertainty is true of all epidemiological studies, which do not show causation but only point to an association. That is why epidemiological studies need to be supported with toxicological studies on a single substance, such as Carrasco's research. His work, along with that of other independent researchers, confirms that Roundup/glyphosate is a reproductive and developmental toxin.

6. Exposure routes an escape for industry and regulators

The German agency BVL tries to dismiss Carrasco's study on the grounds that the exposure routes used (injection and culturing the embryos in solution) are unrealistic and do not reflect real-life conditions of human exposure to glyphosate. In real life, BVL says, pregnant women would be exposed to glyphosate through the skin (dermal) or by inhalation.

Increasingly, industry and its allies in government challenge the findings of independent toxicological studies on the basis that they used injection or some other exposure route that industry argues is unrealistic.[194] [195] Industry prefers oral, dermal, or inhalation exposure routes, on the claimed grounds that they better reflect real-life exposure routes for humans.

As a bonus for industry, these exposure routes can be used to argue for lax allowable daily intake levels, based on the assumption that by the time the chemical has travelled through the protective barriers of the body, such as skin and mucous membranes, and the liver, which helps to break down toxins, very little of the chemical actually reaches the body tissues. Injection, in contrast, allows the substance to bypass these protective barriers. In industry's view, this results in unrealistically high concentrations reaching the tissues. Rejecting injection as an exposure route also allows industry and regulators to exclude many independent studies with inconvenient findings from pesticide risk assessment. A more useful response would be to utilize the signalling role of independent studies and repeat them, substituting the preferred exposure route.

This is the approach recommended by Carrasco, who says that any doubts regarding the realism of his exposure routes could be cleared up by repeating Dallegrave's 2003 study,[196] using inhalation as the exposure route. This would reflect real-life conditions of humans exposed to glyphosate spraying in Argentina, where around 80% of exposure is by inhalation.[197] Dallegrave found skeletal malformations in the foetuses of rats fed orally with high doses of Roundup.[198]

Carrasco suggests that the effects reported by Dallegrave would have been even more striking if treatment had begun on the fifth day of pregnancy, rather than the sixth, as the relevant structures have already begun to form by the fifth day. Beginning treatment on the sixth day is slightly too late to maximize the effects of glyphosate.[199] This is also a shortcoming of the industry teratogenicity tests in the DAR, most of which begin dosing on the sixth or seventh day.[200]

Interestingly, recent study findings suggest that cherry-picking exposure routes may not offer industry much protection. Two recent studies, one on glyphosate, have come up with surprising findings when different exposure routes were tested in the same animal:

- A study on the controversial chemical bisphenol A (BPA) funded by the US government's National Institute of Environmental Health Sciences (NIEHS) tested the effects on rats of the chemical through two different exposure routes, injection and oral dosing. The study was commissioned in response to industry-generated criticism that the injection route of exposure was not relevant to humans, as it would lead to unrealistically high levels of active BPA in the blood. The results showed that while injection showed a seven-fold increased level over oral dosing in the first 30 minutes, after two hours the level of active BPA in the blood was similar for both exposure routes. It is important to note here that the concentration of a chemical found in blood is only an average indicator of its presence in the body and does not provide evidence about its distribution to tissues, where toxic effects occur. Interestingly, in this experiment, both exposure routes resulted in the same pre-cancerous toxic effects on the prostate, seven months after exposure. The study concluded that route of exposure is not as critical as had been thought and therefore, the injection exposure route should be acceptable for human risk assessment.[201 202]
- A study examined the rate at which glyphosate entered the body of rats and what happened to it once it was in the body. Two exposure routes were compared: oral dosage and injection. The study found that injection resulted in a considerable diffusion of glyphosate into the tissues. When given orally, glyphosate was more slowly absorbed but also took longer to clear from blood than when given by injection. Some of this glyphosate was broken down into AMPA (glyphosate's main metabolite/breakdown product). Because glyphosate and AMPA were cleared from blood more slowly after oral dosing, they could be distributed to body tissues to exert systemic toxic effects.[203]

These findings suggest that industry's insistence on oral, dermal, and inhalation routes is based on incorrect assumptions about what happens to toxins inside the body. While received doses may vary according to different exposure routes, this should be tested and not taken on faith.

Nevertheless, as we have seen above (Section 4.2), EFSA recently incorporated industry's

preference for these exposure routes into a Guidance document on the use of science in industry dossiers under the new pesticide regulation 1107/2009.[204] At one stroke, EFSA gave industry permission to exclude from its dossier any study that does not use oral, dermal, or inhalation exposure routes – without any requirement to further investigate the findings by repeating the study with an "approved" exposure route. This will exclude the findings of many independent scientists, including Carrasco, from the risk assessment.

7. The question of doses

BVL says the fact that Carrasco found malformations from concentrations of Roundup and glyphosate below levels used in agriculture is irrelevant to human risk assessment. It says comparison with internal doses received by exposed humans would be more relevant but still cannot tell us what really matters – the doses received by the developing human foetus in the uterus.

However, BVL must know it is asking for the impossible, since it would be considered unethical to perform toxicological experiments on human foetuses to ascertain the doses of glyphosate they receive – and the new EU pesticide regulation forbids human experimentation.

Nevertheless, Carrasco points out that it would be easy to check whether people exposed to Roundup/glyphosate spraying accumulate glyphosate in their blood. If they do, the glyphosate could circulate and expose multiple tissues in the body to different concentrations of the chemical, producing different effects.[205] One study that measured pesticide residues in the blood of pregnant and non-pregnant women found glyphosate residues in the blood of 5% of non-pregnant women.[206] A study on rabbits suggests that glyphosate may accumulate in body tissues, based on its damaging effects on the sperm six weeks after exposure.[207] [208]

7.1. Did Carrasco use inappropriately high doses?

In its response to Carrasco, Monsanto/Dow argues that Carrasco used "inappropriately high" and "unrealistic" doses.[209] These doses, Monsanto/Dow says, are far higher than the already high doses used in other experiments that have been shown not to cause malformations.

Monsanto/Dow first addresses the frog embryo injection experiments. It says that Carrasco's team

> exposed two-cell frog embryos via direct injections of 360 pg and 500 pg glyphosate acid per cell, bypassing the developing amphibian protective gel coat. Assuming a cell diameter of 1mm to determine spherical volume, the cellular doses are approximately 690 to 950 µg/L within each treated cell.[210]

But this is not an inappropriately high dose. This is made clear by some simple calculations based on Monsanto/Dow's own paper. The Monsanto/Dow authors state elsewhere in their paper that a 400 mg/kg dose of glyphosate, delivered through feeding, results in a blood concentration of 4.6 µg/ml. Animal studies typically use between 50 and 500 mg/kg bw/d doses. Making a linear extrapolation (as the authors themselves do for other purposes), a 50 mg/kg dose should result in a blood concentration of 0.575 µg/ml, or 575 µg/L. Therefore the range of blood concentrations achieved in animal studies would be in the range of 575 to 5750 µg/L. Clearly, the concentrations achieved in the frog embryos (690 to 950 µg/L) are comparable to the blood concentrations achieved in animal feeding studies. So the Monsanto/Dow authors' claim that these are unreasonably high concentrations is not warranted.

Above-lethal doses?

Turning to Carrasco's frog embryo incubation experiments, Monsanto/Dow says that the concentrations used were 9–15 times greater than the acute LC50 value for frog embryos of the same species (LC50 is the concentration needed to kill 50% of experimental animals).[211] Monsanto/Dow

cites as its authority for this argument a study by Edginton and colleagues (2004).[212]

But Monsanto/Dow is not comparing like with like. Carrasco points out that Edginton's team used a different glyphosate formulation, which could have different effects and a different LC50 value.[213] Edginton's team stated that the surfactant POEA was the major toxic component of the formulation, so the two experiments are not comparable: it is not known to what extent the toxic effects were due to the POEA. POEA is known to have a synergistic effect with glyphosate, enhancing its toxicity.[214] Carrasco adds that the LC50 value is not relevant to an examination of what happens to the surviving embryos over time.

Moreover, Carrasco says that the doses he used were extremely low. Even the injection doses were far below what has been accepted as lethal.[215] Carrasco reports that treatments at 1/5000 to 1/3000 dilutions of glyphosate herbicide resulted in extremely low mortality of frog embryos, nowhere near the 50% mortality that would be expected at the true LC50.[216] Thus the Monsanto/Dow authors' claim that the effects observed by Carrasco were acute toxicity effects from inappropriately high doses is not supported.

Carrasco's argument is confirmed by the study of Dallegrave (2003), which found similar malformations at sublethal doses.[217] Monsanto/Dow avoids this issue by not even mentioning Dallegrave's study in its response to Carrasco.

The chicken egg experimental doses

Monsanto/Dow says that Carrasco's experiments with fertilized chicken eggs used an "unrealistic" exposure route by "opening a window in the shell and directly dosing 20 µL of 1/3500 and 1/4500 dilutions of glyphosate formulated product (2.0 and 1.6 µg/chicken embryo)." The implication is that due to this choice of exposure route, the doses that the embryos were exposed to were unrealistically high.

But this is untrue. Using the Monsanto/Dow authors' own estimate that 20µL of a 1/4500 dilution of glyphosate formulated product translates into about 2 µg glyphosate injected into the egg, and assuming that the volume of an egg is about 35 mL, the actual concentration of glyphosate within the egg would be about 57 µg/L. This is much lower than the blood concentrations of glyphosate that would be expected in animal toxicity studies (575 to 5750 µg/L, see above), according to Monsanto/Dow's own calculation methods.

Inappropriate comparison with rat study

As evidence for its argument that Carrasco's doses were unrealistically high, Monsanto/Dow cites a study on the fate of glyphosate orally fed to rats. The study found that a 400 mg/kg oral dose of glyphosate resulted in a maximum blood concentration of 4.6 µg/mL.[218] Monsanto/Dow extrapolates from this study to calculate that the dose necessary to produce a blood concentration in rats of 72 µg/mL (as in the low dose of 72000 µg/L in Carrasco's frog embryo culture experiments) would be over 6200 mg/kg bw (72 µg/mL / 4.6 µg/mL x 400 mg/kg bw = 6261 mg/kg bw).

Thus, Monsanto/Dow calculates that the *in vitro* concentration used by Carrasco's team was equivalent to a glyphosate oral dose to rats of 6261 mg/kg bw. Monsanto/Dow says:

> This dose is over an order of magnitude greater than the already high doses of glyphosate shown not to cause developmental or reproductive effects in rats and rabbits (NOAELs), which are used for risk assessment purposes by some regulatory authorities to establish safe human allowable daily intakes (ADIs).[219]

But the comparison made here is not appropriate. It is not justified to assume that an experimental model designed to track the fate of orally administered glyphosate in rats can be used to predict frog embryo uptake of glyphosate from the culture solution. Monsanto/Dow incorrectly attempts to make a parallel between the cells of the rat, bathed in blood containing 4.6 µg/mL of glyphosate, and a frog embryo bathed in a medium containing 72 µg/mL glyphosate, and says that the concentration used for the frog embryos is huge and physiologically inappropriate compared to that used in the rats.

This conclusion depends on the assumption that glyphosate crosses the membrane of the rat cells and the outer membrane of the frog embryo with equal ease. However, these two membranes are very different in structure and function. The frog embryo membrane is the embryo's sole defense against every physical and chemical challenge that it might encounter and must therefore be very protective, while the cells of the rat are defended by many different protective mechanisms, which operate before a challenge ever reaches the individual cells of the rat. This makes it unnecessary for the cellular membrane of rat cells to possess the protective function and structure of the frog embryo membrane.

Thus we would expect that exposing rat cells to blood containing a concentration of 4.6 µg/mL glyphosate would result in a much higher concentration of glyphosate within the rat cells than would be the case if a frog embryo were exposed to that concentration, and that it would be reasonable to expect that a significantly higher concentration of glyphosate, for instance, 72 µg/mL, would be required to achieve a concentration of glyphosate within the frog embryo that would be equivalent to the concentration achieved within the rat cells when exposed to blood containing 4.6 µg/mL of glyphosate.

Thus Monsanto's claim that the concentration used by Carrasco is extremely high and is equivalent to an oral dose of 6261 mg/kg bw is a gross overestimation.

The evidence that the concentrations of glyphosate used in the frog embryo studies were appropriate is Carrasco's observation that mortality of the embryos was very low, yet dose-dependent effects of glyphosate were observed.

Monsanto/Dow claims that "high doses of glyphosate" have been "shown not to cause developmental or reproductive effects in rats and rabbits" in studies used by regulatory authorities to set the acceptable daily intake or ADI. But this is false, as we have shown above (see Section 3). These industry studies did show teratogenic effects of glyphosate, even at low doses. The ADI set by Germany ignores these effects and is incorrect.

Body burdens of glyphosate

Monsanto/Dow dismisses the concerns raised by Carrasco and colleagues about the risk to people living close to fields where glyphosate herbicides are sprayed. Monsanto/Dow uses findings from the Farm Family Exposure Study (FFES)[220] as evidence that the doses used in Carrasco's work and his claim of a link between pesticide exposure and birth defects in Argentina are unrealistic.

The FFES measures urinary glyphosate concentrations for farmers, their spouses, and their children. The study concludes, reassuringly, that the maximum systemic dose to spouses in the FFES was 0.04 µg/kg body weight, with more than 95% of the spouse exposures below the limit of detection.

But the FFES authors themselves acknowledge that the results of their US-based study depend on the method of glyphosate application, the procedures used by the farmers, and the care with which those procedures are carried out. The circumstances in Argentina differ from those in the US on all these counts. Much of the glyphosate application is conducted by aerial spraying and reports from Argentina suggest that little care is taken of impacts on the environment or human health. On this basis, it is not justified to use the FFES as the basis for evaluating Carrasco's work.

The authors of the FFES acknowledge that the nature of the study may well have motivated participating farmers to take extra care in their work and that therefore this study may not reflect real world conditions, even in the US. It should also be remembered that the FFES was sponsored by the pesticide industry, as were other studies that Monsanto/Dow cite to back up their claims of the safety of glyphosate. Sponsors, as stated in the paper, were Bayer, Dow, DuPont, FMC, Monsanto, Syngenta, and the American Chemistry Council. The lead author, Acquavella, was an employee of Monsanto. A second author was an employee of the industry consulting firm Exponent.

For all these reasons, we suggest that the FFES is likely to paint a picture that is not "real-world", but highly idealized. As stated by Mage in his critique of the FFES, a study that randomly and

frequently assesses glyphosate burdens in farmers and their families over a long period of time would provide a more realistic assessment of exposure.[221]

This is borne out by results of another study, which is relevant to this discussion but is not mentioned by the Monsanto/Dow authors. In a study investigating pesticide exposure in farm and non-farm families in Iowa, Curwin (2007) found that 75% of farmers, 67% of wives, and 81% of farmers' children were carrying urinary burdens of more than 900 ppb of glyphosate (0.9 mg/kg bw). In contrast, the FFES reported average daily urinary burdens of glyphosate ranging from 1 to 6.4 ppb on different days of the study for farmers, and with averages close to zero ppb for wives and children (less than 25% of subjects were reported to have any detectable urinary glyphosate burden).

Regarding the FFES, we conclude that, as has been found time and time again, industry-sponsored studies generate results that are unrealistic, when compared with independent studies such as Curwin's.

We also conclude from all the evidence above that Carrasco's doses were realistic and that they add to the existing body of industry and independent studies showing that glyphosate is teratogenic.

8. The choice of experimental animals

BVL says in its response to Carrasco that while developmental mechanisms in frogs and chicken embryos are similar to those of humans, they respond differently to toxins because frogs and chickens lack the protection of a placental barrier – their embryos develop outside the mother's body. BVL says humans and other mammals, in contrast, have a placental barrier that lends some protection against toxins passing from the mother's blood supply to that of the foetus. Therefore, BVL says, findings in frog and chicken embryos cannot be extrapolated to humans and doses of glyphosate reaching the human foetus are unknown.

However, BVL fails to acknowledge research showing that a significant percentage of glyphosate crosses the human placental barrier and enters the foetal compartment.[222] BVL must produce data to back up its implication that the human placental barrier provides protection against glyphosate exposures.

In addition, Dallegrave's 2003 study found skeletal malformations in rats treated with Roundup.[223] Rats are mammals, so BVL cannot dismiss this study on grounds of the wrong choice of experimental animal. But BVL finds another reason to dismiss Dallegrave's study, wrongly claiming that it found no craniofacial malformations (see Section 5, above).

9. South America's responsibility?

BVL implies that the problems with glyphosate raised by Carrasco's research are South America's responsibility. It says, "Even if there were indications for an increase in malformations because of extensive exposure to pesticides in South America, the state authorities in these countries would be responsible to initiate more in-depth investigations. Taking into account the very different application conditions and the uncertainties with regard to the plant protection products and human exposure, such findings would not automatically give rise to concern about the safety of glyphosate-based herbicides in Europe."

It is true that application conditions and exposures in Europe would be different from those in South America. But BVL and the Commission have made no attempt to define how they would differ, especially in the light of the possible cultivation of glyphosate-tolerant crops in the EU. BVL's statement is inadequate, for the following reasons.

Toxicological findings are not confined within national boundaries

In its discussion of possible effects of Roundup/glyphosate on humans, BVL avoids mentioning

the toxicological findings on Roundup and glyphosate. Some of these, such as those of Séralini's team, found effects in human cells and are relevant to humans. While BVL disingenuously confines its discussion of effects on humans to South America, toxicological findings in human cells, and findings in mammals such as in Dallegrave's studies, apply to all countries where Roundup/glyphosate is used.

Also, glyphosate-tolerant crops carrying glyphosate residues enter the European food chain via animal feed and soy products eaten by humans. The Commission must investigate current and potential future exposures and their relationship to findings in the independent scientific literature.

The political climate in South America is problematic

Some South American economies have become highly dependent on the GM soy/glyphosate agricultural model, so central and regional government authorities are reluctant to challenge it. The Argentine government has come to rely on export taxes on soybeans, which reached 35 per cent in 2010.[224]

In Argentina, after Carrasco announced his findings, a group of environmental lawyers launched a lawsuit petitioning the government to ban glyphosate. But Guillermo Cal, executive director of CASAFE (Argentina's crop protection trade association), said a ban would mean "we couldn't do agriculture in Argentina".[225]

Argentine scientists and experts who have produced evidence of problems with the GM soy/glyphosate model report harassment and censorship.[226] [227] [228] But even in these difficult conditions, they and their international colleagues have collectively produced more than enough evidence to indicate that there are serious problems with the GM soy/glyphosate agricultural model.

Europe has a moral responsibility to its supplier countries

As much of the glyphosate-tolerant soy sprayed with glyphosate herbicides in South America is imported to feed European livestock, Europe is to some extent responsible for the situation in South America. The principle of moral responsibility for human rights abuses in supplier countries has been accepted since eighteenth-century debates about the slave trade.

Europe is considering adopting the GM crops/glyphosate farming model

Applications are in the approvals pipeline for the cultivation in Europe of several glyphosate-tolerant GM maize varieties, including Monsanto's NK603[230] and MON89034 x MON88017.[231] If glyphosate-tolerant crops are approved for cultivation in the EU, then the South American experience with GM soy and glyphosate could be replicated in Europe. BVL's attempt to draw a curtain over the South American experience is irresponsible because it ignores the potential impact of this carcinogen and teratogen on European farmers, their families, and the public.

POEA: Case study in regulatory weakness

BVL's only decisive recommendation in its response to Carrasco is that more toxicity tests should be conducted on the effects on aquatic organisms of the Roundup adjuvant or added ingredient, POEA (polyethoxylated tallow amine). POEA is added to glyphosate herbicides as a surfactant or wetting agent, to enable the glyphosate to penetrate the plant. Unfortunately, POEA is highly toxic to human cells as well as increasing the toxicity of glyphosate by allowing it to penetrate the cells more easily.[232]

While action on POEA would be welcome, focusing only on this substance distracts from Carrasco's finding that pure glyphosate is a developmental and reproductive toxin.[233]

The case of POEA shows the weakness of EU regulators in dealing with industry. The German government recommended as long ago as 1999 that POEA should be phased out in the EU. Monsanto disagreed.[234] Eleven years later in 2010, the German government was still asking for action on POEA – and still being ignored by industry and EU regulators.[235] It has resorted to taking its own measures to restrict the use of POEA within Germany.

10. Science divided

Carrasco notes in his reply to Monsanto/Dow that discussion of toxics risk assessment has separated into two diverging strands:

> Rather than pointing out shortcomings of our research, the [Monsanto/Dow] letter illustrates the increasing difficulty in dialogues between those with a vested interest in product sales and independent researchers who wish simply to understand whether the said products are safe.[236]

It is to be expected that industry should look after its own interests. But it is inexcusable for the public body BVL to follow Monsanto/Dow in what seems to be a desperate attempt to dismiss any possibility of Roundup/glyphosate's teratogenicity rather than ordering further investigations to clear up uncertainties. However, the existing body of evidence on Roundup/glyphosate is more than sufficient to justify that BVL advise the EU Commission to invoke the precautionary principle and conduct an immediate review of the herbicide.

11. Another worrying study on Roundup dismissed

BVL's response to Carrasco's study was not a one-off. In 2009, BVL issued a similarly dismissive response[237] to a study by Benachour and Séralini, which found that Roundup caused total cell death in human umbilical, embryonic, and placental cells within 24 hours.[238] In these experiments, Roundup obtained from the market was diluted by 100,000 times – far below the concentrations used when the chemical is sprayed on GM RR crops.

The researchers tested Roundup formulations, as well as pure glyphosate, AMPA (glyphosate's main breakdown product), and the adjuvant POEA. They concluded that the presence of adjuvants increases the permeability of human cells to Roundup and amplifies the toxicity of glyphosate:

> The proprietary mixtures available on the market could cause cell damage and even death around residual levels to be expected, especially in food and feed derived from R (Roundup) formulation-treated crops.[239]

BVL's response to this complex and worrying study was as brief as it was inadequate. Passing over the findings on the toxicity of glyphosate and AMPA, BVL only admitted that POEA ("tallow amines") was a problem. It said it had asked manufacturers of glyphosate herbicides to replace tallow amines with less problematic ingredients within two years. That was the sum of BVL's recommendations.

In choosing to focus solely on the adjuvant POEA, BVL simply ignored all the harmful effects that the researchers found with the Roundup formulations as a whole, their active ingredient glyphosate, and glyphosate's main breakdown product, AMPA. So Roundup continues to be marketed without restriction and people continue to be put at risk.

12. What's wrong with the current approval of glyphosate?

Glyphosate's current approval in the EU is based on the 2002 review, carried out under the old pesticides regulation 91/414.[240] The 2002 review assesses glyphosate, the glyphosate derivative herbicide glyphosate trimesium, and the glyphosate metabolite (breakdown product) AMPA.

The review exemplifies the general failings of the old pesticides approvals system:

- Insulation from independent peer reviewed scientific findings
- Old, outdated, and badly informed claims for glyphosate's safety go unchallenged

- Virtually exclusive reliance on industry studies for the safety assessment, with the inherent conflicts of interest
- Reliance on studies with old and outdated protocols
- Reliance on dubious and outdated assumptions
- Lack of transparency
- Failure to test the complete glyphosate formulations as they are sold.

A detailed breakdown of these factors follows.

12.1 Open peer reviewed scientific literature is denied

There is broad agreement in the scientific community that peer reviewed publication is the best currently available method to ensure reliable scientific data.

There are undoubted flaws with the peer review process – including publication bias, where certain types of results are more likely to be published than others,[241 242 243] and pressure being placed on journal editors not to publish, or to retract, certain findings.[244 245 246] Some journals have been generated or "captured" by industry and use industry-connected peer reviewers.[247]

In spite of these problems, the strength of the peer review process is that studies in the open literature can be evaluated by independent experts. Their findings can be confirmed, built upon, or contradicted by further studies.

The public, too, has been educated to respect the peer review process and to expect scientific claims to be validated in this way. The part-industry-funded UK-based group Sense About Science, which calls itself "an independent charitable trust promoting good science and evidence in public debates"[248] and promotes the safety of controversial technologies like genetically modified foods,[249] set up an entire project to convince the public that peer review is "an essential arbiter of scientific quality".[250] In its guide for the public on peer review, *I Don't Know What to Believe*, Sense About Science says:

> Unpublished research is no help to anyone. Scientists can't repeat or use it and as a society we can't base decisions about our public safety – or our family's health for example – on work that has a high chance of being flawed.[251]

Given such influential messages, it would shock the public to realize that in the pesticide approvals process, peer reviewed open literature is not normally considered. The studies on which the 2002 EU review of glyphosate is based, as is the norm with pesticides, were generated and submitted by industry.[252] The conclusions about the health hazards of glyphosate in the 2002 EU review are strikingly at variance with the findings from the independent scientific literature, as the analysis below shows.

Genotoxicity

The 2002 review flatly states that glyphosate and glyphosate trimesium are "not genotoxic" (causing damage to DNA). It is difficult to understand how this conclusion could be reached, given that even industry studies from the 1980s found that Roundup caused chromosome aberrations and gene mutations in mice lymphoid cells.[253 254]

In addition, a number of studies showing that glyphosate and Roundup are genotoxic existed in the peer reviewed literature even at the time of the 2002 review. Findings include:

- Roundup increases the frequency of gender-linked lethal recessive mutations in fruit flies (these mutations are normally only seen in males).[255]
- Roundup increases the frequency of DNA adducts (the binding to genetic material of reactive molecules that lead to mutations) in the liver and kidneys of mice at all three doses tested. The response was dose-dependent.[256]
- Roundup causes increased frequency of sister chromatid exchanges in human lymphocytes (white blood cells), even at the lowest dose tested.[257]
- Mice injected with glyphosate and Roundup show increased frequency of chromosome damage and increased DNA damage in bone marrow, liver, and kidney.[258]

Numerous additional recent studies confirm genotoxicity:

- Roundup damages the DNA in the blood cells of European eels at environmentally relevant concentrations.[259]
- Roundup has adverse effects on the cells of various organs in fish exposed at sublethal

concentrations of 5–15 ppm (a typical concentration in a post-application site). Effects include hyperplasia (increased proliferation of cells) and increased activity of metabolic enzymes.[260]

- Glyphosate-based herbicides cause increased frequency of DNA strand breaks and cell nucleus abnormalities indicative of mutagenic stress in goldfish at low doses (5–15 ppm).[261]
- Glyphosate-based herbicides cause DNA damage and endocrine disruption in human cells at levels up to 800 times lower than glyphosate residue levels allowed in some GM crops used for animal feed in the United States.[262]
- Glyphosate-based herbicides inhibit RNA transcription and delay hatching in sea urchin embryos at a concentration well below that recommended for commercial spray application. The Roundup surfactant polyoxyethylene amine (POEA) is highly toxic to the embryos when tested alone and so could contribute to the inhibition of hatching.[263]
- Glyphosate-based herbicides and glyphosate's main metabolite (environmental breakdown product), AMPA, alter cell cycle checkpoints in sea urchin embryos by interfering with the physiological DNA repair machinery. Such cell cycle dysfunction is seen from the first cell division in the sea urchin embryos.[264 265 266 267] The failure of cell cycle checkpoints is known to lead to genomic instability and the possible development of cancer in humans. Studies on glyphosate and AMPA suggest that the irreversible damage that they cause to DNA may increase the risk of cancer.[268 269]
- An epidemiological study in Ecuador found a higher degree of DNA damage in people living in an area that was aerially sprayed with glyphosate compared with those living 80 kilometres away.[270]

AMPA, glyphosate's main breakdown product (metabolite), is also genotoxic in isolation. The 2002 review, on the basis of the industry studies, calls AMPA "less toxic than the parent compound".[271] The ECCO Panel states, "AMPA is not of toxicological significance."[272] However, an independent study found that AMPA is genotoxic, damaging DNA in human cells at very low doses and in mice at a dose of 200–400mg/kg.[273]

Carcinogenicity

The 2002 review claims "no evidence" of carcinogenicity for glyphosate and glyphosate trimesium. But glyphosate was known to have carcinogenic effects long before the 2002 review.

Two long-term studies on rats were conducted in 1979–1981 and 1988–1990.[274] The rats received 3, 10 and 32 mg/kg of glyphosate per day in the first study and 100, 410 and 1060 mg/kg per day in the second. The first study found a significant increase in tumours in the testes of rats fed glyphosate, but the same effect was not found in the second test using the higher doses. On this basis, glyphosate was excluded from the carcinogenic category.[275 276]

This move was based on outdated and incorrect assumptions about toxicology. It used to be thought that toxic effects increased in proportion to dose, and that there is a safe level of a chemical, below which toxic effects are not found. But toxicologists now know that these assumptions are not always true. Some chemicals have more potent effects (notably endocrine effects) at low doses than higher doses.[277] In some cases, no safe threshold can be found.[278 279] However, regulators have not revised their conclusions on glyphosate based on up-to-date scientific knowledge.

Studies from the independent literature also show that Roundup and glyphosate have carcinogenic effects:

- Glyphosate induces cancer in mouse skin[280]
- Epidemiological studies show a link between Roundup/glyphosate exposure and two types of cancer: multiple myeloma[281] and non-Hodgkin's lymphoma.[282 283 284]
- Other studies (mentioned under Genotoxicity, above) show that Roundup, glyphosate, and its metabolite AMPA cause changes to cells and DNA that are known to lead to cancer.[285 286 287 288 289 290]

Neurotoxicity

The 2002 review of glyphosate claims "no relevant effects" in tests for delayed neurotoxicity. But glyphosate is an organophosphate, a class of

chemicals known to have neurotoxic effects, so claims of "no relevant" neurotoxic effects demand a strong and transparent evidence base to back them up.

In fact, studies from the open literature have found neurotoxic effects of glyphosate:

- An epidemiological study carried out in Minnesota, USA found that the children of pesticide applicators exposed to glyphosate had an increased incidence of neurobehavioral disorders.[291]
- In an acute poisoning incident, a man who accidentally sprayed himself with glyphosate developed the neurological disorder Parkinsonism.[292]
- A toxicological study on rats found that glyphosate depletes the neurotransmitters serotonin (serotonin is associated with feelings of well-being and is known as the "happiness hormone") and dopamine.[293]
- Glyphosate causes a loss of mitochondrial transmembrane potential (a hallmark of cellular injuries) in rat brain cells.[294]
- Glyphosate and Roundup act synergistically with the organophosphate insecticide diazinon in neuroblastoma (nerve cancer) cells. Glyphosate and Roundup become more neurotoxic when the cells have been pre-exposed to diazinon. Roundup is more toxic than glyphosate and produces effects at a concentration as low as 10 ppb, which is equivalent to a glyphosate concentration of 0.5 nM. Unusual dose-response relationships are found with both glyphosate and Roundup, which the authors say merit further investigation as they indicate that the relationship between concentration and toxicity at low concentrations may not be entirely predictable.[295]

Reproductive and developmental toxicity and endocrine disruption

The 2002 review notes that studies on glyphosate and glyphosate trimesium found reduced pup weight and decrease in litter size and pup body weight gain, but says these effects are confined to high, "parentally toxic doses". The review adds that effects include lower number of viable foetuses and reduced foetal weight, retarded ossification (bone formation), and higher incidence of skeletal and/or visceral (internal organ) anomalies. Effects of glyphosate trimesium include increased post-implantation losses (miscarriage), reduced foetal weight, and increased incidence of rib "variations" at maternally toxic doses.

The 2002 review gives a developmental NOAEL (the highest level at which the effect being looked for is not found) of 300 mg/kg bw/d for glyphosate and 40 mg/kg bw/d for glyphosate trimesium. However, studies from the open literature have found adverse reproductive and developmental effects, in some cases at much lower levels. While we have discussed some of these studies in the above sections, we provide a comprehensive summary as follows:

- Glyphosate herbicide alters hormone levels in female catfish and decreases egg viability. The study concludes that the presence of glyphosate in water is harmful to catfish reproduction.[296]
- Roundup disrupts production of the steroid hormone progesterone in mouse cells by disrupting expression of a regulatory protein.[297]
- Roundup causes decreased sperm numbers and increased abnormal sperms in rats.[298]
- A commercial formulation of glyphosate was found to be a potent endocrine disruptor in rats, causing disturbances in their reproductive development after they were exposed during puberty.[299]
- In human cells, glyphosate-based herbicides prevent the action of androgens, the masculinising hormones, at levels up to 800 times lower than glyphosate residue levels allowed in some GM crops used for animal feed in the United States. DNA damage is found in human cells treated with glyphosate-based herbicides at these levels. Glyphosate-based herbicides also disrupt the action and formation of estrogens, the feminizing hormones.[300] This in vitro study found the first toxic effects of glyphosate-based herbicide at 5 ppm, and the first endocrine disrupting actions at

0.5 ppm – 800 times less than the 400 ppm level authorized by the US Environmental Protection Agency (EPA) in some animal feeds.[301 302]

- Glyphosate acts synergistically with estrogen, disrupting estrogen-regulated gene expression in human cells.[303]
- Glyphosate is toxic to human placental cells and this effect increases in the presence of Roundup adjuvants. Roundup acts as an endocrine disruptor, inhibiting an enzyme responsible for estrogen production. The authors conclude that Roundup could cause reproductive problems in humans at levels below those used in agriculture.[304] The authors suggest that their results could explain epidemiological findings of increased premature births and miscarriages in female members of farming families using glyphosate.[305 306]
- Glyphosate and Roundup damage human embryonic cells and placental cells, in concentrations well below those recommended for agricultural use. The study's authors conclude that Roundup may interfere with human reproduction and embryonic development.[307]
- The foetuses of rats fed orally with high doses of Roundup had increased incidence of skeletal malformations.[308]
- Roundup causes malformations in frog and chicken embryos at doses much lower than those used in agricultural spraying.[309] Malformations were of the craniofacial and neural tube type (of the skull, face, and developing brain and spinal cord).

Conclusion of open peer-reviewed literature on health effects

Both the existing pesticides regulation, 91/414, and the new regulation, 1107/2009, require that a pesticide should not have any harmful effect on human or animal health.[310 311] The new regulation is stricter, since "vulnerable groups" must be considered in the human health assessment and known "cumulative and synergistic effects" of the pesticide must be addressed.[312] Clearly, glyphosate herbicides do not even meet the requirements of the old regulation, so their approval should be reviewed immediately with a view to restricting or banning their use.

12.2. Outdated and badly informed claims go unchallenged

The discussion between industry, the rapporteur Germany, member states, and the ECCO Panel that led to the 2002 review includes numerous old, outdated, and badly informed claims for the safety of glyphosate and its breakdown product AMPA. Many of these claims have been superseded or discredited by independent studies – but they passed through the review process unchallenged and have remained in place in the regulatory system ever since. Similarly, concerns are raised but not followed up.

Anyone who is informed about the current state of knowledge on glyphosate cannot fail to be alarmed by these claims and uninvestigated concerns. There are too many to cover fully in this report, but a few examples follow.

Unresolved concerns about salivary gland lesions

Concerns about repeated findings of salivary gland lesions in experimental animals treated with glyphosate are expressed throughout the DAR materials and mentioned in the 2002 final review report. However, nobody seems to know what the lesions mean, and no attempt is made to find out. A comment by the ECCO Panel is typical:

> Histological effects were observed in salivary glands in the 6 and 12 month dog study, however, since these lesions were considered without functional consequence or long term effects they were not considered to be adverse.[313]

The regulators should have insisted that these experiments be continued for a longer period, so that the true consequences of these lesions were revealed. Salivary gland lesions can be pre-cancerous.

Failure to consider endocrine disruption

The ECCO Panel says, "Various literature

references suggest that glyphosate is an endocrine disruptor." Again, the panel has no idea what to make of these findings: "The group recognised that there was no guidance available regarding how such information should be used so it was agreed that the rapporteur should consult the Chairperson of the mammalian toxicology meeting at the BBA [German Federal Ministry for Food, Agriculture and Consumer Protection] to see if this is a concern."[314] The final review report of 2002 does not mention endocrine disruption – sufficient reason in itself why the current approval of glyphosate is inadequate. However, independent studies show that glyphosate herbicides are endocrine disruptors.[315 316 317]

Failure to consider the impact of glyphosate-resistant weeds

The DAR and 2002 review report were compiled before the problem of glyphosate-resistant weeds became widespread. Monsanto claims in the DAR materials that it has tested over 500 samples and found that only two locations in Australia were affected. The plant involved was an annual rye grass.[318] The UK Pesticides Safety Directorate (PSD) comments, "It is likely that resistance is low, although there have been two further reports of possible cases in America and Asia."[319] Since the EU Commission's 2002 approval of glyphosate, a large number of independent studies and media reports have documented the extensive and serious problems caused by glyphosate-resistant superweeds, especially in North and South America.[320 321 322 323 324 325 326 327 328 329 330 331 332 333 334] Glyphosate's current approval does not take this into consideration and a critical re-assessment is urgently needed.

In addition, the risk assessment should consider the inevitable shift in herbicide use after glyphosate-resistant weed populations become widespread. The published studies and articles cited above show that weeds evolve resistance to glyphosate within 2–6 years of cultivation of genetically modified (GM) Roundup Ready crops. This is less time than the approval period of a pesticide in the EU – formerly ten years, now 15 years. Once resistant weed populations are established, farmers have to resort to other potentially even more toxic herbicides, including 2,4-D, to try to control glyphosate-resistant weeds.[335 336 337 338]

The chemical companies Dow, DuPont, Bayer, BASF, and Syngenta have responded to the superweeds problem by "engineering crop varieties that will enable farmers to spray on the tough old weedkillers freely, instead of having to apply them surgically in order to spare crops", according to a report in the Wall Street Journal.[339] Bayer has patented a GM soybean with tolerance to the herbicide glufosinate ammonium.[340] Studies show that glufosinate ammonium is a neurotoxin[341] and causes birth defects in mice.[342] Monsanto plans to release a dicamba-resistant GM soybean in 2013.[343] These developments are relevant to Europe as Romania is lobbying the EU for permission to cultivate GM soy.[344]

A new generation of herbicide-resistant crops is being engineered with stacked traits to tolerate multiple herbicides.[345] But weed scientists have commented that these new GM crops will only buy growers a little more time until weeds evolve resistance to other herbicides.[346] In fact, weed species resistant to dicamba and 2,4-D already exist.[347 348]

The existing approval of glyphosate fails to take into consideration the chemical treadmill resulting from the emergence of glyphosate-resistant weeds – and the consequences to human health and the environment. While a full consideration of this issue is beyond the scope of this report, it needs to be addressed in the risk assessment of glyphosate as it is a hazard inherent in the use of the herbicide.

Incorrect claim about biological availability of glyphosate

The UK Pesticides Safety Directorate (PSD) notes that the issue of a waiting period between glyphosate spraying and re-entry into fields in order to protect humans, livestock, and plants, is not properly dealt with in Germany's DAR. However, the PSD immediately dismisses this concern:

> This should not be an issue for glyphosate as it is not usually biologically available once it contacts soil.[349]

But this claim was not true even at the time of the DAR. A 1983 study showed that glyphosate persists in sandy loam soil and is not inactivated in the 120 days prior to planting. Plants growing in the glyphosate-treated soil showed decreased nitrogen fixation, root nodule numbers and root weights – indicating that glyphosate was biologically available and toxic to plants 120 days after application.[350]

A new risk assessment should address the issue of the re-entry period.

Incorrect claim about biological activity of AMPA

Monsanto says AMPA's long persistence in soil is of no "regulatory concern" because "AMPA is biologically inactive".[351] But a 2004 study showed that AMPA causes injury to glyphosate-tolerant and non-glyphosate-tolerant soybeans. Findings are the same when the AMPA is deliberately applied and when it forms from the breakdown of applied glyphosate. The study concludes that soybean injury to glyphosate-tolerant soybeans from glyphosate is due to AMPA formed from glyphosate degradation.[352] Therefore AMPA is biologically active.

It is clear that the documents on which the existing approval of glyphosate is based are out of date and out of touch with current scientific knowledge and farmer experience.

12.3. Industry tests have conflicts of interest

There are clear conflicts of interest in the 2002 review of glyphosate in that the companies that commissioned the tests and submitted the data also market the product. The fact that this is the norm in pesticides approvals does not make it acceptable. The main data submitters were Monsanto, Cheminova, Feinchemie, and Syngenta (formerly Zeneca).[353] These companies manufacture and/or sell glyphosate herbicide. Monsanto, Syngenta, and Dow AgroScience (another data submitter) also sell GM glyphosate-tolerant seeds.

12.4. Industry tests are old and use outdated protocols

Anyone who is familiar with the rapid evolution of scientific knowledge relating to glyphosate over the past decade would be shocked to see that its current approval depends mostly on studies dating from the 1990s – some from as far back as the 1970s and 1980s.

In the 1990s glyphosate was still frequently claimed to be safe and environmentally friendly. Few independent studies were in existence to contradict these claims. Even so, by 1996, independent science had moved on to such an extent that a New York court ruled that Monsanto was no longer allowed to claim that Roundup was "safe, non-toxic, harmless or free from risk", or as biodegradable.[354] During the 2000s, a battery of independent scientific studies showed serious toxic effects from Roundup and glyphosate. None of this knowledge has made its way through to the regulatory system.

12.5. The approvals system is not transparent

In theory, the industry dossier of studies on a pesticide and the regulators' discussions and justifications for their final decision are in the public domain. In practice, it is not so straightforward. The authors of this report had difficulty obtaining the materials. When they were finally obtained, a part of Germany's DAR was withheld. The materials were confusingly presented and difficult to interpret. In the DAR itself, justifications for important decisions are not recorded in detail.

Data protection is claimed for many of the industry studies in the 2002 review of glyphosate on grounds of commercial confidentiality. This is standard practice, ostensibly because it prevents data from getting into the hands of competitor companies. Unfortunately, it also prevents the public and independent scientists from evaluating the data. So tests of unknown quality and unknown reliability are used to allow pesticides onto the market.

There is also no transparent system in place for considering independent scientific data that

comes to light after the approval, as is clear from the case of Carrasco's study.

12.6. The complete formulations as they are sold were not tested

The existing review of glyphosate fails to take into account the complete formulations as they are currently sold. Glyphosate herbicides contain adjuvants (added ingredients) which are themselves toxic and which can act synergistically with glyphosate to increase its toxicity. Studies show that Roundup is more toxic than glyphosate alone because the adjuvants enable the glyphosate to penetrate human cells more easily.[355 356 357] These problems are addressed in the new pesticides regulation 1107/2009, which takes into account the toxicity of the formulation as sold. This alone is reason enough to require that glyphosate herbicides be reviewed under the new regulation without delay.

13. Conclusions and recommendations

The existing approval of glyphosate and Roundup is out of date and scientifically unsupportable. The safety assessment began badly, with a dossier of outdated industry-sponsored tests, and was progressively weakened at each stage:

- The German government produced a draft assessment report (DAR) that minimized the harm shown even in inadequate industry studies and set a dangerously high ADI for glyphosate.
- Germany's DAR was in turn whitewashed by the EU's scientific review ECCO Panel.
- Finally, the EU Commission's DG SANCO accepted these misleading reports in its 2002 review, minimizing the reproductive and developmental effects of glyphosate.

Together, these bodies must share responsibility for making claims about the safety of glyphosate that were contradicted even by the scientific knowledge current at the time. Now that scientific knowledge has moved on, glyphosate and Roundup formulations must be reviewed urgently, taking into consideration all independent scientific evidence.

The new pesticides regulation, if implemented objectively and in timely fashion, would likely result in a ban on glyphosate herbicides. But the Commission and EFSA have abnegated their responsibility to the public in allowing glyphosate a free regulatory ride until 2015, with the possibility of no review under up-to-date data requirements until 2030. Their actions flout a democratically established law and put public health at risk.

13.1. Recommendations on Roundup and glyphosate

In the interests of protecting public health, we call upon the Commission to implement the following measures on Roundup and glyphosate:

- Order an immediate withdrawal of Roundup and glyphosate until a new review can be carried out, based on the full range of up-to-date tests.
- Assess all adverse effects of Roundup and glyphosate found in the open peer reviewed scientific literature.
- Base industry tests on the findings in open literature, not only on generalized data requirements. For example, the experiments of Dallegrave should be repeated with modifications.
- Ensure that regulators look critically at the applications for GM Roundup Ready crops that are in the EU approvals pipeline instead of repeating outdated and misleading assurances about the safety of glyphosate and Roundup.

13.2. Recommendations on pesticides regulation

On pesticides regulation in general, we call upon the Commission to:

- Hold an urgent debate with the full range of stakeholders on the question: What is the point of independent science when regulators ignore it in every assessment of a pesticide? Billions of pounds of taxpayers' money go into public sector research. In our view, this type of

research, when peer reviewed and published, represents the most reliable, independent, and up-to-date knowledge on pesticides. But it appears that the Commission and regulatory bodies and agencies disagree with this view. Currently, independent scientists are wasting their time and energy as far as regulation is concerned. The Commission and other regulatory bodies must publicly explain their attitude to independent science.

- Ensure that all studies from the open scientific literature are considered in the risk assessment. Industry and the rapporteur state must not be allowed to "cherry-pick" acceptable studies on the grounds of exposure route, length of study, choice of experimental animal, etc. If there are genuine questions about the methodology of a study finding adverse effects, regulators must order it to be repeated with the desired modifications.
- Publish all industry studies on the internet as a matter of principle.
- Pay independent scientists who are actively researching and publishing in the field to review industry studies and studies from the open literature on the pesticide under review.
- Ensure that the risk assessment is based on the lowest NOAEL found in any study.
- Ensure that "reviews" or comments on studies from the open literature are written by named experts who are accountable for their views.
- Replace the current system, in which industry directly pays contract labs to carry out regulatory studies on pesticides, with a system in which industry pays into a central fund for the studies and the regulators contract out the work to independent researchers.
- Get industry out of the pesticides regulatory process. Industry should provide the pesticide and its basic compositional information – but leave the testing and evaluation (including the peer-reviewed scientific literature search) to regulators and independent scientists.
- Introduce mandatory disclosure of minutes and conclusions of meetings between EU Commission/EFSA and all stakeholders, including industry-affiliated bodies like the International Life Sciences Institute.
- Ensure that all meetings between EFSA and industry or industry-affiliated bodies such as the International Life Sciences Institute (ILSI) are open to the full range of stakeholders, including NGOs and representatives of the general public.
- Ensure full transparency of the decision-making procedure, from the initial submission of the dossier by industry to the final decision made on the pesticide.

Our examination of the evidence leads us to the conclusion that the current approval of glyphosate and Roundup is deeply flawed and unreliable. What is more, we have learned from experts familiar with pesticide assessments and approvals that the case of glyphosate is not unusual. They say that the approvals of numerous pesticides rest on data and risk assessments that are just as scientifically flawed, if not more so. This is all the more reason why the Commission must urgently review glyphosate and other pesticides according to the most rigorous and up-to-date standards.

13.3. Recommendations to the public

Until the pesticide assessment process is fundamentally reformed, we recommend to the public that they do not rely on the messages of governments or industry about pesticide safety. Instead, they should take measures to protect themselves against the harmful effects of Roundup/glyphosate and other pesticides. These include:

- Avoiding using and exposing themselves to pesticides, insofar as they have choice in the matter.
- Lobbying local authorities, farmers, and other pesticide users to disclose what they are spraying and when.
- Lobbying local authorities and other "cosmetic" users of Roundup/glyphosate and other pesticides to switch to less toxic methods of weed and pest control.
- Writing to garden centres, supermarkets, and other stores asking them not to sell Roundup/glyphosate and other pesticides.
- Supporting citizen "truth-in-labelling" schemes to inform consumers about the true risks of pesticides through accurate product labelling.

Note on citations of Germany's DAR on glyphosate

In the interests of transparency and so that readers can check the accuracy of our statements, we have uploaded onto the Internet those parts of Germany's draft assessment report (DAR) on glyphosate that we cite in the text of our report. Please note that page numbers in the references below refer to the page numbers of the pdf document, not the page numbers printed on the original documents that make up the DAR.

Our citations of the DAR begin as follows:

> Rapporteur member state, Germany. 1998. Monograph on Glyphosate. Released by the German Federal Agency for Consumer Protection and Food Safety, BVL.

Then each citation specifies a pdf file within the DAR. The URLs for each pdf file we have uploaded are as follows:

- Volume1_Glyphosat_02.pdf: http://www.scribd.com/doc/57155781
- Volume 2, Part A, Annex A: List of Tests and Studies: http://www.scribd.com/doc/57156365
- Volume 3-1_Glyphosat_05.pdf: http://www.scribd.com/doc/57155616
- Volume 3-1_Glyphosate_04.pdf: http://www.scribd.com/doc/57155694
- FullReport_Glyphosat_03.pdf: http://www.scribd.com/doc/57155540
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in food production, animal toxicological testing appears to be indispensable for the foreseeable future. And if animals are to be used in toxicological testing, it is vital that their lives are not wasted – in other words, that the results are as reliable as possible.

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Appendix: Potential for reform in pesticide use

A new EU regulation (2009/128) on the sustainable use of pesticides[358] has the potential to bring positive reforms to pesticide practices in the EU. EU member states will have to come up with a National Action Plan aimed at reducing "risks and impacts of pesticide use on human health and the environment and at encouraging the development and introduction of integrated pest management and of alternative approaches or techniques in order to reduce dependency on the use of pesticides". Among other measures, member states will have to:

- Set up programmes to monitor the effects of pesticide spraying on the health of exposed groups of people
- Minimize the use of pesticides in parks, school grounds, and public areas
- Require sellers of pesticides (including retailers who sell to the public) to provide buyers with information about the risks of the pesticide, as well as information on less toxic alternatives
- Require pesticide users to progressively reduce dependence on pesticides and to favour less toxic methods of weed and pest management.

The new regulation allows member states to set up systems to inform local people before pesticide spraying takes place, but this provision is voluntary. We argue that it should be mandatory and should order disclosure of the names of substances sprayed and the names and contact details of the parties who commission and carry out the spraying. Pesticide applicators must no longer be allowed to hide such information based on claims of commercial confidentiality.

While the new regulation contains many positive developments, much depends on how it is implemented. For example, even the old pesticide law has strict wording stipulating that a pesticide can only be approved if it has "no harmful effect on human or animal health or on groundwater" when correctly used, but this has never been properly implemented.[359]

Comments of Amis de la Terre/Friends of the Earth-France on the Renewal Assessment Report on Glyphosate 06. 05. 2014

1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)

Identity (B.1, Annex C)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Physical and chemical properties of the active substance (B.2.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Physical, chemical and technical properties of the formulation (B.2.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Further information (B.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations

Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

Further information (B.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, Annex B.3 Data on application and further information, page 7-8	***Amis de la Terre /Friends of the Earth –France*** : Worldwide there are at least 28 weed species (not only 24) for which glyphosate-resistance has been documented, comprising more than 200 populations and infesting millions of hectares (Heap 2014). Although countries with RRcrop cultivation are affected most heavily, cases of glyphosate-resistant weed species are increasingly reported from other countries too. As a result, a massive increase in herbicide amounts applied has been documented. To stop the pesticide treadmill, glyphosate use has to be restricted.	In Europe, there are more cases of glyphosate resistance than depicted in the RAR (16 cases instead of 10 and 6 species instead of 5). Contrary to the RAR, glyphosate-resistant weed species have not been found exclusively in orchards, vineyards or olive groves, but also in other crops, e.g. asparagus (Lolium rigidum in France) and alfalfa (Conyza canadensis in Greece). And Northern and Central Europe will also be affected, with Poland being already the second country after the Czech Republic to report glyphosate-resistant weeds. It will be a question of time when glyphosate-resistant weed biotypes will show up in countries such as Germany. Therefore, evolution of glyphosate-resistance will speed up in Europe too, unless use of glyphosate is severely restricted.

Methods of analysis (B.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

5. Ecotoxicology (B.9)

Birds and mammals (B.9.1 and B.9.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Aquatic organisms (B.9.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	B.9.2.2 Summary of aquatic toxicity data Page 132	***Amis de la Terre /Friends of the Earth –France***: In particular, amphibians, many of which are endangered, have been shown to be affected by glyphosate-based herbicides, possibly both their larval and adult stages (Wagner et al. 2013). Reviewing peer-reviewed studies on glyphosate impacts on amphibian, Plötner and Matschke (2012) concluded that glyphosate is itself toxic to amphibians, and surfactants such as POEA are even more so leading to abnormal behaviour, teratogenic effects and developmental failures. In addition, toxicity of glyphosate and Roundup to aquatic invertebrates such as *Daphnia magna* has been underestimated (Cuhra et al. 2013). Toxicity classification has to be revised.	Cuhra et al. (2013) found EC50 (48) values for glyphosate IPA in *Daphnia magna* that were significantly lower than the values depicted in table B.9.2-59. Testing glyphosate and Roundup for 55 days (instead of only 21 days tested in the long-term studies referred to in table B.9.2-59) led to significant reduction in juvenile size even at the lowest test concentration of 0.05 mg a.i./L. About ten times higher concentrations of Roundup affected fecundity, growth and abortion rate and at1.35 and 4.05 mg a.i./L of both glyphosate and Roundup significant negative effects were seen on most tested parameters, including mortality. Thus even low ambient concentrations of glyphosate will affect aquatic invertebrate ecology.

Section 5 - Ecotoxicology (B.9)

Bees and non-target arthropods (B.9.4 and B.9.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Earthworms and other soil non-target organisms (macro and micro) (B.9.6, B.9.7 and B.9.8)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.9.8 Effects on soil non-target micro-organisms	***Amis de la Terre /Friends of the Earth –France***: As stated in the RAR and reported by Kremer & Means (2009), glyphosate leads to significant shifts in bacterial community composition but it also affects importantfungal species, e.g. beneficial mycorrhizal fungi (Druille et al. 2013a,b). Previous use of glyphosate has been linked to increased Fusarium infection of wheat and barley (Fernandez et al. 2009). Thus impacts of glyphosate use on bacterial and fungal species that are linked to plant health and disease have to be considered too.	

Other non-target organisms (flora and fauna), sewage treatment (B.9.9 and B.9.10)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.9.9.1.4	***Amis de la Terre /Friends of the Earth –France***:	Adverse impacts of (repeated) glyphosate use on the health of non-target

Other non-target organisms (flora and fauna), sewage treatment (B.9.9 and B.9.10)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	Summary of results on non-target plants	Glyphosate can adversely impact micronutrient uptake in plants as it is a strong metal chelator (Tesfamariam et al. 2009, Cakmak et al. 2009). Even low levels of residual glyphosate in soil can greatly impede the availability and uptake of Mn, Fe, Cu, and Zn by plants and lead to their undersupply with these nutrients. Reduced disease resistance and plant growth may be the result (Johal & Huber 2009).	plants have to be taken into account, as reduced disease resistance most likely will increase use of other pesticides, e.g. fungicides that may be highly toxic too.
	Vol. 3, B.9.9.1.6 Indirect effects via trophic interactions	The Farm Scale Evaluations have shown that the quantitative loss of weeds reduces number and diversity of arthropods heavily and interrupts the food chain for farmland birds and mammals. Ample evidence of negative impacts of glyphosate on biodiversity has been collected in areas where glyphosate is used extensively, e.g. in combination with genetically modified glyphosate-resistant crops. The all-time low in the number of monarch butterflies in 2013/2014 has been attributed to the loss of their food plant (*Asclepias syriaca*) in vast areas of the United States where glyphosate-resistant crops are grown (Wade 2014).	As glyphosate is the herbicide most widely used, these massive negative impacts on biodiversity have to be considered and used as reason not to re-authorize the substance. Mitigation measures, such as buffer strips, that would be up to the individual member states will not reduce the risk of impacting biodiversity to an acceptable level – even if farmers accepted to spare buffer strips from glyphosate application which they often don't.

Section 5 - Ecotoxicology (B.9)

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	B.9.11 Surface-active substances in glyphosate-based formulations	***Amis de la Terre /Friends of the Earth –France:*** There is ample evidence that formulated products can exhibit higher toxicity. In particular, polyethoxylated alkylamines (POEA) are known to be highly toxic to cells and organisms (Mesnage et al. 2013). Glyphosate has endocrine disrupting properties which cannot only be attributed to the surfactants. Paganelli et al (2010) showed that both formulated products and the active substance have adverse effects and that glyphosate acts as an endocrine disruptor. To make agriculture in Europe more environmentally benign, it is of utmost importance that pesticide use is restricted to a much greater extent than it is actually the case. As herbicides make up the largest share of pesticides and glyphosate is the most used herbicide, regulators are obliged to not renew the approval of this chemical.	To argue, that the lead formulation MON52276 for the assessment of glyphosate does not contain POEA and that POEA-formulated products "are not expected to be neither notified nor registered in the future", is not comforting, as such products are still on the market and data about the nature and toxicity of other surfactants that replace POEA are not provided to the public. In addition, predicted environmental concentrations for glyphosate and its metabolite AMPA do not take into account the highly toxic surfactants that are released into the environment in combination with the active ingredient. Therefore, data about environmental concentrations of surfactants should have been collected and their impact on the environment should have been considered before drafting the RAR .

Amis de la Terre/Friends of the Earth-France : Comments to the Renewal Assessment Report (RAR) – Glyphosate

Introduction

The Renewal Assessment Report (RAR) prepared by the Rapporteur Member State (RMS) has been opened by EFSA to comments from the public. Some parts of the final report have been blackened, presumably names that refer to studies provided by the applicants. Unfortunately, in **Volume 1 Report and Proposed Decision** the very last chapter, **3.2 Proposed Decision,** has been blackened too. This means the public will not get informed about what kind of decision the RMS and the Co-RMS propose. Thus the public can only speculate about details of the proposal.

Amis de la Terre/Friends of the Earth-France is commenting on specific sections of the renewal assessment report (RAR), in particular those that deal with environmental impacts of glyphosate.

Development of resistance

In **Volume 1, Section 2.3.2 Summary of information on the development of resistance**, and **Volume 3 Annex B.3 Data on application and further information**, the topics "development of resistance and appropriate management strategies" are being discussed.

Comments:

The simplicity and effectiveness of weed control through glyphosate will be undermined by shifts in weed communities and populations resulting from the selection pressure of the applied herbicides. Glyphosate has long been considered to be a low risk herbicide in terms of the evolution of resistant weed populations (Beckie 2006), but ever increasing use of glyphosate has favored the development of glyphosate-resistance in weeds. It has taken 8-20 years of glyphosate use in conventional systems until the first glyphosate-resistant weed, rigid ryegrass (*Lolium rigidum*), was found in 1996 in Australia (Pratley et al. 1999). Since then, at least 28 cases of glyphosate-resistant weed species (comprising more than 200 populations) have been recorded worldwide (Heap 2014). The resistant weeds infest millions of hectares at many different places in various countries. Although countries, such as the US, Argentina, Australia, and Brazil, where glyphosate-resistant crops are cultivated are affected most heavily, countries without GM crop cultivation increasingly report cases of glyphosate-resistant weed species.

Glyphosate-resistance in weeds has been found to be based on several mechanisms, such as target site insensitivity, overproduction of the target protein EPSPS (5-enolpyruvylshikimate-3-phosphate synthase), amplification of the EPSPS gene, reduced glyphosate translocation, and increased sequestration of glyphosate in plant cell vacuoles (Perez-Jones & Mallory-Smith 2010). Resistance mechanisms can co-occur, in particular, when related resistant weed species hybridize. In addition, multiple-resistance to other herbicide mode of actions than glyphosate has been reported too (Heap 2014).

In the RAR, reference is made to the development of glyphosate-resistance in Europe. But in reality, the situation is far more severe than depicted in the RAR document (as of September 2012). There are not only 10 cases of resistance known in Europe, but meanwhile the number is 16 and it is not

only five species that have been found, but there are six (Heap 2014). With five resistant species that have infested hundreds of hectares, Spain is the most afflicted country. Contrary to the RAR presentation, glyphosate-resistant weed species have not been found exclusively in orchards, vineyards or olive groves, but also in other crops such as asparagus (*Lolium rigidum* in France) and alfalfa (*Conyza canadensis* in Greece). It is also not quite true, that "*Apart from one case (C. canadensis) in the Czech Republic, Northern and Central Europe are not affected by glyphosate resistance up to now*", since resistant *C. canadensis* has also been reported from Poland railways. This indicates that evolution of glyphosate-resistance will speed up in Europe too, unless use of glyphosate is severely restricted.

In the US, not only the broad adoption of glyphosate-resistant crops but also the continuous rise in the number of resistant species and areas inflicted by resistant weeds has resulted in a massive increase in herbicide amounts applied (Benbrook 2012a). A similar scenario has been depicted for Europe in case genetically modified glyphosate-resistant crops would be authorized for cultivation here too (Benbrook 2012b). Therefore, to stop the pesticide treadmill, glyphosate use has to be restricted.

Environmental effects

In **Volume 1, Section 2.9 Effects on non-target species and Volume 3, Annex B.9 Ecotoxicology),** data on ecotoxicology studies are discussed, evaluated, and summarized.

Environmental impacts on non-target organisms

The risk assessment for birds and mammals is based on the active ingredient glyphosate acid in the product MON 52276 for the intended uses in several crops including pre-planting, pre-emergence, pre-harvest and row-application in orchards and vineyards. From the data provided by the applicants, the RMS comes to the conclusion that after use of the lead formulation MON 52276 in the indications according to the label there is an acceptable acute risk for birds and mammals due to uptake of contaminated food and an acceptable risk resulting from an exposure of small herbivorous mammals, non-target arthropods, and aquatic organisms. Use under the proposed conditions will result in a negligible exposure of honeybees or has no unacceptable acute or chronic effects on colony survival and development. The RMS concludes further, that for the evaluation of the formulation MON 52276 on non-target plants data are still required, in particular, as a valid study with this product to non-target plants is lacking and the formulants in the product may enhance toxicity.

The RMS concedes that, depending on the agricultural and ecological conditions, the use of glyphosate may affect populations of non-target terrestrial arthropods and vertebrate species (especially farmland birds) via trophic interactions and suggests mitigation measures. The RAR reads at this point: *These effects trace back to the intended effect of the herbicides – eliminating competing plants – and the interruption of the food web going along with it*.

In Volume 1, Section 3 Proposed decision, the RMS states: *It is considered that Article 4 of Regulation (EC) No 1107/2009 is complied with. Specifically the RMS considers that authorization in at least one Member State is expected to be possible for at least one plant protection product containing the active substance for at least one of the representative uses*. But the approval should be subject to conditions and restrictions. According to the RMS, glyphosate is not a candidate for substitution.

This statement has been made although the RMS identifies data gaps with regard to the ecotoxicology risk assessment (e.g. aquatic organisms, microorganisms, and non-target plants such as tomato) and concludes that certain areas of the risk assessment could not be finalized on the basis of the available data, among them effects of glyphosate towards microorganisms, on non-target plants and on biodiversity.

For all uses, the RMS acknowledges that the impacts of glyphosate on biodiversity is a critical area of concern and recommends that member states should pay attention to such potential indirect effects and may consider adequate risk mitigation measures.

Comments

It is not acceptable that glyphosate that is known to negatively impact biodiversity to such an extent should be re-authorized in the EU. Glyphosate exhibits acute and chronic toxicity, in particular, to aquatic species and non-target plants. As stated in the RAR and reported by Kremer & Means (2009), glyphosate leads to significant shifts in bacterial community composition but it also affects some fungal species, e.g. beneficial mycorrhizal fungi (Druille et al. 2013a,b). Previous use of glyphosate has been linked to increased Fusarium infection of wheat and barley (Fernandez et al. 2009). Amphibians, many of which are endangered, have been shown to be affected, possibly both their larval and adult stages (Wagner et al. 2013). Plötner and Matschke (2012) concluded that glyphosate is itself toxic to amphibians, and surfactants such as POEA are even more so causing abnormal behavior, teratogenic effects and developmental failures.

Glyphosate can adversely impact micronutrient uptake in plants as it is a strong metal chelator (Tesfamariam et al. 2009, Cakmak et al. 2009). Even low levels of residual glyphosate in soil can greatly impede the availability and uptake of Mn, Fe, Cu, and Zn by plants and lead to their undersupply with these nutrients. Reduced disease resistance and plant growth may be the result (Johal & Huber 2009). Adverse impacts of (repeated) glyphosate use on the health of non-target plants have to be taken into account, as reduced disease resistance most likely will increase use of other pesticides, e.g. fungicides that may be highly toxic too.

It is well known that weeds offer considerable benefits for the agro ecosystem, as they support a range of organisms, among them decomposers, predators, pollinators, and parasitoids, by providing food and shelter for them (Marshall et al. 2003). The Farm Scale Evaluations performed in the UK showed that broad-spectrum herbicides such as glyphosate impact abundance and diversity of weeds more severely than conventional herbicide regimes (Heard et al. 2003). The quantitative loss of weeds reduces number and diversity of arthropods heavily and interrupts the food chain for farmland birds and mammals. Ample evidence of negative impacts of glyphosate on biodiversity has been collected in areas where glyphosate is used extensively, e.g. in combination with genetically modified glyphosate-resistant crops. The all-time low in the number of monarch butterflies in the winter 2013/2014 has been attributed to the loss of their food plant (*Asclepias syriaca*) in vast areas of the United States where glyphosate-resistant crops are grown (Wade 2014).

As glyphosate is the herbicide most widely used, these massive negative impacts on biodiversity have to be considered and used as reason not to re-authorize the substance. Mitigation measures, such as buffer strips, that would be up to the individual member states could not reduce the risk of impacting

biodiversity to an acceptable level – even if farmers accepted to spare buffer strips from glyphosate application which they often don't.

Subclause: Formulated glyphosate products (Annex B.9.11 Surface-active substances in glyphosate-based formulations)

In the RAR, solely the active ingredient glyphosate is being considered for authorization, although in the field, only formulated products are applied. The final glyphosate products contain high amounts of surfactants that have surface-active properties. According to the German government[1], in addition to the 5000 t of glyphosate used in Germany in 2010, 1700 t of polyethoxylated alkylamines (POEA) had been applied. Therefore, it is of importance to not only test the toxicity of the active ingredient glyphosate but to take into account the toxicity of the various formulated products that are used.

There is ample evidence that formulated products can exhibit higher toxicity. In particular, polyethoxylated alkylamines (POEA) are known to be highly toxic to cells and organisms (Mesnage et al. 2013). The RMS considers several of the observed effects on endpoints regarding genotoxicity, mutagenicity, and development or reproduction of non-target organisms to be mediated by the surfactant included in the formulations. Thus the RMS concedes that "*the toxicity of glyphosate-based products is greatly enhanced if the active substance is formulated with alkylamine ethoxylates"* and "*the authorization of glyphosate-based products with alkylamine ethoxylated surfactants might require the generation of further data"*. But to argue, that the lead formulation MON52276 for the assessment of glyphosate does not contain this surfactant and that nowadays POEA-formulated products "*are not expected to be neither notified nor registered in the future"*, are not comforting statements, as such products are still on the market and data about the nature and toxicity of other surfactants that replace POEA are not provided to the public. In addition, predicted environmental concentrations for glyphosate and its metabolite AMPA are calculated only for these substances, not taking into account the highly toxic surfactants that are released into the environment together with the active ingredient. Therefore, it is important to collect data about environmental concentrations of surfactants and to consider their impact on the environment already during the authorization process.

Conclusions

To make agriculture in Europe more environmentally benign, it is of utmost importance that pesticide use is restricted to a much greater extent than it is actually the case. As herbicides make up the largest share of pesticides and glyphosate, in particular, is the most used herbicide, regulators are obliged to not renew the approval of this chemical.

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1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)

Identity (B.1, Annex C)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Physical and chemical properties of the active substance (B.2.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Physical, chemical and technical properties of the formulation (B.2.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Further information (B.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Methods of analysis (B.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Other comments (B.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol.3, B.6, Toxicology and metabolism, page 2	UIM: in the classification of studies the categories 2, 3 and E are made subject to the so-called Klimisch-criteria. We do not agree with using Klimisch criteria since it uses no test protocol criteria, just the circular logic that OECD/GLP = good . Academic studies rarely use these standard protocols as they restrict the testing of hypotheses. Do the hundreds of thousands of scientists in academia do irrelevant or poor work? RMS say yes, but do not prove it	Studies need to be assessed on their scientific value and not be dismissed without reading them because they are not GLP/OECD studies. Next a 'weight of the evidence' approach should be followed, including all scientifically qualified studies available, especially independent studies.
2.	Vol.3, B 6	UIM: Industry's financial interests in selling their	White, J. and Bero, L.A., 2010, 'Corporate manipulation of research:

Other comments (B.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		products conflicts with the interests of truth when they perform the agent's safety tests. Specific techniques are used to allow their mission of getting products approved to prevail. White (2010) extends the well-known strategies of the tobacco industry to other sectors. A RMS must be ready to counter these strategies, yet we didn't note a very critical approach of RMS to the applicants.	Strategies are similar across five industries', *Stanford Law & Policy Review*, (21/1) 105–134. We are disappointed that the RMS agreed on the completeness of the dossier while demanding extra tests and confirmatory information would be the proper approach, especially when the outcomes of industry-sponsored studies differ from academic studies.
3.	Vol.3, B.6	The tests performed by the applicants will probably be based on good laboratory practice (GLP), but this doesn't guarantee quality and reliability. In the past several cases of industry laboratory fraud (IBT, Craven) were discovered by regulators (including tests on Glyphosate). Although these fraudulent tests were replaced by new ones, we still have our doubts on their quality and reliability. GLP, in the end, is just a management system, forcing laboratories to be transparent, but no-one can guarantee what is written down exactly, and what happened or is observed in the tests.	The Commission therefore needs to explain what guarantees they have used to ensure quality and reliability of tests, both old and new. Many outcomes of studies comparing GLP-studies and studies from open (independent) literature have different outcomes, this is an unaddressed concern so far.

2. Mammalian toxicology (B.6)

Toxicokinetics (B.6.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Acute toxicity (B.6.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol.3, B.6.2.3, page 240	UIM: we do not understand that the exposure of test animals at 1000 ppm is called "low". With a current ADI of 0,3 ppm we challenge the value of this type of experiments with extreme high doses. This also means that effects seen at doses people are exposed to in practice are not tested and given the fact that Glyphosate has endocrine disrupting properties, adverse effects of low doses at vulnerable periods of development cannot be excluded.	We do not understand what we can learn from exposure of 20.000 ppm. Can any effect seen at this unrealistic dose be extrapolated to lower doses, thousand times lower and more, to predict an effect? We do not think that this type of mechanistic linear dose-response thinking has any basis in science. A body is no machine but an interrelated system with three major communication systems with triggers and feedback. OECD-tests are very insensitive and should be replaced by realistic dose tests on those elements (with very specific and sensitive endpoints) derived from the hazard assessment (mainly based on academic studies)

Short-term toxicity (B.6.3)

Section 2 - Mammalian toxicology (B.6)

No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Genotoxicity (B.6.4)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
1.	Vol.3, B.6.4, genotoxicty, page 359	UIM: In Table B 6.4-15 an experiment is disqualified for having too low doses. This is difficult to understand since the dose is still above ADI and far more relevant than the many dozens studies at extreme high dose.	Also remarkable is that at these doses effects are seen. They are subsequently qualified as not relevant using an industry-invented tool called "historical control data" allowing adverse effects being dismissed. Historical control data are never used by scientists; they rely on normal controls.
2.	Vol.3, B.6.4, genotoxicty, page 382	UIM: The study discussed showing clastogenicity is done at lower levels than usual. It concludes that effects are seen al lower levels while no effects are seen at higher levels. This again would be reason to reconsider the old paradigms of linear dose-response and use of high unrealistic doses.	
3.	Vol.3, B.6.4, genotoxicity, page 384	UIM: the study of Clemens shows mutagenicity in tadpoles and the occurrence of this effect is not excluded by the RMS. However, in the next lines many questionable assumptions and reasoning are added by the RMS and finally the effects are dismissed for humans. We cannot	We think the only proper approach in case of uncertainties would be to demand the test to be repeated and confirmed by independent laboratories and blind testing. The approval process should be stopped until various aspects are clarified.

Genotoxicity (B.6.4)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		agree with assumptions being made of questionable grounds; expert judgement should be based on science and not feelings.	
4.	Vol.3, B.6.4, genotoxicty, page 385	UIM: we think it is not justified to dismiss studies (genotoxic effects in germ cells in Drosophila) that challenge industry findings by immediately pointing at the "large database of existing studies`. This gives the impression the RMS had already made up their mind about mutagenicity and is now just looking for reasons to dismiss studies not confirming the RMS´s feelings.	All studies should be used for a weight of the evidence approach in an open scientific approach without prior opinions or feelings. We think independent experts are needed to do this weight of the evidence evaluation - scientists who were not involved in drafting the RAR and are linked to the industry. The same biased approach is taken on page 386 for another critical study.
5.	Vol.3, B.6.4, genotoxicty, page 386	UIM: we can understand that the applicants will claim that any adverse effect seen is due to the co-formulant tallowamine and because of this, these studies should not be considered. We do not understand the claim of the RMS that it can "certainly be assumed" that an effect will be caused by the co-formulant. RMS's should not assume but assess. And if they have no data to prove it was the co-formulant, the effects should be contributed to the active ingredient.	Again, there is all reason to demand the applicant to repeat academic studies showing adverse effects by exposing the active substance. This should be done in an independent laboratory with blind testing.
6.	Vol.3, B.6.4, genotoxicty, page 389	UIM: The claim in the RAR of a lack of mutagenicity or even that results of studies are consistently and unequivocally negative (Vol.1) is false. On the contrary, genotoxic effects	It cannot be that the RMS uses the unscientific Klimisch-criteria for academic studies. Anyone knows the outcome: all dismissed! Given the conflict of interest of the applicant on safety testing, and the potential bias in studies or interpretation of studies, we propose

Genotoxicity (B.6.4)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		have been known for a long time and study results are available to the reviewers. Kale (1995) showed mutations in fruit flies, Vigfussen (1980) showed sister chromatin exchanges in human lymphocytes, just as Bolognesi in 1997. Peluso in 1998 showed increased DNA adducts in mice. Gasnier (2009) showed DNA damage, as well as Manas (2009). Some are captured in the industry review, others not, for unknown reasons. All are dismissed in the end. Numerous other studies have confirmed DNA damage in mouse, bovine, fish, caiman, tadpole, fruit fly, sea urchin, onion, and bacterial cells.	EFSA starts their peer-review with independent literature for doing a hazard assessment. Independent literature is less biased because it lacks certain ambitions and should be qualified as more reliable than industry-sponsored studies with an inherent conflict of interest. It is strange to note that Table 2.6-6 in Volume 1 only summarises industry-sponsored studies.
7.	Vol.3, B.6.4.8.10, weight of the evidence	UIM: While the RMS discusses a few of the academic studies that show adverse effects, in the 'weight of the evidence' approach taken by the RMS as a standard procedure plays down the positive effects seen by assumptions and reasoning's such as the effects being indirect, or being beyond a certain threshold, not relevant for humans, suggests that the effect are toxic but not mutagenic. None of these assumptions are based on science but just part of the old paradigm used by regulators.	The RMS has high confidence in industry-sponsored studies and very low in academic studies, with the result that only industry-sponsored studies with their favourable outcome for industry are counted in the final evaluation.

Section 2 - Mammalian toxicology (B.6)

Genotoxicity (B.6.4)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations

Long-term toxicity and carcinogenicity (B.6.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
1	Vol 3, B 6.5. Long-term toxicity and carcinogenicity, page 435	UIM: A major failure in the testing systems used is the lack of exposure in-utero of the test animals. It is well-known that many chronic diseases develop in-utero (not only cancer) and as such tests lacking in-utero exposure cannot be qualified as a 'state-of-the art' scientific approach. The conclusion that the substance is not carcinogen needs to be justified. We therefore propose EFSA requires the applicant to test again with in-utero exposure, performed with blind testing in an independent laboratory.	EU legislation provides for a high level of human health protection based on the precautionary principle and requires special attention for the vulnerable, the unborn and the elderly. The test system disregards the effects on vulnerable groups of society.
2	Vol 3, B 6.5. Long-term toxicity and carcinogenicity, page 435	UIM: Extremely high doses are used in the applicants testing. More evidence is available in the literature (see Vandenberg et al. 2012 review) that low doses can harm, in many cases during the development phase of the organism. Since Glyphosate has endocrine disrupting properties, EFSA should perform a thorough	EFSA should require the applicant to do new testing of the substance including a range of low doses.

Long-term toxicity and carcinogenicity (B.6.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		review ion the data in independent literature, and require applicant to do a series of low dose testing on endocrine adverse effects.	
3	Vol 3, B 6.5. Long-term toxicity and carcinogenicity, page 435	UIM: Another point on carcinogenicity is the need to expose and follow test animals during their entire lifetime. Most diseases develop after incinerating the test animals (e.g. ACS (American Cancer Society): *Cancer Facts & Figures 2012*. Atlanta: American Cancer Society; 2012. [http://cancer.org/acs/groups/content/@epidemiologysurveilance/documents/document/acspc-031941.pdf].	EFSA should require the applicant to do new testing of the substance including lifetime exposure and monitoring.
4.	Vol 3, B 6.5. Long-term toxicity and carcinogenicity, page 502	UIM: No evidence in rat according to the RAR (only industry-sponsored studies analysed) but the malignant lymphoma seen in mice were dismissed. It was not the chemical (Glyphosate) that should be blamed according to the RMS but the strain of mice. We think this has nothing to do with a scientific evaluation but more with a determination to get to a certain outcome. Given the many articles in peer-reviewed literature on the long-term effects and cancer, a more balanced approach would have been justified.	We propose that based on the studies of the open literature hazard assessments are carried out to find out what long-term effects and type of cancers can be expected to occur by the use of Glyphosate. And finally those long-term and carcinogenicity studies qualifying for capturing the adverse effects should be used for a final conclusion. No study should be dismissed for being non-GLP or non-OECD. Every study counts, also the one of Seralini. While the Rapporteur might not like the outcome, there is no scientific failure in the tests of Seralini.

Long-term toxicity and carcinogenicity (B.6.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
5.	Vol 3, B 6.5. Long-term toxicity and carcinogenicity, page 502	UIM: Glyphosate has a history of being related to cancer. The first carcinogenicity study submitted to US-EPA (1981) by the applicant Monsanto showed an increase in testicular tumours in male rats as well as an increase in the frequency of a thyroid cancer in females. Both results occurred at the highest dose tested (30 mg/kg of body weight per day). The second study (1983) found an increasing trend in the frequency of a rare kidney tumour in male mice. A later study (1990) found an increase in pancreas and liver tumours in male rats together with an increase of the same thyroid cancer found in the 1983 study in females.	We ask EFSA to take a look at these older studies. There is good reason for EFSA to start the cancer analysis from scratch including all evidence from the past and from independent literature. Knowing the potential of Glyphosate to cause these effects, are the currently evaluated safety tests designed to capture these effects?
6.	Vol 3, B 6.5. Long-term toxicity and carcinogenicity page 524	UIM: In the RAR all epidemiology studies showing a relation between Glyphosate and cancer are considered irrelevant, such as the Hardell-studies on the Non-Hodgkin's-lymphoma - the unscientific Klimisch-approach is used for this qualification. This is unjustified. Now industry has created a situation in which people are exposed to thousands of chemicals at the same time, epidemiology studies cannot by nature be sensitive anymore. This means if a relation is shown, even weak, this should be reason for concern and reason to demand the	Industry should monitor the use of Glyphosate, analyse all environmental components and organisms, and do a large epidemiology study focused on clarifying the evidence available. There is good evidence on the relation with non-Hodgkin's lymphoma, Nordstrom, 1998, Hardell, 1999 and 2002, McDuffie, 2001, De Roos, 2003 and Eriksson, 2008, and multiple myeloma, De Roos, 2005, and a large study should be initiated to find out more.

Long-term toxicity and carcinogenicity (B.6.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		applicant to do independent monitoring to obtain more information	

Reproductive toxicity (B.6.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
1	Vol.3 B.6.6 Reproductive toxicity. page 538	UIM: a big omission in the German RAR is the lack of a hazard characterization of Glyphosate. In the opinion of the EFSA it is stated that the first step of risk assessment is the hazard characterization. We observe that Germany just moves on directly to risk characterisation and standard setting, and ignores the evidence on hazards	A hazard characterization is important to learn about the mechanism of toxicity of Glyphosate. Without the knowledge of the hazards it will be difficult to select in the next steps of risk assessment what data are useful and not. Germany just puts all evidence in the "Klimisch-mill" with the obvious effect of all independent science disregarded.
2	Vol.3 B.6.6 Reproductive toxicity. page 538	UIM: We urge the EFSA to include a hazard characterisation in the peer-review. This should be done by using all in-vitro studies available, disregarding none, and all mechanistic studies available. The peer-review should focus on what evidence exists on teratogenicity, on DNA-damage., etc.	The study of Paganelli et al. 2010 presents interesting evidence on the mechanism of action. During early embryonic development, retinoic acid generated in a specific region of the embryo helps determine position along the embryonic anterior/posterior axis by serving as an intercellular signalling molecule that guides development of the posterior portion of the embryo. It acts through Hox genes, which ultimately control anterior/posterior patterning in early developmental

Reproductive toxicity (B.6.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
			stages. The findings of Marc et al. '05 support this, offering a general mechanism of action for teratogenicity.
3.	Vol.3 B.6.6 Reproductive toxicity. page 539	UIM: many multi-generation tests in the RAR with their very high (and unrealistic) doses, endpoints which are not the state-of-the-art cannot provide the final answer on reproductive toxicity. The results are not clear anyway with a study that shows effects at low doses but is dismissed in the end by the Rapporteur. Studies showing effects on the offspring are also accepted because they are observed at high doses. Combined with the many studies found in the open literature on malformations of the offspring and developmental effects, a peer-review by EFSA of all evidence is more than necessary.	The industry-sponsored OECD tests are known for their insensitivity and this could explain the very remarkable difference seen between the industry-sponsored studies and independent literature. The high doses used are close to the acute poisoning doses and poisoning effects are common in these tests, while more subtle effects could be missed.
4	Vol.3 B.6.6 Reproductive toxicity. page 548	UIM: we again question the use of extreme high exposure doses such as 15.000 ppm or 1000 mg/kg, more than 1000x the ADI. Animals should be tested at realistic doses and no extrapolation used	The high doses are close to the acute poisoning doses used and poisoning effects are common in these tests, while more subtle effects could be missed.
5	Vol.3 B.6.6 Reproductive toxicity. page 596	UIM: We especially encourage EFSA to take a look at teratogenicity. The pre-2001 studies of Monsanto show teratogenic effects, a range of independent studies report these effects, these effects are also observed in areas with Roundup	In the first DAR on Glyphosate in 2001, the UK experts commented that -based on the Monsanto studies- a single study might not raise concerns, but that the teratogenic effects that kept being observed in the Monsanto-studies, pointed at a pattern that should not be dismissed in the risk assessment.

Reproductive toxicity (B.6.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		monocultures (soy bean) in epidemiology studies and even in bioindustry where piglets fed on soy show these effects.	
6.	Vol.3 B.6.6.9, Reproductive toxicity. page 597	UIM: specific endocrine disrupting tests should be demanded from the applicant. Just basing conclusions on outdated OECD-protocols on reproduction and development is not justified. The science on endocrine disruption differs a lot from other fields and specific exposure windows, doses and specific endpoints should be used. In the traditional tests with traditional experts these effects will be missed.	
7.	Vol.3 B.6.6.9 Reproductive toxicity. page 597	UIM: A large body of evidence on endocrine disrupting effects of Glyphosate is disregarded and dismissed in the RAR. Walsh, 2002 showed the disruption of the steroid hormone progesterone, as well as Romano, 2010 on testosterone. Richard, 2005 also concludes Glyphosate is an endocrine disruptor by affecting aromatase at very low doses. Also Benachour, 2005 and Gasnier, 2007 came to the same conclusion.	Hokanson (2007), demonstrated a synergistic effect of Glyphosate with oestrogen, with implications for pregnancy-induced hypertension and foetal growth retardation. The implications of these effects on reproduction and the developing foetus are profound, with work by Mose (2008) confirming that Glyphosate does cross the placenta.
8	Vol.3 B.6.6.10 Reproductive toxicity. page 613	UIM: the study in rabbits shows that at a level of 10 mg/kg 20% of the litters have malformations while this is 5% in the control (this also counts for the foetus, 3.1% vs. 0.7%).	The malformations should be more thoroughly investigated and this study already shows that the NOEAL of 10 mg/kg should be adopted for standard setting. Suggesting a NOEAL of 100 mg/kg by the applicant is absurd.

Reproductive toxicity (B.6.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		While this dose is at least less enormous than the regular dose, it is still above a realistic dose and we think additional studies should be done at lower doses	
9.	Vol.3 B.6.6.10 Reproductive toxicity. page 619	UIM: this study in rabbit again shows most effects at the lowest dose tested (18 vs. 13 of the litter tested with malformations), 50 mg/kg. While this dose is still unrealistic high, lower doses should be tested on malformations of the foetus.	
10.	Vol.3 B.6.6.10 Reproductive toxicity. page 629	UIM: this study on rabbits also shows malformations at the lowest level tested (82 foetus with 'minor' defects vs 58 in the control), 100 mg/kg. This "low" dose is of course unrealistically high.	There is a clear pattern of malformations of the foetus in all rabbit studies.
11.	Vol.3 B.6.6.10 Reproductive toxicity. page 642	UIM: this study confirms previous observations that malformations of the foetus are highest in the lowest dose tested: 50 mg/kg, (17.7% vs. 11.7% in the control). We object to the use of historical control data. The only scientific approach is to compare the outcome in the tests against the control.	Why the RMS values historical control data more than the normal (negative) control is a mystery. While it is highly questionable if the industry-sponsored studies are reproducible at all, historical control data mix different labs, operators, protocols and strains and create an unrealistic wide range of "controls'. No scientist will ever use this type of tools.
12.	Vol.3 B.6.6.10 Reproductive toxicity. page 650	UIM: this study shows effects at the lowest dose tested, 20 mg/kg, upper cleft palate, 15% vs. 5% in the control, and dilated heart, 23.1% vs. 0% in the control.	There is a clear pattern of malformations of the foetus in all rabbit studies.

Section 2 - Mammalian toxicology (B.6)

Reproductive toxicity (B.6.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
13.	Vol.3 B.6.6.12, Reproductive toxicity, Published data, page 658	UIM: it is remarkable that the RMS now easily rejects all claims made by EOS in their report "is the public kept in the dark" and let most independent literature fall under the 'Klimisch-axe". In their reaction in July 2011, the RMS called the report: The recently published report "Roundup and birth defects: Is the public kept in the dark?" is a challenging critical summary of adverse health (mainly teratological and reproductive) findings that are attributed by the authors to the compound glyphosate and/or to herbicides such as Roundup that contain glyphosate as active ingredient.	The RMS ends their report by saying: An adequate response to the criticism and the many accusations in the report would require a general discussion of the established paradigms for the toxicological evaluation of chemicals. These general discussions should be initiated by the Commission before we start with the re-evaluation of glyphosate within the AIR2 project. We fail to see any general discussion about the established paradigms, neither by the RMS nor by the Commission. We therefore urge the EFSA to start such a discussion before drafting the peer review on Glyphosate.
14.	Vol.3 B.6.6.12, Reproductive toxicity, Published data, page 658	UIM: the industry review made by the applicant is not commented by the RMS. Given the many missing studies and the standard use of Klimisch to dismiss studies on a large scale, an intervention of the RMS would have been needed very much.	We urge EFSA to review all independent studies and stop using the entirely unscientific Klimisch-tool and do a purely scientific assessment of each study looking at the quality of the study, disregarding protocols and GLP-administration systems.

Neurotoxicity (B.6.7)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
1.	Vol.3, B.6.7.1,	UIM: Epidemiological studies have been	There is evidence of developmental neurotoxicity of Glyphosate and

Neurotoxicity (B.6.7)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	Neurotoxicity, Published data, page 702.	published pointing out that Glyphosate causes mental disorders of children of pesticide applicators in the US (Garry, 2002). Even acute poisoning can lead to brain damage (Barbosa, 2001). Animal studies have demonstrated that Glyphosate depletes serotonin and dopamine, (Anadon, 2008) and causes a loss of mitochondrial transmembrane potential in rat brain cells, especially in the substantia nigra region of the brain (Astiz, 2009).	the EFSA should pay good attention to this adverse effect in their peer-review.
2.	Vol.3, B.6.7.1, Neurotoxicity, Published data, page 702.	UIM: We regret that an assessment of the literature by the RMS is missing. We think the assessment of the applicant is totally inadequate, playing down any adverse effects and using the "Klimisch-axe" to ensure it is ignored. This abrogates the idea of scientific evaluation.	

Other toxicological studies & Medical data (B.6.8-B.6.9)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>,	<< Identifier >>: <<comment>>	

Other toxicological studies & Medical data (B.6.8-B.6.9)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	<<description>>		

Summary of mammalian toxicology and setting ADI, AOEL, ARfD (B.6.10)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Toxicity of the product(s) (B.6.11)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Dermal absorption (B.6.12)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>,	<< Identifier >>: <<comment>>	

Section 2 - Mammalian toxicology (B.6)

Dermal absorption (B.6.12)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	<<description>>		

Toxicity of non-active substances (B.6.13)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Exposure data (B.6.14)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>,	<< Identifier >>: <<comment>>	

Section 2 - Mammalian toxicology (B.6)

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	<<description>>		

5. Ecotoxicology (B.9)

Birds and mammals (B.9.1 and B.9.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Aquatic organisms (B.9.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Bees and non-target arthropods (B.9.4 and B.9.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.9.4	UIM: the endocrine disrupting effects of Glyphosate on birds and other non-target organisms are disregarded.	

Section 5 - Ecotoxicology (B.9)

Earthworms and other soil non-target organisms (macro and micro) (B.9.6, B.9.7 and B.9.8)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Other non-target organisms (flora and fauna), sewage treatment (B.9.9 and B.9.10)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.9, Annex, page 298	UIM: many studies show that Glyphosate has endocrine disrupting properties. The RMS conveniently states that all endocrine disrupting effects are likely to be caused by the surfactant. The study of Paganelli, 2010, clearly shows that formulations and active substance have the same adverse effect, and clearly point out that that Glyphosate is an endocrine disruptor.	EFSA should demand studies from the applicant (by independent laboratories, blind testing) for a range of endocrine disruption screening test for Glyphosate.
(2)	RAR_40_list of	UIM: all studies should be publicly available; there	Transparency ought to be guaranteed – this applies to **all** studies

Section 5 - Ecotoxicology (B.9)

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	studies_version 1_CA-CP_2013-12-18	is no reason why industry-based studies should be kept secret	
	RAR_40_list of studies_version 1_CA-CP_2013-12-18, e.g. page 3, 15, 68, 85, 127	UIM: how can the authors of a study be anonymous?	Please improve the transparency – applicants should be asked to supply all details

2. Mammalian toxicology (B.6)

Toxicokinetics (B.6.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Acute toxicity (B.6.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Short-term toxicity (B.6.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Genotoxicity (B.6.4)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Long-term toxicity and carcinogenicity (B.6.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Reproductive toxicity (B.6.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Neurotoxicity (B.6.7)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Other toxicological studies & Medical data (B.6.8-B.6.9)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Section 2 - Mammalian toxicology (B.6)

Summary of mammalian toxicology and setting ADI, AOEL, ARfD (B.6.10)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.6.10, Pages 808 und 849, 8th of May, 2014	GER, Ministry of Lower Saxony, Germany An ADI of 0.5 mg/kg – as proposed by Germany (BfR) – is not acceptably. Our proposal – see detailed letter of the Ministry to EFSA from the 7th of May 2014 – is to minimize the ADI to 0.1mg/kg.	This proposal from Lower Saxony should be considered in Vol.1 , Page 93, too

Toxicity of the product(s) (B.6.11)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Dermal absorption (B.6.12)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Toxicity of non-active substances (B.6.13)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>,	<< Identifier >>: <<comment>>	

Section 2 - Mammalian toxicology (B.6)

Toxicity of non-active substances (B.6.13)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	<<description>>		

Exposure data (B.6.14)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

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6. Mai 2014

Glyphosat

Öffentliche Konsultation des Bewertungsberichts (Renewal Assessment Report Glyphosate 2013)

5 Anlagen

Sehr geehrte Damen und Herren,

zum Bewertungsbericht des Pflanzenschutzmittelwirkstoffs Glyphosat der Bundesrepublik Deutschland („Renewal Assessment Report Glyphosate 2013") gibt es – insb. zum Bereich Toxikologie - aus Niedersachsen ergänzende Informationen, die von Experten (Toxikologie, Geologie / Bodenkunde) für das Niedersächsische Umweltministerium erarbeitet wurden. Die Ergebnisse sind diesem Schreiben in Berichtsform beigefügt. Wichtige Erkenntnisse ergeben sich zu folgenden Themen:

- Glyphosatgehalte in menschlichem Urin – Aufnahmewege – Konsequenzen,
- Auswirkungen von Glyphosat in Böden und Ökosystemen,
- Dysbiose,
- Anwendungseinschränkungen
- Teratogene Wirkung

Ein zusammenfassender Text ist ergänzend beigefügt.

Ich bitte um Berücksichtigung dieser Argumente im Rahmen der öffentlichen Konsultation zum Pflanzenschutzmittelwirkstoff Glyphosat.

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Ausführlicher Bericht über Erkenntnisse aus den Arbeiten der niedersächsischen Expertengruppe zum Thema Glyphosat

1. Anlass und Auftrag:

Fragen zum Pflanzenbehandlungsmittel „Glyphosat" wurden im Jahr 2013 sowohl in der Umweltministerkonferenz als auch in der Agrarministerkonferenz behandelt. Anlass sind kontroverse Aussagen über Wirkungen / Auswirkungen bei der Anwendung glyphosathaltiger Mittel in verschiedenen Publikationen, die im Rahmen der Verlängerung der Zulassung des Pflanzenschutzmittelwirkstoffes Glyphosat von Regierungsorganisationen / Nicht-Regierungsorganisationen (GO`s / NGO`s) und verschiedenen Einrichtungen / Verfassern sowie darauf aufbauend von der Presse herausgestellt wurden und die Haltung der Bewertungsstelle BfR in Frage stellen. Das Bundesinstitut für Risikobewertung (BfR) hat auf verschiedene Publikationen reagiert und sie in mehreren Stellungnahmen kommentiert. Zu klären ist die Frage, ob die Haltung des BfR zu den Ergebnissen der o. a. Publikationen aus fachlicher niedersächsischer Sicht nachvollziehbar ist oder ob die Bundesstelle Hinweisen auf bestimmte Wirkungen von Glyphosat „nicht ausreichend" nachgegangen ist.

Eine Reihe von Informationen über Wirkungen, die dem Einsatz von Glyphosat zugeschrieben wurden, sind in einem Vortrag der Universität Leipzig – Inst. f. Mikrobiologie – zusammengeführt und wurden im Rahmen der Frühjahres-UMK 2013 verschiedenen Teilnehmern übergeben, so auch an Herrn Minister Wenzel.

Im Spannungsfeld der Vorwürfe von NGO`s und anderen Einrichtungen zu den Auffassungen des BfR wurde im MU beschlossen, diese Fragen von einem zu bildenden ad hoc Expertenkreis untersuchen zu lassen.

Folgende Fragen sollten geklärt werden:

- Wo liegen die Risiken von Glyphosat?
- Ist die herbe Kritik an Glyphosat gerechtfertigt oder nicht?
- Werden aus den vorliegenden Erkenntnissen die richtigen Schlüsse gezogen?

Die Untersuchungen durch den Expertenkreis sollen insb. die von der Universität Leipzig in ihrem Vortrag „Glyphosat- Wirkung des Totalherbizids auf Menschen und Tiere" zusammengestellten Aussagen und die darauf erfolgten Reaktionen des BfR zu Glyphosatgehalten in Körperflüssigkeiten in der Normalbevölkerung einer kritischen Untersuchung umfassen.

2. Umsetzung (Einrichtung einer Expertenarbeitsgruppe)

Für den Expertenkreis wurden mehrere Personen des Landesdienstes gewonnen, die aufgrund ihrer Kenntnisse qualifiziert sind, an der Untersuchung der o. a. Fragen mitzuwirken.

3. Vorgehensweise und Ablauf

Die Arbeit der Experten wurde von einem Begleitkreis unter Vorsitz eines Vertreters des MU geleitet.

Der Begleitkreis sollte die Arbeiten der Expertengruppe organisieren und steuern.

Zwischen Dezember 2013 und März 2014 ist die AG fünfmal zusammengekommen. In den Treffen wurde Aufgabenstellung, Arbeitsweise – insb. der Austausch der relevanten Literatur – und Abläufe vor einem engen Zeithorizont koordiniert.

Die Experten haben verschiedene fachbezogene Themen, zu denen sie die Aussagen aus Veröffentlichungen / Studien und die Reaktion des BfR dazu prüfen wollten, im Rahmen der Sitzungen weitgehend festgelegt.

Es zeigt sich, dass insb. die Einsichtnahme in die Originalliteratur unbedingt erforderlich ist, um die Ausführungen der Experimentatoren ausreichend interpretieren zu können. Hierzu waren erhebliche Anstrengungen bei der Literaturbeschaffung notwendig. Es zeigt sich als sehr misslich, dass der Bewertungsbericht des federführenden Bundesinstituts für Verbraucherschutz und Lebensmittelsicherheit (BVL), der Anfang Februar 2014 über die Webseiten der Europ. Lebensmittelbehörde EFSA eingesehen werden können sollte, erst sehr spät (Mitte März 2014) veröffentlicht wurde.

Zur Arbeit der Experten im Detail:

Untersuchte Themen: (Boden)

Auswirkungen von Glyphosat / glyphosathaltigen Mitteln auf das Schutzgut Boden für

- Boden/Pflanze
-. Grundwasser / Oberflächenwasser
-. Biologische Vielfalt / Nichtzielorganismen / Resistenzmanagement

Dabei untersuchte Arbeitsthesen:

- Die häufige Anwendung von Totalherbiziden reduziert die Nahrungsgrundlage von Tieren insbesondere Insekten mit der Folge, dass eine Gefährdung von Arten nicht auszuschließen ist.
- Die regelmäßige Anwendung von Glyphosat erhöht den Selektionsdruck für die Entwicklung glyphosatresistenter Wildpflanzen.

Untersuchte Themen (Toxikologie)

– Welche begründeten Hinweise sind publiziert, dass Glyphosat eine Dysbiose auslösen/verursachen kann und somit die Tiergesundheit beeinflusst?

- Ist eine Festlegung (Erhöhung) von ADI-Werten auf Basis von Erkenntnissen aus Sicht der Reproduktionstoxikologie gerechtfertigt? Ist eine Festlegung des ADI-Wertes auf Basis der Gesamtschau toxikologischer Studien gerechtfertigt?
- Sind die in Studien gezeigte Dysbiosewirkung (Vermehrung schädlicher Bakterien oder Reduzierung nützlicher Bakterien) und Chelatbildung durch Glyphosat in höheren Lebewesen und die dadurch bedingten gesundheitlichen Beeinträchtigungen bei Tier / Mensch wissenschaftlich begründet?
- Sind die in mehreren Studien diesbezüglich gezeigten und publizierten Wirkungen von Glyphosat (Dysbiose und Chelatbildung) vom BfR hinreichend berücksichtigt und widerlegt worden?
- Welche wissenschaftlich begründeten Hinweise für teratogene Effekte durch Glyphosat / glyphosathaltige PSM liegen vor? Sind die begründeten Hinweise auf teratogene Effekte bei der Bewertung von Glyphosat hinreichend berücksichtigt oder widerlegt worden?
- Ist eine Festlegung (Anhebung) des ADI-Wertes auf Basis der Gesamtschau toxikologischer Studien gerechtfertigt oder wäre eine Absenkung geboten?

Die Untersuchungen erfolgten vor dem Hintergrund besonderer Qualifikationen der Experten und der verfügbaren Originalliteratur. In so weit sind einige der Feststellungen als vorläufig zu betrachten. Ebenso ist ein enger Zeitrahmen für die Bearbeitung der Themen zu berücksichtigen.

Die übersendeten Berichte der Experten wurden nach bestem Wissen ausgewertet und zu dieser Darstellung verwendet.

Erkenntnisse und Schlussfolgerungen

Vorbemerkung:

Die Expertenmeinungen sind in Bezug auf die teratogene Wirkung nicht übereinstimmend. Während für einen Experten weitere Prüfungen zur Absicherung des Ergebnisses der Bewertungsstellen unbedingt notwendig sind, sind aus der Sicht eines anderen Experten weitere Prüfungen nicht erforderlich, da es keine Anzeichen für teratogene Wirkungen gibt.

Vorhandene Untersuchungen zeigen auf, dass das Kaninchen die empfindlichste Spezies für reproduktionstoxische Prüfungen ist. Die Reihe von Untersuchungen an anderen Spezies ändert bei kritischer Betrachtung nichts an der Forderung, weitere langfristige in vivo-Untersuchungen insb. an Kaninchen durchführen zu müssen, um vorliegende Hinweise auf solche Wirkungen bestätigen oder ausschließen zu können. „Die Kaninchen zeigten sich sehr empfindlich gegenüber Glyphosat. Toxische Effekte bei den Muttertieren zeigten sich bei fast allen Studien bereits bei der mittleren getesteten Dosis. Der NO(A)EL der Muttertiere war somit jeweils die niedrigste Dosis.
Bei den Föten zeigten sich in fast allen Studien Abnormalitäten in den Eingeweiden (zumeist beim Herzen sowie in den großen kardiovaskulären Gefäßen) und im Skelett". In Kontrollen trat der Effekt nicht auf. Historische Kontrolldaten wurden zu diesem Effekt in der Studie nicht angegeben. Die Autoren stellten deshalb fest, dass

für die Föten der NO(A)EL unterhalb der niedrigsten Dosis liegen würde und setzen 20 mg/kg/Tag als LO(A)EL fest.

Dabei weist die Expertin darauf hin, dass – ähnlich wie beim Thalidomid („Contergan") Schadwirkungen nur in einem kleinen Zeitfenster der Applikation zu spezifischen Schädigungen führen könnten. Dort war von Bedeutung, dass die Dosis für das Ausmaß der Schädigung nicht relevant war. Nur der genaue Zeitpunkt der Einwirkung während der Embryonalentwicklung war entscheidend, ob und welche z. T. sehr spezifische Schädigung verursacht wurde. Eine Dosis-Wirkungs-Beziehung trat bei Thalidomid nicht auf. So kommt ein Experte zur Auffassung, dass die im RAR beschriebenen Effekte an Kaninchen – wie auch in anderen epidemiologischen Studien- Hinweise auf eine teratogene Wirkung aufzeigen würden, auch wenn methodische Defizite ersichtlich sind. „Die Gesamtschau der Daten ergibt zumindest begründete Hinweise, dass Glyphosat eine teratogene Wirkung haben könnte". Die eindeutige Aussage des BfR, bei Glyphosat handele es sich nicht um einen Stoff mit teratogener Wirkung, sei mit den vorliegenden Daten nicht belegt.

Das BfR bewertete im RAR 2013 die Situation anders mit dem Hinweis, dass es keine eindeutige Dosis-Beziehung geben würde.

Ein Experte sieht keine überzeugenden Hinweise für das Vorliegen einer teratogenen Wirkung.

Übereinstimmend sehen die Experten für toxikologische Fragestellungen weitere Untersuchungen als notwendig an, um den widersprüchlichen Hinweisen auf Störungen der bakteriellen Mikroflora - der Balance im Magen-Darm-Trakt – zu klären. Vorliegende Studien zeigen widersprüchliche Erkenntnisse, die weitere wissenschaftliche experimentelle Untersuchungen zum Effekt einer Dysbiose erforderlich machen. Das BfR kommentierte 2012 die Frage, ob bei der Risikobewertung potentiell schädliche Effekte von Glyphosat auf Bakterien des Magen-Darm-Traktes berücksichtigt worden sind. Danach liegen dem BfR keine Studien vor, die einen schädlichen Einfluss auf Bakterien im Tiermodell belegen. Diese Feststellungen sind mit Bezug auf den RAR (18.12.2013) sowie auf bereits Mitte 2012 vorliegende Studien und die vorhandene Datenlage nicht zutreffend.

Die vorliegenden Ergebnisse geben Hinweise, dass die anwendungsfertigen Zubereitungen („Formulierungen") glyphosathaltiger Mittel ein höheres Gefährdungspotential besitzen als der Wirkstoff.

Im Einzelnen:

Der Prozess der toxikologischen Risikoabschätzung beinhaltet die Ermittlung des Gefährdungspotentials, die Expositionsabschätzung, die Erfassung einer Dosis-Wirkungsbeziehung und die Risikocharakterisierung. Es muss dabei zwischen dem Gefährdungspotential und dem tatsächlich gegebenem Risiko (als dosisabhängige Größe) unterschieden werden. Grundsätzlich muss auch zwischen der Beurteilung des Wirkstoffes und der Toxizität der Pflanzenbehandlungsmittelformulierung unterschieden werden. Die Ergebnisse der Bewertungsstellen wurden von Deutschland als federführender „Rapporteur Member State" im Renewal Assessment Report (RAR) dargelegt.

Von den Herstellern des Stoffes bzw. der Formulierungen wurden seit der Zulassung 150 neue toxikologische Studien vorgelegt, bisherige bewertende Studien re-evaluiert sowie neu hinzugekommene Publikationen in der offenen wissenschaftlichen Literatur hinsichtlich ihrer Relevanz, Qualität und Zuverlässigkeit bewertet. Studien, die nicht unter den Qualitätsbedingungen der Guten Labor Praxis durchgeführt wurden, sind nicht mit einem Ausschlusskriterium zu versehen, wenn sie den etablierten Anforderungen an die Qualität und der Zuverlässigkeit entsprechen.

Den Beurteilungen der zuständigen Stellen zufolge wird Glyphosat nach oraler Gabe zu ca. 20% resorbiert und findet sich in den höchsten Konzentrationen in Knochengewebe, Niere und Leber. Die Ausscheidung erfolgt mit dem Urin nach etwa 48 Stunden. Der Metabolit AMPA findet sich nur in geringen Anteilen neben nicht-absorbiertem Glyphosat in den Feces. Es finden sich keine Hinweise auf eine Akkumulation im Organismus.

Der Stoff weist in den Studien eine geringe akute Toxizität nach oraler, dermaler oder inhalativer Exposition auf. Die LD50-Werte wurden mit >2000mg/kg (oral und dermal), ein LC50-Wert mit >5mg/kg Luft bestimmt. Glyphosat verursacht Augenreizungen.

In Kurzzeitstudien (bis 28 Tage) wurde eine niedrige Toxizität (Ratte, Maus und Hund) beobachtet. Die Dosis, bei der keine gesundheitlichen Auswirkungen festgestellt wurde (NOAEL: No Observed Adverse Effect Level) lag zwischen 300 – 500 mg/kg Körpergewicht und Tag. Bei einer Mortalitätsstudie an Hunden mit 1000mg/kg und Tag wurden Effekte auf die Körpergewichtsverteilung, die Blase und die Ohrspeicheldrüse beobachtet. Veränderte klinisch-chemische Parameter waren indikativ für Lebertoxizität, die aber nicht durch hämatologische Befunde unterstützt wurden. Bei subakuten dermalen Prüfungen wurden bei Dosen von 1000 bzw. 5000mg/kg und Tag keine systemische Toxizität sondern nur leichte Hautreizungen beobachtet.

Erbgutverändernde Eigenschaften (Gentoxizität) wurde in vitro in Bakterien und Säugerzellen getestet. Ergebnisse von 14 Studien (Ames-Test) waren negativ. Bei Prüfungen in Vivo an Ratte und Maus spielen Mikrokerntestsysteme und Untersuchungen zum Nachweis von Chromosomenabberationen eine wichtige Rolle. Unter den Bedingungen der Prüfungen in der Gesamtheit der Mikrokerntests in vivo und der Chromosomenabberationen in vivo zeigte sich Glyphosat nicht genotoxisch. Einige in vivo-Untersuchungen, die zu einem Ausschluss positiver Befunde geführt haben, hat das BfR begründet.

Die chronische Toxizität und die Kanzerogenität wurden in Studien an Ratten und Mäusen untersucht. Gegenüber der Risikobewertung 1998 sind fünf neue Studien an Ratten und drei Studien an Mäusen hinzugekommen. Bei der Re-Evaluierung alter Studien von 1998 wurde nun auf den NAOEL statt auf den NOEL (No Observed Effect Level) abgestellt (mit Blick auf die aktuellen regulatorischen Standards). Die

Folge sind höhere NOAEL-Werte. Auf Basis der chronischen Rattenstudien kann nach Ansicht der RAR-Autoren ein robuster NOAEL-Wert von 100mg/kg und Tag angenommen werden. Eine Monsantostudie aus 1981, für die ein NOEL von 31,5mg/kg und Tag benannt wurde, wurde wegen zu niedrig geprüfter Dosen und Mängeln bei der Berichterstattung nicht mehr berücksichtigt. Die kombinierten chronischen Kanzerogenitätsstudien an Ratten und Mäusen erbrachten keinen wissenschaftlichen Beweis für Kanzerogenität.

Es wurden etliche epidemiologische Studien mit unterschiedlicher Differenzierung der Exposition in Pestizide, gruppenspezifische Pestizide und Glyphosat (Glyphosat-Formulierungen) in Bezug auf Krebs durchgeführt. Eine bekannte Schwäche dieser Untersuchungen ist ihre Schwäche bei der Beschreibung der Exposition. So ist dabei neben der Aufnahme von Glyphosat auch von einer Aufnahme weiterer Pestizide auszugehen. Es ist daher grundsätzlich äußerst schwierig, belastbare Aussagen in Bezug auf den Endpunkt Kanzerogenität und Glyphosat zu erhalten. In einigen Studie liegen uneinheitliche Aussagen zu einem Zusammenhang zwischen Glyphosat und dem Non-Hodgkin-Syndrom (Sammelbezeichnung von Krankheiten des Lympathischen Systems, die kein Morbus Hodgkin sind) vor. Die umfangreichste davon (USA) umfasste 57000 Landwirte und Pestizidanwender. Den Auswertungen zufolge gibt es keine Hinweise für eine Assoziation spezifischer Kebsformen zu Glyphosat.

Daraus folgend kann geschlossen werden, dass Glyphosat kein gentoxisches Kanzerogen ist.

Reproduktionstoxikologie:

Es liegen Multigenerationenstudien mit verschiedenen Spezies und Studien zur Entwicklungstoxizität und Teratogenität (d. h. exogene Induktion grobstruktureller Abnormitäten) vor. Wie alle toxischen Wirkungen sind fetotoxische Wirkungen (Wirkungen in der Embryo- und Fötalzeit im Zeitabschnitt zwischen Konzeption und Befruchtung) dosisabhängig. Als Besonderheit der Teratogenität gelten die Phasenspezifität und die Dosisspezifität neben der Stoffspezifität und der Speziesspezifität. Phasenspezifität bedeutet, dass Fehlbildungen nur in einem bestimmten Entwicklungsfenster erkannt werden können. Dosisspezifität bedeutet, dass unterhalb eines Dosisbereichs (unterhalb des NAOEL) keine Fehlbildungen auftreten. Bestimmte teratogene Effekte können bei höheren Dosen überdeckt werden durch einen stärkeren Effektschweregrad, so dass für ihre Erkennung die Wahl eines geeigneten Dosisbereichs entscheidende Voraussetzung ist

Die Datenlage aus Studien zur Reproduktionstoxikologie wird von einem Experten als ausreichend angesehen (s. hierzu die Anmerkungen in der Vorbemerkung). Die Bewertung aller validen Studien führt zu einem zusammenfassenden elterlichen NOAEL von 300-400mg/kg Körpergewicht und Tag sowie zu einem NOAEL in Nachkommen im gleichen Bereich wie für die Elterngeneration ermittelt.

Die früheren Studienergebnisse wurden bestätigt. In Studien mit Schlundsondenverabreichung wurden teratogene Effekte in Dosen >1000mg/kg und Tag beobachtet, der NOAEL liegt bei 300mg/kg und Tag.

Fünf Studien der früheren EU-Evaluierung zum Entwicklungspotential in Kaninchen wurden in jüngster Zeit kritisch diskutiert. Von diesen wurden drei als ergänzend und

eine weitere bewertet. In Konsequenz wurden einige LOAEL und NOAEL-Werte revidiert. Die Einstufungen als „ergänzend" wurden in zwei Fällen wegen hoher Sterblichkeit der Mütter bereits in einer mittleren und einer Hochdosisgruppe oder Defiziten in der Berichterstattung vorgenommen. Die hohe maternale Toxizität hatte insofern einen prägenden Einfluss auf die Bewertung von Daten in den Fällen, wo formal statistische Relevanz für teratogene Effekte vorlag. Die Bedeutung dieser Effekte wurde in Bezug auf die Rolle maternaler Toxizität als Ursache einer Entwicklungstoxizität kontrovers diskutiert. Das OECD Guidance Document (2008) zu reproduktionstoxischen Prüfungen und ihrer Bewertung sagt dazu, dass bei schwerer maternaler Toxizität, die das Wohlbefinden des Fötus gefährdet, die Daten zur Reproduktionstoxizität schwierig zu interpretieren sind.

Die nunmehr vier Studien der älteren EU-Bewertung zur Entwicklungstoxizität in Kaninchen zeigen zusammenfassend maternale NOAEL im Bereich 20-250mg/kg und Tag und für entwicklungstoxische NOAEL von 100-250mg/kg und Tag. Bei neuen Untersuchungen in Kaninchen liegt die maternale Toxizität bei 50-100mg/kg und Tag und entwicklungstoxische NOAEL im Bereich 50-300mg/kg und Tag. Die erkannten und berücksichtigten Prüfungen zur Entwicklungstoxizität zeigen eine besondere Empfindlichkeit von trächtigen Kaninchen gegenüber Glyphosat im Vergleich mit anderen getesteten Spezies. Die Autoren des RAR leiten darauf einen Gesamt-NOAEL von 50mg/kg und Tag für die maternale und die Entwicklungstoxizität ab.

Einige kritische Publikationen berichten über in Vivo-Studien zur Reproduktions-/ Entwicklungstoxizität, die als Beleg für ein entsprechendes Risiko gesehen werden. Sie wurden mit handelsüblichen Formulierungen durchgeführt. Evaluierungen dieser Studien wurden auf nationaler wie auf EU-Ebene durchgeführt. Die Studien erbrachten in Bezug auf die Beurteilung des Risikos für den Menschen keine überzeugenden Beweise (Anwendung unrealistisch hoher Dosen, unphysiologische Art der Applikation im Vergleich zur Möglichkeit der Exposition des Menschen, keine ausreichend validierten Prüfsysteme). Es ergab sich jedoch sowohl die Erkenntnis der höheren Toxizität von Formulierungen im Vergleich zur aktiven Substanz Glyphosat.

Epidemioloische Studien zu Endpunkten der Reproduktionstoxizität / der Entwicklungstoxizität waren ähnlich wie bei beim Endpunkt Krebs ohne statistisch signifikante Assoziation zu Glyphosat.

In weiteren Studien konnte kein neurotoxisches Potential für Glyphosat belegt werden.

Auf die kontroversen Auffassungen der beiden Toxikologen zur Frage der Teratogenität sei ausdrücklich nochmals hingewiesen. Hier ist keine einheitliche Auffassung erzielbar.

Ableitung eines ADI-Wertes

Die Ableitung eines ADI-Wertes zur Bewertung einer chronischen Exposition geht allg. von der höchsten Dosis einer bestmöglich geeigneten Studie aus, bei der keine adversen Effekte bei der empfindlichsten Spezies beobachtet werden. Derzeit sind verschiedene Institutionen in der regulatorischen Praxis zu unterschiedlichen ADI-Ableitungen gekommen. Dabei können unterschiedliche NOAEL/LOAEL-Ableitungen

oder Extrapolationsfaktoren zur Übertragung von Studien bei Tieren auf den Menschen die gefundene Höhe des Wertes begründen. Das trifft auch auf Glyphosat zu. Der gültige ADI-Wert liegt bei 0,3mg/kg und Tag und wurde auf Basis eines NOEL von 30mg/kg und Tag durch chronische Studien an Ratten abgeleitet. Die WHO/FAO haben 2004 einen ADI von 1mg/kg auf Basis eine Zweijahresstudie an Ratten festgelegt. Die US-EPA hatte 2009 einen Referenzwert von 1,75mg/kg auf Grundlage einer Studie zur Entwicklungstoxizität an Kaninchen mit einem NOAEL von 175mg/kg und Tag abgeleitet. Im aktuellen RAR 2013 wird auf Grundlage eines Gesamt-NOAEL von 50mg/kg und Tag sowohl für eine maternale als auch entwicklungstoxische Effekte ein ADI von 0,5mg/kg und Tag vorgeschlagen.

In Bezug auf Unsicherheiten auf die langfristig-orale Exposition wird ein zusätzlicher Sicherheitsfaktor von zwei empfohlen. Daraus würde ein ADI-Wert von 0,25mg/kg und Tag gegenüber dem im RAR 2013 vorgeschlagenen ADI von 0,5mg/kg und Tag resultieren.

Erfassung der inneren Belastung des Menschen

Es liegen Daten zur Belastung des Menschen vor. Sie wurden bei der Bewertung vom BfR berücksichtigt. Für Deutschland und Niedersachsen ist die Datenlage nicht ausreichend bzw. sind nicht bekannt. Eine Untersuchung mit dem Ergebnis, dass 7 von 10 Proben in Deutschland positiv waren, fand starke mediale Beachtung. Das BfR hat befunden, dass die Höhe der Glyphosatfunde in deutschen Proben nicht mit einem gesundheitlichen Risiko verbunden seien. Dennoch geben die Befunde einen Hinweis darauf, dass eine Exposition des Menschen insb. über die Lebensmittel gegeben ist und die grundsätzlich als Mehrfachbelastung gegenüber Pestiziden anzusehen ist. Ergebnisse von Trinkwasseruntersuchungen in Niedersachsen (2011-2012) zeigten hier keine Nachweise von Glyphosat (703 Proben) als auch vom Metaboliten AMPA (700 Proben).

Zusammenfassend wird festgestellt, dass die Datenlage zur Charakterisierung des toxikologischen Profils gegenüber Glyphosat als gut bezeichnet werden kann. Es fehlen trotz einer Reihe publizierter in vitro-Tests, die vor allem mit Glyphosat-Formulierungen vorgenommen wurden, Ergebnisse zu systematischen Untersuchungen zur Abklärung des Potentials von Glyphosat hinsichtlich der Teratogenität und einer möglichen endokrinen Aktivität.

Dysbiose:

Clostridium botulinum ist die taxonomische Zuordnung für einen Komplex von anaeroben Bakterien, denen die Bildung von Botulinum—Neurotoxinen gemeinsam ist. Einige Typen sind tierpatogen. Unter der Bezeichnung Chronischer Botulismus wird in der wissenschaftlichen Literatur eine Hypothese zur Erklärung unspezifischer Krankheitserscheinungen in Rinderbeständen (Verdauungsstörungen, Labmagenverlagerungen, Abmagerung, Klauen- und Gelenkerkrankungen etc) diskutiert. Auch beim Menschen wurden chronische Krankheitsbilder beobachtet. Betroffen waren Landwirte und Familienangehörige, in deren Betrieben Rinder erkrankt sind.

Die Ursache für die meist unspezifischen Symptome bei erkrankten Menschen ist bislang unklar geblieben. Erst seit 2009 wird in Arbeiten ein Zusammenhang des visceralen Botulismus bei Menschen als neues Krankheitsbild in Folge einer Übertragung des chronischen Botulismus vom Tier auf den Menschen hergestellt. Die Deutsche Gesellschaft für Neurologie hat 2012 in einer Stellungnahme festgestellt, dass bisher in keinem Fall das Vorliegen eines humanen chronischen Botulisnus durch eine Erregerübertragung belegt ist. Die beschriebenen unspezifischen Erkrankungsformen sind derzeit wissenschaftlich nicht als eigenständiges Krankheitsbild etabliert.

Bodenbereich:

Es sei angemerkt, dass die Bewertungen nur schlaglichtartig erfolgen und einen Anspruch auf Vollständigkeit nicht erfüllen können.

Als wesentliches Umweltrisiko der umfangreichen Anwendung glyphosathaltiger Herbizide im Ackerbau können mögliche indirekte Auswirkungen auf die biologische Vielfalt sicher identifiziert werden. Nach dem nationalen Aktionsplan Pflanzenschutz (BMEL, 2013) ist Pflanzenschutz umfassend zu verstehen und nicht nur auf die Anwendung von Pflanzenschutzmitteln einzugrenzen.

Die ökonomische Vorzüglichkeit der Anwendung von Totalherbiziden gegenüber anderen herbizid-wirksamen Maßnahmen im Ackerbau, wie Bodenbearbeitung und Fruchtfolgegestaltung, hat zu einem weitreichenden Einsatz geführt. National und international fordern Herbologen (STEINMANN, 2013; HARKER et al., 2012) auch aus Gründen des Resistenzmanagements einen verantwortungsvolleren Umgang mit dem Wirkstoff Glyphosat. Vor diesem Hintergrund sollten Anwendungen für die keine Indikation nach dem Pflanzenschutzrecht vorliegt (z. B. Sikkation) in jedem Fall unterbleiben.

Bei einer Einschränkung der Anwendung von Glyphosat aus Gründen des Artenschutzes muss im Einzelfall eine Abwägung mit den Zielen des Bodenschutzes und des Gewässerschutzes erfolgen. Glyphosat hat als derzeit einziger zugelassener systemischer Totalherbizidwirkstoff die Einführung reduzierter, pflugloser Bodenbearbeitungssysteme ermöglicht. Die reduzierte Bodenbearbeitung ist ein wichtiges Instrument im Rahmen des Gewässerschutzes um erosive Nährstoffeinträge zu vermindern. Des Weiteren fördern reduzierte Bodenbearbeitungssyteme die Bodenstruktur und Regenwurmpopulationen und sowie die Befahrbarkeit von Böden. Die Verwendung von Glyphosat ermöglicht durch Einhaltung der Bodenruhe eine Verminderung der herbstlichen Stickstoffmineralisation bei Anbau von Feldfrüchten wie Raps, die aus Sicht des nitratbezogenen Grundwasserschutzes problematisch sind.

Nach BMEL (2013a) wurden im Jahr 2012 5.941 t Glyphosat an berufliche Verwender und 40 t an nicht berufliche Anwender abgesetzt. Die entsprechenden Mengen der formulierten Pflanzenschutzmittel betrugen 17.867 t im beruflichen und 811 t im nichtberuflichen Bereich. Im nichtberuflichen Anwendungsbereich wurden in der Vergangenheit häufig nicht zugelassene Herbizidanwendungen auf Nichtkulturland wie versiegelten Flächen festgestellt. Diese Anwendungen sind mit erheblichen Risiken der Abschwemmung und des Direkteintrages von

Pflanzenschutzmitteln in Gewässer behaftet. Es muss hinterfragt werden, ob ein Einsatz von Herbiziden im Haus- und Kleingartenbereich notwendig ist. Im Haus- und Kleingartenbereich sind insgesamt 17 Herbizidwirkstoffe in 235 Präparaten zugelassen (BVL 2014). Neben Glyphosat sind unter anderem 2,4 D, MCPA und Dicamba zugelassen.

Bei Überlegungen, den Wirkstoff Glyphosat aus dem Anwendungsgebiet im Haus- und Kleingartenbereich herauszunehmen, ist abzuwägen, ob damit nicht eine Substitution durch möglicherweise aus Gewässerschutzsicht problematischere Wirkstoffe erreicht wird. Sinnvoller wäre, die Abgabe von Herbiziden an nichtsachkundige Personen nicht weiter zuzulassen.

Zu den konkreten Fragen:

Wo liegen die Risiken von Glyphosat?

Für den deutschen Verbraucher ist vor dem Hintergrund der festgestellten inneren Belastung mit Blick auf den ADI-Wert zwar nicht von einem akuten Risiko auszugehen (bei von nds. Experten umstrittener teratogener Wirkung sowie offenen Fragen zum Thema Dysbiose). Wegen des Nachweises des Vorkommens von Glyphosat bei Mensch und Nutztieren ist aber eine Minimierung der Glyphosat-Belastung anzustreben. Erkannte kritische Bestandteile von Formulierungen (z. B. oberflächenaktive Substanzen) müssen abschließend gesetzlich geregelt werden.

Werden aus den vorliegenden Erkenntnissen die richtigen Schlüsse gezogen?

Hinsichtlich der Bewertungen der Humantoxizität seitens der Bewertungsstellen: ja

(bei uneinheitlicher Auffassung der nieders. Experten zu Teratogenität und einiger nicht abschließend geklärter Fragen).

Zusammenfassung von Kritikpunkten:

Die Experten berichten über Defizite des Erkenntnisstands bei folgenden Themen:

- Dysbiose: Die vorliegenden Publikationen geben Anlass, Hinweise auf Dysbiose ernst nehmen zu müssen. Es fehlen Untersuchungen
- teratogene Wirkungen: Es liegen kontroverse Auffassungen der Experten vor. Stand: Die Ergebnisse geben Anlass, eine mögliche teratogene Wirkung von Glyphosat weiter untersuchen zu lassen bzw. die vorliegenden Erkenntnisse reichen für endgültige Aussagen „keine teratogene Wirkung erkennbar" aus
- den Hinweisen auf mögliche endokrine Wirkungen sollte nachgegangen werden
- die Wirkung von im anwendungsfertigen Mittel enthaltenen Beistoffen und der auf dem Markt angebotenen Formulierungen sollte stärker auf die Wirkungen untersucht und kritische Beistoffe geregelt werden,

- es sind Güterabwägungen vorzunehmen, um Argumente des pro und contra für chemische oder physikalische Bodenbearbeitungsverfahren zu werten. Bei einer Einschränkung der Anwendung von Glyphosat aus Gründen des Artenschutzes muss im Einzelfall eine Abwägung mit den Zielen des Bodenschutzes und des Gewässerschutzes erfolgen. Auch aus gründen des Resistenzmanagements muss ein verantwortlicher Umgang mit dem Wirkstoff Glyphosat erreicht werden.
- Umfang und Ursachen für die Belastung von Mensch und Tieren mit Glyphosat sind durch entsprechende eigene Untersuchungen festzustellen – Quellen und Umfang der Belastung müssen minimiert werden.

Erläuterungen:

NOEL (No Observed Effect Level): Toxikologischer Endpunkt in der Toxizitätsbestimmung: entspricht der höchsten Dosis oder Expositionskonzentration eines Stoffes in subchronischen oder chronischen („längerfristigen") Studien, bei der keine statistisch signifikante behandlungsbedingte Wirkung beobachtet wird.

NOAEL: (No Observed Adverse Effect Level): Expositionshöhe, bei der keine signifikanten adversen Effekte an Testorganismen beobachtet werden.

Landesamt für
Bergbau, Energie
und Geologie

L3.3 Landwirtschaft und Bodenschutz, Landesplanung

Dr. K. Meyer

Hannover, 24.03..2014

Arbeitsgruppe ‚Glyphosat' (MU Ref. 37) zur Risikobewertung des Herbizidwirkstoffes

Teilbeitrag des LBEG zu nichttoxikologischen Fragestellungen

Hinweis:

Die folgenden Aussagen stützen sich auf eine Sichtung und Auswertung der frei verfügbaren Literatur sowie Daten des Landes Niedersachsen. Der von Deutschland an die EFSA übergebene Bewertungsbericht (RAR) konnte erst am 14.3.2014 nach der Freigabe durch die EFSA heruntergeladen werden und kann daher nur in Teilen in die Bewertung einfließen. Es ist ausdrücklich festzuhalten, dass die Bewertungen nur schlaglichtartig erfolgen und einen Anspruch auf Vollständigkeit nicht erfüllen können.

1. Auswirkungen von Glyphosatanwendungen auf das System Boden/Pflanze

These: Glyphosatanwendungen reduzieren die Pflanzenverfügbarkeit von Mikronährstoffen

In verschiedenen Studien (z. B. ZOBIOLE et al. 2010; BOTT et al. 2008) wurden verminderte Spurenelementkonzentrationen (u. a. Mangan und Zink) in der Pflanzenmasse gentechnisch veränderter Sojasorten bei Glyphosatapplikation ermittelt. Die Studien wurden an tropischen Böden mit insgesamt geringer Nährstoffverfügbarkeit und starker Sorption über Eisenoxidoberflächen vorgenommen. Die in den Studien verwandten glyphosattoleranten Sojasorten zeichneten sich durch ein geringeres Nährstoffaneignungsvermögen aus als die zum Vergleich herangezogenen nichtveränderten Elternlinien.

An dieser Stelle kann nicht abschließend beantwortet werden, ob ein Zusammenhang zwischen Glyphosatapplikation und der Induktion eines bestimmten Nährstoffmangels auch unter den hiesigen Standortbedingungen und Anbaufrüchten zu erwarten ist. Entsprechende Hinweise aus der landwirtschaftlichen Praxis sind nicht bekannt.

These: Glyphosat kann von behandelten Pflanzen in die Rhizosphäre abgegeben werden und Folgekulturen (Nichtzielpflanzen) schädigen

NEUMANN et al. (2006) zeigten in Labor- und Gewächshausversuchen, dass Glyphosat nach Blattapplikation schnell vom Spross in die Wurzeln der Zielpflanzen verlagert und anschließend in die Rhizosphäre abgegeben wird. Die Autoren sehen als negativen Nebeneffekt eine gehemmte Aneignung von Mikronährstoffen wie Mangan, Zink, Eisen und Bor in der Folgekultur, die insbesondere für Böden mit verminderter Verfügbarkeit von Mikronährstoffen prognostiziert wird.

Eine Remobilisierung von im Boden sorbiertem Glyphosat bei einer mineralischen Phosphatdüngung wurde in Modellversuchen von BOTT et al. (2011) nachgewiesen. In Folge der Wiederfreisetzung von Glyphosat wurden an den angebauten Nichtzielpflanzen Wachstumsstörungen beobachtet. Die Effekte wurden an vier extrem phosphatarmen

(< 1 mg P/100 g Boden) teilweise tropischen Böden festgestellt, während an einem Boden mit erhöhten verfügbaren Phosphatgehalten keine Schädigungen auftraten.

These: Glyphosat kann den Befall mit Fusarien erhöhen

Ein möglicher Einfluss der Glyphosatapplikation auf pilzliche Schaderreger der Gattung *Fusarium* wird in der Literatur widersprüchlich diskutiert. FERNANDEZ et al. (2009) fanden in Kanada bei reduzierter Bodenbearbeitung und Glyphosateinsatz einen erhöhten Befall mit Fusarien bei Weizen, konnten aber die Wechselwirkung zwischen den Einflussfaktoren Bodenbearbeitung und Herbizidapplikation nicht auflösen. Dagegen stellten BÉRUBÉ et al. (2012) einen signifikanten Einfluss der Bodenbearbeitung auf den Gehalt an Deoxynivalenol als kennzeichnendes Fusariumtoxin im Getreidekorn fest, fanden aber keinen erhöhten Fusariumbefall bei Glyphosatapplikation in der Vorfrucht.

Aus der landwirtschaftlichen Praxis in Deutschland ist seit längerem bekannt, das konservierende Bodenbearbeitung den Befall mit Fusarien im Getreidebau fördern kann, Einflüsse der Glyphosatanwendung in der Vorfrucht auf das Infektionsverhalten der Folgekultur (Infektionszeitpunkt Frühjahr bis Getreideblüte) sind nicht bekannt.

These: Glyphosatapplikation beeinflusst die Bodenmikroflora

Einflüsse von Glyphosat auf die Bodenmikroflora und den Kohlenstoff- und Stickstoffumsatz im Boden wurde sowohl in den von der Glyphosat Task Force eingereichten Studien als auch in einer Reihe weiterer Studien untersucht. Ein signifikanter Einfluss von Glyphosat auf die Stickstoffmineralisation wurde in der regulatorischen Studie mit dem formulierten Produkt (MON 52276) nicht festgestellt, eine Studie mit dem aktiven Wirkstoff (unformuliert) war nicht valide gemäß der OECD Guideline. Im RAR (2013) werden weitere Studien mit der aktiven Substanz gefordert, da Glyphosat im Boden als persistent einzustufen ist (DT_{50} > 60 d).

MALKOMES (2007) untersuchte die Wirkung unterschiedlich formulierter Glyphosatprodukte und eines Vergleichsherbizids (Dinoterb) auf biomassebezogene mikrobielle Aktivitäten (Dehydrogenase, Substrat-induzierte Kurzzeitatmung) bzw. die Kohlenstoff- und Stickstoffmineralisierung. Während das Vergleichsmittel die biomassebezogenen mikrobiellen Aktivitäten generell stark hemmte und die Mineralisierung erhöhte, wirkten die Glyphosat-Varianten (Formulierung, Dosierung) nur zeitweise geringfügig auf diese Messgrößen. Lediglich die N-Mineralisierung wurde durch die höhere Dosierung zeitweise erhöht und die Relation der C- zur N-Mineralisierung entsprechend verringert.

LANE et al. (2012) stellten in einem Gewächshausexperiment mit glyphosattoleranter (GR-) Soja keinen Einfluss der Glyphosatanwendung auf die Struktur der Mikroorganismengemeinschaft fest. Bei erstmaliger Anwendung von Glyphosat auf einem vorher nicht mit Glyphsat behandelten Boden wurde im Rhizosphärenbereich eine Minderung der mikrobiellen Biomasse festgestellt.

WARDLE & PARKINSON (1992) fanden im Feldversuch keinen Einfluss der Glyphosatanwendung auf die mikrobielle Biomasse und -aktivität, während Wirkungen des Vergleichsmittels 2,4 D festgestellt werden konnten. In einem Versuch mit langjähriger Applikation verschiedener Pestizide in Rothamsted (u. a. Glyphosat) stellten HART & BROOKES (1996) keinen messbaren Langzeiteffekt auf die mikrobielle Biomasse und Aktivitätsparameter (C- und N-Mineralisation) fest.

2. Austrag von Glyphosat in das Grundwasser und Oberflächengewässer

These: Glyphosat wird aufgrund der physiko-chemischen Eigenschaften wenig in Grund- und Oberflächengewässer ausgetragen

Für das Land Niedersachsen liegen Daten zu Funden von Glyphosat und dem Metaboliten AMPA (Aminomethylphosphonat) des Gewässerüberwachungssystems (GÜN) vor. Im Zeitraum 2008 bis 2013 wurden 1163 Grundwassermessstellen auf die genannten Parameter untersucht. An sechs Messstellen wurde Glyphosat in Konzentrationen von mehr als 0,03 µg/l gefunden, davon an einer Messstelle mit einer Konzentration von mehr als 0,1 µg/l. AMPA wurde an 10 Grundwassermessstellen in Konzentrationen von mehr als 0,03 µg/l, davon an drei Messstellen > 0,1 µg/l gefunden (NLWKN, 2014). Die höchste gefundene Konzentration von Glyphosat (15 µg/l) und AMPA (9 µg/l) an einer Grundwassermessstelle im Jahr 2010 wurde bei der Folgeuntersuchung im Jahr 2011 nicht bestätigt (Glyphosat: 0,7 µg/l; AMPA: 1,4 µg/l). Für die genannte Grundwassermessstelle kann eine unsachgemäße Anwendung von Glyphosat im Einzugsgebiet nicht ausgeschlossen werden. Ergebnisse einer möglicherweise erfolgten Fundaufklärung sind nicht bekannt.

Für das Grundwasser ergibt sich danach eine Fundhäufigkeit (Funde über Bestimmungsgrenze) von 0,5 % für Glyphosat und 1,1 % für AMPA. Verglichen mit Funden anderer Pflanzenschutzmittelwirkstoffe oder Metabolite im Grundwasser im Rahmen des GÜN-Monitorings sind die Funde von Glyphosat und AMPA als gering einzustufen.

Untersuchungen des NLWKN an 140 Oberflächengewässermessstellen in den Jahren 2010 und 2011 mit insgesamt 554 Einzelmessungen ergaben Fundhäufigkeiten über der Bestimmungsgrenze von 0,05 µg/l bei Glyphosat von 28 % bzw. 54 % bei AMPA. Der Anteil der Einzelfunde > 0,1 µg/l lag bei 8 % für Glyphosat und 41 % für AMPA. Auch hinsichtlich der gefundenen Maximalkonzentrationen wurden deutliche Unterschiede zwischen Glyphosat (1,1 µg/l) und AMPA (4,3 µg/l) festgestellt (NLWKN, 2012).

Zeitreihenuntersuchungen des LANUV an der Ruhr (Messstelle Mülheim) in Nordrhein-Westfalen ließen einen tendenziell ansteigenden Trend der AMPA-Konzentrationen im Wasser erkennen (LANUV, 2013). Insgesamt zeigten die Daten aber keine Korrelation zwischen den gemessenen AMPA- und Glyphosatkonzentrationen. Das LANUV hält es daher für unwahrscheinlich, dass Abbauprodukte von Glyphosat die Hauptquelle für die AMPA-Belastung der Ruhr sind. Es wird vermutet, dass ein wesentlicher Teil der AMPA-Belastung der Ruhr aus Abbauprodukten von phosphonathaltigen Haushaltsreinigern stammt, zumal der Einsatz von Phosphonaten einen deutlichen Anstieg aufweist (Tab. 1).

Tab. 1: Einsatzmengen von Phosphonaten in Wasch- und Reinigungsmitteln in Deutschland (IKW, 2013)

Jahr	Einsatzmenge [t]
1989	2000
1994	1900
2005	3207
2007	4043
2010	4115
2012	*ca. 4208**

*vorläufige Angabe, bislang nicht veröffentlichte Daten (Auskunft UBA, 20.03.2014)

Nach FÜRHACKER et al. (2005) können folgende Phosphonsäuren als mögliche Vorläufersubstanzen für AMPA angesehen werden:

- Hydroxyethandiphosphonsäure (HEDP)
- Aminotrimethylenphosphonsäure (ATMP)
- Ethylendiamintetra(methylenphosphonsäure) (EDTMP)
- Diethylentriaminpenta(methylenphosphonsäure) (DTPMP)

Nach KNEPPER et al. (2002) finden HEDP, EDTMP und DTPMP überwiegend im Wasch- und Reinigungsmittelbereich und in der industriellen Reinigung Verwendung, während ATMP als Additiv in Kühl- und Kesselwasser genutzt wird.

Im Rückschluss auf die Ergebnisse niedersächsischer Oberflächengewässeruntersuchungen kann auch hier ein Einfluss nichtglyphosatbürtiger Phosphonate auf die gefundenen AMPA-Konzentrationen nicht ausgeschlossen werden.

3. Wirkungen von Glyphosat auf die Biologische Vielfalt und Nichtzielorganismen

These: Die häufige Anwendung von Breitbandherbiziden reduziert die Nahrungsgrundlage von Tieren insbesondere Insekten mit der Folge, dass eine Gefährdung von Arten nicht auszuschließen ist.

Die Verwendung von Glyphosat und anderen Breitbandherbiziden kann negative Auswirkungen auf die Biodiversität haben. Betroffen hiervon sind insbesondere terrestrische Arthropoden (z. B. Insekten, Schmetterlinge, Spinnen) und Feldvögel. Der Entzug der Nahrungsgrundlage von Nichtzielorganismen als indirekte Folge von Herbizidanwendungen ist der wesentliche Kritikpunkt zu den Umweltwirkungen des Wirkstoffes Glyphosat im Bewertungsbericht zum Antrag auf Wiederzulassung (RAR, 2013).

Die Gefährdungssituation von Tier- und Pflanzenarten wird seit 1977 systematisch in den Roten Listen des Bundesamtes für Naturschutz dokumentiert. Bei den wirbellosen Tieren gelten aktuell 45,8% der untersuchten Arten als bestandsgefährdet, extrem selten oder bereits verschollen oder ausgestorben (BfN, 2012). Der Anteil der gefährdeten Arten hat gegenüber dem Vergleichsjahr 1998 deutlich zugenommen. Auch die Bestandssituation zahlreicher bodenbrütender Vogelarten der Agrarlandschaft wie Feldlerche, Kiebitz oder Wiesenpieper wird als nach wie vor ungünstig eingestuft.

Die negativen Wirkungen des Herbizideinsatzes auf die Biodiversität sind kein Spezifikum des Wirkstoffes Glyphosat, sondern gelten für Breitbandherbizide allgemein und könnten auch auf andere wildkrautregulierende ackerbauliche Maßnahmen, wie z. B. häufiger Pflugeinsatz und winterliche Schwarzbrache übertragen werden.

Angesichts der seit den 1990er Jahren stark angestiegenen Anwendung von Glyphosat kommt diesem Wirkstoff bei Fragen zu Wirkungen auf die Biodiversität aufgrund der im Vergleich zu anderen Wirkstoffen häufigeren Anwendung besondere Bedeutung zu. Im Jahr 2012 betrug die Absatzmenge von Glyphosat 5.981 t. Nach einer Auswertung von STEINMANN et al. (2012) lag den Anteil von Glyphosat an den insgesamt eingesetzten Herbizidwirkstoffmengen bei etwa 30 %.

4. Bewertung der Glyphosatanwendung vor dem Hintergrund von Herbizidsesistenzen

These: Die regelmäßige Anwendung von Glyphosat erhöht den Selektionsdruck für die Entwicklung glyphosatresistenter Wildpflanzen.

In Europa ist in zehn Fällen das Auftreten glyphosatresistenter Pflanzen beobachtet worden. Die Funde traten im Weinbau, Obstbau und Olivenanbau in Italien, Spanien und Frankreich sowie an Bahngleisen in Tschechien auf (RAR, 2013). HEAP (2014) dokumentiert weitere Funde in Griechenland, Portugal und Polen. Resistenzen wurden bislang an Arten des Berufskrauts (*Conyza bonariensis, C. canadensis, C. sumatrensis*) sowie an den Weidelgräsern *Lolium multiflorum* (Welsches Weidelgras) und *L. rigidum* (Steif-Loch) gefunden. Weltweit sind bislang 28 glyphosatresistente Arten bekannt. In Deutschland sind bisher keine resistenten Arten bekannt (HEAP, 2014). BENBROOK (2012) stellte für die USA im Zeitraum 1996 bis 2011 eine deutliche Zunahme des Herbizideinsatzes fest (Pestizideinsatz insg. +7 %) und führte dies auf die vermehrte Entwicklung resistenter Wildkräuter im Zusammenhang mit dem Anbau glyphosattoleranter gentechnisch veränderter Kulturpflanzen zurück.

HARKER et al. (2012) fordern zur Unterdrückung weiterer Resistenzentwicklungen eine Reduktion der herbiziden Behandlungsintensität, welche durch geeignete ackerbauliche Maßnahmen (Diversifizierung von Fruchtfolgen, Bodenbearbeitung) flankiert sein sollte. Nach einer Studie von STEINMANN et al. (2012) erfolgt in Deutschland ein Einsatz von Glyphosat auf etwa 40 % der Ackerfläche (4,3 Mio. ha), wobei mit 23 % der Ackerfläche (entsprechend 68 % der Applikationsfläche) eine Nachernteanwendung die höchste Bedeutung hat. Vorsaatanwendungen (7 % der Ackerfläche) haben vor allem im Zuckerrüben- und Maisanbau erhöhte Bedeutung. Vor dem Hintergrund der Erfahrungen mit Resistenzentwicklungen gegenüber Herbiziden wird u. a. von STEINMANN (2013) eine Begrenzung der Anwendungsintensität gefordert. Bezogen auf Glyphosat wird ein großes Reduktionspotenzial in der genannten Nachernteanwendung gesehen.

5. Schlussfolgerungen und Empfehlungen

Als wesentliches Umweltrisiko der umfangreichen Anwendung glyphosathaltiger Herbizide im Ackerbau können mögliche indirekte Auswirkungen auf die biologische Vielfalt sicher identifiziert werden. Nach dem nationalen Aktionsplan Pflanzenschutz (BMEL, 2013) ist Pflanzenschutz umfassend zu verstehen und nicht nur auf die Anwendung von Pflanzenschutzmitteln einzugrenzen.

Die ökonomische Vorzüglichkeit der Anwendung von Totalherbiziden gegenüber anderen herbizid wirksamen Maßnahmen im Ackerbau, wie Bodenbearbeitung und Fruchtfolgegestaltung, hat zu einem weitreichenden Einsatz geführt. National und international fordern Herbologen (STEINMANN, 2013; HARKER et al., 2012) auch aus Gründen des Resistenzmanagements einen verantwortungsvolleren Umgang mit dem Wirkstoff Glyphosat. Vor diesem Hintergrund sollten Anwendungen für die keine Indikation nach dem Pflanzenschutzrecht vorliegt (z. B. Sikkation) in jedem Fall unterbleiben.

Bei einer Einschränkung der Anwendung von Glyphosat aus Gründen des Artenschutzes muss im Einzelfall eine Abwägung mit den Zielen des Bodenschutzes und des Gewässerschutzes erfolgen. Glyphosat hat als derzeit einziger zugelassener systemischer Totalherbizidwirkstoff die Einführung reduzierter, pflugloser Bodenbearbeitungssysteme

ermöglicht. Die reduzierte Bodenbearbeitung ist ein wichtiges Instrument im Rahmen des Gewässerschutzes um erosive Nährstoffeinträge zu vermindern. Des Weiteren fördern reduzierte Bodenbearbeitungssyteme die Bodenstruktur und Regenwurmpopulationen und sowie die Befahrbarkeit von Böden. Die Verwendung von Glyphosat ermöglicht durch Einhaltung der Bodenruhe eine Verminderung der herbstlichen Stickstoffmineralisation bei Anbau von Feldfrüchten wie Raps, die aus Sicht des nitratbezogenen Grundwasserschutzes problematisch sind.

Nach BMEL (2013a) wurden im Jahr 2012 5.941 t Glyphosat an berufliche Verwender und 40 t an nicht berufliche Anwender abgesetzt. Die entsprechenden Mengen der formulierten Pflanzenschutzmittel betrugen 17.867 t im beruflichen und 811 t im nichtberuflichen Bereich. Im nichtberuflichen Anwendungsbereich wurden in der Vergangenheit häufig nicht zugelassene Herbizidanwendungen auf Nichtkulturland wie versiegelten Flächen festgestelllt. Diese Anwendungen sind mit erheblichen Risiken der Abschwemmung und des Direkteintrages von Planzenschutzmitteln in Gewässer behaftet. Es muss hinterfragt werden, ob ein Einsatz von Herbiziden im Haus- und Kleingartenbereich notwendig ist. Im Haus- und Kleingartenbereich sind insgesamt 17 Herbizidwirkstoffe in 235 Präparaten zugelassen (BVL 2014). Neben Glyphosat sind unter anderem 2,4 D, MCPA und Dicamba zugelassen.

Bei Überlegungen, den Wirkstoff Glyphosat aus dem Anwendungsgebiet im Haus- und Kleingartenbereich herauszunehmen, ist abzuwägen, ob damit nicht eine Substitution durch möglicherweise aus Gewässerschutzsicht problematischere Wirkstoffe erreicht wird. Sinnvoller wäre, die Abgabe von Herbiziden an nichtsachkundige Personen nicht weiter zuzulassen.

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Das Thema „Glyphosat" wurde 2013 sowohl in der Umweltministerkonferenz als auch in der Agrarministerkonferenz behandelt. Anlass sind kontroverse Aussagen über Wirkungen / Auswirkungen bei der Anwendung glyphosathaltiger Mittel in verschiedenen Publikationen, die im Rahmen der Verlängerung der Zulassung des Pflanzenschutzmittelwirkstoffes Glyphosat von Regierungsorganisationen / Nicht-Regierungsorganisationen (GO`s / NGO`s) und verschiedenen Einrichtungen / Verfassern sowie der Presse herausgestellt wurden und die Haltung der Bewertungsstelle BfR dazu kritisieren.

Im Spannungsfeld der Vorwürfe von NGO`s und anderen Einrichtungen und den Antworten des BfR - etwa zur Frage, ob den Vorwürfen in genügender Weise nachgegangen wurde oder ob diese vom BfR nicht in ausreichender Weise im Rahmen des Zulassungsverfahrens gewürdigt wurden, wurde im MU beschlossen, diese Fragen von einem zu bildenden Expertenkreis untersuchen zu lassen.

MU bat um die Klärung der folgenden Fragen:

- Wo liegen die Risiken von Glyphosat?

- Ist die herbe Kritik an Glyphosat gerechtfertigt oder nicht?

- Werden aus den vorliegenden Erkenntnissen die richtigen Schlüsse gezogen?

Aus einer Vielzahl von unterschiedlichen toxikologischen Wirkungen / Auswirkungen, bei denen ein Zusammenhang mit Glyphosat intensiv kontrovers diskutiert wird, musste aufgrund einer relativ engen Terminsetzung in dem Expertenkreis eine Auswahl von Themen getroffen werden, die näher behandelt werden sollten.

Folgende Themen/Fragen sollten von mir näher behandelt werden:

1. Sind die in Studien gezeigte Dysbiosewirkung (Vermehrung schädlicher Bakterien oder Reduzierung nützlicher Bakterien) und Chelatbildung durch Glyphosat in höheren Lebewesen und die dadurch bedingten gesundheitlichen Beeinträchtigungen bei Tier / Mensch wissenschaftlich begründet? Sind die in mehreren Studien diesbezüglich gezeigten und publizierten Wirkungen von Glyphosat (Dysbiose und Chelatbildung) vom BfR hinreichend berücksichtigt und widerlegt worden?
2. Welche wiss. begründeten Hinweise für teratogene Effekte durch Glyphosat /glyphosathaltige PSM liegen vor? Sind die begründeten Hinweise auf teratogene Effekte bei der Bewertung von Glyphosat hinreichend berücksichtigt oder widerlegt worden?
3. Ist eine Festlegung (Anhebung) des ADI-Wertes auf Basis der Gesamtschau toxikologischer Studien gerechtfertigt oder wäre eine Absenkung geboten?

Der „Renewal Assessment Report" (RAR) 2013 für Glyphosat wurde erst am 14. März 2014 über die EFSA-Seite zur Verfügung gestellt. Dennoch wurden die relevanten Bereiche in dem Bericht zur Stellungnahme von Punkt/Frage 1 und 2 gründlich von mir durchgearbeitet. In Bezug auf Punkt/Frage 3 aufgrund der engen Zeitsetzung zumindest insoweit, dass auch hier eine erste vorläufige Aussage gemacht werden konnte.

Außerdem wurde der „Draft Assessment Report" (DAR), welcher 1998 von Deutschland aufgrund des durch die Industrie eingereichten Dossiers verfasst wurde, inklusive der United-Kingdom-Kommentierung zum DAR für Punkt/Frage 2 gründlich durchgesehen. Ferner wurden zahlreichen Publikationen zu Punkt/Frage 1 und 2 durchgesehen und bewertet.

Bei dem RAR 2013 handelt es sich um ein Dossier, welches von der „Glyphosate Task Force" (GTF) zusammengestellt und von Deutschland als RMS („Rapporteur Member State"), im Fall des Toxikologie-Parts vom BfR, kommentiert wurde. Das RAR enthält durch die GTF verfasste (teilweise relativ ausführliche) Zusammenfassungen und Bewertungen der zur Bewertung von Glyphosat eingereichten Studien. Die eigentlichen Studien inklusive der Rohdaten liegen nicht vor.

Aufgrund der äußerst engen Terminsetzung zur Erstellung der Einschätzung der Experten und aufgrund der Komplexität der Thematik, kann die Ausführung zu den einzelnen Punkten derzeit leider nicht in der ggf. erforderlichen Ausführlichkeit erfolgen. Detailliertere Angaben können (/müssen) ggf. zu einem späteren Zeitpunkt erfolgen. Zu den einzelnen Punkten:

1. Sind die in Studien gezeigte Dysbiosewirkung (Vermehrung schädlicher Bakterien oder Reduzierung nützlicher Bakterien) und Chelatbildung durch Glyphosat in höheren Lebewesen und die dadurch bedingten gesundheitlichen Beeinträchtigungen bei Tier / Mensch wissenschaftlich begründet? Sind die in mehreren Studien diesbezüglich gezeigten und publizierten Wirkungen von Glyphosat (Dysbiose und Chelatbildung) vom BfR hinreichend berücksichtigt und widerlegt worden?

Glyphosat (N-(Phosphonomethyl)-Glycin) ist eine chemische Verbindung aus der Gruppe der Phosphonate. Glyphosat wirkt unselektiv gegen Pflanzen; Nutzpflanzen können mittels Gentechnik eine Resistenz gegen Glyphosat erhalten. Die gewünschte herbizide und auch teilweise mikrobizide Wirkung beruht auf folgendem Wirkmechanismus: Glyphosat blockiert das Enzym 5-Enolpyruvylshikimat-3-phosphat-Synthase (EPSPS), das zur Synthese der aromatischen Aminosäuren Phenylalanin, Tryphtophan und Tyrosin über den Shikimatweg benötigt wird. Der Shikimatweg kommt bei Pflanzen und den meisten Mikroorganismen (einigen Bakterien und Pilzen) vor, bei höheren Tieren und dem Menschen hingegen nicht.

Bakterien bilden zwei unterschiedliche EPSPS-Klassen, die weniger als 30% Aminosäurehomologie besitzen. Die Klasse I kommt in Pflanzen und einigen Bakterien vor und ist sensitiv gegen Glyphosat. In anderen Bakterien wurde die EPSPS Klasse II identifiziert, welche weitgehend resistent gegen Glyphosat ist.

In zahlreichen publizierten Studien, u.a. Studien der Universität Leipzig, wurde gezeigt, dass oftmals pathogene Bakterien, wie z. B. E. coli, Streptococcus pneumoniae, Staphylococcus aureus, Clostridium perfringens sowie einige andere Clostridien-, Salmonellen- und Pseudomonas-Arten weitgehend resistent bzw. tolerant gegenüber Glyphosat sind. Zahlreiche nützliche Bakterien (wie z.B. Enterococcus spp., Lactobacillus ssp.) wurden dagegen durch Glyphosat gehemmt, sie besaßen offensichtlich die Klasse I ESPS und sind sensitiv gegenüber Glyphosat.

In verschiedenen Studien (u.a. von der Arbeitsgruppe von Frau Prof. Krüger der Universität Leipzig) wurden Hinweise publiziert, dass chronische Applikationen von (im Futter) enthaltenden Glyphosatmengen zu einer Dysbiose (Störung der Darmflora) und dadurch auch zu sogenanntem „Viszeralen / Chronischem Botulismus" (offiziell auch als multifaktorieller Symptomenkomplex bezeichnet) vor allem bei Rindern führen könnte, wie sie seit Mitte der 90iger Jahre verstärkt in Deutschland und auch anderen Ländern auftritt.

Mechanistisch kann dies durch selektive mikrobizide Wirkung auf die normale Darmflora und höhere Resistenz bei pathogenen Keimen, wie Clostridium botulinum, erklärt werden (siehe oben).

Von der Universität Leipzig wurden ihre entsprechenden Erkenntnisse als wissenschaftlich gut begründete und mit experimentell ermittelten Daten belegte Thesen publiziert. Empfohlen wurde, dass noch weitere Untersuchungen, vor allem in-vivo, folgen müssten.

Ist die Darmflora nicht im Gleichgewicht, kann es grundsätzlich zu zahlreichen - teils schwerwiegenden - gesundheitlichen Einschränkungen und Krankheiten bei Mensch und Tier kommen.

Eine nicht intakte bzw. eine noch nicht voll ausgebildete Darmflora wird als Ursache für den sogenannten „Säuglings-Botulismus" genannt, der in Vielem der bei Rindern beschriebenen Form des „Chronischen Botulismus" ähnelt.

„Wegen der wachsenden öffentlichen Besorgnis über diese Rinderkrankheit vor allem in Deutschland und weil eine Wirkung auf die Mikroorganismen durch EPSP Hemmung nicht ausgeschlossen werden kann" [übersetzt aus RAR 2013], hatte das BfR - ohne Ausschreibung - eine in-vitro-Studie in einem künstlichen kontinuierlichem Rumensystem bei der Tierärztlichen Hochschule Hannover, Physiologisches Institut (bei Prof. Breves), in Auftrag gegeben, um die diesbezüglichen Bedenken auszuräumen und zu widerlegen.

Die Ergebnisse der Studie „Einfluss eines glyphosathaltigen Pflanzenschutzmittels auf die ruminale Fermentation und mikrobielle Gemeinschaft in vitro unter besonderer Berücksichtigung von Clostridia" sind nicht publiziert, wurden allerdings in einem Vortrag auf dem BfR-Symposium am 20.01.2014 in Berlin präsentiert. Außerdem stellte Herr Prof. Breves seine Ergebnisse auch den Teilnehmern der „Glyphosat-AG" im MU vor und stand für Fragen und Erläuterungen zur Verfügung.

Aus einer Reihe verschiedener Gründe ist die vorgestellte Studie allerdings nicht geeignet, die begründeten Thesen zu widerlegen. Auch können mit der Studie aufgrund der verwandten Methoden und des gewählten Organismus, die dargestellten Schlussfolgerungen zum Teil nicht gezogen werden:

- Es handelt sich um eine in-vitro-Studie. Auch, wenn das gewählte kontinuierliche System wohl das am besten geeignete in-vitro-System ist, die in-vivo-Situation kann auch hiermit nicht vollständig dargestellt werden

- Es ist keine OECD-Guideline-Studie und wurde nicht nach GLP durchgeführt

- Es wurde ausschließlich ein nicht näher definiertes PSM und nicht (auch) der Wirkstoff Glyphosat alleine getestet

- Es wurde eine SSCP (single strand conformation polymorphism) Analyse durchgeführt. Hierbei werden nur Bakterien identifiziert, deren DNA-Anteil über 10% an der Gesamt-DNA ausmacht. Es bedarf einer relativ hohen Anzahl von Keimen, damit sich eine Bande darstellt. Wenn sich aber wenige pathogene Clostridien in der Suspension befinden, kann man die damit nicht darstellen

- Als Testorganismus wurde Clostridium sporogenes, ein nicht Toxin-bildender, also nicht-pathogener Keim, gewählt. Er sollte als Surrogat für Clostridium botulinum, ein Neurotoxin-bildender, pathogener Keim dienen. Für die Untersuchung der ruminalen Fermentation im Rind ist er allerdings nicht als solcher geeignet:
C. sporogenes gehört zur physiologische Gruppe I (proteolytische Clostridien). Es ist damit phylogenetisch nur nah verwandt mit C. botulinum Typ A und F, die beim Menschen vorkommen. Die hauptsächlich bei Rindern vorkommenden C. botulinum Typ C und D (Gruppe III, nicht-proteolytische (saccharolytische) Clostridien) und andere saccharolytische C. botulinum, wie Typ B (Gruppe II), welche auch bei Rindern vorkommen, werden durch C. sporogenes nicht abgebildet.
Proteolytische (Gruppe I) und saccharolytische (Gruppe II und III) Clostridien gehören zwar alle zum Cluster I, aber jeweils zu den phylogenetisch am weitesten entfernten Ästen, sind also am wenigsten verwandt.

- C. sporogenes ist auch deshalb ungeeignet, da bekannt ist, dass durch proteolytische Enzyme der Pansenflora das Botulinumneurotoxin degradiert wird, nicht der Erreger und nicht die Spore. Es wurde in einer Studie sogar gezeigt, dass C. sporogenes C. botulinum hemmt. Letztendlich würde C. sporogenes somit sogar zu den nützlichen Bakterien gehören

- Es wurde nur eine sehr kurze Testdauer von 5 Tagen nach Inkubation mit C. sporogenes gewählt. Das Krankheitsbild des „Chronischen Botulismus" zeichnet sich aber durch einen chronisch schleichenden, sehr langsamen Verlauf aus.
Um verlässliche Aussagen treffen zu können, hätte eine deutlich längere Testdauer gewählt werden müssen.

Es soll hier noch Folgendes angemerkt werden:
Nicht richtig ist die Behauptung des BfR in der BfR-Stellungnahme Nr. 033/2012 vom 14. August 2012: „Dem BfR liegen keine Studien vor, die einen adversen Einfluss von Glyphosat auf Bakterien des Magen-Darm-Traktes belegen. In Langzeitstudien an Nagern, an Hunden oder aber auch in Fütterungsstudien an Kühen oder Ziegen hätten sich nach Kenntnis des BfR Krankheitssymptome wie Gewichtsverlust, Durchfall oder Erbrechen manifestiert. Das war aber nicht der Fall."

In fast allen Studien zeigten sich sehr wohl Symptome wie Durchfall und andere gastrointestinale Krankheitssymptome - meist bereits ab den niedrigen Dosierungen [siehe DAR 1998 und RAR 2013].

Glyphosat wurde 1964 ursprünglich als Chelatbildner patentiert. (Erst 10 Jahr später erfolgte die Erteilung zur Nutzung als Herbizid.) Glyphosat ist ein starker Chelatbildner mit besonderen Metall-Chelatbildungseigenschaften: Es bildet stabile Glyphosat-Metall-Komplexe sowohl mit zweiwertigen Kationen von Metallen (Zn > Cu > Ca > Mg) als auch mit dreiwertigen Kationen von Metallen

(Co > Fe > Cr > Al). Es wurde in Untersuchungen gezeigt, dass sich neben tetraedrische auch oktaedrische Glyphosat-Metall-Komplexe bildeten.

Es wurde gezeigt, dass der Abbau von Glyphosat, wenn es als Glyphosat-Metall-Komplex vorliegt - z.B. in hartem Wasser oder metallhaltigen Böden -, ganz erheblich verzögert wird.

Ebenso behindern bzw. erschweren Metalle wegen der Chelatbildung die Analytik von Glyphosat und machen hier weitere Aufbereitungsschritte erforderlich. Andernfalls wird die Glyphosatmenge erheblich unterschätzt bzw. ist nicht nachweisbar.

Es erscheint deshalb durchaus wahrscheinlich und plausibel, dass Glyphosat auch in Organismen mit Metallen Glyphosat-Metall-Komplexe bildet und so z.B. Metalle, die für bestimmte Enzyme essentiell sind, komplexiert und so zu schädlichen Wirkungen durch Spurenelementmangel führen kann, wie sie in den Untersuchungen der Universität Leipzig an Rindern festgestellt wurden.

Fazit:

Die wissenschaftlich gut begründeten Bedenken, dass Glyphosat möglicherweise eine Dysbiose (Vermehrung von Schadorganismen wie z.B. Clostridium botulinum bei gleichzeitiger Schädigung „nützlicher, gesundheitsfördernder bzw. nicht-krankmachender Organismen") auslösen kann, sind nicht ausgeräumt worden (- auch nicht durch die in-vitro-Studie der Tierärztlichen Hochschule Hannover: "Einfluss eines glyphosathaltigen Pflanzenschutzmittels auf die ruminale Fermentation und mikrobielle Gemeinschaft in vitro unter besonderer Berücksichtigung von Clostridia").

Für eine abschließende Klärung wäre die Durchführung weiterer Untersuchungen - längerfristige in-vitro-Studien mit pathogen, toxinbildenden Bakterien und vor allem in-vivo-Studien - sinnvoll und notwendig, um die vermutete Wirkung zu bestätigen oder zu widerlegen.

Ebenso wenig wurden wissenschaftlich begründete Bedenken ausgeräumt, dass Glyphosat als erwiesenermaßen starker Chelatbildner schädliche Wirkungen (z. B. Spurenelementmangel) in höheren Organismen verursachen kann. Auch hier sind weitere Studien zur Klärung erforderlich.

2. Welche wiss. begründeten Hinweise für teratogene Effekte durch Glyphosat /glyphosathaltige PSM liegen vor? Sind die begründeten Hinweise auf teratogene Effekte bei der Bewertung von Glyphosat hinreichend berücksichtigt oder widerlegt worden?

Die im RAR 2013 zur Untersuchung der Teratogenität eingereichten Studien an Kaninchen geben wissenschaftlich begründete Hinweise für teratogene Effekte durch den Wirkstoff Glyphosat:
Zur Untersuchung der Teratogenität an Kaninchen liegen im RAR 2013 7 Studien vor, alle durchgeführt mit dem Wirkstoff. Im DAR 1998 wurden 5 Studien eingereicht, von denen eine jetzt als nicht akzeptabel aus der aktuellen Bewertung herausgenommen wurden. 3 „neue" Studien kamen hinzu. Die 7 Studien datieren zwischen 1980 und 1996. 6 Studien wurden nach OECD-Guideline durchgeführt, 5 Studien gemäß GLP.

Die 7 Studien wurden an 3 verschiedenen Kaninchenrassen durchgeführt: 5 Studien mit „Weißen Neuseeländern", 1 mit „Weißen Japanern" und 1 mit

„Gestreiften Holländern". Ob die verschiedenen Kaninchenrassen die gleiche Sensitivität hinsichtlich teratogener Effekte haben, ist zweifelhaft. Die teratogene Wirkung von Thalidomid (Wirkstoff von Contergan) beispielsweise konnte im Tierversuch ausschließlich an „Weißen Neuseeländern" gezeigt werden.

Die Kaninchen zeigten sich sehr empfindlich gegenüber Glyphosat. Toxische Effekte bei den Muttertieren zeigten sich bei fast allen Studien bereits bei der mittleren getesteten Dosis. Der NO(A)EL der Muttertiere war somit jeweils die niedrigste Dosis. Ausnahme war die Studie mit den „Weißen Japanern".

Bei den Föten zeigten sich in fast allen Studien Abnormalitäten in den Eingeweiden (zumeist beim Herzen sowie in den großen kardiovaskulären Gefäßen) und im Skelett.

In 3 der 5 Studien an „Weißen Neuseeländern" (Suresh 1993, TOX0551106; Broker et al. 1991, TOX9552391; Bhide & Patil 1989, TOX9551960) zeigten sich adverse Erweiterungen am Herzen. (In der 4. Studie an „Weißen Neuseeländern" (Cole & Dolemann 1996, ASB2012-11499) ist aufgrund von Defiziten in der Berichterstattung nicht klar, ob das Herz bei den viszeralen Untersuchungen überhaupt untersucht wurde (siehe Kommentierung des RMS/BfR im RAR 2013).) In einer der drei Studien (Suresh 1993) waren diese adversen Effekte („dilated heart") in allen getesteten Dosen (20, 100, 500 mg/kg/Tag) signifikant erhöht - also auch unterhalb der Dosis, bei der maternale Toxizität auftrat.
In der Kontrolle trat der Effekt nicht auf. Historische Kontrolldaten wurden zu diesem Effekt in der Studie nicht angegeben. Die Autoren dieser Studie stellten deshalb fest, dass für die Föten der NO(A)EL unterhalb der niedrigsten Dosis liegen würde und setzen 20 mg/kg/Tag als LO(A)EL fest.

Dennoch bewertete das BfR im RAR 2013 die Situation anders mit dem Hinweis, dass es keine eindeutige Dosis-Beziehung geben würde. Allerdings ist bei teratogen Effekten, z. B. bei Thalidomid (Contergan) gezeigt worden, dass die Dosis für das Ausmaß der Schädigung nicht relevant ist. Alleine der genaue Zeitpunkt der Einwirkung während der Embryonalentwicklung ist entscheidend, ob eine und welche - teils sehr spezifische - Schädigung verursacht wird. Eine Dosis-Beziehung trat bei Thalidomid nicht auf.

Außerdem wurde vom BfR bemängelt, dass sich die Terminologie um die Herzmissbildungen zu beschreiben (z. B. „dilated heart") in der Studie von der üblicherweise in der Teratologie benutzten Terminologie unterscheiden würde. Allerdings wurde erst Mitte der 90iger Jahre begonnen, eine international einheitliche Terminologie in der Reproduktionstoxikologie (also auch der Teratologie) festzulegen. 1993 gab es diese nicht.

In einer anderen Studie an „Weißen Neuseeländern" (Brooker et al. 1991) wurden ebenfalls signifikant erhöhte fetotoxische Effekte („Post-implantation loss") bei allen getesteten Dosen (50, 150, 450 mg/kg/Tag) festgestellt - also auch unterhalb der Dosis, bei der maternale Toxizität auftrat. Auch in dieser Studie konnte für die Föten also kein NO(A)EL festgelegt werden. Der LO(A)EL lag hier bei 50 mg/kg/Tag.
Auch dies wurde vom BfR, - m.E. nicht korrekterweise -, anders gesehen mit dem Hinweis auf eine fehlende Dosis-Beziehung (siehe oben) und auf historische Kontrolldaten. Bei 2 Dosen (50 und 450 mg/kg/Tag) lagen die Werte allerdings auch außerhalb der historischen Kontrolldaten.

Auch bei anderen Studien wurden signifikant erhöhte teratogene/fetotoxische Effekte mit Hinweis auf historische Kontrolldaten nicht berücksichtigt.

Im RAR 2013 wurden zwar die Bereiche der Kontrolldaten in den Tabellen angegeben, allerdings ist nicht klar, ob die historischen Kontrolldaten die Kriterien für historische Kontrolldaten gemäß „Guidance ReprTox 2008" erfüllen: Studien müssen im gleichen Labor, unter den gleichen Bedingungen (z.B. Spezies, Rasse, Lieferant der Tiere, Alter, Vehikel, Applikationsroute, Applikationsdauer, technisches Personal usw.) und innerhalb eines Zeitraums von +- 2 Jahren in Bezug auf die jeweilige Studie durchgeführt werden. Historische Kontrolldaten mit behandelten Tieren (wie z. B. mit 200 mg/kg Acetylsalicylsäure), wie in einer der Studien, können definitiv nicht als historische Kontrolldaten genutzt werden.

Auch in neueren (Labor- aber auch epidemiologischen) Studien mehren sich die Hinweise, dass Glyphosat (und/oder glyphosathaltige PSM) eine teratogene Wirkung haben könnte - auch wenn die Studien zweifelsohne teilweise methodische Mängel wie auch Defizite in der Berichterstattung aufweisen. Die in diesen Studien gezeigten teratogenen Effekte entsprechen (in großen Teilen) den Befunden in den Kaninchenstudien im RAR 2013.

Die Gesamtschau der Daten ergibt zumindest begründete Hinweise, dass Glyphosat eine teratogene Wirkung haben könnte. Die eindeutige Aussage des BfR, bei Glyphosat handelt es sich nicht um eine teratogene Substanz, ist mit den vorliegenden Daten nicht belegt.

Fazit:
Die im RAR beschriebenen teratogenen Studien an Kaninchen geben begründete Hinweise für mögliche teratogene Effekte durch den Wirkstoff Glyphosat. Auch in neueren (Labor- aber auch epidemiologischen) Studien mehren sich die Hinweise, dass Glyphosat (und/oder glyphosathaltige PSM) eine teratogene Wirkung haben könnte - auch wenn diese Studien zweifelsohne teilweise methodische Mängel wie auch Defizite in der Berichterstattung aufweisen. Die Gesamtschau der Daten ergibt zumindest begründete Hinweise, dass Glyphosat eine teratogene Wirkung haben könnte. Die eindeutige Aussage des BfR, bei Glyphosat handelt es sich nicht um eine teratogene Substanz, ist mit den vorliegenden Daten nicht belegt.

Um die teratogene Wirkung von Glyphosat zu bestätigen bzw. auszuschließen sind weitere Studien dringend erforderlich. Das können z. B. teratogene Studien an Schweinen sein, die laut einer noch nicht publizierten Studie ebenfalls reprotoxische Wirkungen zeigten (Aussage von Frau Prof. Krüger, Universität Leipzig). Außerdem wären epidemiologische Studien in diesem Zusammenhang wichtig.

3. Ist eine Festlegung (Anhebung) des ADI-Wertes auf Basis der Gesamtschau toxikologischer Studien gerechtfertigt oder wäre eine Absenkung geboten?

Im RAR 2013 werden - anders als noch im DAR 1998 trotz nahezu unveränderter Datenlage - zur Ermittlung des ADI-Wertes nun auch die teratogenen Studien an Kaninchen herangezogen und das Kaninchen als sensibelste Spezies berücksichtigt.

Aus den teratogenen Studien würde sich nach den Ausführungen unter Punkt 2 ein niedrigerer NO(A)EL ergeben und dieser würde auch zu einem geringeren ADI-Wert führen.

[Suresh 1993: LO(A)EL 20 mg/kg/Tag -> /Faktor 2 --> NO(A)EL 10 mg/kg/Tag. Sicherheitsfaktor 100 (ohne Berücksichtigung Teratogenität) => ADI = 0,1 mg/kg bw]

Sollte sich die teratogene Wirkung von Glyphosat in weiteren Studien bestätigen, wäre ein größerer Sicherheitsfaktor als 100 geboten und der ADI-Wert würde dann deutlich unter dem vorgeschlagenem Wert von 0,5 mg/kg bw liegen müssen.

Fazit:

Allein aus den Ausführungen unter Punkt 2 ergibt sich, dass eine Absenkung des ADI aufgrund der im RAR vorliegenden Studien auf mindestens 0,1 mg/kg bw gerechtfertigt wäre. Sollte sich die teratogene Wirkung von Glyphosat in weiteren Studien bestätigen, wäre dann auch ein größerer Sicherheitsfaktor als der üblich veranschlagte Wert von 100 geboten und der ADI-Wert würde dann deutlich unter dem im RAR vorgeschlagenem Wert von 0,5 mg/kg bw liegen müssen.

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Staatliches Gewerbeaufsichtsamt Hildesheim

Niedersächsisches Landesgesundheitsamt Hannover, 24.03.2014

Abt. 3 Umweltmedizin, Umwelthygiene und Umweltepidemiologie

Dr. K.-M. Wollin

Glyphosat, Dysbiose und *Chronischer Botulismus*

Clostridium botulinum ist die taxonomische Zuordnung für einen Komplex von anaeroben, sporen- und stäbchenbildenden Bakterien, denen die Bildung von einem oder mehreren Botulinum-Neurotoxinen (BoNT) gemeinsam ist (Brown et al. 2012). C. botulinum umfasst vier phylogenetisch und physiologisch unterschiedliche Gruppen. Zu unterscheiden sind sieben verschiedene BoNT (A, B, C1/C2, D, E, F und G), wobei nur die Typen A, B, E und F humanpathogen sind. Die Typen C und D sind tierpathogen. Hinsichtlich der Pathogenese beim Menschen werden der lebensmittelbedingte Botulismus (Aufnahme des Toxins) sowie der Wundbotulismus und der Säuglingsbotulismus (Wundkontamination durch Sporen oder Sporenaufnahme über die Nahrung durch den Säugling) unterschieden.

Unter der Bezeichnung *chronischer Botulismus* (auch: *visceraler Botulismus*, die Baucheingeweide betreffend) wird in der wissenschaftlichen Literatur seit einiger Zeit eine Hypothese zur Erklärung unspezifischer Krankheitserscheinungen in Rinderbeständen (Verdauungsstörungen, Labmagenverlagerungen, Abmagerung, Festliegen, Klauen- und Gelenkserkrankungen, Lähmungen, gespannte Bauchdecke, hochgezogenes Abdomen, Schluckstörungen sowie fieberhafte akute Entzündungen der Milchdrüsen (Mastitiden)) insbesondere im Zusammenhang mit dem Bakterium Clostridium botulinum diskutiert (http://www.fli.bund.de/fileadmin/dam_uploads/IBIZ/FLI_Botulismus_Informationen_20111005en.pdf). Die Erkrankungen sind zuerst bei Hochleistungsrindern, später auch bei Kälbern beschrieben worden.

Auch beim Menschen wurden chronische Krankheitsbilder beobachtet. Betroffen waren Landwirte und Familienangehörige, in deren Betrieben Rinder erkrankt sind (z.B. Krüger et al. 2012, Rodloff und Krüger 2012). Krüger et al. (2012) berichteten den Botulinum-Toxin - E-Nachweis in 16 von 77 Humanproben, während in den Rinderfaeces der BoNT-Typ A dominierte. Vier Personen zeigten unspezifische Krankheitssymptome

Die Ursache für die meist unspezifischen Symptome bei den erkrankten Menschen ist bislang weitgehend unklar geblieben. Eine 2009 veröffentlichte Übersichtsarbeit (Dressler und Saberi 2009) zum Thema Botulinum-Toxin postulierte den visceralen Botulismus im Menschen als neues Krankheitsbild in der Folge der Übertragung des chronischen Botulismus von Tier zu Mensch. Als mögliche Ursache der Symptome nennen Dressler und Saberi (2009) eine Besiedlung des Magen-Darm-Trakts mit dem BoNT-produzierenden Bakterium C. botulinum oder eine kontinuierliche exogene Zufuhr von Botulinumtoxin.

Die Deutsche Gesellschaft für Neurologie (DGN) hat 2012 in ihrer Stellungnahme festgestellt, dass bisher in keinem einzigen Fall das Vorliegen eines humanen chronischen Botulismus durch eine Erregerübertragung belegt ist. (http://www.dgn.org/component/content/article/23/1941-

pressemitteilung-08022012.html) Derzeit seien wesentliche Kriterien für einen kausalen Zusammenhang (z.B. Kohärenz, Konsistenz, Spezifität, Stärke des Zusammenhangs) zwischen dem postulierten Krankheitsbild und einer Toxikoinfektion aufgrund einer Besiedlung mit C. botulinum bzw. einer kontinuierlichen exogenen Zufuhr von Botulinumtoxin nicht erfüllt. Diese Position ist in den aktuellen DGN-Leitlinien in den Ausführungen zu Botulismus wiedergegeben (http://www.dgn.org/component/content/article/45-leitlinien-der-dgn-2012/2401-ll-39-2012-botulismus.html?q=botulismus, Stand: September 2012, gültig bis 2014): „Das Syndrom eines *chronischen Botulismus* bei Menschen, die in der Landwirtschaft tätig sind, wird postuliert, ohne dass bisher ein eindeutiger Beweis für seine Existenz gelungen ist". Ob das Krankheitsbild des *chronischen Botulismus*, das in der Veterinärmedizin seit mehr als zehn Jahren kontrovers diskutiert wird, auch bei Menschen, die in der Landwirtschaft in engem Rinder- bzw. Tierkontakt stehen, tatsächlich existiert und damit eine gesundheitspolitische Relevanz hätte, ist derzeit noch nicht völlig verstanden.

Die als chronischer oder visceraler Botulismus beschriebenen unspezifischen Erkrankungsformen sind bislang wissenschaftlich nicht als eigenständiges Krankheitsbild etabliert. Als eine mögliche Ursache der beobachteten Krankheitserscheinungen wird die Toxikoinfektion mit C. botulinum vermutet, die als noch nicht bestätigt gilt. Andere Wissenschaftler gehen demgegenüber von einem multifaktoriellen Ablauf der Erkrankung mit Beteiligung von verschiedenen Faktoren an dem Krankheitsgeschehen aus.

Jüngere Untersuchungen zum multifaktoriellen Symptomenkomplex des visceralen Botulismus deuten auf dysbiotische Zustände in der Magen-Darm-Mikrobiota hin (Krüger et al. 2012, Shehata et al. 2013, Krüger et al. 2013).

Bakterielle Fehlbesiedlungen (Dysbiose) des Darms bzw. des Gastrointestinaltraktes (GIT) sind charakterisiert durch a) qualitative und quantitative Änderungen der bakteriellen Darmflora selbst, b) Veränderungen ihrer metabolischen Aktivitäten und c) Veränderungen ihrer lokalen Verteilung. Die GIT-Mikroflora hat wichtige Funktionen und ist beteiligt an der Stimulierung des Immunsystems, der Vitaminsynthese, der Verbesserung der GIT-Motilität, der Verdauung und Absorption der Nahrung, der Inhibierung von Pathogenen, der Metabolisierung von Pflanzenbestandteilen und Arzneimitteln und der Produktion von kurzkettigen Fettsäuren und Polyaminen. Grundsätzlich ist die GIT-Mikroflora des Rindes noch mangelhaft charakterisiert und es finden sich auch deutliche, individuelle Unterschiede zwischen den Tieren (Jami und Mizrahi 2012, Durso et al. 2010). Eine Untersuchung in einem Rinderbestand über den Zeitraum von 8 Jahren berichtet starke natürliche jährliche Schwankungen der fäkalen Biota bei vergleichbarem Fütterungs- und Behandlungsregime (Rudi et al. 2012), so dass andere nicht kontrollierte Faktoren dafür wichtig sind.

Die Beeinflussung der Darmflora und ihrer Aktivität werden als Faktoren angesehen, die in Beziehung zu chronischen und degenerativen Erkrankungen gesetzt werden (Hawrelak et al. 2004). Dieses können beim Menschen unmittelbar Funktionsstörungen des GIT sein wie das Reizdarmsyndrom (Irritable Bowel Syndrom, IBS) oder entzündliche Darmerkrankungen (Inflammatory Bowel Disease, IBD) oder aber systemische Formen wie die rheumatoide Arthritis, die Spondylitis ankylosans (Morbus Bechterew) oder die Fettsucht (Hawrelak et al. 2004, Packey und Sartor 2009, Tannock 2010, Fava und Danese 2011, Harris et al. 2011). Faktoren, die die GIT-Flora schädigen können, sind z.B. Antibiotika, psychischer und physischer Stress sowie

Ernährungsumstellungen. Der negative Einfluss von Antibiotika ist gut bekannt wie ebenso der einer tierprotein- und zuckerreichen Ernährung (Hawrelak et al. 2004). Umgekehrt waren in einem Maus-Modell induzierte akute Leberschädigungen mit Veränderungen des intestinalen Mikrobioms assoziiert (Fouts et al. 2012). In Anbetracht des Antibiotika-Einsatzes in der Tierhaltung bei hochleistenden Tieren scheint von vorn herein die Möglichkeit der Beeinflussung der natürlichen Darmflora gegeben zu sein.

Aktuell wird in der wissenschaftlichen Literatur in Übersichtsarbeiten ein Zusammenhang zwischen der Dysbiose im GIT auch für Glyphosat als wahrscheinlich diskutiert (Seneff et al. 2013, Samsel und Seneff 2013, D'Brant 2014). Eine Schlüsselfunktion scheint die Störung der Expression der Cytochrom-P450-Enzymfamilie durch Glyphosat und nachfolgend die Beeinflussung der Biosynthese von aromatischen Aminosäuren durch die GIT-Bakterien zu haben.

In experimentellen Studien in vitro konnte gezeigt werden, dass a) kommensale Bakterien (die für den Wirt per Definition vorteilhafte Wirkungen entfalten) das Wachstum von C. botulinum inhibieren (Shehata et al. 2013) und b) bei Exposition gegenüber Glyphosat eine Hemmung der vorteilhaften Bakterien erfolgt (Shehata et al. 2013, Krüger et al. 2013). Shehata et al. (2013) zufolge könnte die Toxizität von Glyphosat gegenüber den am häufigsten vorkommenden Enterokokken (Enterococcus spp.) ein signifikanter Prädispositionsfaktor für C. botulinum-assoziierte Erkrankungen infolge der Suppression der gesundheitsfördernden Bakterien im GIT sein.

Den Ergebnissen der Arbeitsgruppe um M. Krüger stehen bisher in der Literatur nicht publizierte Daten von Breves und Riede (2014) (http://www.bfr.bund.de/cm/343/einfluss-eines-glyphosathaltigen-pflanzenschutzmittels.pdf) gegenüber. Mittels Rumen – Simulationstechnik, einem System, das die Verhältnisse im Wiederkäuerpansen abbilden soll (hier wird von einem Spendertier der Panseninhalt entnommen und direkt eingesetzt), wurde der Einfluss von Glyphosat auf die mikrobielle Gemeinschaft in vitro untersucht. Die Rumen - Simulationstechnik repräsentiert die Verhältnisse im Tier (d.h., die Bedingungen in vivo) realitätsnäher. Breves und Riede (2014) fanden keine Hinweise auf einen negativen Einfluss von Glyphosat - es handelte sich um ein kommerzielles Produkt, das zugleich das Netzmittel Tallowamine enthielt - auf die mikrobielle Gemeinschaft insgesamt sowie auf C. sporogenes (einem etablierten nichttoxischen Surrogat für C. botulinum (Brown et al. 2012)) selbst bei hoher Glyphosat-Dosis (2,92 mg/d).

Glyphosat wurde in einer weiteren Studie (Untersuchungen an dänischen Milchkühen, Krüger et al. 2013) mit veränderten Enzymgehalten und anderen veränderten Parametern, die indikativ für Nieren- und Lebertoxizität sind, sowie Spurenelementgehalten im Blutserum in Verbindung gebracht. In 240 Tieren aus acht Betrieben wurde Glyphosat in stark differierenden Konzentrationen im Urin gemessen. Die Interpretation der gemessenen Abweichungen der untersuchten diagnostischen Parameter ist schwierig, da die Herkunft der Referenzwerte in der Publikation nicht mitgeteilt wird und Angaben dazu fehlen, ob die gemessenen Werte bereits einen entsprechenden Krankheitswert mit entsprechenden klinischen Beobachtungen hatten. Dies betrifft insbesondere die ermittelten Spurenelementgehalte zu Mangan und Cobalt, die auf einen Spurenelementmangel hindeuten. Wegen der Übereinstimmungen der „postulated reference level" mit den Referenzbereichen der Medizinischen Tierklinik (MTK) Leipzig - diese wiederum stammen aus aktuellen Lehrbüchern und aus dem MTK-Labor

(http://www.vetmed.uni-leipzig.de/ik/wmedizin/labor/diagnostik/referenzwerte.htm) - kann vermutet werden, dass diese MTK-Werte verwendet wurden. Die Ursache der verminderte Cobalt- und Mangan-Blutserum-Werte könnte in Verbindung mit der Glyphosat-Aufnahme mit dem Futter stehen und der Komplexierung der Spurenstoffe stehen. Analysen zu den Inhaltsstoffen des Futters und Informationen zum Haltungsregime wurden in der Studie nicht berichtet.

Zusammenfassung

Glyphosat steht im Verdacht, im Magen-Darm-Trakt die Balance (Homöostase) der bakteriellen Mikroflora zu stören. In der Konsequenz könnte z.B. C. botulinum einen Wachstumsvorteil erzielen. Die bisher vorliegenden *experimentellen* Untersuchungen, die gezielt dieser These nachgehen, sind widersprüchlich und bei weitem nicht ausreichend. Sie bedürfen weiterer wissenschaftlicher Bestätigung, um eine belastbare Aussage in Richtung „Induzierung von Dysbiosen im GIT durch Glyphosat" treffen zu können oder, um diese These ausschließen zu können. Folglich können erst nach dieser Klärung weitere Überlegungen in Richtung der möglichen Ätiologie des *chronischen Botulismus* insbesondere unter Einbeziehung der Thematik Eubiose (= ausgeglichene Magendarm-Flora)/Dysbiose in die Gesamtschau des multifaktoriellen Geschehens folgen.

Das BfR kommentierte 2012 die Frage, ob bei der Risikobewertung potentielle schädliche Effekte von Glyphosat auf Bakterien des Magen-Darm-Traktes berücksichtigt worden sind. Nach Aussage des BfR lägen keine Studien vor, die einen schädlichen Einfluss von Glyphosat auf Bakterien des GIT im Tiermodell belegen. In Langzeitstudien an Nagern und Hunden oder auch in Fütterungsstudien an Kühen oder Ziegen hätten sich Krankheitssymptome wie Gewichtsverlust, Durchfall oder Erbrechen manifestieren müssen. Das sei jedoch nicht der Fall.

Diese vorgenannten Aussagen des BfR (2012) sind mit Bezug auf den Renewal Assessment Report Glyphosate (18. December 2013, RMS: Germany) sowie die bereits Mitte 2012 vorliegenden Studien und die existierende Datenlage nicht zutreffend.

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Abt. 3 Umweltmedizin, Umwelthygiene und Umweltepidemiologie

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Glyphosat, Risikobewertung Toxizität

Vorbemerkung

Der Prozess der toxikologischen Risikoabschätzung beinhaltet die Ermittlung des Gefährdungspotentials (engl. „Hazard Identification"), Erfassung der Dosis-Wirkungsbeziehung ("Dose-Response Assessment"), Expositionsabschätzung („Exposure Assessment") und Risikocharakterisierung („Risk Characterisation"). Dieses, auch als NAS-Paradigma bezeichnete Schema gestattet eine sequentielle Analyse wissenschaftlicher Daten. Von Bedeutung ist die eindeutige Unterscheidung des *Gefährdungspotentials* eines Stoffes vom tatsächlich gegebenen *Risiko*, das eine dosisabhängige Größe ist, damit aber in besonderer Weise von der tatsächlichen Exposition abhängig ist. Somit ist Toxizität die intrinsische Eigenschaft eines Stoffes, die erst dann wirksam wird und zu einem Schaden in einem Zielorgan führen kann, wenn der Stoff den Menschen überhaupt mit einer entsprechend hohen Dosis erreicht hat. Dieser Sachverhalt bleibt in der öffentlichen (medialen) Diskussion toxikologischer Studien zu Glyphosat sehr häufig unbeachtet.

Glyphosat ist als aktive Komponente in einer Reihe von Pflanzenschutzmitteln (PSM) eine toxikologisch gut untersuchte Substanz und es liegen zu allen bewertungs- und einstufungsrelevanten toxikologischen Endpunkten geeignete Studien vor, um Aussagen zum Stoff-Hazard und schließlich zum Risiko für den Menschen vornehmen zu können. Grundsätzlich ist die Beurteilung des aktiven Bestandteils Glyphosat von der Toxizität der PSM-Formulierungen zu unterscheiden. Eine aktuelle Zusammenfassung der Datenlage ist im Renewal Assessment Report (RAR) Glyphosate vom 18. Dezember 2013 zu finden (http://dar.efsa.europa.eu/dar-web/consultation). Deutschland war federführend als „Rapporteur Member State", die Slowakei war „C- Rapporteur Member State". Es wurden von den Herstellern und des Stoffes bzw. der Formulierungen (Glyphosat Task Force, GFC) seit der Zulassung 150 neue toxikologische Studien vorgelegt sowie diejenigen der bisherigen Bewertung unter Berücksichtigung aktueller Qualitätsstandards wie den neuesten OECD- und EU-Prüfrichtlinien re-evaluiert. Hinzu kommen etwa 900 publizierte wissenschaftliche Veröffentlichungen. Die neu hinzugekommenen Publikationen in der offenen wissenschaftlichen Literatur (ab 2000 bis August 2013) wurden im RAR analog zu den OECD-/EU-Guideline-Studien hinsichtlich ihrer Relevanz, Qualität und Zuverlässigkeit bewertet. Die Durchführung unter den Bedingungen der Guten Laborpraxis (GLP) ist ein Qualitätsmerkmal von toxikologischen Prüfungen, war aber kein Ausschlusskriterium, wenn eine Studie nicht unter GLP durchgeführt worden ist, aber den etablierten Anforderungen an Qualität und Zuverlässigkeit entspricht.

Glyphosat – intrinsische Toxizität (Hazard): Ergebnisse der Re-Evaluierung Dezember 2013

Glyphosat wird nach oraler Gabe an Ratten zu etwa 20% rasch absorbiert mit den höchsten Konzentrationen im Knochengewebe, Niere und Leber. Die Ausscheidung erfolgt mit dem Urin nach etwa 48 h. Glyphosat wird nahezu nicht metabolisiert, der Metabolit Aminomethylphosphonsäure (AMPA) findet sich nur in geringen Anteilen neben nichtabsorbiertem Glyphosat in den Faeces. Es gibt keine Hinweise auf eine Akkumulation von Glyphosat im Organismus.

Die Substanz weist nach oraler, dermaler und inhalativer Exposition in allen getesteten Spezies eine geringe akute Toxizität mit Werten der letalen Dosis (LD50) größer 2000 mg/kg KG (oral und dermal) bzw. LC50 (letale Konzentration) von größer 5 mg/mL Luft auf. Glyphosat ist nicht hautreizend und hautsensibilisierend, verursacht aber schwere Augenreizungen. Die Augenreizungen sind bei den Salzen des Glyphosats deutlich schwächer ausgeprägt.

In Kurzzeitstudien (subakute Exposition bis zu 28 Tage) nach wiederholter Gabe über alle Aufnahmepfade (oral, dermal, inhalativ) wurde in allen untersuchten Spezies (Ratte, Maus, Hund) eine niedrige Toxizität beobachtet. Die No Observed Adverse Effect Level (NOAEL), also die höchste Dosis ohne gesundheitliche Wirkungen, lagen zwischen 300 – 500 mg/kg Körpergewicht/d. Mortalität wurde in einer Hundestudie nach Applikation von Glyphosat in Kapseln bei der Dosis 1000 mg/kg KG/d festgestellt, die in einer weiteren Hundestudie nicht bestätigt wurde. Die Gabe über das Futter wird allgemein besser toleriert gegenüber der Bolusgabe in Form von Kapseln. Die Zielorgane der Toxizität in den Kurzzeitstudien waren der Gastrointestinaltrakt, die Blase und die Ohrspeicheldrüse. Weiter wurden Effekte auf die Körpergewichtsentwicklung, den Futterverbrauch und hämatologische Parameter beobachtet. Veränderte klinisch-chemische Parameter waren indikativ für Lebertoxizität, die aber nicht durch histologische Befunde unterstützt wurde. In subakuten dermalen Prüfungen wurden bis zu höchsten Dosen von 1000 bzw. 5000 mg/kg KG/d wurde keine systemische Toxizität, sondern nur leichte Hautreizungen beobachtet.

Erbgutverändernde Eigenschaften (Gentoxizität) wurde in vitro in Bakterien und Säugerzellen getestet. Die Ergebnisse von 14 als valide bewerteten Studien in S. typhimurium (Ames-Test) waren mit und ohne metabolische Aktivierung konsistent negativ. Ebenfalls negative Ergebnisse wurden in verschiedenen in vitro Testsystemen mit Säugerzellen erhalten. In vivo (Prüfungen an der Maus und Ratte) spielen Mikrokern-Testsysteme und Untersuchungen zum Nachweis von Chromosomenaberrationen eine wichtige Rolle. Unter den Bedingungen der durchgeführten Prüfungen war in der Gesamtheit aller Mikrokern-Tests in vivo und der Untersuchungen zu Chromosomenaberrationen in vivo Glyphosat nicht gentoxisch. Die Gründe, die zum Ausschluss von positiven Resultaten in vivo ursächlich waren, wurden transparent erläutert und sind nachvollziehbar.

Chronische Toxizität und Kanzerogenität wurden in Studien in der Ratte und Maus untersucht. Gegenüber der Risikobewertung in 1998 sind fünf neue Studien an der Ratte und 3 Studien an der Maus hinzugekommen. Die Re-Evaluierung der Studien, die bereits 1998 bewertet wurden, wurde nun durchgehend in Bezug auf den NOAEL anstelle des NOEL (No Observed Effect Level) in Übereinstimmung mit aktuellen regulatorischen Standards abgestellt. Die Folge sind höhere

NOAEL. Auf der Basis der chronischen Rattenstudien kann nach Ansicht der RAR-Autoren ein robuster, umfassender NOAEL von 100 mg/kg KG/d angenommen werden. Eine Monsanto-Studie aus 1981, für die ein NOEL von 31,5 mg/kg KG/d benannt worden war, wurde wegen der zu niedrig geprüften Dosen und Mängel in der Berichterstattung nicht mehr berücksichtigt.

Die kombinierten chronischen/Kanzerogenitätsstudien an der Ratte und Maus einschließlich der neu durchgeführten erbrachten keinen wissenschaftlichen Beweis für Kanzerogenität.

Es wurden etliche epidemiologischen Studien mit unterschiedlicher Differenzierung der Exposition in Pestizide allgemein, gruppenspezifische Pestizide und Glyphosat (in aller Regel Glyphosat-Formulierungen) in Bezug auf Krebs durchgeführt. Eine bekannte, inhärente Schwäche vieler dieser Studien ist ihre Schwäche in der Beschreibung der Exposition. So ist neben der Exposition gegenüber Glyphosat auch von der Aufnahme weiterer Pestizide oder anderer unbekannter Pestizide auszugehen. Es ist daher grundsätzlich schwierig, belastbare Aussagen in Bezug auf den Endpunkt Kanzerogenität und Glyphosat zu erhalten. Uneinheitliche Aussagen wurden in einigen Studien erhalten, die gezielt den Zusammenhang zwischen Glyphosat und dem Non-Hodgkin-Lymphom untersuchten. Die größte in den USA durchgeführte epidemiologische Untersuchung (AHS-Studie) zu Pestiziden – Glyphosat eingeschlossen – umfasste 57000 Landwirte und Pestizidanwender. Die späteren Auswertungen der AHS-Daten zu spezifischen Krebsformen erbrachten keine Assoziationen zu Glyphosat. In der Gesamtschau aller Studien gibt es keine Hinweise für eine Assoziation von Glyphosat und dem Endpunkt *Krebs gesamt* und einer Vielzahl spezifischer Krebsformen.

Aus den Ergebnissen der Gentoxizitäts- und Kanzerogenitätsprüfungen kann gefolgert werden, dass Glyphosat kein gentoxisches Kanzerogen ist.

Zur Reproduktionstoxikologie liegen Multigenerationsstudien in verschiedenen Spezies und Studien zur Entwicklungstoxizität und Teratogenität (d.h., die exogene Induktion von grob-strukturellen Abnormitäten) vor. Wie alle toxischen Wirkungen, sind fetotoxische Wirkungen (Wirkungen in der Embryo- und Fötalzeit in dem Zeitabschnitt zwischen Konzeption und Befruchtung) streng dosisabhängig. Als Besonderheit der Teratogenität gelten die Phasen-Spezifität und die Dosis-Spezifität neben der Substanz-Spezifität und der Spezies-Spezifität, wobei die beiden letzteren auch auf andere toxischen Wirkungen zutreffen (Neubert 1997, Schönfelder und Neubert 2013). Die Phasen-Spezifität bedeutet, dass Fehlbildungen nur in einem bestimmten Entwicklungsfenster erkannt werden können; Dosis-Spezifität heißt, dass unterhalb eines bestimmten Dosisbereichs (unterhalb des NOAEL) keine Fehlbildungen auftreten. Bestimmte teratogene Effekte können bei bestimmten höheren Dosen überdeckt werden durch solche eines stärkeren Effektschweregrades, so dass für ihre Erkennung die Wahl eines geeigneten Dosisbereichs die entscheidende Voraussetzung ist. Bei den meisten Stoffen werden teratogene Wirkungen in einem vergleichsweise engen Dosisbereich ausgelöst, die Dosis-Wirkungsbeziehungen sind durch eine große Steilheit gekennzeichnet. Diese Steilheit ist auch bei Thalidomidderivaten (z. B. EM12) im untersten Dosisbereich zu beobachten, wenngleich die teratogene Wirkung hier über einen Dosisbereich von etwa 3 Zehnerpotenzen, aber in unterschiedlicher Häufigkeit ausgelöst werden kann.

Die Datenlage aus Studien zur Reproduktionstoxikologie (Multigenerationen-Studien) ist ausreichend; von den ehemals acht Studien an der Ratte wurden nach Re-Evaluierung vier als

geeignet bewertet, die drei neuen Studien zur Reproduktionstoxizität wurden als uneingeschränkt valide bewertet. Die Bewertung aller Studien führt zu einem zusammenfassenden elterlichen NOAEL im Bereich von 300-400 mg/kg KG/d sowie zu NOAEL in den Nachkommen in dem gleichen Bereich, wie für die Elterngeneration ermittelt.

Aus der früheren EU-Bewertung (1998) wurden drei von 5 Studien zur Entwicklungstoxizität an der Ratte als akzeptabel und eine weitere als unterstützend bewertet. Zwei neue wurden als akzeptabel gewertet. Die früheren Bewertungen wurden bestätigt; in den Studien mit Schlundsonden-Verabreichung wurden teratogene Effekte in höheren Dosen (> 1000 mg/kg KG/d) beobachtet; der NOAEL liegt bei 300 mg/kg KG/d. Die beiden in 2012 neu bewerteten Studien ergaben einmal bis zur höchsten getesteten Dosis (1000 mg/kg KG/d, NOAEL für Entwicklungstoxizität) keine Effekte bzw. in der zweiten Studie einen NOAEL von 300 mg/kg KG/d.

Die fünf Studien der früheren EU-Evaluierung zur Entwicklungstoxizität im Kaninchen wurden in jüngerer Zeit in der wissenschaftlichen Literatur kritisch diskutiert. Von diesen fünf wurden aktuell drei als *ergänzend* (also abgestuft in Bezug auf ihre Validität) und eine als *valide* Studie bewertet. Die Konsequenz ist, dass einige LOAEL/NOAEL für Toxizität bei den Müttern und für Entwicklungstoxizität revidiert wurden.

Die Einstufungen als *Ergänzend* erfolgten in zwei Fällen wegen hoher Sterblichkeit der Mütter (maternale Toxizität) bereits in der mittleren und in der Hochdosisgruppe oder Defiziten in der Berichterstattung. Die hohe maternale Toxizität hatte insofern auch einen prägenden Einfluss auf Bewertung der Daten in den Fällen, wo formal statistische Signifikanz für teratogene Effekte vorlag. Die Bedeutung dieser Effekte wurde in Bezug auf die Rolle maternaler Toxizität als Ursache für Entwicklungstoxizität kontrovers diskutiert. Das OECD-Guidance Document (2008) zu reproduktionstoxikologischen Prüfungen und ihrer Bewertung sagt dazu aus, dass bei schwerer maternaler Toxizität, die das Wohlbefinden des Fötus gefährdet, die Daten zur Entwicklungstoxizität schwierig zu interpretieren sind. Die Verordnung EG 1272/2008 führt aus, dass eine maternale Toxizität von oberhalb von 10% überhöht ist und die Daten dieser Dosisgruppen normalerweise nicht für die weitere Evaluierung berücksichtigt werden sollen.

Diese Situation betrifft insbesondere die Studie *Feinchemie* (1993) (TOX9551106), wo zudem der teratogene Effekt in der höchsten Dosisgruppe – Herzerweiterung (dilated heart) - im Studienbericht nicht unzweifelhaft eindeutig anhand klarer und quantitativer Kriterien beschrieben wurde, was wiederum in der kritischen Literatur als eindeutiger Effekt reklamiert worden ist. Der v. g. Effekt ist in anderen Studien nicht bestätigt worden.

Ein grundsätzliches Problem ist die noch nicht abgeschlossene internationale Harmonisierung der Nomenklatur zur Beschreibung der neonatalen und fötalen Morphologie (OECD 2008).

Die nunmehr vier Studien der älteren EU-Bewertung zur Entwicklungstoxizität im Kaninchen zeigen zusammenfassend maternale NOAEL im Bereich 20-250 mg/kg KG/d und entwicklungstoxische NOAEL Bereich 100-250 mg/kg KG/d. Die entsprechenden Daten zu den drei neuen Studien zur Entwicklungstoxizität im Kaninchen der aktuellen Bewertung sind: maternale NOAEL im Bereich 50-100 mg/kg KG/d und entwicklungstoxische NOAEL Bereich 50-300 mg/kg KG/d.

Die bereits bekannten und neu berücksichtigten Prüfungen zur Entwicklungstoxizität zeigen eine besondere Empfindlichkeit von trächtigen Kaninchen gegenüber Glyphosat im Vergleich zu anderen getesteten Spezies. Die Autoren des RAR leiten auf der Basis aller Untersuchungen einen Gesamt-NOAEL für maternale Toxizität von 50 mg/kg KG/d und für Entwicklungstoxizität in Höhe von ebenfalls 50 mg/kg KG/d ab. Die Befunde zu Fehlbildungen des Herzens, die viel Diskussion auslösten, sind zwingend im Kontext maternale Toxizität zu sehen.

In der wissenschaftlichen Literatur wurden weitere in vivo Studien zu Reproduktions-/Entwicklungstoxizität veröffentlicht, die in der Öffentlichkeit als Beleg für ein entsprechendes *Risiko* von Glyphosat gesehen wurden (Dallegrave et al. 2003, Romano et al. 2010, Paganelli et al. 2012). Sie wurden mit kommerziellen Formulierungen durchgeführt. Entsprechende Evaluierungen der Studien erfolgten bereits auf EU- oder nationaler Ebene. Diese Studien erbrachten in Bezug auf die Beurteilung des Risikos von Glyphosat für den Menschen keine überzeugenden Beweise (unrealistisch hohe Dosen, unphysiologische Art der Applikation im Vergleich zur Möglichkeit der Exposition des Menschen, nicht ausreichend validierte Prüfsysteme), wohl aber die Erkenntnis der höheren Toxizität von Formulierungen im Vergleich zur aktiven Substanz Glyphosat allein.

Epidemiologische Studien zu Endpunkten der Reproduktions-/Entwicklungstoxizität waren, aus praktisch identischen Gründen wie diejenigen für den Endpunkt Krebs berichtet, ohne statistisch signifikante Assoziation zu Glyphosat.

Zur Bewertung der Neurotoxizität lagen jeweils eine akute (= Einmalgabe von Glyphosat) und eine subchronische (90 Tagesstudie) an der Ratte sowie eine Studie zur verzögerten Neurophatie (einer Erkrankung des peripheren Nervensystems) vor. Sie belegen, dass Glyphosat kein neurotoxizisches Potental aufweist.

Begründung/Ableitung eines Acceptable Daily Intake (ADI)

Die Ableitung eines ADI zur Bewertung von chronischen stofflichen Expositionen geht allgemein von der höchsten Dosis aus einer bestgeeignetsten Studie aus, bei der keine adversen (gesundheitsschädlichen) Wirkungen in der empfindlichsten Spezie aus tierexperimentellen Untersuchungen, im günstigsten Fall aus Beobachtungen beim Menschen, beobachtet worden sind. Es ist aber angemessener, aus allen validen Studien eines toxikologischen Endpunktes für die verschiedenen Spezies einen umfassenden LOAEL/NOAEL zu bilden.

Es ist festzustellen, dass in der regulatorischen Praxis selbst bei identischer Studienlage verschiedene Institutionen zu unterschiedlichen ADI-Ableitungen gekommen sind, wobei bereits in Bezug auf die Festlegung des NOAEL/LOAEL verschieden Bewertungen erfolgen können wie ebenso unterschiedliche Extrapolationsfaktoren für die Übertragung der Situation vom Tier auf den Menschen und die Berücksichtigung vulnerabler Personengruppen gewählt worden sind, die direkt die Höhe des ADI beeinflussen.

Dieser Sachverhalt trifft ebenfalls auf Glyphosat zu. Der gültige ADI in der EU beträgt 0,3 mg/kg KG/d und wurde seinerzeit auf der Grundlage der chronischen Studien an der Ratte nach oraler Exposition (NOEL 30 mg/kg KG/d) abgeleitet. Die WHO/FAO haben 2004 einen ADI von 1,0

mg/kg KG auf Basis einer 2-Jahres-Studie an der Ratte festgelegt, Ausgangspunkt war ein NOAEL von 100 mg/kg KG/d (JMPR 2004). Die U.S. EPA hat 2009 eine (chronische) Reference Dose (RfD) (identisch mit ADI) für Glyphosat in Höhe von 1,75 mg/kg KG abgeleitet; Grundlage war eine Studie zur Entwicklungstoxizität am Kaninchen mit einem NOAEL von 175 mg/kg KG/d (Federal Register /Vol. 76, No. 68 / Friday, April 8, 2011 /Rules and Regulations).

Die Ableitung eines ADI für Glyphosat auf Grundlage der chronischen Rattenstudien würde – da nunmehr die NOAEL als Ausgangspunkt (Point Of Departure, POD) betrachtet werden – zwangsläufig zu einem höheren ADI führen, wenn der Gesamt-*NOAEL* aller validen Tests in Höhe von 100 mg/kg KG/d als POD anstelle des früheren *NOEL* von 30 mg/kg KG/d dient. Allerdings ist die besondere Empfindlichkeit trächtiger Kaninchen zu berücksichtigen. Eine Dosis von 100 mg/kg KG/d führte bereits zu ausgeprägter maternaler Toxizität (Mortalität) (Feinchemie 1993, (TOX9551106) und ist als LOAEL ausgewiesen. Die maternalen LOAEL aus weiteren Prüfungen zur Entwicklungstoxizität liegen in einem etwas höheren Bereich von 150-200 mg/kg KG/d, waren dennoch niedriger als in allen anderen Studientypen in vivo, die mit Glyphosat durchgeführt worden sind. Im aktuellen RAR 2013 wird dann auf der Grundlage des Gesamt-NOAEL in Höhe von 50 mg/kg KG/d für sowohl maternale als auch entwicklungstoxische Effekte als POD mit einem Extrapolationsfaktor von 100 ein ADI von 0,5 mg/kg KG/d vorgeschlagen.

Der POD in Höhe von 50 mg/kg KG/d scheint gut begründet, in Hinblick auf Unsicherheiten in Bezug auf die langfristig – orale Exposition/systemische Wirkungen wird jedoch von uns ein zusätzlicher *Sicherheitsfaktor* von 2 empfohlen. Es würde dann ein ADI in Höhe von 0,25 mg/kg KG/d gegenüber den im RAR vorgeschlagenen ADI von 0,5 mg/kg KG/d resultieren.

Daten zur Erfassung der inneren Belastung des Menschen

Daten zur inneren Belastung des Menschen liegen vor und fanden so auch bei der Bewertung der Glyphosat-Nachweise in deutschen Urinproben Berücksichtigung. Für Deutschland und insbesondere Niedersachsen ist die Datenlage insgesamt nicht ausreichend bzw. sind Daten nicht bekannt; ein jüngerer Berichte zu 7 belasteten von 10 Urinproben aus Deutschland insgesamt fand mit seiner Vereinfachung – 70% der deutschen Proben waren belastet - starke mediale Beachtung (http://www.bund.net/nc/presse/pressemitteilungen/detail/artikel/glyphosat-im-urin-von-grossstaedtern-aus-18-europaeischen-staaten-nachgewiesen-70-prozent-aller-pro/). Die Höhe der Glyphosat-Nachweise in den deutschen Proben war nicht mit einem gesundheitlichen Risiko verbunden. Dennoch sind diese Ergebnisse ein Hinweis darauf, dass eine Exposition des Menschen vor allem über Lebensmittel gegeben ist und die grundsätzlich im Kontext zu Mehrfachbelastungen gegenüber PSM zu sehen ist. Die Ergebnisse zu Trinkwasseruntersuchungen in Niedersachsen für die Jahre 2011-2013 (Auswertungsstand 21.01.2014) zeigen keine Nachweise sowohl für Glyphosat (703 Proben) als auch den Metaboliten AMPA (700 Proben).

Zusammenfassung

Bezogen auf die frühere Risikobewertung der EU 1998/2002 sind seitdem zahlreiche neu, bewertungsrelevante Studien zur Toxizität von Glyphosat vorgelegt bzw. publiziert worden. Es ist vor dem Hintergrund zahlreicher in vivo Studien, die alle relevanten Endpunkte und relevanten Expositionszeiträume (akute bis chronische Exposition) abdecken, von einer sehr guten Datenlage zur Charakterisierung des toxikologischen Profils von Glyphosat auszugehen. Darüber hinaus sind im RAR 2013 Ergebnisse aus der offenen wissenschaftlichen Literatur, also i.d.R. Nicht-Guideline-Studien und solchen, die nicht unter den Bedingungen der Guten Laborpraxis durchgeführt worden sind, berücksichtigt und ausgewertet worden. Es fehlt allerdings trotz einer Reihe publizierter in vitro Tests, die vor allem mit Glyphosat-Formulierungen vorgenommen wurden, noch Ergebnisse zu systematischen Untersuchungen zur Abklärung des Potentials des aktiven Bestandteils Glyphosat hinsichtlich seiner endokrinen Aktivität. Ein entsprechendes Programm ist von der U.S. EPA begonnen worden. Erste dokumentierte Ergebnisse zu einigen bereits geprüften Endpunkten erbrachten in diesem Programm kein entsprechendes Potential von Glyphosat.

Die Fragen der Aufgabenstellung MU werden zusammenfassend wie folgt beantwortet.

1. Wo liegen die Risiken von Glyphosat?

Die Unterscheidung der Begriffe Risiko und stoffliches Gefährdungspotential wurde in der Vorbemerkung erläutert, das Stoff-Hazard auf Basis des aktuellen Kenntnisstands nachfolgend umrissen. Für den Verbraucher in Deutschland ist vor dem Hintergrund der aktuell bekannten und gemessen inneren Belastung und mit Blick auf den Bewertungsmaßstab ADI nicht von einem Risiko auszugehen. Die Minimierung der Glyphosat-Belastung ist vor dem Hintergrund des Nachweises im Menschen anzustreben. Die Regulierung kritischer Bestandteile in Glyphosat-Formulierungen (oberflächenaktive Bestandteile) ist abschließend gesetzlich zu regeln; unbestritten weisen kommerzielle Glyphosat-Formulierungen (und die anderer PSM-Formulierungen) eine höhere Toxizität auf.

2. Ist die herbe Kritik an Glyphosat gerechtfertigt oder nicht?

In Bezug auf den Endpunkt Humantoxizität – nein. In der öffentlich-medialen Diskussion erfolgte u.a. eine Überbewertung von Effekten in in vitro Studien.

3. Werden aus den vorliegenden Erkenntnissen die richtigen Schlüsse gezogen?

Hinsichtlich der Bewertungen zur Humantoxizität seitens der Bewertungsbehörden BVL und BfR sowie der europäischen Lebensmittelbehörde EFSA – ja.

Dr. Klaus-Michael Wollin, 24.03.2014

(Dipl.-Chemiker, Fachtoxikologe DGPT/ERT)

2. Mammalian toxicology (B.6)

Reproductive toxicity (B.6.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B 6.6.12., Published data (released since 2000), p. 659	Dr. P. Clausing: The important findings by Beuret et al (2005) – increased lipid peroxidation - are not taken into consideration. Instead the reduced reduced food consumption "that could have affected the altered enzyme concentrations" is criticized. This is a **wrong, misleading assessment**, because studies with restricted diets (see references in column 3) show that reduced food consumption actually **decreases** lipid peroxidation whereas here an **increase** of lipid peroxidation and of the corresponding enzyme activity is shown. In other words, it is highly likely that this change was caused by the test item and not by the reduced food intake	See Rao et al. (1990): J. Nutr. 120:602-609; Xia et al. (1995): J. Nutr. 125 195-201; Kim et al. (1996): Aging 8:123-129 concerning the reduction of lipid peroxidation under reduced food consumption. The results (increased lipid peroxidation) are important in the light of epidemiological findings indicating possible increased tumor incidences in glyphosate exposed populations. Effects of glyphosate on lipid peroxidation should be thoroughly assessed.
(2)	Vol. 3, B 6.6.12., Published data (released since 2000), p. 659	Dr. P. Clausing: The findings by Dallegrave et al. (2003) were dismissed because of "reporting deficiencies and inconsistencies" without giving any further details. While there is an obvious mistake in the publication concerning the number of foetuses vs. implantation sites and corpora lutea (which probably is related to the count of corpora lutea and/or implantation sites) this *per se* does not affect the finding of a statistically significant increase of skeletal alterations. Therefore, this study should not be dismissed.	For safety assessments concerning occupational health it is important to take into consideration results from exposure to formulations (in addition to studies using the active ingredient)

1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)

Identity (B.1, Annex C)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)			

Physical and chemical properties of the active substance (B.2.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Physical, chemical and technical properties of the formulation (B.2.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Further information (B.3)

No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Methods of analysis (B.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Other comments (B.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol.3, B.6, Toxicology and metabolism, page 2	PAN Germany: In the classification of studies the categories 2, 3 and E are made subject to the so-called Klimisch-criteria. These criteria are based on a proposition published in 1997 by employees of the chemical company BASF. We do not agree that most independent scientific studies are excluded as “unreliable” because they do not meet the Klimisch (= OECD/GLP) criteria. It can’t be that the scientific evidence of independent academic scientists is not considered in the risk	Studies need to be assessed on their scientific value and not being dismissed because they do not meet the Klimisch (= OECD/GLP) criteria which had been set mainly by chemical industry. Next a 'weight of the evidence' approach should be followed, including all scientifically qualified studies available, especially independent studies.

Other comments (B.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		assessment.	
(2)	Vol.3, B 6	PAN Germany: A RMS must always have a high level of critical awareness regarding industrial studies knowing that Industry is led by its interests in selling products and making profit top priority over society's interests for a living without chemical harm and a healthy environment.	We are disappointed that the RMS agreed on the completeness of the dossier while demanding extra tests and confirmatory information would be the proper approach, especially in case the outcome of industry-sponsored studies differ from academic studies.
(3)	Vol.3, B.6	The tests performed by the applicants based on good laboratory practice (GLP) don't automatically guarantee quality & reliability. Several cases of industry laboratory fraud (IBT, Craven) were discovered by regulators (including tests on Glyphosate). Fraudulent tests had been replaced but our doubt on their quality and reliability remains. GLP is just a management system, forcing laboratories to be transparent; no-one can guarantee what happens or is written down in the tests.	Commission therefore needs to explain what guarantees they have used to ensure quality and reliability of tests, both old and new. Many outcomes of studies comparing GLP-studies and studies from open (independent) literature have different outcomes. A differentiated examination of the described different outcomes is missing.

2. Mammalian toxicology (B.6)

Toxicokinetics (B.6.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Acute toxicity (B.6.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol.3, B.6.2.3, page 240	PAN Germany: we do not understand that the exposure of test animals at 1000 ppm is called "low". With a current ADI of 0,3 ppm we challenge the value of this type of experiments with extreme high doses. This also means that effects seen at doses people are exposed to in practice are not tested and given the fact that Glyphosate has endocrine disrupting properties, adverse effects of low doses at vulnerable periods of development cannot be excluded.	We do not understand what we can learn from exposure of 20.000 ppm. Can any effect seen at this unrealistic dose be extrapolated to lower doses, thousand times lower and more, to predict an effect? We do not think that this type of mechanistic linear dose-response thinking has any basis in science. A body is no machine but an interrelated system with three major communication systems with triggers and feedback. OECD-tests are very insensitive and should be replaced by realistic dose tests on those elements (with very specific and sensitive endpoints) derived from the hazard assessment (mainly based on academic studies).

Section 2 - Mammalian toxicology (B.6)

Short-term toxicity (B.6.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Genotoxicity (B.6.4)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol.3, B.6.4, genotoxicty, page 359	PAN Germany: In Table B 6.4-15 an experiment is disqualified for having too low doses. This is difficult to understand since the dose is still above ADI and far more relevant than the many dozens studies at extreme high dose.	Also remarkable is that at these doses effects are seen. They are subsequently qualified as not relevant using an industry-invented tool called "historical control data" allowing adverse effects being dismissed. Historical control data are never used by active scientists; they rely on normal controls.
(2)	Vol.3, B.6.4, genotoxicty, page 382	PAN Germany: The study discussed showing clastogenicity is done at lower levels than usual. It concludes that effects are seen al lower levels while no effects are seen at higher levels. This again would be reason to reconsider the old paradigms of linear dose-response and use of high unrealistic doses.	
(3)	Vol.3, B.6.4, genotoxicity, page 384	PAN Germany: The study of Clemens shows mutagenicity in tadpoles and the occurrence of this effect is not excluded by the RMS. However in the next lines many questionable assumptions and reasoning are added by the	We think the only proper approach in case of uncertainties would be to demand the test to be repeated and confirmed in independent laboratories and blind testing. And the process of approval halted until more clarity is given.

Genotoxicity (B.6.4)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		RMS and finally the effects dismissed for humans. We cannot agree with this.	
(4)	Vol.3, B.6.4, genotoxicty, page 385	PAN Germany: We think it is not justified to dismiss studies (genotoxic effects in germ cells in Drosophila) that challenge industry findings by immediately pointing at the "large database of existing studies`. This gives the impression the RMS had already made up his mind about mutagenicity and is now just looking for reasons to dismiss critical studies.	All studies should be used for a weight of the evidence approach in an open scientific approach without prior opinions or feelings. We think independent experts, who were not involved in drafting the RAR and who have no contacts with industry, are needed to do this weight of the evidence evaluation. The same approach is taken on page 386 for another critical study.
(5)	Vol.3, B.6.4, genotoxicty, page 386	PAN Germany: We can understand that the applicant will claim that any adverse effect seen is due to the co-formulant and as such these studies should not count. We do not understand the claim of the RMS that it can "certainly be assumed" that an effect will be caused by the co-formulant. RMS's should not assume but assess. And if they have no data to prove that it was the co-formulant, the effects should be counted for the active ingredient.	Again, there is all reason to demand the applicant to repeat academic studies showing adverse effects by exposing the active substance. This should be done in an independent laboratory with blind testing.
(6)	Vol.3, B.6.4, genotoxicty, page 389	PAN Germany: The claim in the RAR of a “lack of mutagenicity” or even that results of studies are consistently and unequivocally negative (Vol.1) is false. Genotoxic effects on the contrary are already long known and available to the reviewers. (see references in column 3)	Kale, 1995, showed mutations in fruit flies, Vigfussen, 1980, showed sister chromatin exchanges in human lymphocytes, just as Bolognesi in 1997. Peluso in 1998 showed increased DNA adducts in mice. Gasnier, 2009, showed DNA damage, as well as Manas, 2009. Some are captured in the industry review, others not, for unknown reason. All are dismissed in the end. Literature references will be provided on

Genotoxicity (B.6.4)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		Numerous other studies have confirmed DNA damage in mouse, bovine, fish, caiman, tadpole, fruit fly, sea urchin, onion, and bacterial cells. We propose EFSA starts her peer-review with independent literature.	request but should also be part of the review of the applicant on peer-reviewed literature. We only mention, Grisolia, 2002, Sivikova, 2006, Belle, 2007, Cavas, 2007, Cavalcante, 2008, Guilherme, 2009, Poletta, 2009, Monroy, 2005. It is really a joke the RMS uses the unscientific Klimisch-criteria for academic studies. Anyone knows the outcome: all dismissed! Given the conflict of interest of the applicant on safety testing, and the potential bias in studies or interpretation of studies, we propose EFSA starts her peer-review with independent literature for doing a hazard assessment. Independent literature has less chance on bias because of lacking motives and should be qualified as more reliable than industry-sponsored studies with an inherent conflict of interest. It is strange to note that Table 2.6-6 in Volume 1 only summarises industry-sponsored studies.
(7)	Vol.3, B.6.4.8.10, weight of the evidence	PAN Germany: While the RMS discusses a few of the academic studies that show adverse effects, in the 'weight of the evidence' approach taken by the RMS as a standard procedure plays down the positive effects seen by assumptions and reasoning's such as the effects being indirect, or being beyond a certain threshold, not relevant for humans, suggests that the effect are toxic but not mutagenic. None of these assumptions is based on science but just part of the old paradigm used by regulators.	The RMS has high confidence in industry-sponsored studies and very low in academic studies, with the result that only industry-sponsored studies with their favourable outcome for industry are counted in the final evaluation.

Genotoxicity (B.6.4)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations

Long-term toxicity and carcinogenicity (B.6.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol 3, B 6.5. Long-term toxicity and carcinogenicity, page 435	PAN Germany: A major failure in the testing systems used is the lack of exposure in-utero of the test animals. It is well-known that many chronic diseases develop in-utero (not only for cancer) and as such tests lacking in-utero exposure cannot be qualified as a 'state-of-the art' scientific approach. The conclusion that the substance is not carcinogen needs to be justified. We propose EFSA requires the applicant to test again (in-utero exposure, with blind testing in an independent laboratory.)	EU legislation provides for a high level of human health protection based on the precautionary principle and requires special attention for the vulnerable, the unborn and the elderly. The test system disregards the effects on the vulnerable groups in society.
(2)	Vol 3, B 6.5. Long-term toxicity and carcinogenicity, page 435	PAN Germany: Next point is the extreme high doses used in notifier's testing. Evidence is available in literature (see Vandenberg et al. 2012 review) that low doses can harm, many times in the developing phase of the organism and many times for endocrine disrupting chemicals. Since Glyphosate has endocrine disrupting properties, EFSA should perform a	EFSA should require the applicant to do new testing of the substance including a range of low doses.

Long-term toxicity and carcinogenicity (B.6.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		thorough review on the data in independent literature, and require applicant to do a series of low dose testing on endocrine adverse effects.	
(3)	Vol 3, B 6.5. Long-term toxicity and carcinogenicity, page 435	PAN Germany: Another point on carcinogenicity is the need to expose and follow test animals during their entire lifetime. Most diseases develop after notifier's tests incinerate the test animals (e.g. ACS (American Cancer Society): *Cancer Facts & Figures 2012*. Atlanta: American Cancer Society; 2012. [http://cancer.org/acs/groups/content/@epidemiologysurveilance/documents/document/acspc-031941.pdf].	EFSA should require the applicant to do new testing of the substance including lifetime exposure and monitoring.
(4)	Vol 3, B 6.5. Long-term toxicity and carcinogenicity, page 502	PAN Germany: No evidence in rat according to the RAR (only industry-sponsored studies analysed) but the malignant lymphoma seen in mice was dismissed. It was not the chemical (Glyphosate) that should be blamed according to the RMS but the strain of mice. We think this has nothing to do with a scientific evaluation but more with a determination to get to a certain outcome. Given the many articles in peer-reviewed literature on long-term effects and cancer, a more balanced approach would have been justified.	We propose that based on the studies in open literature a hazard assessment is done to find out what long-term effects and cancers can be expected to occur by the use of Glyphosate. Next, an analysis needs to be done if the long-term and carcinogenicity animal tests will really capture the expected effects. And finally those long-term and carcinogenicity tests qualifying for capturing the adverse effects should be used for a final conclusion. No study should be dismissed for being non-GLP or non-OECD. Every study counts, also the one of Seralini.

Section 2 - Mammalian toxicology (B.6)

Long-term toxicity and carcinogenicity (B.6.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(5)	Vol 3, B 6.5. Long-term toxicity and carcinogenicity, page 502	PAN Germany: Glyphosate has a history of links with cancer. The first carcinogenicity study submitted to US-EPA (1981) by applicant Monsanto showed an increase in testicular tumours in male rats as well as an increase in the frequency of a thyroid cancer in females. Both results occurred at the highest dose tested (30 mg/kg of body weight per day). The second study (1983) found an increasing trend in the frequency of a rare kidney tumour in male mice (see further examples in column 3)	A later study (1990)found an increase in pancreas and liver tumours in male rats together with an increase of the same thyroid cancer found in the 1983 study in females. We ask EFSA to take a look at these older studies. There is good reason for EFSA to start the cancer analysis from scratch including all evidence from the past and from independent literature. Knowing the potential of Glyphosate to cause these effects, are the currently evaluated safety tests designed to capture these effects?
(6)	Vol 3, B 6.5. Long-term toxicity and carcinogenicity page 524	PAN Germany: In the RAR all epidemiology studies showing a relation between Glyphosate and cancer are considered irrelevant, such as the Hardell-studies on the link with non-Hodgkin's, and even the unscientific Klimisch-approach is used for this qualification. This is unjustified. Now industry has created a situation in which people are exposed to thousands of chemicals at the same time. This means if a relation is shown, even weak, this should be reason for concern, monitoring and more information.	If a relation is shown, this should be reason to demand the applicant to do independent monitoring to get more information Industry should monitor the use of Glyphosate, analyse all environmental compartments and organisms, and do a large epidemiology study focussed on clarifying the evidence available. There is good evidence on the relation with non-Hodgkin's lymphoma, Nordstrom, 1998, Hardell, 1999 and 2002, McDuffie, 2001, De Roos, 2003 and Eriksson, 2008, and multiple myeloma, De Roos, 2005, and a large study should be initiated to find out more.
(7)			

Long-term toxicity and carcinogenicity (B.6.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations

Reproductive toxicity (B.6.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol.3 B.6.6 Reproductive toxicity. page 538	PAN Germany: A big omission in the German RAR is the lack of a hazard characterization of Glyphosate. In many EFSA opinions it is stated that the first step of risk assessment is the hazard characterization. We observe that the RMS just moves on directly to risk characterisation and standard setting, and ignores the evidence on hazards.	A hazard characterization is important to learn about the mechanism of toxicity of Glyphosate. Without the knowledge of the hazards it will be difficult to select in the next steps of risk assessment what data are useful and not. Germany as RMS just puts all evidence in the "Klimisch-mill" with the obvious effect of all independent science disregarded.
(2)	Vol.3 B.6.6 Reproductive toxicity. page 538	PAN Germany: We urge EFSA to include a hazard characterisation in the peer-review. This should be done by using all in-vitro studies available, disregarding none, and all mechanistic studies available. The peer-review should focus on what mechanistic evidence is present on teratogenicity, on DNA-damage., etc.?	The study of Paganelli et al. 2010 presents interesting evidence on the mechanism of action. During early embryonic development, retinoic acid generated in a specific region of the embryo helps determine position along the embryonic anterior/posterior axis by serving as an intercellular signalling molecule that guides development of the posterior portion of the embryo. It acts through Hox genes, which ultimately control anterior/posterior patterning in early developmental stages. The findings of Marc et al. '05 support this, offering a general mechanism of action for teratogenicity.
(3)	Vol.3 B.6.6	PAN Germany: Many multi-generation tests in the	The industry-sponsored OECD tests are known for their insensitivity

Reproductive toxicity (B.6.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	Reproductive toxicity. page 539	RAR with their very high (and unrealistic) doses, endpoints which are not the state-of-the-art, cannot provide for the final answer on reproductive toxicity. Study results that showed effects at low doses were dismissed by the RMS. Studies showing effects on the offspring were accepted because they are observed at high doses. Combined with the many studies in open literature on malformations of the offspring and developmental effects, a peer-review by EFSA of all evidence is more than necessary.	and this could explain the very remarkable difference seen between the industry-sponsored studies and independent literature. The high doses used are close to the acute poisoning doses and poisoning effects are common in these tests, while more subtle effects could be missed.
(4)	Vol.3 B.6.6 Reproductive toxicity. page 548	PAN Germany, we again question the use of extreme high exposure doses such as 15.000 ppm or 1000 mg/kg, more than 1000x the ADI. Animals should be tested at realistic doses and no extrapolation used	The high doses are close to the acute poisoning doses used and poisoning effects are common in these tests, while more subtle effects could be missed.
(5)	Vol.3 B.6.6 Reproductive toxicity. page 596	PAN Germany: We especially encourage EFSA to take a look at teratogenicity. The pre-2001 studies of Monsanto show teratogen effects, a range of independent studies report these effects, these effects are also observed in areas with Roundup monocultures (soy) in epidemiology studies and even in "bioindustry" where piglets fed on soy have these effects.	In the first DAR on Glyphosate in 2001, the UK experts commented that -based on the Monsanto studies- a single study might not raise concerns, but that the teratogenic effects that kept being observed in the Monsanto-studies, pointed at a pattern that should not be dismissed in the risk assessment. EFSA should assess if in the two-generation studies the animals are properly exposed during vulnerable windows during development and if a large range and relevant endpoints are considered for teratogenicity and development during later life of the offspring.

Reproductive toxicity (B.6.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(6)	Vol.3 B.6.6.9, Reproductive toxicity. page 597	PAN Germany: Specific endocrine disrupting tests should be demanded from the applicant. Just basing conclusions on outdated OECD-protocols on reproduction and development is not justified. The science on endocrine disruption differs a lot from other fields and specific exposure windows, doses and specific endpoints should be used. In the traditional tests with traditional experts these effects will be missed.	
(7)	Vol.3 B.6.6.9 Reproductive toxicity. page 597	PAN Germany: A large body of evidence on endocrine disrupting effects of Glyphosate is disregarded and dismissed in the RAR. Walsh, 2002 showed the disruption of the steroid hormone progesterone, as well as Romano, 2010 on testosterone. Richard, 2005 also concludes Glyphosate is an endocrine disruptor by affecting aromatase at very low doses. Also Benachour, 2005 and Gasnier, 2007 came to the same conclusion.	Hokanson, 2007, demonstrated a synergistic effect of Glyphosate with oestrogen, with implications for pregnancy-induced hypertension and foetal growth retardation. The implications of these effects on reproduction and the developing foetus are profound, with work by Mose, 2008, confirming that Glyphosate does cross the placenta.
(8)	Vol.3 B.6.6.10 Reproductive toxicity. page 613	PAN Germany: the study in rabbits shows that at a level of 10 mg/kg 20% of the litters have malformations while this is 5% in the control (this also counts for the foetus, 3,1% vs. 0,7%). While this dose is at least less enormous than the regular dose, it is still above a realistic dose	The malformations should be more thoroughly investigated and this study already shows that the LOAEL of 10 mg/kg should be adopted for standard setting. A suggesting NOEAL of 100 mg/kg by the applicant is absurd.

Reproductive toxicity (B.6.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		and we think additional studies should be done with lower loses.	
(9)	Vol.3 B.6.6.10 Reproductive toxicity. page 619	PAN Germany: This study in rabbits again shows most effects at the lowest dose tested (18 vs. 13 of the litters tested with malformations), 50 mg/kg. While this dose is still unrealistic high, lower doses should be tested on malformations of the foetus.	
(10)	Vol.3 B.6.6.10 Reproductive toxicity. page 629	PAN Germany: This study in rabbits also shows malformations at the lowest level tested (82 foetus with 'minor' defects vs, 58 in the control), 100 mg/kg. This "low" dose is of course unrealistically high.	There is a clear pattern of malformations of the foetus in all rabbit studies.
(11)	Vol.3 B.6.6.10 Reproductive toxicity. page 642	PAN Germany: This study confirms previous observations that malformations of the foetus is highest in the lowest dose tested, 50 mg/kg, (17.7% vs. 11,7% in the control). We object to the use of historical control data. The only scientific approach is to compare the outcome in the tests against the control.	Why the RMS values historical control data over the normal (negative) control is a mystery. While it is highly questionable if the industry-sponsored studies are reproducible at all, historical control data mix different labs, operators, protocols and strains and create an unrealistic wide range of "controls'. No scientist will ever use this type of tools.
(12)	Vol.3 B.6.6.10 Reproductive toxicity. page 650	PAN Germany: Also this study shows effects at the lowest dose tested, 20 mg/kg, upper cleft palate, 15% vs. 5% in the control, and dilated heart, 23,1% vs. 0% in the control.	There is a clear pattern of malformations of the foetus in all rabbit studies.
(13)	Vol.3 B.6.6.12,	PAN Germany: It is remarkable that the RMS	The RMS ends their report by saying: "An adequate response to the

Reproductive toxicity (B.6.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	Reproductive toxicity, Published data, page 658	now easily rejects all claims made by EOS in their report "The recently published report "Roundup and birth defects: Is the public kept in the dark?"" and let most independent literature fall under the 'Klimisch-axe". In their reaction in July 2011, the RMS called the report: "… a challenging critical summary of adverse health (mainly teratological and reproductive) findings that are attributed by the authors to the compound glyphosate and/or to herbicides such as Roundup that contain glyphosate as active ingredient."	criticism and the many accusations in the report would require a general discussion of the established paradigms for the toxicological evaluation of chemicals, including the postulated shortcomings in the legal system, the recourse to independent science, the Commitology system, GLP, the alleged insufficiency of the toxicological approach. These general discussions should be initiated by the Commission before we start with the re-evaluation of glyphosate within the AIR2 project." (http://www.bfr.bund.de/cm/343/neue_daten_zu_gesundheitlichen_aspekten_von_glyphosat.pdf) We fail to have seen any general discussion on established paradigms, not by the RMS and not by Commission. We therefore urge EFSA to start such a discussion before drafting the peer review on Glyphosate.
(14)	Vol.3 B.6.6.12, Reproductive toxicity, Published data, page 658	PAN Germany: It is sad to note that the industry review made by the applicant is not commented by the RMS. Given the many missing studies and the standard use of Klimisch to dismiss studies on a large scale, an intervention of the RMS was needed very much.	We urge EFSA to review all independent studies and stop using the entirely unscientific Klimisch-tool and do a purely scientific assessment of each study looking at the quality of the study, disregarding protocols and GLP-administration systems.
(15)	Vol. 3, B 6.6.12., Published data (released since 2000), p. 659	PAN Germany: Relevant findings by Beuret et al (2005) – increased lipid peroxidation – had not been taken into consideration. Instead the reduced food consumption "that could have affected the altered enzyme concentrations" is	See Rao et al. (1990): J. Nutr. 120:602-609; Xia et al. (1995): J. Nutr. 125 195-201; Kim et al. (1996): Aging 8:123-129 concerning the reduction of lipid peroxidation under reduced food consumption. It is very likely that the described change was caused by the test item and not by the reduced food intake.

Reproductive toxicity (B.6.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		criticized. This is a wrong, misleading assessment. Studies with restricted diets show that reduced food consumption actually decreases lipid peroxidation whereas here an increase of lipid peroxidation and of the corresponding enzyme activity is shown. (see further explanation in column 3).	The results (increased lipid peroxidation) are important in the light of epidemiological findings indicating possible increased tumor incidences in glyphosate exposed populations. Effects of glyphosate on lipid peroxidation should be thoroughly assessed.
(16)	Vol. 3, B 6.6.12., Published data (released since 2000), p. 659	PAN Germany**:** Findings by Dallegrave et al. (2003) were dismissed because of "reporting deficiencies and inconsistencies" without giving any further details. The obvious mistake in the publication concerning the number of foetuses vs. implantation sites and corpora lutea (which probably is related to the count of corpora lutea and/or implantation sites) does not *per se* affect the finding of a statistically significant increase of skeletal alterations. Therefore, this study should not be dismissed	For safety assessments concerning occupational health it is important to take into consideration results from exposure to formulations (in addition to studies using the active ingredient)

Neurotoxicity (B.6.7)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol.3, B.6.7.1, Neurotoxicity, Published data, page 702.	PAN Germany: Epidemiology studies have been published pointing at Glyphosate of causing mental disorders of children born to pesticide applicators in the US, Garry, 2002. Even acute poisoning could lead to brain damage, Barbosa, 2001. Animal studies have demonstrated that Glyphosate depletes serotonin and dopamine, Anadon, 2008, and causes a loss of mitochondrial transmembrane potential in rat brain cells, especially in the substantia nigra region of the brain, Astiz, 2009.	There is evidence of developmental neurotoxicity of Glyphosate and EFSA should pay good attention to this adverse effect in their peer-review.
(2)	Vol.3, B.6.7.1, Neurotoxicity, Published data, page 702.	PAN Germany: We regret that an assessment of the literature by the RMS is missing. We think the assessment of the applicant is totally inadequate, playing down any adverse effects and using the "Klimisch-axe" to ensure it is ignored. This abrogates the idea of scientific evaluation.	

Section 2 - Mammalian toxicology (B.6)

Other toxicological studies & Medical data (B.6.8-B.6.9)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Summary of mammalian toxicology and setting ADI, AOEL, ARfD (B.6.10)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Toxicity of the product(s) (B.6.11)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Dermal absorption (B.6.12)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations

Section 2 - Mammalian toxicology (B.6)

Dermal absorption (B.6.12)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Toxicity of non-active substances (B.6.13)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Exposure data (B.6.14)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations

Section 2 - Mammalian toxicology (B.6)

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol.3, B.6 review public data	PAN Germany: We did our own literature search (see explanations) and found remarkable differences with the one conducted by the applicant. The notifier only found 52% of the 145 significant glyphosate toxicity studies we found, despite the mandate to find all. Worse– the notifier finds a published study but never mentions it (not even placing its main numerical finding in a table, as sometimes occurred). So the fraction of those we found that were also discussed is just 31%.	To check compliance with the new mandate on literature review, we performed a simple search of PubMed: "<pesticide common name> toxicity". The later is a specific keyword in PubMed, while almost all studies use, inter alia, the common name of a chemical. In our experience this simple search term captures on average 95% of all *published* studies relating to the risks of a chemical. After eliminating the obviously irrelevant, we saved the remaining abstracts (by publication date) as a public PubMed collection, and listed by endpoint in a table the studies that the notifier and RMS did & did not find or discuss, critiquing the reasons for the former.

5. Ecotoxicology (B.9)

Birds and mammals (B.9.1 and B.9.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Aquatic organisms (B.9.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Bees and non-target arthropods (B.9.4 and B.9.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.9.4	PAN Germany: The endocrine disrupting effects of Glyphosate on birds and other non-target organisms are disregarded.	

Earthworms and other soil non-target organisms (macro and micro) (B.9.6, B.9.7 and B.9.8)

Section 5 - Ecotoxicology (B.9)

No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Other non-target organisms (flora and fauna), sewage treatment (B.9.9 and B.9.10)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.9, Annex, page 298	PAN Germany: Many studies show that Glyphosate has endocrine disrupting properties. The RMS conveniently states that all endocrine disrupting effects are likely caused by the surfactant. The study of Paganelli, 2010, for instance clearly shows that formulations and active substance have the same adverse effect, and clearly point at Glyphosate as being an endocrine disruptor.	EFSA should demand studies from the applicant (in independent laboratories, blind testing) for a range of endocrine disruption screening test for Glyphosate.

Section 5 - Ecotoxicology (B.9)

1. **Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)**
2. **Mammalian toxicology (B.6)**
3. **Residues (B.7)**

4. **Environmental fate and behaviour (B.8)**

PEC in surface water and ground water (B.8.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.8.6.3.1, Ground water and Surface water monitoring data	CTR: On page 313 it states that " in Germany.. high rates.. of noncompliance regarding the application of plant protection products on walks and places in housing areas." From this, RMS concludes that other MS should be "aware of the problem". It is not fully clear whether this is referring to the "problem" of misuse – which would not be compound- specific (& therefore shouldn't be assigned to glyphosate alone?) – or water quality. No evidence has been provided that residential use is a "problem" in terms of water quality. UK data indicate otherwise, hence the conclusion given is not accurate.	A water monitoring study in England contradicts the conclusion of the RMS. (http://onlinelibrary.wiley.com/doi/10.1002/ps.3724/full) Despite occasional over-dosing occurring, when Ready-to-Use glyphosate was applied in a residential area, glyphosate losses to drains were lower than other reported losses in urban areas receiving treatment by professional users. A higher proportion of jointing in the surfaces/presence of gravel in the catchment was considered to increase retention and thus comparatively reduce losses to the drains.

5. **Ecotoxicology (B.9)**

1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)

Identity (B.1, Annex C)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Physical and chemical properties of the active substance (B.2.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Physical, chemical and technical properties of the formulation (B.2.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

Further information (B.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Methods of analysis (B.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Other comments (B.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol.3, B.6, Toxicology and metabolism, page 2	SA: in the classification of studies the categories 2,3 and E are made subject to the so-called Klimisch-criteria. We do not agree with using Klimisch criteria since it uses no test protocol criteria, just the circular logic that OECD/GLP = good . Academic studies rarely use these standard protocols as they restrict the testing of hypothesis. Do the hundreds of thousands scientists in academia do irrelevant or poor work? RMS say yes, but do not prove it	Studies need to be assessed on their scientific value and not dismissed without reading because not being GLP/OECD. Next a 'weight of the evidence' approach should be followed, including all scientifically qualified studies available, especially independent studies.
2.	Vol.3, B 6	SA: Industry's financial interests in selling their	White, J. and Bero, L.A., 2010, 'Corporate manipulation of research:

Other comments (B.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		products conflicts with the interests of truth when they perform the agent's safety tests. Specific techniques are used to allow their mission of getting products approved to prevail. White, 2010, extends the well-known strategies of the tobacco industry to other sectors. A RMS must be ready to counter these strategies, yet we didn't note a very critical approach of RMS to the applicant.	Strategies are similar across five industries', *Stanford Law & Policy Review*, (21/1) 105–134. We are disappointed that the RMS agreed on the completeness of the dossier while demanding extra tests and confirmatory information would be the proper approach, especially in case the outcome of industry-sponsored studies differ from academic studies.
3.	Vol.3, B.6	The tests performed by the applicants will probably be based on good laboratory practice (GLP), but this doesn't guarantee quality and reliability. In the past several cases of industry laboratory fraud (IBT, Craven) were discovered by regulators (including tests on Glyphosate). Although these fraudulent tests were replaced by new ones, we still have our doubts on their quality and reliability. GLP, in the end, is just a management system, forcing laboratories to be transparent, but no-one can guarantee what is written down exactly, and what happened or is observed in the tests.	Commission therefore needs to explain what guarantees they have used to ensure quality and reliability of tests, both old and new. Many outcomes of studies comparing GLP-studies and studies from open (independent) literature have different outcomes, an unaddressed concern.

2. Mammalian toxicology (B.6)

Toxicokinetics (B.6.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Acute toxicity (B.6.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol.3, B.6.2.3, page 240	SA, we do not understand that the exposure of test animals at 1000 ppm is called "low". With a current ADI of 0,3 ppm we challenge the value of this type of experiments with extreme high doses. This also means that effects seen at doses people are exposed to in practice are not tested and given the fact that Glyphosate has endocrine disrupting properties, adverse effects of low doses at vulnerable periods of development cannot be excluded.	We do not understand what we can learn from exposure of 20.000 ppm. Can any effect seen at this unrealistic dose be extrapolated to lower doses, thousand times lower and more, to predict an effect? We do not think that this type of mechanistic linear dose-response thinking has any basis in science. A body is no machine but an interrelated system with three major communication systems with triggers and feedback. OECD-tests are very insensitive and should be replaced by realistic dose tests on those elements (with very specific and sensitive endpoints) derived from the hazard assessment (mainly based on academic studies)

Short-term toxicity (B.6.3)

No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Genotoxicity (B.6.4)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
1.	Vol.3, B.6.4, genotoxicty, page 359	SA: In Table B 6.4-15 an experiment is disqualified for having too low doses. This is difficult to understand since the dose is still above ADI and far more relevant than the many dozens studies at extreme high dose.	Also remarkable is that at these doses effects are seen. They are subsequently qualified as not relevant using an industry-invented tool called "historical control data" allowing adverse effects being dismissed. Historical control data are never used by active scientists; they rely on normal controls.
2.	Vol.3, B.6.4, genotoxicty, page 382	SA: The study discussed showing clastogenicity is done at lower levels than usual. It concludes that effects are seen al lower levels while no effects are seen at higher levels. This again would be reason to reconsider the old paradigms of linear dose-response and use of high unrealistic doses.	
3.	Vol.3, B.6.4, genotoxicity, page 384	SA: the study of Clemens shows mutagenicity in tadpoles and the occurrence of this effect is not excluded by the RMS. However in the next lines many questionable assumptions and reasoning are added by the RMS and finally the effects dismissed for humans. We cannot agree	We think the only proper approach in case of uncertainties would be to demand the test to be repeated and confirmed in independent laboratories and blind testing. And the process of approval halted until more clarity is given.

Genotoxicity (B.6.4)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		with assumptions being made of questionable grounds; expert judgement should be based on science and not feelings.	
4.	Vol.3, B.6.4, genotoxicty, page 385	SA: we think it is not justified to dismiss studies (genotoxic effects in germ cells in Drosophila) that challenge industry findings by immediately pointing at the "large database of existing studies`. This gives the impression the RMS had already made up his mind about mutagenicity and is now just looking for reasons to dismiss studies not confirming the RMS´s feelings.	All studies should be used for a weight of the evidence approach in an open scientific approach without prior opinions or feelings. We think independent experts are needed to do this weight of the evidence evaluation, who were not involved in drafting the RAR and contacts with industry. The same biased approach is taken on page 386 for another critical study.
5.	Vol.3, B.6.4, genotoxicty, page 386	SA: we can understand that the applicant will claim that any adverse effect seen is due to the co-formulant tallowene and as such these studies should not count. We do not understand the claim of the RMS that it can "certainly be assumed" that an effect will be caused by the co-formulant. RMS's should not assume but assess. And if they have no data to prove it was the co-formulant, the effects should be counted for the active ingredient.	Again, there is all reason to demand the applicant to repeat academic studies showing adverse effects by exposing the active substance. This should be done in an independent laboratory with blind testing.
6.	Vol.3, B.6.4, genotoxicty, page 389	SA: The claim in the RAR of a lack of mutagenicity or even that results of studies are consistently and unequivocally negative (Vol.1) is false. Genotoxic effects on the contrary are	Given the conflict of interest of the applicant on safety testing, and the potential bias in studies or interpretation of studies, we propose EFSA starts her peer-review with independent literature for doing a hazard assessment. Independent literature has less chance on bias

Genotoxicity (B.6.4)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		already long known and available to the reviewers. Kale, 1995, showed mutations in fruit flies, Vigfussen, 1980, showed sister chromatin exchanges in human lymphocytes, just as Bolognesi in 1997. Peluso in 1998 showed increased DNA adducts in mice. Gasnier, 2009, showed DNA damage, as well as Manas, 2009. Some are captured in the industry review, others not, for unknwon reason. All are dismissed in the end. Numerous other studies have confirmed DNA damage in mouse, bovine, fish, caiman, tadpole, fruit fly, sea urchin, onion, and bacterial cells.	because of lacking motives and should be qualified as more reliable than industry-sponsored studies with an inherent conflict of interest. It is strange to note that Table 2.6-6 in Volume 1 only summarises industry-sponsored studies.
7.	Vol.3, B.6.4.8.10, weight of the evidence	SA: While the RMS discusses a few of the academic studies that show adverse effects, in the 'weight of the evidence' approach taken by the RMS as a standard procedure plays down the positive effects seen by assumptions and reasoning's such as the effects being indirect, or being beyond a certain threshold, not relevant for humans, suggests that the effect are toxic but not mutagenic. None of these assumptions is based on science but just part of the old paradigm used by regulators.	The RMS has high confidence in industry-sponsored studies and very low in academic studies, with the result only industry-sponsored studies with their favourable outcome for industry are counted in the final evaluation.

Section 2 - Mammalian toxicology (B.6)

Genotoxicity (B.6.4)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations

Long-term toxicity and carcinogenicity (B.6.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
1	Vol 3, B 6.5. Long-term toxicity and carcinogenicity, page 435	SA: A major failure in the testing systems used is the lack of exposure in-utero of the test animals. It is well-known that many chronic diseases develop in-utero (not only for cancer) and as such tests lacking in-utero exposure cannot be qualified as a 'state-of-the art' scientific approach. The conclusion that the substance is not carcinogen needs to be justified. We therefore propose EFSA requires the applicant to test again with in-utero exposure, performed with blind testing in an independent laboratory.	EU legislation provides for a high level of human health protection based on the precautionary principle and requires special attention for the vulnerable, the unborn and the elderly. The test system disregards the effects on the vulnerable groups in society.
2	Vol 3, B 6.5. Long-term toxicity and carcinogenicity, page 435	SA: More and evidence is available in literature (see Vandenberg et al. 2012 review) that low doses can harm, many times in the developing phase of the organism and many times for endocrine disrupting chemicals. Since Glyphosate has endocrine disrupting properties, EFSA should perform a thorough review ion the data in independent literature,	EFSA should require the applicant to do new testing of the substance including a range of low doses.

Long-term toxicity and carcinogenicity (B.6.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		and require applicant to do a series of low dose testing on endocrine adverse effects.	
3	Vol 3, B 6.5. Long-term toxicity and carcinogenicity, page 435	SA: Another point on carcinogenicity is the need to expose and follow test animals during their entire lifetime. Most diseases develop after notifier's tests incinerate the test animals (e.g. ACS (American Cancer Society): *Cancer Facts & Figures 2012*. Atlanta: American Cancer Society; 2012. [http://cancer.org/acs/groups/content/@epidemiologysurveilance/documents/document/acspc-031941.pdf].	EFSA should require the applicant to do new testing of the substance including lifetime exposure and monitoring.
4.	Vol 3, B 6.5. Long-term toxicity and carcinogenicity, page 502	SA: No evidence in rats according to the RAR (only industry-sponsored studies analysed) but the malignant lymphoma seen in mice were dismissed. It was not the chemical (Glyphosate) that should be blamed according to the RMS but the strain of mice. We think this has nothing to do with a scientific evaluation but more with a determination to get to a certain outcome. Given the many articles in peer-reviewed literature on long-term effects and cancer, a more balanced approach would have been justified.	We propose that based on the studies in open literature, a hazard assessment is done to find out what long-term effects and cancers can be expected to occur by the use of Glyphosate. Next, an analysis need to be done if the long-term and carcinogenicity animal tests will really capture the expected effects. And finally those long-term and carcinogenicity tests qualifying for capturing the adverse effects should be used for a final conclusion. No study should be dismissed for being non-GLP or non-OECD. Every study counts, also the one of Seralini. While the Rapporteur might not like the outcome, there is no scientific failure in the tests of Seralini.

Long-term toxicity and carcinogenicity (B.6.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
5.	Vol 3, B 6.5. Long-term toxicity and carcinogenicity, page 502	SA: Glyphosate has a history of links with cancer. The first carcinogenicity study submitted to US-EPA (1981) by applicant Monsanto showed an increase in testicular tumours in male rats as well as an increase in the frequency of a thyroid cancer in females. Both results occurred at the highest dose tested (30 mg/kg of body weight per day). The second study (1983) found an increasing trend in the frequency of a rare kidney tumour in male mice. A later study (1990) found an increase in pancreas and liver tumours in male rats together with an increase of the same thyroid cancer found in the 1983 study in females.	We ask EFSA to take a look at these older studies. There is good reason for EFSA to start the cancer analysis from scratch including all evidence from the past and from independent literature. Knowing the potential of Glyphosate to cause these effects, are the currently evaluated safety tests designed to capture these effects?
6.	Vol 3, B 6.5. Long-term toxicity and carcinogenicity page 524	SA: In the RAR all epidemiology studies showing a relation between Glyphosate and cancer are considered irrelevant, such as the Hardell-studies on the link with non-Hodgkin's, and even the unscientific Klimisch-approach is used for this qualification. This is unjustified. Now industry has created a situation in which people are exposed to thousands of chemicals at the same time, epidemiology studies cannot by nature be sensitive anymore. This means if a relation is shown, even weak, this should be reason for concern and reason to demand the	Industry should monitor the use of Glyphosate, analyse all environmental compartments and organisms, and do a large epidemiology study focussed on clarifying the evidence available. There is good evidence on the relation with non-Hodgkin's lymphoma, Nordstrom, 1998, Hardell, 1999 and 2002, McDuffie, 2001, De Roos, 2003 and Eriksson, 2008, and multiple myeloma, De Roos, 2005, and a large study should be initiated to find out more.

Long-term toxicity and carcinogenicity (B.6.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		applicant to do independent monitoring to et more information	
7.			

Reproductive toxicity (B.6.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
1	Vol.3 B.6.6 Reproductive toxicity. page 538	SA: a big omission in the German RAR is the lack of a hazard characterization of Glyphosate. In many EFSA opinions it is stated that the first step of risk assessment is the hazard characterization. We observe that Germany just moves on directly to risk characterisation and standard setting, and ignores the evidence on hazards	A hazard characterization is important to learn about the mechanism of toxicity of Glyphosate. Without the knowledge of the hazards it will be difficult to select in the next steps of risk assessment what data are useful and not. Germany just puts all evidence in the "Klimisch-mill" with the obvious effect of all independent science disregarded.
2	Vol.3 B.6.6 Reproductive toxicity. page 538	SA: We urge EFSA to include a hazard characterisation in the peer-review. This should be done by using all in-vitro studies available, disregarding none, and all mechanistic studies available. The peer-review should focus on what mechanistic evidence is present on teratogenicity, on DNA-damage., etc.?	The study of Paganelli et al. 2010 presents interesting evidence on the mechanism of action. During early embryonic development, retinoic acid generated in a specific region of the embryo helps determine position along the embryonic anterior/posterior axis by serving as an intercellular signaling molecule that guides development of the posterior portion of the embryo. It acts through Hox genes, which ultimately control anterior/posterior patterning in early developmental stages. The findings of Marc et al. '05 support this, offering a general

Reproductive toxicity (B.6.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
			mechanism of action for teratogenicity.
3.	Vol.3 B.6.6 Reproductive toxicity. page 539	SA: many multi-generation tests in the RAR with their very high (and unrealistic) doses, endpoints which are not the state-of-the-art cannot provide for the final answer on reproductive toxicity. The results are not clear anyway with a study that shows effects at low doses but is dismissed in the end by the Rapporteur. And studies showing effects on the offspring also accepted because they are observed at high doses. Combined with the many studies in open literature on malformations of the offspring and developmental effects, a peer-review by EFSA of all evidence is more than necessary.	The industry-sponsored OECD tests are known for their insensitivity and this could explain the very remarkable difference seen between the industry-sponsored studies and independent literature. The high doses used are close to the acute poisoning doses and poisoning effects are common in these tests, while more subtle effects could be missed.
4	Vol.3 B.6.6 Reproductive toxicity. page 548	SA, we question the use of extremely high exposure doses such as 15.000 ppm or 1000 mg/kg, more than 1000x the ADI. Animals should be tested at realistic doses and no extrapolation used	The high doses are close to the acute poisoning doses used and poisoning effects are common in these tests, while more subtle effects could be missed.
5	Vol.3 B.6.6 Reproductive toxicity. page 596	SA: We especially encourage EFSA to take a look at teratogenicity. The pre-2001 studies of Monsanto show teratogen effects, a range of independent studies report these effects, these effects are also observed in areas with Roundup monocultures (soya).	In the first DAR on Glyphosate in 2001, the UK experts commented that -based on the Monsanto studies- a single study might not raise concerns, but that the teratogenic effects that kept being observed in the Monsanto-studies, pointed at a pattern that should not be dismissed in the risk assessment. EFSA should asses if in the two-generation studies the animals are

Reproductive toxicity (B.6.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
			properly exposed during vulnerable windows during development and if a large range and relevant endpoints are considered for teratogenicity and development during later life of the offspring.
6.	Vol.3 B.6.6.9, Reproductive toxicity. page 597	SA: specific endocrine disrupting tests should be demanded from the applicant. Just basing conclusions on outdated OECD-protocols on reproduction and development is not justified. The science on endocrine disruption differs a lot from other fields and specific exposure windows, doses and specific endpoints should be used. In the traditional tests with traditional experts these effects will be missed.	
7.	Vol.3 B.6.6.9 Reproductive toxicity. page 597	SA: A large body of evidence on endocrine disrupting effects of Glyphosate is disregarded and dismissed in the RAR. Walsh, 2002 showed the disruption of the steroid hormone progesterone, as well as Romano, 2010 on testosterone. Richard, 2005 also concludes Glyphosate is an endocrine disruptor by affecting aromatase at very low doses. Also Benachour, 2005 and Gasnier, 2007 came to the same conclusion.	Hokanson, 2007, demonstrated a synergistic effect of Glyphosate with oestrogen, with implications for pregnancy-induced hypertension and foetal growth retardation. The implications of these effects on reproduction and the developing foetus are profound, with work by Mose, 2008, confirming that Glyphosate does cross the placenta.
8	Vol.3 B.6.6.10 Reproductive toxicity. page 613	SA: the study in rabbits shows that at a level of 10 mg/kg 20% of the litters have malformations while this is 5% in the control (this also counts for the foetus, 3,1% vs. 0,7%). While this dose	The malformations should be more thoroughly investigated and this study already shows that the LOAEL of 10 mg/kg should be adopted for standard setting. A suggesting NOEAL of 100 mg/kg by the applicant is absurd.

Reproductive toxicity (B.6.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		is at least less enormous than the regular dose, it is still above a realistic dose and we think additional studies should be done with lower and m	
9.	Vol.3 B.6.6.10 Reproductive toxicity. page 619	SA: this study in rabbit again shows most effects at the lowest dose tested (18 vs. 13 of the litters tested with malformations), 50 mg/kg. While this dose is still unrealistic high, lower doses should be tested on malformations of the foetus.	
10.	Vol.3 B.6.6.10 Reproductive toxicity. page 629	SA: this study in rabbit also shows malformations at the lowest level tested (82 foetus with 'minor' defects vs, 58 in the control), 100 mg/kg. This "low" dose is of course unrealistically high.	There is a clear pattern of malformations of the foetus in all rabbit studies.
11.	Vol.3 B.6.6.10 Reproductive toxicity. page 642	SA: this study confirms previous observations that malformations of the foetus is highest in the lowest dose tested, 50 mg/kg, (17.7% vs. 11,7% in the control). We object to the use of historical control data. The only scientific approach is to compare the outcome in the tests against the control.	Why the RMS values historical control data over the normal (negative|) control is a mystery. While it is highly questionable if the industry-sponsored studies are reproducible at all, historical control data mix different labs, operators, protocols and strains and create an unrealistic wide range of "controls'. No scientist will ever use this type of tools.
12.	Vol.3 B.6.6.10 Reproductive toxicity. page 650	SA: also this study shows effects at the lowest dose tested, 20 mg/kg, upper cleft palate, 15% vs. 5% in the control, and dilated heart, 23,1% vs. 0% in the control.	There is a clear pattern of malformations of the foetus in all rabbit studies.

Reproductive toxicity (B.6.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
13.	Vol.3 B.6.6.12, Reproductive toxicity, Published data, page 658	SA: it is remarkable that the RMS now rejects all claims made by EOS in their report "is the public kept in the dark" and let most independent literature fall under the 'Klimisch-axe". In their reaction in July 2011, the RMS called the report: The recently published report "Roundup and birth defects: Is the public kept in the dark?" is a challenging critical summary of adverse health (mainly teratological and reproductive) findings that are attributed by the authors to the compound glyphosate and/or to herbicides such as Roundup that contain glyphosate as active ingredient.	The RMS ends their report by saying: An adequate response to the criticism and the many accusations in the report would require a general discussion of the established paradigms for the toxicological evaluation of chemicals. These general discussions should be initiated by the Commission before we start with the re-evaluation of glyphosate within the AIR2 project. We fail to have seen any general discussion on established paradigms, not by the RMS and not by Commission. We therefore urge EFSA to start such a discussion before drafting the peer review on Glyphosate.
14.	Vol.3 B.6.6.12, Reproductive toxicity, Published data, page 658	SA: it is sad to note that the industry review made by the applicant is not commented by the RMS. Given the many missing studies and the standard use of Klimisch to dismiss studies on a large scale, an intervention of the RMS was needed very much.	We urge EFSA to review all independent studies and stop using the entirely unscientific Klimisch-tool and do a purely scientific assessment of each study looking at the quality of the study, disregarding protocols and GLP-administration systems.

Neurotoxicity (B.6.7)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
1.	Vol.3, B.6.7.1,	SA: Epidemiology studies have been published	There is evidence of developmental neurotoxicity of Glyphosate and

Neurotoxicity (B.6.7)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	Neurotoxicity, Published data, page 702.	pointing at Glyphosate of causing mental disorders of children born to pesticide applicators in the US, Garry, 2002. Even acute poisoning could lead to brain damage, Barbosa, 2001. Animal studies have demonstrated that Glyphosate depletes serotonin and dopamine, Anadon, 2008, and causes a loss of mitochondrial transmembrane potential in rat brain cells, especially in the substantia nigra region of the brain, Astiz, 2009.	EFSA should pay good attention to this adverse effect in their peer-review.
2.	Vol.3, B.6.7.1, Neurotoxicity, Published data, page 702.	SA: We regret that an assessment of the literature by the RMS is missing. We think the assessment of the applicant is totally inadequate, playing down any adverse effects and using the "Klimisch-axe" to ensure it is ignored. This abrogates the idea of scientific evaluation.	

Other toxicological studies & Medical data (B.6.8-B.6.9)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data	<< Identifier >>: <<comment>>	

Other toxicological studies & Medical data (B.6.8-B.6.9)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	point>>, <<description>>		

Summary of mammalian toxicology and setting ADI, AOEL, ARfD (B.6.10)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Toxicity of the product(s) (B.6.11)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Dermal absorption (B.6.12)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data	<< Identifier >>: <<comment>>	

Section 2 - Mammalian toxicology (B.6)

Dermal absorption (B.6.12)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	point>>, <<description>>		

Toxicity of non-active substances (B.6.13)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Exposure data (B.6.14)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Other comments

Section 2 - Mammalian toxicology (B.6)

No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol.3, B.6 review public data		

5. Ecotoxicology (B.9)

Birds and mammals (B.9.1 and B.9.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Aquatic organisms (B.9.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Bees and non-target arthropods (B.9.4 and B.9.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.9.4	SA: the endocrine disrupting effects of Glyphosate on birds and other non-target organisms are disregarded.	

Section 5 - Ecotoxicology (B.9)

Earthworms and other soil non-target organisms (macro and micro) (B.9.6, B.9.7 and B.9.8)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Other non-target organisms (flora and fauna), sewage treatment (B.9.9 and B.9.10)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.9, Annex, page 298	SA: many studies show that Glyphosate has endocrine disrupting properties. The RMS conveniently states that all endocrine disrupting effects are likely caused by the surfactant. The study of Paganelli, 2010, for instance clealrly shows that formulations and active substance have the same adverse effect, and clearly point at Glyphosate as being an endocrine disruptor.	EFSA should demand studies from the applicant (in independent laboratories, blind testing) for a range of endocrine disruption screening test for Glyphosate.

Comments of *Friends of the Earth (Cyprus)* on the Renewal Assessment Report on Glyphosate 06. 05. 2014

1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)

Identity (B.1, Annex C)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Physical and chemical properties of the active substance (B.2.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Physical, chemical and technical properties of the formulation (B.2.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

Further information (B.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, Annex B.3 Data on application and further information, page 7-8	***Friends of the Earth (Cyprus)***: Worldwide there are at least 28 weed species (not only 24) for which glyphosate-resistance has been documented, comprising more than 200 populations and infesting millions of hectares (Heap 2014). Although countries with RRcrop cultivation are affected most heavily, cases of glyphosate-resistant weed species are increasingly reported from other countries too. As a result, a massive increase in herbicide amounts applied has been documented. To stop the pesticide treadmill, glyphosate use has to be restricted.	In Europe, there are more cases of glyphosate resistance than depicted in the RAR (16 cases instead of 10 and 6 species instead of 5). Contrary to the RAR, glyphosate-resistant weed species have not been found exclusively in orchards, vineyards or olive groves, but also in other crops, e.g. asparagus (Lolium rigidum in France) and alfalfa (Conyza canadensis in Greece). And Northern and Central Europe will also be affected, with Poland being already the second country after the Czech Republic to report glyphosate-resistant weeds. It will be a question of time when glyphosate-resistant weed biotypes will show up in countries such as Germany. Therefore, evolution of glyphosate-resistance will speed up in Europe too, unless use of glyphosate is severely restricted.

Methods of analysis (B.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

5. Ecotoxicology (B.9)

Birds and mammals (B.9.1 and B.9.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Aquatic organisms (B.9.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	B.9.2.2 Summary of aquatic toxicity data Page 132	***Friends of the Earth (Cyprus)***: In particular, amphibians, many of which are endangered, have been shown to be affected by glyphosate-based herbicides, possibly both their larval and adult stages (Wagner et al. 2013). Reviewing peer-reviewed studies on glyphosate impacts on amphibian, Plötner and Matschke (2012) concluded that glyphosate is itself toxic to amphibians, and surfactants such as POEA are even more so leading to abnormal behaviour, teratogenic effects and developmental failures. In addition, toxicity of glyphosate and Roundup to aquatic invertebrates such as *Daphnia magna* has been underestimated (Cuhra et al. 2013). Toxicity classification has to be revised.	Cuhra et al. (2013) found EC50 (48) values for glyphosate IPA in *Daphnia magna* that were significantly lower than the values depicted in table B.9.2-59. Testing glyphosate and Roundup for 55 days (instead of only 21 days tested in the long-term studies referred to in table B.9.2-59) led to significant reduction in juvenile size even at the lowest test concentration of 0.05 mg a.i./L. About ten times higher concentrations of Roundup affected fecundity, growth and abortion rate and at1.35 and 4.05 mg a.i./L of both glyphosate and Roundup significant negative effects were seen on most tested parameters, including mortality. Thus even low ambient concentrations of glyphosate will affect aquatic invertebrate ecology.

Section 5 - Ecotoxicology (B.9)

Bees and non-target arthropods (B.9.4 and B.9.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Earthworms and other soil non-target organisms (macro and micro) (B.9.6, B.9.7 and B.9.8)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.9.8 Effects on soil non-target micro-organisms	***Friends of the Earth (Cyprus)***: As stated in the RAR and reported by Kremer & Means (2009), glyphosate leads to significant shifts in bacterial community composition but it also affects importantfungal species, e.g. beneficial mycorrhizal fungi (Druille et al. 2013a,b). Previous use of glyphosate has been linked to increased Fusarium infection of wheat and barley (Fernandez et al. 2009). Thus impacts of glyphosate use on bacterial and fungal species that are linked to plant health and disease have to be considered too.	

Section 5 - Ecotoxicology (B.9)

Other non-target organisms (flora and fauna), sewage treatment (B.9.9 and B.9.10)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.9.9.1.4 Summary of results on non-target plants	***Friends of the Earth (Cyprus)***: Glyphosate can adversely impact micronutrient uptake in plants as it is a strong metal chelator (Tesfamariam et al. 2009, Cakmak et al. 2009). Even low levels of residual glyphosate in soil can greatly impede the availability and uptake of Mn, Fe, Cu, and Zn by plants and lead to their undersupply with these nutrients. Reduced disease resistance and plant growth may be the result (Johal & Huber 2009).	Adverse impacts of (repeated) glyphosate use on the health of non-target plants have to be taken into account, as reduced disease resistance most likely will increase use of other pesticides, e.g. fungicides that may be highly toxic too.
	Vol. 3, B.9.9.1.6 Indirect effects via trophic interactions	The Farm Scale Evaluations have shown that the quantitative loss of weeds reduces number and diversity of arthropods heavily and interrupts the food chain for farmland birds and mammals. Ample evidence of negative impacts of glyphosate on biodiversity has been collected in areas where glyphosate is used extensively, e.g. in combination with genetically modified glyphosate-resistant crops. The all-time low in the number of monarch butterflies in 2013/2014 has been attributed to the loss of their food plant (*Asclepias syriaca*) in vast areas of the United States where glyphosate-resistant crops are grown (Wade 2014).	As glyphosate is the herbicide most widely used, these massive negative impacts on biodiversity have to be considered and used as reason not to re-authorize the substance. Mitigation measures, such as buffer strips, that would be up to the individual member states will not reduce the risk of impacting biodiversity to an acceptable level – even if farmers accepted to spare buffer strips from glyphosate application which they often don't.

Section 5 - Ecotoxicology (B.9)

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	B.9.11 Surface-active substances in glyphosate-based formulations	***Friends of the Earth (Cyprus):*** There is ample evidence that formulated products can exhibit higher toxicity. In particular, polyethoxylated alkylamines (POEA) are known to be highly toxic to cells and organisms (Mesnage et al. 2013). Glyphosate has endocrine disrupting properties which cannot only be attributed to the surfactants. Paganelli et al (2010) showed that both formulated products and the active substance have adverse effects and that glyphosate acts as an endocrine disruptor. To make agriculture in Europe more environmentally benign, it is of utmost importance that pesticide use is restricted to a much greater extent than it is actually the case. As herbicides make up the largest share of pesticides and glyphosate is the most used herbicide, regulators are obliged to not renew the approval of this chemical.	To argue, that the lead formulation MON52276 for the assessment of glyphosate does not contain POEA and that POEA-formulated products "are not expected to be neither notified nor registered in the future", is not comforting, as such products are still on the market and data about the nature and toxicity of other surfactants that replace POEA are not provided to the public. In addition, predicted environmental concentrations for glyphosate and its metabolite AMPA do not take into account the highly toxic surfactants that are released into the environment in combination with the active ingredient. Therefore, data about environmental concentrations of surfactants should have been collected and their impact on the environment should have been considered before drafting the RAR .

Friends of the Earth (Cyprus): Comments to the Renewal Assessment Report (RAR) – Glyphosate

Introduction

The Renewal Assessment Report (RAR) prepared by the Rapporteur Member State (RMS) has been opened by EFSA to comments from the public. Some parts of the final report have been blackened, presumably names that refer to studies provided by the applicants. Unfortunately, in **Volume 1 Report and Proposed Decision** the very last chapter, **3.2 Proposed Decision,** has been blackened too. This means the public will not get informed about what kind of decision the RMS and the Co-RMS propose. Thus the public can only speculate about details of the proposal.

Friends of the Earth (Cyprus) is commenting on specific sections of the renewal assessment report (RAR), in particular those that deal with environmental impacts of glyphosate.

Development of resistance

In **Volume 1, Section 2.3.2 Summary of information on the development of resistance**, and **Volume 3 Annex B.3 Data on application and further information**, the topics "development of resistance and appropriate management strategies" are being discussed.

Comments:

The simplicity and effectiveness of weed control through glyphosate will be undermined by shifts in weed communities and populations resulting from the selection pressure of the applied herbicides. Glyphosate has long been considered to be a low risk herbicide in terms of the evolution of resistant weed populations (Beckie 2006), but ever increasing use of glyphosate has favored the development of glyphosate-resistance in weeds. It has taken 8-20 years of glyphosate use in conventional systems until the first glyphosate-resistant weed, rigid ryegrass (*Lolium rigidum*), was found in 1996 in Australia (Pratley et al. 1999). Since then, at least 28 cases of glyphosate-resistant weed species (comprising more than 200 populations) have been recorded worldwide (Heap 2014). The resistant weeds infest millions of hectares at many different places in various countries. Although countries, such as the US, Argentina, Australia, and Brazil, where glyphosate-resistant crops are cultivated are affected most heavily, countries without GM crop cultivation increasingly report cases of glyphosate-resistant weed species.

Glyphosate-resistance in weeds has been found to be based on several mechanisms, such as target site insensitivity, overproduction of the target protein EPSPS (5-enolpyruvylshikimate-3-phosphate synthase), amplification of the EPSPS gene, reduced glyphosate translocation, and increased sequestration of glyphosate in plant cell vacuoles (Perez-Jones & Mallory-Smith 2010). Resistance mechanisms can co-occur, in particular, when related resistant weed species hybridize. In addition, multiple-resistance to other herbicide mode of actions than glyphosate has been reported too (Heap 2014).

In the RAR, reference is made to the development of glyphosate-resistance in Europe. But in reality, the situation is far more severe than depicted in the RAR document (as of September 2012). There are not only 10 cases of resistance known in Europe, but meanwhile the number is 16 and it is not

only five species that have been found, but there are six (Heap 2014). With five resistant species that have infested hundreds of hectares, Spain is the most afflicted country. Contrary to the RAR presentation, glyphosate-resistant weed species have not been found exclusively in orchards, vineyards or olive groves, but also in other crops such as asparagus (*Lolium rigidum* in France) and alfalfa (*Conyza canadensis* in Greece). It is also not quite true, that "*Apart from one case (C. canadensis) in the Czech Republic, Northern and Central Europe are not affected by glyphosate resistance up to now*", since resistant *C. canadensis* has also been reported from Poland railways. This indicates that evolution of glyphosate-resistance will speed up in Europe too, unless use of glyphosate is severely restricted.

In the US, not only the broad adoption of glyphosate-resistant crops but also the continuous rise in the number of resistant species and areas inflicted by resistant weeds has resulted in a massive increase in herbicide amounts applied (Benbrook 2012a). A similar scenario has been depicted for Europe in case genetically modified glyphosate-resistant crops would be authorized for cultivation here too (Benbrook 2012b). Therefore, to stop the pesticide treadmill, glyphosate use has to be restricted.

Environmental effects

In **Volume 1, Section 2.9 Effects on non-target species and Volume 3, Annex B.9 Ecotoxicology),** data on ecotoxicology studies are discussed, evaluated, and summarized.

Environmental impacts on non-target organisms

The risk assessment for birds and mammals is based on the active ingredient glyphosate acid in the product MON 52276 for the intended uses in several crops including pre-planting, pre-emergence, pre-harvest and row-application in orchards and vineyards. From the data provided by the applicants, the RMS comes to the conclusion that after use of the lead formulation MON 52276 in the indications according to the label there is an acceptable acute risk for birds and mammals due to uptake of contaminated food and an acceptable risk resulting from an exposure of small herbivorous mammals, non-target arthropods, and aquatic organisms. Use under the proposed conditions will result in a negligible exposure of honeybees or has no unacceptable acute or chronic effects on colony survival and development. The RMS concludes further, that for the evaluation of the formulation MON 52276 on non-target plants data are still required, in particular, as a valid study with this product to non-target plants is lacking and the formulants in the product may enhance toxicity.

The RMS concedes that, depending on the agricultural and ecological conditions, the use of glyphosate may affect populations of non-target terrestrial arthropods and vertebrate species (especially farmland birds) via trophic interactions and suggests mitigation measures. The RAR reads at this point: *These effects trace back to the intended effect of the herbicides – eliminating competing plants – and the interruption of the food web going along with it*.

In Volume 1, Section 3 Proposed decision, the RMS states: *It is considered that Article 4 of Regulation (EC) No 1107/2009 is complied with. Specifically the RMS considers that authorization in at least one Member State is expected to be possible for at least one plant protection product containing the active substance for at least one of the representative uses*. But the approval should be subject to conditions and restrictions. According to the RMS, glyphosate is not a candidate for substitution.

This statement has been made although the RMS identifies data gaps with regard to the ecotoxicology risk assessment (e.g. aquatic organisms, microorganisms, and non-target plants such as tomato) and concludes that certain areas of the risk assessment could not be finalized on the basis of the available data, among them effects of glyphosate towards microorganisms, on non-target plants and on biodiversity.

For all uses, the RMS acknowledges that the impacts of glyphosate on biodiversity is a critical area of concern and recommends that member states should pay attention to such potential indirect effects and may consider adequate risk mitigation measures.

Comments

It is not acceptable that glyphosate that is known to negatively impact biodiversity to such an extent should be re-authorized in the EU. Glyphosate exhibits acute and chronic toxicity, in particular, to aquatic species and non-target plants. As stated in the RAR and reported by Kremer & Means (2009), glyphosate leads to significant shifts in bacterial community composition but it also affects some fungal species, e.g. beneficial mycorrhizal fungi (Druille et al. 2013a,b). Previous use of glyphosate has been linked to increased Fusarium infection of wheat and barley (Fernandez et al. 2009). Amphibians, many of which are endangered, have been shown to be affected, possibly both their larval and adult stages (Wagner et al. 2013). Plötner and Matschke (2012) concluded that glyphosate is itself toxic to amphibians, and surfactants such as POEA are even more so causing abnormal behavior, teratogenic effects and developmental failures.

Glyphosate can adversely impact micronutrient uptake in plants as it is a strong metal chelator (Tesfamariam et al. 2009, Cakmak et al. 2009). Even low levels of residual glyphosate in soil can greatly impede the availability and uptake of Mn, Fe, Cu, and Zn by plants and lead to their undersupply with these nutrients. Reduced disease resistance and plant growth may be the result (Johal & Huber 2009). Adverse impacts of (repeated) glyphosate use on the health of non-target plants have to be taken into account, as reduced disease resistance most likely will increase use of other pesticides, e.g. fungicides that may be highly toxic too.

It is well known that weeds offer considerable benefits for the agro ecosystem, as they support a range of organisms, among them decomposers, predators, pollinators, and parasitoids, by providing food and shelter for them (Marshall et al. 2003). The Farm Scale Evaluations performed in the UK showed that broad-spectrum herbicides such as glyphosate impact abundance and diversity of weeds more severely than conventional herbicide regimes (Heard et al. 2003). The quantitative loss of weeds reduces number and diversity of arthropods heavily and interrupts the food chain for farmland birds and mammals. Ample evidence of negative impacts of glyphosate on biodiversity has been collected in areas where glyphosate is used extensively, e.g. in combination with genetically modified glyphosate-resistant crops. The all-time low in the number of monarch butterflies in the winter 2013/2014 has been attributed to the loss of their food plant (*Asclepias syriaca*) in vast areas of the United States where glyphosate-resistant crops are grown (Wade 2014).

As glyphosate is the herbicide most widely used, these massive negative impacts on biodiversity have to be considered and used as reason not to re-authorize the substance. Mitigation measures, such as buffer strips, that would be up to the individual member states could not reduce the risk of impacting biodiversity to an acceptable level – even if farmers accepted to spare buffer strips from glyphosate application which they often don't.

Subclause: Formulated glyphosate products (Annex B.9.11 Surface-active substances in glyphosate-based formulations)

In the RAR, solely the active ingredient glyphosate is being considered for authorization, although in the field, only formulated products are applied. The final glyphosate products contain high amounts of surfactants that have surface-active properties. According to the German government[1], in addition to the 5000 t of glyphosate used in Germany in 2010, 1700 t of polyethoxylated alkylamines (POEA) had been applied. Therefore, it is of importance to not only test the toxicity of the active ingredient glyphosate but to take into account the toxicity of the various formulated products that are used.

There is ample evidence that formulated products can exhibit higher toxicity. In particular, polyethoxylated alkylamines (POEA) are known to be highly toxic to cells and organisms (Mesnage et al. 2013). The RMS considers several of the observed effects on endpoints regarding genotoxicity, mutagenicity, and development or reproduction of non-target organisms to be mediated by the surfactant included in the formulations. Thus the RMS concedes that "*the toxicity of glyphosate-based products is greatly enhanced if the active substance is formulated with alkylamine ethoxylates"* and "*the authorization of glyphosate-based products with alkylamine ethoxylated surfactants might require the generation of further data"*. But to argue, that the lead formulation MON52276 for the assessment of glyphosate does not contain this surfactant and that nowadays POEA-formulated products "*are not expected to be neither notified nor registered in the future"*, are not comforting statements, as such products are still on the market and data about the nature and toxicity of other surfactants that replace POEA are not provided to the public. In addition, predicted environmental concentrations for glyphosate and its metabolite AMPA are calculated only for these substances, not taking into account the highly toxic surfactants that are released into the environment together with the active ingredient. Therefore, it is important to collect data about environmental concentrations of surfactants and to consider their impact on the environment already during the authorization process.

Conclusions

To make agriculture in Europe more environmentally benign, it is of utmost importance that pesticide use is restricted to a much greater extent than it is actually the case. As herbicides make up the largest share of pesticides and glyphosate, in particular, is the most used herbicide, regulators are obliged to not renew the approval of this chemical.

[1] http://dipbt.bundestag.de/dip21/btd/17/071/1707168.pdf

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1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)

Identity (B.1, Annex C)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Physical and chemical properties of the active substance (B.2.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Physical, chemical and technical properties of the formulation (B.2.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

Further information (B.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Methods of analysis (B.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Other comments (B.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol.3, B.6, Toxicology and metabolism, page 2	Agrar Koordination: in the classification of studies the categories 2,3 and E are made subject to the so-called Klimisch-criteria. We do not agree with using Klimisch criteria since it uses no test protocol criteria, just the circular logic that OECD/GLP = good . Academic studies rarely use these standard protocols as they restrict the testing of hypothesis. Do the hundreds of thousands scientists in academia do irrelevant or poor work? RMS say yes, but do not prove it	Studies need to be assessed on their scientific value and not dismissed without reading because not being GLP/OECD. Next a 'weight of the evidence' approach should be followed, including all scientifically qualified studies available, especially independent studies.
2.	Vol.3, B 6	Agrar Koordination: Industry's financial interests	White, J. and Bero, L.A., 2010, 'Corporate manipulation of research:

Other comments (B.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		in selling their products conflicts with the interests of truth when they perform the agent's safety tests. Specific techniques are used to allow their mission of getting products approved to prevail. White, 2010, extends the well-known strategies of the tobacco industry to other sectors. A RMS must be ready to counter these strategies, yet we didn't note a very critical approach of RMS to the applicant.	Strategies are similar across five industries', *Stanford Law & Policy Review*, (21/1) 105–134. We are fi. disappointed that the RMS agreed on the completeness of the dossier while demanding extra tests and confirmatory information would be the proper approach, especially in case the outcome of industry-sponsored studies differ from academic studies.
3.	Vol.3, B.6	Agrar Koordination: The tests performed by the applicants will probably be based on good laboratory practice (GLP), but this doesn't guarantee quality and reliability. In the past several cases of industry laboratory fraud (IBT, Craven) were discovered by regulators (including tests on Glyphosate). Although these fraudulent tests were replaced by new ones, we still have our doubts on their quality and reliability. GLP, in the end, is just a management system, forcing laboratories to be transparent, but no-one can guarantee what is written down exactly, and what happened or is observed in the tests.	Commission therefore needs to explain what guarantees they have used to ensure quality and reliability of tests, both old and new. Many outcomes of studies comparing GLP-studies and studies from open (independent) literature have different outcomes, an unaddressed concern.

2. Mammalian toxicology (B.6)

Toxicokinetics (B.6.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Acute toxicity (B.6.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol.3, B.6.2.3, page 240	Agrar Koordination: We do not understand that the exposure of test animals at 1000 ppm is called "low". With a current ADI of 0,3 ppm we challenge the value of this type of experiments with extreme high doses. This also means that effects seen at doses people are exposed to in practice are not tested and given the fact that Glyphosate has endocrine disrupting properties, adverse effects of low doses at vulnerable periods of development cannot be excluded.	We do not understand what we can learn from exposure of 20.000 ppm. Can any effect seen at this unrealistic dose be extrapolated to lower doses, thousand times lower and more, to predict an effect? We do not think that this type of mechanistic linear dose-response thinking has any basis in science. A body is no machine but an interrelated system with three major communication systems with triggers and feedback. OECD-tests are very insensitive and should be replaced by realistic dose tests on those elements (with very specific and sensitive endpoints) derived from the hazard assessment (mainly based on academic studies)

Short-term toxicity (B.6.3)

Section 2 - Mammalian toxicology (B.6)

No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Genotoxicity (B.6.4)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
1.	Vol.3, B.6.4, genotoxicty, page 359	Agrar Koordination: In Table B 6.4-15 an experiment is disqualified for having too low doses. This is difficult to understand since the dose is still above ADI and far more relevant than the many dozens studies at extreme high dose.	Also remarkable is that at these doses effects are seen. They are subsequently qualified as not relevant using an industry-invented tool called "historical control data" allowing adverse effects being dismissed. Historical control data are never used by active scientists; they rely on normal controls.
2.	Vol.3, B.6.4, genotoxicty, page 382	Agrar Koordination: The study discussed showing clastogenicity is done at lower levels than usual. It concludes that effects are seen al lower levels while no effects are seen at higher levels. This again would be reason to reconsider the old paradigms of linear dose-response and use of high unrealistic doses.	
3.	Vol.3, B.6.4, genotoxicity, page 384	Agrar Koordination: the study of Clemens shows mutagenicity in tadpoles and the occurrence of this effect is not excluded by the RMS. However in the next lines many questionable assumptions and reasoning are added by the	We think the only proper approach in case of uncertainties would be to demand the test to be repeated and confirmed in independent laboratories and blind testing. And the process of approval halted until more clarity is given.

Genotoxicity (B.6.4)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		RMS and finally the effects dismissed for humans. We cannot agree with assumptions being made of questionable grounds; expert judgement should be based on science and not feelings.	
4.	Vol.3, B.6.4, genotoxicty, page 385	Agrar Koordination: we think it is not justified to dismiss studies (genotoxic effects in germ cells in Drosophila) that challenge industry findings by immediately pointing at the "large database of existing studies`. This gives the impression the RMS had already made up his mind about mutagenicity and is now just looking for reasons to dismiss studies not confirming the RMS´s feelings.	All studies should be used for a weight of the evidence approach in an open scientific approach without prior opinions or feelings. We think independent experts are needed to do this weight of the evidence evaluation, who were not involved in drafting the RAR and contacts with industry. The same biased approach is taken on page 386 for another critical study.
5.	Vol.3, B.6.4, genotoxicty, page 386	Agrar Koordination: we can understand that the applicant will claim that any adverse effect seen is due to the co-formulant tallowene and as such these studies should not count. We do not understand the claim of the RMS that it can "certainly be assumed" that an effect will be caused by the co-formulant. RMS's should not assume but assess. And if they have no data to prove it was the co-formulant, the effects should be counted for the active ingredient.	Again, there is all reason to demand the applicant to repeat academic studies showing adverse effects by exposing the active substance. This should be done in an independent laboratory with blind testing.
6.	Vol.3, B.6.4, genotoxicty, page 389	Agrar Koordination: The claim in the RAR of a lack of mutagenicity or even that results of	Literature references will be provided by PAN Europe on request but should also be part of the review of the applicant on peer-reviewed

Genotoxicity (B.6.4)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		studies are consistently and unequivocally negative (Vol.1) is false. Genotoxic effects on the contrary are already long known and available to the reviewers. Kale, 1995, showed mutations in fruit flies, Vigfussen, 1980, showed sister chromatin exchanges in human lymphocytes, just as Bolognesi in 1997. Peluso in 1998 showed increased DNA adducts in mice. Gasnier, 2009, showed DNA damage, as well as Manas, 2009. Some are captured in the industry review, others not, for unknwon reason. All are dismissed in the end. Numerous other studies have confirmed DNA damage in mouse, bovine, fish, caiman, tadpole, fruit fly, sea urchin, onion, and bacterial cells.	literature. We only mention, Grisolia, 2002, Sivikova, 2006, Belle, 2007, Cavas, 2007, Cavalcante, 2008, Guilherme, 2009, Poletta, 2009, Monroy, 2005. It is really a joke the RMS uses the unscientific Klimisch-criteria for academic studies. Anyone knows the outcome: all dismissed! Given the conflict of interest of the applicant on safety testing, and the potential bias in studies or interpretation of studies, we propose EFSA starts her peer-review with independent literature for doing a hazard assessment. Independent literature has less chance on bias because of lacking motives and should be qualified as more reliable than industry-sponsored studies with an inherent conflict of interest. It is strange to note that Table 2.6-6 in Volume 1 only summarises industry-sponsored studies.
7.	Vol.3, B.6.4.8.10, weight of the evidence	Agrar Koordination: While the RMS discusses a few of the academic studies that show adverse effects, in the 'weight of the evidence' approach taken by the RMS as a standard procedure plays down the positive effects seen by assumptions and reasoning's such as the effects being indirect, or being beyond a certain threshold, not relevant for humans, suggests that the effect are toxic but not mutagenic. None of these assumptions is based on science but just part of the old paradigm used by regulators.	The RMS has high confidence in industry-sponsored studies and very low in academic studies, with the result only industry-sponsored studies with their favourable outcome for industry are counted in the final evaluation.

Section 2 - Mammalian toxicology (B.6)

Genotoxicity (B.6.4)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations

Long-term toxicity and carcinogenicity (B.6.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
1	Vol 3, B 6.5. Long-term toxicity and carcinogenicity, page 435	Agrar Koordination: A major failure in the testing systems used is the lack of exposure in-utero of the test animals. It is well-known that many chronic diseases develop in-utero (not only for cancer) and as such tests lacking in-utero exposure cannot be qualified as a 'state-of-the art' scientific approach. The conclusion that the substance is not carcinogen needs to be justified. We therefore propose EFSA requires the applicant to test again with in-utero exposure, performed with blind testing in an independent laboratory.	EU legislation provides for a high level of human health protection based on the precautionary principle and requires special attention for the vulnerable, the unborn and the elderly. The test system disregards the effects on the vulnerable groups in society.
2	Vol 3, B 6.5. Long-term toxicity and carcinogenicity, page 435	Agrar Koordination: Next point is the extreme high doses used in notifier's testing. More evidence is available in literature (see Vandenberg et al. 2012 review) that low doses can harm, many times in the developing phase of the organism and many times for endocrine	EFSA should require the applicant to do new testing of the substance including a range of low doses.

Long-term toxicity and carcinogenicity (B.6.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		disrupting chemicals. Since Glyphosate has endocrine disrupting properties, EFSA should perform a thorough review on the data in independent literature, and require applicant to do a series of low dose testing on endocrine adverse effects.	
3	Vol 3, B 6.5. Long-term toxicity and carcinogenicity, page 435	Agrar Koordination: Another point on carcinogenicity is the need to expose and follow test animals during their entire lifetime. Most diseases develops after notifier's tests incinerate the test animals (e.g. ACS (American Cancer Society): *Cancer Facts & Figures 2012*. Atlanta: American Cancer Society; 2012. [http://cancer.org/acs/groups/content/@epidemiologysurveilance/documents/document/acspc-031941.pdf].	EFSA should require the applicant to do new testing of the substance including lifetime exposure and monitoring.
4.	Vol 3, B 6.5. Long-term toxicity and carcinogenicity, page 502	Agrar Koordination: No evidence in rat according to the RAR (only industry-sponsored studies analysed) but the malignant lymphoma seen in mice were dismissed. It was not the chemical (Glyphosate) that should be blamed according to the RMS but the strain of mice. We think this has nothing to do with a scientific evaluation but more with a determination to get to a certain outcome. Given the many articles in peer-reviewed literature on long-term effects	We propose that based on the studies in open literature a hazard assessment is done to find out what long-term effects and cancers can be expected to occur by the use of Glyphosate. Next, an analysis need to be done if the long-term and carcinogenicity animal tests will really capture the expected effects. And finally those long-term and carcinogenicity tests qualifying for capturing the adverse effects should be used for a final conclusion. No study should be dismissed for being non-GLP or non-OECD. Every study counts, also the one of Seralini. While the Rapporteur might not like the outcome, there is no scientific failure in the tests of Seralini.

Long-term toxicity and carcinogenicity (B.6.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		and cancer, a more balanced approach would have been justified.	
5.	Vol 3, B 6.5. Long-term toxicity and carcinogenicity, page 502	Agrar Koordination: Glyphosate has a history of links with cancer. The first carcinogenicity study submitted to US-EPA (1981) by applicant Monsanto showed an increase in testicular tumours in male rats as well as an increase in the frequency of a thyroid cancer in females. Both results occurred at the highest dose tested (30 mg/kg of body weight per day). The second study (1983) found an increasing trend in the frequency of a rare kidney tumour in male mice. A later study (1990) found an increase in pancreas and liver tumours in male rats together with an increase of the same thyroid cancer found in the 1983 study in females.	We ask EFSA to take a look at these older studies. There is good reason for EFSA to start the cancer analysis from scratch including all evidence from the past and from independent literature. Knowing the potential of Glyphosate to cause these effects, are the currently evaluated safety tests designed to capture these effects?
6.	Vol 3, B 6.5. Long-term toxicity and carcinogenicity page 524	Agrar Koordination: In the RAR all epidemiology studies showing a relation between Glyphosate and cancer are considered irrelevant, such as the Hardell-studies on the link with non-Hodgkin's, and even the unscientific Klimisch-approach is used for this qualification. This is unjustified. Now industry has created a situation in which people are exposed to thousands of chemicals at the same time, epidemiology studies cannot by nature be	Industry should monitor the use of Glyphosate, analyse all environmental compartments and organisms, and do a large epidemiology study focussed on clarifying the evidence available. There is good evidence on the relation with non-Hodgkin's lymphoma, Nordstrom, 1998, Hardell, 1999 and 2002, McDuffie, 2001, De Roos, 2003 and Eriksson, 2008, and multiple myeloma, De Roos, 2005, and a large study should be initiated to find out more.

Long-term toxicity and carcinogenicity (B.6.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		sensitive anymore. This means if a relation is shown, even weak, this should be reason for concern and reason to demand the applicant to do independent monitoring to add more information	
7.			

Reproductive toxicity (B.6.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
1	Vol.3 B.6.6 Reproductive toxicity. page 538	Agrar Koordination: a big omission in the German RAR is the lack of a hazard characterization of Glyphosate. In many EFSA opinions it is stated that the first step of risk assessment is the hazard characterization. We observe that Germany just moves on directly to risk characterisation and standard setting, and ignores the evidence on hazards	A hazard characterization is important to learn about the mechanism of toxicity of Glyphosate. Without the knowledge of the hazards it will be difficult to select in the next steps of risk assessment what data are useful and not. Germany just puts all evidence in the "Klimisch-mill" with the obvious effect of all independent science disregarded.
2	Vol.3 B.6.6 Reproductive toxicity. page 538	Agrar Koordination: We urge EFSA to include a hazard characterisation in the peer-review. This should be done by using all in-vitro studies available, disregarding none, and all mechanistic	The study of Paganelli et al. 2010 presents interesting evidence on the mechanism of action. During early embryonic development, retinoic acid generated in a specific region of the embryo helps determine position along the embryonic anterior/posterior axis by serving as an

Reproductive toxicity (B.6.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		studies available. The peer-review should focus on what mechanistic evidence is present on teratogenicity, on DNA-damage., etc.?	intercellular signaling molecule that guides development of the posterior portion of the embryo. It acts through Hox genes, which ultimately control anterior/posterior patterning in early developmental stages. The findings of Marc et al. '05 support this, offering a general mechanism of action for teratogenicity.
3.	Vol.3 B.6.6 Reproductive toxicity. page 539	Agrar Koordination: many multi-generation tests in the RAR with their very high (and unrealistic) doses, endpoints which are not the state-of-the-art cannot provide for the final answer on reproductive toxicity. The results are not clear anyway with a study that shows effects at low doses but is dismissed in the end by the Rapporteur. And studies showing effects on the offspring also accepted because they are observed at high doses. Combined with the many studies in open literature on malformations of the offspring and developmental effects, a peer-review by EFSA of all evidence is more than necessary.	The industry-sponsored OECD tests are known for their insensitivity and this could explain the very remarkable difference seen between the industry-sponsored studies and independent literature. The high doses used are close to the acute poisoning doses and poisoning effects are common in these tests, while more subtle effects could be missed.
4	Vol.3 B.6.6 Reproductive toxicity. page 548	Agrar Koordination: we again question the use of extreme high exposure doses such as 15.000 ppm or 1000 mg/kg, more than 1000x the ADI. Animals should be tested at realistic doses and no extrapolation used	The high doses are close to the acute poisoning doses used and poisoning effects are common in these tests, while more subtle effects could be missed.
5	Vol.3 B.6.6 Reproductive toxicity. page 596	Agrar Koordination: We especially encourage EFSA to take a look at teratogenicity. The pre-2001 studies of Monsanto show teratogen	In the first DAR on Glyphosate in 2001, the UK experts commented that -based on the Monsanto studies- a single study might not raise concerns, but that the teratogenic effects that kept being observed in

Reproductive toxicity (B.6.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		effects, a range of independent studies report these effects, these effects are also observed in areas with Roundup monocultures (soy) in epidemiology studies and even in bioindustry where piglets fed on soy have these effects.	the Monsanto-studies, pointed at a pattern that should not be dismissed in the risk assessment. EFSA should asses if in the two-generation studies the animals are properly exposed during vulnerable windows during development and if a large range and relevant endpoints are considered for teratogenicity and development during later life of the offspring.
6.	Vol.3 B.6.6.9, Reproductive toxicity. page 597	Agrar Koordination: specific endocrine disrupting tests should be demanded from the applicant. Just basing conclusions on outdated OECD-protocols on reproduction and development is not justified. The science on endocrine disruption differs a lot from other fields and specific exposure windows, doses and specific endpoints should be used. In the traditional tests with traditional experts these effects will be missed.	
7.	Vol.3 B.6.6.9 Reproductive toxicity. page 597	Agrar Koordination: A large body of evidence on endocrine disrupting effects of Glyphosate is disregarded and dismissed in the RAR. Walsh, 2002 showed the disruption of the steroid hormone progesterone, as well as Romano, 2010 on testosterone. Richard, 2005 also concludes Glyphosate is an endocrine disruptor by affecting aromatase at very low doses. Also Benachour, 2005 and Gasnier, 2007 came to the same conclusion.	Hokanson, 2007, demonstrated a synergistic effect of Glyphosate with oestrogen, with implications for pregnancy-induced hypertension and foetal growth retardation. The implications of these effects on reproduction and the developing foetus are profound, with work by Mose, 2008, confirming that Glyphosate does cross the placenta.

Reproductive toxicity (B.6.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
8	Vol.3 B.6.6.10 Reproductive toxicity. page 613	Agrar Koordination: the study in rabbits shows that at a level of 10 mg/kg 20% of the litters have malformations while this is 5% in the control (this also counts for the foetus, 3,1% vs. 0,7%). While this dose is at least less enormous than the regular dose, it is still above a realistic dose and we think additional studies should be done with lower and m	The malformations should be more thoroughly investigated and this study already shows that the LOAEL of 10 mg/kg should be adopted for standard setting. A suggesting NOEAL of 100 mg/kg by the applicant is absurd.
9.	Vol.3 B.6.6.10 Reproductive toxicity. page 619	Agrar Koordination: this study in rabbit again shows most effects at the lowest dose tested (18 vs. 13 of the litters tested with malformations), 50 mg/kg. While this dose is still unrealistic high, lower doses should be tested on malformations of the foetus.	
10.	Vol.3 B.6.6.10 Reproductive toxicity. page 629	Agrar Koordination: this study in rabbit also shows malformations at the lowest level tested (82 foetus with 'minor' defects vs, 58 in the control), 100 mg/kg. This "low" dose is of course unrealistically high.	There is a clear pattern of malformations of the foetus in all rabbit studies.
11.	Vol.3 B.6.6.10 Reproductive toxicity. page 642	Agrar Koordination: this study confirms previous observations that malformations of the foetus is highest in the lowest dose tested, 50 mg/kg, (17.7% vs. 11,7% in the control). We object to the use of historical control data. The only scientific approach is to compare the outcome in the tests against the control.	Why the RMS values historical control data over the normal (negative|) control is a mystery. While it is highly questionable if the industry-sponsored studies are reproducible at all, historical control data mix different labs, operators, protocols and strains and create an unrealistic wide range of "controls'. No scientist will ever use this type of tools.

Reproductive toxicity (B.6.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
12.	Vol.3 B.6.6.10 Reproductive toxicity. page 650	Agrar Koordination: also this study shows effects at the lowest dose tested, 20 mg/kg, upper cleft palate, 15% vs. 5% in the control, and dilated heart, 23,1% vs. 0% in the control.	There is a clear pattern of malformations of the foetus in all rabbit studies.
13.	Vol.3 B.6.6.12, Reproductive toxicity, Published data, page 658	Agrar Koordination: it is remarkable that the RMS now easily rejects all claims made by EOS in their report "is the public kept in the dark" and let most independent literature fall under the 'Klimisch-axe". In their reaction in July 2011, the RMS called the report: The recently published report "Roundup and birth defects: Is the public kept in the dark?" is a challenging critical summary of adverse health (mainly teratological and reproductive) findings that are attributed by the authors to the compound glyphosate and/or to herbicides such as Roundup that contain glyphosate as active ingredient.	The RMS ends their report by saying: An adequate response to the criticism and the many accusations in the report would require a general discussion of the established paradigms for the toxicological evaluation of chemicals. These general discussions should be initiated by the Commission before we start with the re-evaluation of glyphosate within the AIR2 project. We fail to have seen any general discussion on established paradigms, not by the RMS and not by Commission. We therefore urge EFSA to start such a discussion before drafting the peer review on Glyphosate.
14.	Vol.3 B.6.6.12, Reproductive toxicity, Published data, page 658	Agrar Koordination: it is sad to note that the industry review made by the applicant is not commented by the RMS. Given the many missing studies and the standard use of Klimisch to dismiss studies on a large scale, an intervention of the RMS was needed very much.	We urge EFSA to review all independent studies and stop using the entirely unscientific Klimisch-tool and do a purely scientific assessment of each study looking at the quality of the study, disregarding protocols and GLP-administration systems.

Section 2 - Mammalian toxicology (B.6)

Neurotoxicity (B.6.7)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
1.	Vol.3, B.6.7.1, Neurotoxicity, Published data, page 702.	Agrar Koordination: Epidemiology studies have been published pointing at Glyphosate of causing mental disorders of children born to pesticide applicators in the US, Garry, 2002. Even acute poisoning could lead to brain damage, Barbosa, 2001. Animal studies have demonstrated that Glyphosate depletes serotonin and dopamine, Anadon, 2008, and causes a loss of mitochondrial transmembrane potential in rat brain cells, especially in the substantia nigra region of the brain, Astiz, 2009.	There is evidence of developmental neurotoxicity of Glyphosate and EFSA should pay good attention to this adverse effect in their peer-review.
2.	Vol.3, B.6.7.1, Neurotoxicity, Published data, page 702.	Agrar Koordination: We regret that an assessment of the literature by the RMS is missing. We think the assessment of the applicant is totally inadequate, playing down any adverse effects and using the "Klimisch-axe" to ensure it is ignored. This abrogates the idea of scientific evaluation.	

Other toxicological studies & Medical data (B.6.8-B.6.9)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations

Section 2 - Mammalian toxicology (B.6)

Other toxicological studies & Medical data (B.6.8-B.6.9)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Summary of mammalian toxicology and setting ADI, AOEL, ARfD (B.6.10)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Toxicity of the product(s) (B.6.11)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Dermal absorption (B.6.12)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations

Section 2 - Mammalian toxicology (B.6)

Dermal absorption (B.6.12)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Toxicity of non-active substances (B.6.13)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Exposure data (B.6.14)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Other comments

Section 2 - Mammalian toxicology (B.6)

No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol.3, B.6 review public data	Agrar Koordination: PAN did its own literature search (see explanations) and found remarkable differences with the one conducted by the applicant. The notifier only found 52% of the 145 significant glyphosate toxicity studies PAN found, despite the mandate to find all. Worse– the notifier finds a published study but never mentions it (not even placing its main numerical finding in a table, as sometimes occurred). So the fraction of those PAN found that were also discussed is just 31%.	To check compliance with the new mandate on literature review, PAN performed a simple search of PubMed: "<pesticide common name> toxicity". The later is a specific keyword in PubMed, while almost all studies use, inter alia, the common name of a chemical. In our experience this simple search term captures on average 95% of all *published* studies relating to the risks of a chemical. After eliminating the obviously irrelevant, PAN saved the remaining abstracts (by publication date) as a public PubMed collection, and listed by endpoint in a table the studies that the notifier and RMS did & did not find or discuss, criticizing the reasons for the former.

5. Ecotoxicology (B.9)

Birds and mammals (B.9.1 and B.9.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Aquatic organisms (B.9.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Bees and non-target arthropods (B.9.4 and B.9.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.9.4	Agrar Koordination: the endocrine disrupting effects of Glyphosate on birds and other non-target organisms are disregarded.	

Earthworms and other soil non-target organisms (macro and micro) (B.9.6, B.9.7 and B.9.8)

Section 5 - Ecotoxicology (B.9)

No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Other non-target organisms (flora and fauna), sewage treatment (B.9.9 and B.9.10)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.9, Annex, page 298	Agrar Koordination: many studies show that Glyphosate has endocrine disrupting properties. The RMS conveniently states that all endocrine disrupting effects are likely caused by the surfactant. The study of Paganelli, 2010, for instance clearly shows that formulations and active substance have the same adverse effect, and clearly point at Glyphosate as being an endocrine disruptor.	EFSA should demand studies from the applicant (in independent laboratories, blind testing) for a range of endocrine disruption screening test for Glyphosate.

Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)

Identity (B.1, Annex C)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Physical and chemical properties of the active substance (B.2.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)			

Physical, chemical and technical properties of the formulation (B.2.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Further information (B.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Methods of analysis (B.5)

Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

2. Mammalian toxicology (B.6)

Report and Proposed Decision (Volume 1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
1	Vol. 1, 2.6.9 Summary of further toxicological studies (Mechanistic studies)	On page 85, it is stated: “So far, a link of glyphosate residues in ruminant diet to a new disease in cattle that was mainly reported from Northern parts of Germany has not been established and is not likely”. We agree that the link is not established, but disagree that a link can be ruled out as “not likely”. What is the scientific foundation for this statement? We believe that the statement should be: “A link can neither be established nor excluded with the present knowledge”.	Our scientific foundation for not excluding “a link of glyphosate residues in ruminant diet to a new disease in cattle“ is that several pathogenic bacterial species (for example Clostridium botulinum) have been reported to be less inhibited by glyphosate than a range of commensal (harmless, non-pathogenic) species (Shehata et al., 2013; Krüger et al., 2013, Anaerobe 20, 74-78). Such different glyphosate tolerance between commensal and pathogenic bacterial species may cause a detrimental disturbance of rumen microbiota and a disease outcome cannot be excluded with the present knowledge. Our position on this matter is further elaborated in a memorandum of February 4, 2014 to the Danish Ministry of Food, Agriculture and Fisheries (http://dca.au.dk/fileadmin/DJF/Notat_gmofoder__uk_version_Memorandum_on_The_feeding_of_genetically_modified_glyphosate_resistant_soy_products_to_livestock.pdf).

Report and Proposed Decision (Volume 1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
2	Vol. 1, 2.6.9 Summary of further toxicological studies (Mechanistic	On page 85, results of Riede et al. 2013 are referred. Our calculations show that if half the cow’s diet consists of soybean meal and barley	We have not been able to track the Riede et al. 2013 reference and therefore cannot evaluate these data. Our calculations for the cow are based on a diet with 50 % of the feed originating from glyphosat

Report and Proposed Decision (Volume 1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	studies)	with 20 mg glyphosate residue per kg (MRL) then the glyphosate concentration would be 1.8-3.5 mg per L in the rumen/intestine content. This concentration is close to a level (~one order of magnitude below minimum inhibitory concentrations, MIC) where effects on bacteria growth generally are observed (Fredborg et al. 2013, J Clinical Microbiology 51, 2047).	resistant GM soy products (soybean meal) and barley (glyphosate treated 10 days pre-harvest) which is realistic for a lactating cow. Calculations for pigs on a diet with 20 mg glyphosate residue per kg (~100 % of the feed originating from glyphosat resistant GM soy products and barley preharvest-treated with glyphosate) show stomach and intestine concentrations of 5-21 mg/Litre. These concentrations are within the one tenth MIC range for commensal bacteria. In the calculations for both cow and pig, it is assumed that 20% of the ingested glyphosate is absorbed from the small intestine and that rumen/intestine breakdown of glyphosate is negligible. Thus, we disagree with your statement in Vol. 3 Annex B.6 page 778 that “Residues of glyphosate may occur in feedstuffs for ruminants and, so far the MRLs are not exceeded, are allowed and of no concern”. In addition our concern is also, and not the least, valid for monogastric animals. Our position on this matter is further elaborated in a memorandum of February 4, 2014 to the Danish Ministry of Food, Agriculture and Fisheries (http://dca.au.dk/fileadmin/DJF/Notat_gmofoder__uk_version_Memorandum_on_The_feeding_of_genetically_modified_glyphosate_resistant_soy_products_to_livestock.pdf).

Toxicokinetics (B.6.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations

Section 2 - Mammalian toxicology (B.6)

Toxicokinetics (B.6.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
1	Vol. 3, Annex B.6.1 Toxicology and metabolism	B.6.8.3.3 on p 778 it is stated that "Residues of glyphosate may occur in feedstuffs for ruminants and, so far the MRLs are not exceeded, are allowed and of no concern". With reference to our calculations on rumen/intestine glyphosate concentrations we believe that the calculations based on ADI and NOAEL (page 778-779) are irrelevant for the conditions in the rumen and intestines of livestock. We thus conclude that with the present knowledge, MRL levels of glyphosate in feed are of concern.	Our position on this matter is further elaborated in a memorandum of February 4, 2014 to the Danish Ministry of Food, Agriculture and Fisheries (http://dca.au.dk/fileadmin/DJF/Notat_gmofoder__uk_version_Memorandum_on_The_feeding_of_genetically_modified_glyphosate_resistant_soy_products_to_livestock.pdf).

Toxicokinetics (B.6.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
2	Vol. 3, Annex B.6.1 Toxicology and metabolism	B.6.8.3.3 on p 779 it is stated that "…the authors claimed very low levels of several trace elements such as cobalt or manganese, a possible chelating mode of action of glyphosate was suspected. However these considerations appear purely speculative". Glyphosate do chelate trace minerals, and we know of no evidence that can justify excluding that levels of glyphosate in the mg/L-range in rumen/intestine	With reference to our comments in column 2, we conclude that it cannot be excluded that MRL levels of glyphosate in feed for livestock may affect trace mineral availability. Our position on this matter is further elaborated in a memorandum of February 4, 2014 to the Danish Ministry of Food, Agriculture and Fisheries (http://dca.au.dk/fileadmin/DJF/Notat_gmofoder__uk_version_Memorandum_on_The_feeding_of_genetically_modified_glyphosate_resistant_soy_products_to_livestock.pdf).

Section 2 - Mammalian toxicology (B.6)

Toxicokinetics (B.6.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		content (see our calculations above) may affect trace mineral availability in livestock.	

Acute toxicity (B.6.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Short-term toxicity (B.6.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Genotoxicity (B.6.4)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Section 2 - Mammalian toxicology (B.6)

Long-term toxicity and carcinogenicity (B.6.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Reproductive toxicity (B.6.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Neurotoxicity (B.6.7)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Other toxicological studies & Medical data (B.6.8-B.6.9)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Section 2 - Mammalian toxicology (B.6)

Summary of mammalian toxicology and setting ADI, AOEL, ARfD (B.6.10)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Toxicity of the product(s) (B.6.11)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Dermal absorption (B.6.12)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Toxicity of non-active substances (B.6.13)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>,	<< Identifier >>: <<comment>>	

Section 2 - Mammalian toxicology (B.6)

Toxicity of non-active substances (B.6.13)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	<<description>>		

Exposure data (B.6.14)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)			

3. Residues (B.7)

Storage Stability (B.7.0)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Metabolism in plants (B.7.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Metabolism in livestock (B.7.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Residue definition (B.7.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>,	<< Identifier >>: <<comment>>	

Section 3 - Residues (B.7)

Residue definition (B.7.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	<<description>>		

Use pattern, critical GAP, residues trials (B.7.4 to B.7.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Processing (B.7.7)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Livestock feeding (B.7.8)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Section 3 - Residues (B.7)

Succeeding/Rotational crops (B.7.9)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

4. Environmental fate and behaviour (B.8)

Route and rate of degradation in soil (B.8.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Adsorption, desorption and mobility in soil (B.8.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

PEC in soil (B.8.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Fate and behaviour in water and impact on water treatment procedures (B.8.4 – B.8.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations

Section 4 - Environmental fate and behaviour (B.8)

Fate and behaviour in water and impact on water treatment procedures (B.8.4 – B.8.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

PEC in surface water and ground water (B.8.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Fate and behaviour in air and PEC in air (B.8.7 – B.8.8)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Definition of the residues (B.8.9)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Section 4 - Environmental fate and behaviour (B.8)

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

5. Ecotoxicology (B.9)

Birds and mammals (B.9.1 and B.9.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Aquatic organisms (B.9.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Bees and non-target arthropods (B.9.4 and B.9.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Earthworms and other soil non-target organisms (macro and micro) (B.9.6, B.9.7 and B.9.8)

Section 5 - Ecotoxicology (B.9)

No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Other non-target organisms (flora and fauna), sewage treatment (B.9.9 and B.9.10)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Comments of Friends of the Earth Europe on the Renewal Assessment Report on Glyphosate 09.05. 2014

1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)

Identity (B.1, Annex C)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Physical and chemical properties of the active substance (B.2.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Physical, chemical and technical properties of the formulation (B.2.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Further information (B.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, Annex B.3 Data	***Name of your group***: Worldwide there are at least	In Europe, there are more cases of glyphosate resistance than depicted in

Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

Further information (B.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	on application and further information, page 7-8	28 weed species (not only 24) for which glyphosate-resistance has been documented, comprising more than 200 populations and infesting millions of hectares (Heap 2014). Although countries with RRcrop cultivation are affected most heavily, cases of glyphosate-resistant weed species are increasingly reported from other countries too. As a result, a massive increase in herbicide amounts applied has been documented. To stop the pesticide treadmill, glyphosate use has to be restricted.	the RAR (16 cases instead of 10 and 6 species instead of 5). Contrary to the RAR, glyphosate-resistant weed species have not been found exclusively in orchards, vineyards or olive groves, but also in other crops, e.g. asparagus (Lolium rigidum in France) and alfalfa (Conyza canadensis in Greece). And Northern and Central Europe will also be affected, with Poland being already the second country after the Czech Republic to report glyphosate-resistant weeds. It will be a question of time when glyphosate-resistant weed biotypes will show up in countries such as Germany. Therefore, evolution of glyphosate-resistance will speed up in Europe too, unless use of glyphosate is severely restricted.

Methods of analysis (B.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

5. Ecotoxicology (B.9)

Birds and mammals (B.9.1 and B.9.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Aquatic organisms (B.9.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	B.9.2.2 Summary of aquatic toxicity data Page 132	***FoEE*** : In particular, amphibians, many of which are endangered, have been shown to be affected by glyphosate-based herbicides, possibly both their larval and adult stages (Wagner et al. 2013). Reviewing peer-reviewed studies on glyphosate impacts on amphibian, Plötner and Matschke (2012) concluded that glyphosate is itself toxic to amphibians, and surfactants such as POEA are even more so leading to abnormal behaviour, teratogenic effects and developmental failures. In addition, toxicity of glyphosate and Roundup to aquatic invertebrates such as *Daphnia magna* has been underestimated (Cuhra et al. 2013). Toxicity classification has to be revised.	Cuhra et al. (2013) found EC50 (48) values for glyphosate IPA in *Daphnia magna* that were significantly lower than the values depicted in table B.9.2-59. Testing glyphosate and Roundup for 55 days (instead of only 21 days tested in the long-term studies referred to in table B.9.2-59) led to significant reduction in juvenile size even at the lowest test concentration of 0.05 mg a.i./L. About ten times higher concentrations of Roundup affected fecundity, growth and abortion rate and at1.35 and 4.05 mg a.i./L of both glyphosate and Roundup significant negative effects were seen on most tested parameters, including mortality. Thus even low ambient concentrations of glyphosate will affect aquatic invertebrate ecology.

Section 5 - Ecotoxicology (B.9)

Bees and non-target arthropods (B.9.4 and B.9.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Earthworms and other soil non-target organisms (macro and micro) (B.9.6, B.9.7 and B.9.8)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.9.8 Effects on soil non-target micro-organisms	***FoEE***: As stated in the RAR and reported by Kremer & Means (2009), glyphosate leads to significant shifts in bacterial community composition but it also affects importantfungal species, e.g. beneficial mycorrhizal fungi (Druille et al. 2013a,b). Previous use of glyphosate has been linked to increased Fusarium infection of wheat and barley (Fernandez et al. 2009). Thus impacts of glyphosate use on bacterial and fungal species that are linked to plant health and disease have to be considered too.	

Other non-target organisms (flora and fauna), sewage treatment (B.9.9 and B.9.10)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.9.9.1.4 Summary of results on	***Name of your group***: Glyphosate can adversely impact micronutrient	Adverse impacts of (repeated) glyphosate use on the health of non-target plants have to be taken into account, as reduced disease resistance most

Other non-target organisms (flora and fauna), sewage treatment (B.9.9 and B.9.10)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	non-target plants	uptake in plants as it is a strong metal chelator (Tesfamariam et al. 2009, Cakmak et al. 2009). Even low levels of residual glyphosate in soil can greatly impede the availability and uptake of Mn, Fe, Cu, and Zn by plants and lead to their undersupply with these nutrients. Reduced disease resistance and plant growth may be the result (Johal & Huber 2009).	likely will increase use of other pesticides, e.g. fungicides that may be highly toxic too.
	Vol. 3, B.9.9.1.6 Indirect effects via trophic interactions	The Farm Scale Evaluations have shown that the quantitative loss of weeds reduces number and diversity of arthropods heavily and interrupts the food chain for farmland birds and mammals. Ample evidence of negative impacts of glyphosate on biodiversity has been collected in areas where glyphosate is used extensively, e.g. in combination with genetically modified glyphosate-resistant crops. The all-time low in the number of monarch butterflies in 2013/2014 has been attributed to the loss of their food plant (*Asclepias syriaca*) in vast areas of the United States where glyphosate-resistant crops are grown (Wade 2014).	As glyphosate is the herbicide most widely used, these massive negative impacts on biodiversity have to be considered and used as reason not to re-authorize the substance. Mitigation measures, such as buffer strips, that would be up to the individual member states will not reduce the risk of impacting biodiversity to an acceptable level – even if farmers accepted to spare buffer strips from glyphosate application which they often don't.

Section 5 - Ecotoxicology (B.9)

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	B.9.11 Surface-active substances in glyphosate-based formulations	***FoEE:*** There is ample evidence that formulated products can exhibit higher toxicity. In particular, polyethoxylated alkylamines (POEA) are known to be highly toxic to cells and organisms (Mesnage et al. 2013). Glyphosate has endocrine disrupting properties which cannot only be attributed to the surfactants. Paganelli et al (2010) showed that both formulated products and the active substance have adverse effects and that glyphosate acts as an endocrine disruptor. To make agriculture in Europe more environmentally benign, it is of utmost importance that pesticide use is restricted to a much greater extent than it is actually the case. As herbicides make up the largest share of pesticides and glyphosate is the most used herbicide, regulators are obliged to not renew the approval of this chemical.	To argue, that the lead formulation MON52276 for the assessment of glyphosate does not contain POEA and that POEA-formulated products "are not expected to be neither notified nor registered in the future", is not comforting, as such products are still on the market and data about the nature and toxicity of other surfactants that replace POEA are not provided to the public. In addition, predicted environmental concentrations for glyphosate and its metabolite AMPA do not take into account the highly toxic surfactants that are released into the environment in combination with the active ingredient. Therefore, data about environmental concentrations of surfactants should have been collected and their impact on the environment should have been considered before drafting the RAR .

Name of your group Friends of the Earth Europe: Comments to the Renewal Assessment Report (RAR) – Glyphosate

Introduction

The Renewal Assessment Report (RAR) prepared by the Rapporteur Member State (RMS) has been opened by EFSA to comments from the public. Some parts of the final report have been blackened, presumably names that refer to studies provided by the applicants. Unfortunately, in **Volume 1 Report and Proposed Decision** the very last chapter, **3.2 Proposed Decision,** has been blackened too. This means the public will not get informed about what kind of decision the RMS and the Co-RMS propose. Thus the public can only speculate about details of the proposal.

Friends of the Earth Europe is commenting on specific sections of the renewal assessment report (RAR), in particular those that deal with environmental impacts of glyphosate.

Development of resistance

In **Volume 1, Section 2.3.2 Summary of information on the development of resistance**, and **Volume 3 Annex B.3 Data on application and further information**, the topics "development of resistance and appropriate management strategies" are being discussed.

Comments:

The simplicity and effectiveness of weed control through glyphosate will be undermined by shifts in weed communities and populations resulting from the selection pressure of the applied herbicides. Glyphosate has long been considered to be a low risk herbicide in terms of the evolution of resistant weed populations (Beckie 2006), but ever increasing use of glyphosate has favored the development of glyphosate-resistance in weeds. It has taken 8-20 years of glyphosate use in conventional systems until the first glyphosate-resistant weed, rigid ryegrass (*Lolium rigidum*), was found in 1996 in Australia (Pratley et al. 1999). Since then, at least 28 cases of glyphosate-resistant weed species (comprising more than 200 populations) have been recorded worldwide (Heap 2014). The resistant weeds infest millions of hectares at many different places in various countries. Although countries, such as the US, Argentina, Australia, and Brazil, where glyphosate-resistant crops are cultivated are affected most heavily, countries without GM crop cultivation increasingly report cases of glyphosate-resistant weed species.

Glyphosate-resistance in weeds has been found to be based on several mechanisms, such as target site insensitivity, overproduction of the target protein EPSPS (5-enolpyruvylshikimate-3-phosphate synthase), amplification of the EPSPS gene, reduced glyphosate translocation, and increased sequestration of glyphosate in plant cell vacuoles (Perez-Jones & Mallory-Smith 2010). Resistance mechanisms can co-occur, in particular, when related resistant weed species hybridize. In addition, multiple-resistance to other herbicide mode of actions than glyphosate has been reported too (Heap 2014).

In the RAR, reference is made to the development of glyphosate-resistance in Europe. But in reality, the situation is far more severe than depicted in the RAR document (as of September 2012). There are not only 10 cases of resistance known in Europe, but meanwhile the number is 16 and it is not

only five species that have been found, but there are six (Heap 2014). With five resistant species that have infested hundreds of hectares, Spain is the most afflicted country. Contrary to the RAR presentation, glyphosate-resistant weed species have not been found exclusively in orchards, vineyards or olive groves, but also in other crops such as asparagus (*Lolium rigidum* in France) and alfalfa (*Conyza canadensis* in Greece). It is also not quite true, that "*Apart from one case (C. canadensis) in the Czech Republic, Northern and Central Europe are not affected by glyphosate resistance up to now*", since resistant *C. canadensis* has also been reported from Poland railways. This indicates that evolution of glyphosate-resistance will speed up in Europe too, unless use of glyphosate is severely restricted.

In the US, not only the broad adoption of glyphosate-resistant crops but also the continuous rise in the number of resistant species and areas inflicted by resistant weeds has resulted in a massive increase in herbicide amounts applied (Benbrook 2012a). A similar scenario has been depicted for Europe in case genetically modified glyphosate-resistant crops would be authorized for cultivation here too (Benbrook 2012b). Therefore, to stop the pesticide treadmill, glyphosate use has to be restricted.

Environmental effects

In **Volume 1, Section 2.9 Effects on non-target species and Volume 3, Annex B.9 Ecotoxicology),** data on ecotoxicology studies are discussed, evaluated, and summarized.

Environmental impacts on non-target organisms

The risk assessment for birds and mammals is based on the active ingredient glyphosate acid in the product MON 52276 for the intended uses in several crops including pre-planting, pre-emergence, pre-harvest and row-application in orchards and vineyards. From the data provided by the applicants, the RMS comes to the conclusion that after use of the lead formulation MON 52276 in the indications according to the label there is an acceptable acute risk for birds and mammals due to uptake of contaminated food and an acceptable risk resulting from an exposure of small herbivorous mammals, non-target arthropods, and aquatic organisms. Use under the proposed conditions will result in a negligible exposure of honeybees or has no unacceptable acute or chronic effects on colony survival and development. The RMS concludes further, that for the evaluation of the formulation MON 52276 on non-target plants data are still required, in particular, as a valid study with this product to non-target plants is lacking and the formulants in the product may enhance toxicity.

The RMS concedes that, depending on the agricultural and ecological conditions, the use of glyphosate may affect populations of non-target terrestrial arthropods and vertebrate species (especially farmland birds) via trophic interactions and suggests mitigation measures. The RAR reads at this point: *These effects trace back to the intended effect of the herbicides – eliminating competing plants – and the interruption of the food web going along with it*.

In Volume 1, Section 3 Proposed decision, the RMS states: *It is considered that Article 4 of Regulation (EC) No 1107/2009 is complied with. Specifically the RMS considers that authorization in at least one Member State is expected to be possible for at least one plant protection product containing the active substance for at least one of the representative uses*. But the approval should be subject to conditions and restrictions. According to the RMS, glyphosate is not a candidate for substitution.

This statement has been made although the RMS identifies data gaps with regard to the ecotoxicology risk assessment (e.g. aquatic organisms, microorganisms, and non-target plants such as tomato) and concludes that certain areas of the risk assessment could not be finalized on the basis of the available data, among them effects of glyphosate towards microorganisms, on non-target plants and on biodiversity.

For all uses, the RMS acknowledges that the impacts of glyphosate on biodiversity is a critical area of concern and recommends that member states should pay attention to such potential indirect effects and may consider adequate risk mitigation measures.

Comments

It is not acceptable that glyphosate that is known to negatively impact biodiversity to such an extent should be re-authorized in the EU. Glyphosate exhibits acute and chronic toxicity, in particular, to aquatic species and non-target plants. As stated in the RAR and reported by Kremer & Means (2009), glyphosate leads to significant shifts in bacterial community composition but it also affects some fungal species, e.g. beneficial mycorrhizal fungi (Druille et al. 2013a,b). Previous use of glyphosate has been linked to increased Fusarium infection of wheat and barley (Fernandez et al. 2009). Amphibians, many of which are endangered, have been shown to be affected, possibly both their larval and adult stages (Wagner et al. 2013). Plötner and Matschke (2012) concluded that glyphosate is itself toxic to amphibians, and surfactants such as POEA are even more so causing abnormal behavior, teratogenic effects and developmental failures.

Glyphosate can adversely impact micronutrient uptake in plants as it is a strong metal chelator (Tesfamariam et al. 2009, Cakmak et al. 2009). Even low levels of residual glyphosate in soil can greatly impede the availability and uptake of Mn, Fe, Cu, and Zn by plants and lead to their undersupply with these nutrients. Reduced disease resistance and plant growth may be the result (Johal & Huber 2009). Adverse impacts of (repeated) glyphosate use on the health of non-target plants have to be taken into account, as reduced disease resistance most likely will increase use of other pesticides, e.g. fungicides that may be highly toxic too.

It is well known that weeds offer considerable benefits for the agro ecosystem, as they support a range of organisms, among them decomposers, predators, pollinators, and parasitoids, by providing food and shelter for them (Marshall et al. 2003). The Farm Scale Evaluations performed in the UK showed that broad-spectrum herbicides such as glyphosate impact abundance and diversity of weeds more severely than conventional herbicide regimes (Heard et al. 2003). The quantitative loss of weeds reduces number and diversity of arthropods heavily and interrupts the food chain for farmland birds and mammals. Ample evidence of negative impacts of glyphosate on biodiversity has been collected in areas where glyphosate is used extensively, e.g. in combination with genetically modified glyphosate-resistant crops. The all-time low in the number of monarch butterflies in the winter 2013/2014 has been attributed to the loss of their food plant (*Asclepias syriaca*) in vast areas of the United States where glyphosate-resistant crops are grown (Wade 2014).

As glyphosate is the herbicide most widely used, these massive negative impacts on biodiversity have to be considered and used as reason not to re-authorize the substance. Mitigation measures, such as buffer strips, that would be up to the individual member states could not reduce the risk of impacting

biodiversity to an acceptable level – even if farmers accepted to spare buffer strips from glyphosate application which they often don't.

Subclause: Formulated glyphosate products (Annex B.9.11 Surface-active substances in glyphosate-based formulations)

In the RAR, solely the active ingredient glyphosate is being considered for authorization, although in the field, only formulated products are applied. The final glyphosate products contain high amounts of surfactants that have surface-active properties. According to the German government[1], in addition to the 5000 t of glyphosate used in Germany in 2010, 1700 t of polyethoxylated alkylamines (POEA) had been applied. Therefore, it is of importance to not only test the toxicity of the active ingredient glyphosate but to take into account the toxicity of the various formulated products that are used.

There is ample evidence that formulated products can exhibit higher toxicity. In particular, polyethoxylated alkylamines (POEA) are known to be highly toxic to cells and organisms (Mesnage et al. 2013). The RMS considers several of the observed effects on endpoints regarding genotoxicity, mutagenicity, and development or reproduction of non-target organisms to be mediated by the surfactant included in the formulations. Thus the RMS concedes that "*the toxicity of glyphosate-based products is greatly enhanced if the active substance is formulated with alkylamine ethoxylates"* and "*the authorization of glyphosate-based products with alkylamine ethoxylated surfactants might require the generation of further data"*. But to argue, that the lead formulation MON52276 for the assessment of glyphosate does not contain this surfactant and that nowadays POEA-formulated products "*are not expected to be neither notified nor registered in the future"*, are not comforting statements, as such products are still on the market and data about the nature and toxicity of other surfactants that replace POEA are not provided to the public. In addition, predicted environmental concentrations for glyphosate and its metabolite AMPA are calculated only for these substances, not taking into account the highly toxic surfactants that are released into the environment together with the active ingredient. Therefore, it is important to collect data about environmental concentrations of surfactants and to consider their impact on the environment already during the authorization process.

Conclusions

To make agriculture in Europe more environmentally benign, it is of utmost importance that pesticide use is restricted to a much greater extent than it is actually the case. As herbicides make up the largest share of pesticides and glyphosate, in particular, is the most used herbicide, regulators are obliged to not renew the approval of this chemical.

[1] http://dipbt.bundestag.de/dip21/btd/17/071/1707168.pdf

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1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)

Identity (B.1, Annex C)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 1 and Vol 3, pdf files	BfN: The provided pdf files did not allow to copy and paste text or to set bookmarks. This severely impeded working with the documents and commenting on the DAR.	
(1)	Vol. 1, 1.4.8, effects on harmful organisms	BfN: On page 14 it is stated that glyphosate binds to and blocks the activity of its target enzyme EPSPS. Glyphosate's herbicidal activity might also be due to binding manganese, a cofactor for the EPSPS. This aspect should be added here and a cross-reference made to chapter 2.3.4, mentioning glyphosate's chelating activity.	See Johal and Huber (2009) for glyphosate's herbicidal activity. Europ. J. Agronomy 31: 144–152). See also Toy and Uhing (1964; US Patent 3.130.632) for the ability of glyphosate and related compounds to chelate minerals.

Physical and chemical properties of the active substance (B.2.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.2.1, physical and chemical properties of the active substance	BfN: Table 2.1.-1 on page 1 ff.: The ability of glyphosate to bind minerals is an important chemical ability and should be mentioned here.	Glyphosate and chemically related compounds have a wide variety of uses including as chelating agents and due to these uses they were patented already back in 1964 (Toy and Uhing; US Patent 3.130.632).

Physical, chemical and technical properties of the formulation (B.2.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Further information (B.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.3.1.5, mode of action	BfN: A cross-reference should be made to B.3.2.2 and B.3.2.8. Cf. comment above on Vol. 1, 1.4.8, effects on harmful organisms	
(2)	Vol. 3, B.3.2.2, effects on harmful organisms	BfN: A cross-reference should be made to B.3.1.5 and B.3.2.8. Cf. comment on Vol. 1, 1.4.8, effects on harmful organisms.	
(3)	Vol. 3, B.3.2.8, waiting periods for succeeding crops	BfN: A a cross-reference should be made to B.3.1.5 and B.3.2.2. Cf. comment on Vol. 1, 1.4.8, effects on harmful organisms	

Methods of analysis (B.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

2. Mammalian toxicology (B.6)

Toxicokinetics (B.6.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.6.1, absorption, excretion and distribution studies	BfN: In terms of dermal exposure the summarising Vol. 1 says on page 41: "Following dermal exposure, glyphosate is poorly absorbed, but the actual extent depends very much on the product in which the active ingredient is formulated". This might also be in case of oral exposure so that more glyphosate gets absorbed and less excreted if applied as formulated product. If we followed the DAR correctly, oral exposure was only studied using glyphosate rather than formulated products. If true, the actual extent of glyphosate absorption following oral exposure of formulated products would remain unknown.	None of the considered studies indicated the potential for accumulation of glyphosate following oral administration. However, this conclusion should be reassessed in light of a pilot study which found glyphosate in US mothers' breast milk. http://sustainablepulse.com/2014/04/06/worlds-number-1-herbicide-discovered-u-s-mothers-breast-milk/
(2)	Vol. 3, B.6.1.1, Toxicokinetic and metabolism studies in rats that were not previously evaluated in the EU	BfN: The seven studies mentioned here were performed in 1995 and 1996. Acc. to Vol. 1. Chapter 2.6.2, page 37 these studies were used to re-estimate oral absorption of glyphosate from urine excretion to be 20% rather than 30% (former evaluation).	Why were those studies evaluated now but not during the last evaluation?

Section 2 - Mammalian toxicology (B.6)

Acute toxicity (B.6.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Short-term toxicity (B.6.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Genotoxicity (B.6.4)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Long-term toxicity and carcinogenicity (B.6.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Section 2 - Mammalian toxicology (B.6)

Reproductive toxicity (B.6.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.6.6.2, published data since 2000	BfN: Lopez et al. (2012) reported an increase in malformations, but also in cancer incidence from certain regions in South America. When these results are discussed in Vol. 1 on page 80, it is argued that even if the claimed increases could be substantiated in future, "it is unlikely they were due to glyphosate, taking into account the extensive toxicological database and the long history of its worldwide safe use."	No reference (e.g. health monitoring of glyphosate) is provided to support the claim of glyphosate's long history of worldwide safe use.

Neurotoxicity (B.6.7)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Other toxicological studies & Medical data (B.6.8-B.6.9)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.6.8.3.,Further published data>>	BfN: On page 778-782 several studies of Krueger et al. investigating effects of glyphosate on cattle and ruminant microorganisms are discussed. Because of methodological deficiencies, the RMS concludes that no adverse effects can be drawn from these studies. DAR mentions that a study in	The conclusion in Vol. 1 is not supported by any data or reference and obviously premature. As the conclusion is not supported by data and the study design is not provided the relevance and significance of the study is not comprehensible.

Section 2 - Mammalian toxicology (B.6)

Other toxicological studies & Medical data (B.6.8-B.6.9)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		an artificial rumen system was commissioned by BfR, without presenting any details of the study design. While it is mentioned on page 782, that results were not available until October 2013, it is already summarized in Vol. 1 on page 36 that no adverse effects on animal health are to be anticipated	

Summary of mammalian toxicology and setting ADI, AOEL, ARfD (B.6.10)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Toxicity of the product(s) (B.6.11)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Section 2 - Mammalian toxicology (B.6)

Dermal absorption (B.6.12)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Toxicity of non-active substances (B.6.13)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Exposure data (B.6.14)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Section 5 - Ecotoxicology (B.9)

5. Ecotoxicology (B.9)

Birds and mammals (B.9.1 and B.9.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.9.1.7.7, indirect effects via trophic interactions	BfN: (i) It is appreciated that this issue is raised here. (ii) The text says that effective and reasonable mitigation measures are available and highlights later the need for risk mitigation measures by the Member States.	The proposed measures might mitigate indirect effects of glyphosate application. However, their effectiveness to mitigate indirect effects of glyphosate application in a given situation remains to be shown.
(2)	Vol. 3, B.9.1.7.7, scientific evidence of indirect effects of PPP on farmland bird and mammal species	BfN: Also amphibians can be directly negatively affected when they pass over fields or when their breeding ponds, which might be embedded in the agrarian landscape, are over-sprayed. Amphibians can also suffer from indirect effects, when weeds are killed and therefore shelter is lost.	Wagner and Lötters (2013) Possible correlation of the worldwide amphibian decline and the increasing use of glyphosate in the agrarian industry. BfN-Skripten 343. http://www.bfn.de/fileadmin/MDB/documents/service/skript_343.pdf

Aquatic organisms (B.9.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Bees and non-target arthropods (B.9.4 and B.9.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3,6.5.6.3,	<< Identifier >>: <<comment>>	

Section 5 - Ecotoxicology (B.9)

Bees and non-target arthropods (B.9.4 and B.9.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	<<description>>		

Earthworms and other soil non-target organisms (macro and micro) (B.9.6, B.9.7 and B.9.8)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, 9.8, Effects on soil non-target microorganisms	BfN: Vol 1, 3.1.1.2 proposes on page 134: "The submission of a study assessing the effects of the active substance towards microorganisms and a study with the representative plant protection product MON 52276 assessing the effects on non-target plants is considered to be confirmatory in nature … to increase confidence in the decision."	To investigates long-term and cumulative effects of glyphosate on soil microorganisms, soil fertility and plant health (endpoints), a study is required which considers multiple glyphosate application on the same field plots over consecutive years using different soil types. As these aspects have not been investigated sufficiently so far, the requested studies and evidence is not regarded to be confirmatory in nature, but genuinely required.
(2)	Vol. 3, 9.8.2, Literature Review	BfN: The RMS rejects most of the studies collected by the notifier on soil non-target microorganisms, because they deal with rhizobia of glyphosate-resistant crops and – according to the RMS – are not assignable to risk assessment in the European Union.	This approach to not consider those studies is not comprehensible given that there are some applications in the EU for the approval of GM crops with glyphosate resistance including cultivation.

Other non-target organisms (flora and fauna), sewage treatment (B.9.9 and B.9.10)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, 9.9.2., Effects on amphibians	BfN: As rightly pointed out on page 289, (i) only few data exist assessing the effect of glyphosate and glyphosate-based products on terrestrial stages of	Amphibians seem to be at higher risk due to dermal uptake. For this purpose, mammals and birds do not seem to suit, and it is suggested to include at least 2 amphibian species from different families in

Other non-target organisms (flora and fauna), sewage treatment (B.9.9 and B.9.10)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		amphibians and (ii) the conclusions of the risk assessment for birds and mammals for a specific product do not cover necessarily the risk of exposed terrestrial amphibian stages.	standardized test batteries to study dermal administration (cf. Wagner et al. 2013: Environ Toxicol Chem Vol. 32, No. 8, pp. 1688–1700 and the references therein).

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Comments of Friends of the Earth Latvia on the Renewal Assessment Report on Glyphosate 06. 05. 2014

1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)

Identity (B.1, Annex C)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Physical and chemical properties of the active substance (B.2.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Physical, chemical and technical properties of the formulation (B.2.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Further information (B.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, Annex B.3 Data	**Friends of the Eath Latvia**: Worldwide there are at	In Europe, there are more cases of glyphosate resistance than depicted in

Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

Further information (B.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	on application and further information, page 7-8	least 28 weed species (not only 24) for which glyphosate-resistance has been documented, comprising more than 200 populations and infesting millions of hectares (Heap 2014). Although countries with RRcrop cultivation are affected most heavily, cases of glyphosate-resistant weed species are increasingly reported from other countries too. As a result, a massive increase in herbicide amounts applied has been documented. To stop the pesticide treadmill, glyphosate use has to be restricted.	the RAR (16 cases instead of 10 and 6 species instead of 5). Contrary to the RAR, glyphosate-resistant weed species have not been found exclusively in orchards, vineyards or olive groves, but also in other crops, e.g. asparagus (Lolium rigidum in France) and alfalfa (Conyza canadensis in Greece). And Northern and Central Europe will also be affected, with Poland being already the second country after the Czech Republic to report glyphosate-resistant weeds. It will be a question of time when glyphosate-resistant weed biotypes will show up in countries such as Germany. Therefore, evolution of glyphosate-resistance will speed up in Europe too, unless use of glyphosate is severely restricted.

Methods of analysis (B.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

5. Ecotoxicology (B.9)

Birds and mammals (B.9.1 and B.9.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Aquatic organisms (B.9.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	B.9.2.2 Summary of aquatic toxicity data Page 132	**Friends of the Earth Latvia** : In particular, amphibians, many of which are endangered, have been shown to be affected by glyphosate-based herbicides, possibly both their larval and adult stages (Wagner et al. 2013). Reviewing peer-reviewed studies on glyphosate impacts on amphibian, Plötner and Matschke (2012) concluded that glyphosate is itself toxic to amphibians, and surfactants such as POEA are even more so leading to abnormal behaviour, teratogenic effects and developmental failures. In addition, toxicity of glyphosate and Roundup to aquatic invertebrates such as *Daphnia magna* has been underestimated (Cuhra et al. 2013). Toxicity classification has to be revised.	Cuhra et al. (2013) found EC50 (48) values for glyphosate IPA in *Daphnia magna* that were significantly lower than the values depicted in table B.9.2-59. Testing glyphosate and Roundup for 55 days (instead of only 21 days tested in the long-term studies referred to in table B.9.2-59) led to significant reduction in juvenile size even at the lowest test concentration of 0.05 mg a.i./L. About ten times higher concentrations of Roundup affected fecundity, growth and abortion rate and at1.35 and 4.05 mg a.i./L of both glyphosate and Roundup significant negative effects were seen on most tested parameters, including mortality. Thus even low ambient concentrations of glyphosate will affect aquatic invertebrate ecology.

Section 5 - Ecotoxicology (B.9)

Bees and non-target arthropods (B.9.4 and B.9.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Earthworms and other soil non-target organisms (macro and micro) (B.9.6, B.9.7 and B.9.8)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.9.8 Effects on soil non-target micro-organisms	**Friends of the Earth Latvia**: As stated in the RAR and reported by Kremer & Means (2009), glyphosate leads to significant shifts in bacterial community composition but it also affects importantfungal species, e.g. beneficial mycorrhizal fungi (Druille et al. 2013a,b). Previous use of glyphosate has been linked to increased Fusarium infection of wheat and barley (Fernandez et al. 2009). Thus impacts of glyphosate use on bacterial and fungal species that are linked to plant health and disease have to be considered too.	

Other non-target organisms (flora and fauna), sewage treatment (B.9.9 and B.9.10)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.9.9.1.4 Summary of results on	**Friends of the Earth Latvia**: Glyphosate can adversely impact micronutrient	Adverse impacts of (repeated) glyphosate use on the health of non-target plants have to be taken into account, as reduced disease resistance most likely will increase use of other pesticides, e.g. fungicides that may be

Other non-target organisms (flora and fauna), sewage treatment (B.9.9 and B.9.10)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	non-target plants	uptake in plants as it is a strong metal chelator (Tesfamariam et al. 2009, Cakmak et al. 2009). Even low levels of residual glyphosate in soil can greatly impede the availability and uptake of Mn, Fe, Cu, and Zn by plants and lead to their undersupply with these nutrients. Reduced disease resistance and plant growth may be the result (Johal & Huber 2009).	highly toxic too.
	Vol. 3, B.9.9.1.6 Indirect effects via trophic interactions	The Farm Scale Evaluations have shown that the quantitative loss of weeds reduces number and diversity of arthropods heavily and interrupts the food chain for farmland birds and mammals. Ample evidence of negative impacts of glyphosate on biodiversity has been collected in areas where glyphosate is used extensively, e.g. in combination with genetically modified glyphosate-resistant crops. The all-time low in the number of monarch butterflies in 2013/2014 has been attributed to the loss of their food plant (*Asclepias syriaca*) in vast areas of the United States where glyphosate-resistant crops are grown (Wade 2014).	As glyphosate is the herbicide most widely used, these massive negative impacts on biodiversity have to be considered and used as reason not to re-authorize the substance. Mitigation measures, such as buffer strips, that would be up to the individual member states will not reduce the risk of impacting biodiversity to an acceptable level – even if farmers accepted to spare buffer strips from glyphosate application which they often don't.

Section 5 - Ecotoxicology (B.9)

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	B.9.11 Surface-active substances in glyphosate-based formulations	**Friends of the Earth Latvia:** There is ample evidence that formulated products can exhibit higher toxicity. In particular, polyethoxylated alkylamines (POEA) are known to be highly toxic to cells and organisms (Mesnage et al. 2013). Glyphosate has endocrine disrupting properties which cannot only be attributed to the surfactants. Paganelli et al (2010) showed that both formulated products and the active substance have adverse effects and that glyphosate acts as an endocrine disruptor. To make agriculture in Europe more environmentally benign, it is of utmost importance that pesticide use is restricted to a much greater extent than it is actually the case. As herbicides make up the largest share of pesticides and glyphosate is the most used herbicide, regulators are obliged to not renew the approval of this chemical.	To argue, that the lead formulation MON52276 for the assessment of glyphosate does not contain POEA and that POEA-formulated products "are not expected to be neither notified nor registered in the future", is not comforting, as such products are still on the market and data about the nature and toxicity of other surfactants that replace POEA are not provided to the public. In addition, predicted environmental concentrations for glyphosate and its metabolite AMPA do not take into account the highly toxic surfactants that are released into the environment in combination with the active ingredient. Therefore, data about environmental concentrations of surfactants should have been collected and their impact on the environment should have been considered before drafting the RAR .

Friends of the Earth Latvia: Comments to the Renewal Assessment Report (RAR) – Glyphosate

Introduction

The Renewal Assessment Report (RAR) prepared by the Rapporteur Member State (RMS) has been opened by EFSA to comments from the public. Some parts of the final report have been blackened, presumably names that refer to studies provided by the applicants. Unfortunately, in **Volume 1 Report and Proposed Decision** the very last chapter, **3.2 Proposed Decision,** has been blackened too. This means the public will not get informed about what kind of decision the RMS and the Co-RMS propose. Thus the public can only speculate about details of the proposal.

Friends of the Earth Latvia is commenting on specific sections of the renewal assessment report (RAR), in particular those that deal with environmental impacts of glyphosate.

Development of resistance

In **Volume 1, Section 2.3.2 Summary of information on the development of resistance**, and **Volume 3 Annex B.3 Data on application and further information**, the topics "development of resistance and appropriate management strategies" are being discussed.

Comments:

The simplicity and effectiveness of weed control through glyphosate will be undermined by shifts in weed communities and populations resulting from the selection pressure of the applied herbicides. Glyphosate has long been considered to be a low risk herbicide in terms of the evolution of resistant weed populations (Beckie 2006), but ever increasing use of glyphosate has favored the development of glyphosate-resistance in weeds. It has taken 8-20 years of glyphosate use in conventional systems until the first glyphosate-resistant weed, rigid ryegrass (*Lolium rigidum*), was found in 1996 in Australia (Pratley et al. 1999). Since then, at least 28 cases of glyphosate-resistant weed species (comprising more than 200 populations) have been recorded worldwide (Heap 2014). The resistant weeds infest millions of hectares at many different places in various countries. Although countries, such as the US, Argentina, Australia, and Brazil, where glyphosate-resistant crops are cultivated are affected most heavily, countries without GM crop cultivation increasingly report cases of glyphosate-resistant weed species.

Glyphosate-resistance in weeds has been found to be based on several mechanisms, such as target site insensitivity, overproduction of the target protein EPSPS (5-enolpyruvylshikimate-3-phosphate synthase), amplification of the EPSPS gene, reduced glyphosate translocation, and increased sequestration of glyphosate in plant cell vacuoles (Perez-Jones & Mallory-Smith 2010). Resistance mechanisms can co-occur, in particular, when related resistant weed species hybridize. In addition, multiple-resistance to other herbicide mode of actions than glyphosate has been reported too (Heap 2014).

In the RAR, reference is made to the development of glyphosate-resistance in Europe. But in reality, the situation is far more severe than depicted in the RAR document (as of September 2012). There are not only 10 cases of resistance known in Europe, but meanwhile the number is 16 and it is not

only five species that have been found, but there are six (Heap 2014). With five resistant species that have infested hundreds of hectares, Spain is the most afflicted country. Contrary to the RAR presentation, glyphosate-resistant weed species have not been found exclusively in orchards, vineyards or olive groves, but also in other crops such as asparagus (*Lolium rigidum* in France) and alfalfa (*Conyza canadensis* in Greece). It is also not quite true, that "*Apart from one case (C. canadensis) in the Czech Republic, Northern and Central Europe are not affected by glyphosate resistance up to now*", since resistant *C. canadensis* has also been reported from Poland railways. This indicates that evolution of glyphosate-resistance will speed up in Europe too, unless use of glyphosate is severely restricted.

In the US, not only the broad adoption of glyphosate-resistant crops but also the continuous rise in the number of resistant species and areas inflicted by resistant weeds has resulted in a massive increase in herbicide amounts applied (Benbrook 2012a). A similar scenario has been depicted for Europe in case genetically modified glyphosate-resistant crops would be authorized for cultivation here too (Benbrook 2012b). Therefore, to stop the pesticide treadmill, glyphosate use has to be restricted.

Environmental effects

In **Volume 1, Section 2.9 Effects on non-target species and Volume 3, Annex B.9 Ecotoxicology),** data on ecotoxicology studies are discussed, evaluated, and summarized.

Environmental impacts on non-target organisms

The risk assessment for birds and mammals is based on the active ingredient glyphosate acid in the product MON 52276 for the intended uses in several crops including pre-planting, pre-emergence, pre-harvest and row-application in orchards and vineyards. From the data provided by the applicants, the RMS comes to the conclusion that after use of the lead formulation MON 52276 in the indications according to the label there is an acceptable acute risk for birds and mammals due to uptake of contaminated food and an acceptable risk resulting from an exposure of small herbivorous mammals, non-target arthropods, and aquatic organisms. Use under the proposed conditions will result in a negligible exposure of honeybees or has no unacceptable acute or chronic effects on colony survival and development. The RMS concludes further, that for the evaluation of the formulation MON 52276 on non-target plants data are still required, in particular, as a valid study with this product to non-target plants is lacking and the formulants in the product may enhance toxicity.

The RMS concedes that, depending on the agricultural and ecological conditions, the use of glyphosate may affect populations of non-target terrestrial arthropods and vertebrate species (especially farmland birds) via trophic interactions and suggests mitigation measures. The RAR reads at this point: *These effects trace back to the intended effect of the herbicides – eliminating competing plants – and the interruption of the food web going along with it*.

In Volume 1, Section 3 Proposed decision, the RMS states: *It is considered that Article 4 of Regulation (EC) No 1107/2009 is complied with. Specifically the RMS considers that authorization in at least one Member State is expected to be possible for at least one plant protection product containing the active substance for at least one of the representative uses*. But the approval should be subject to conditions and restrictions. According to the RMS, glyphosate is not a candidate for substitution.

This statement has been made although the RMS identifies data gaps with regard to the ecotoxicology risk assessment (e.g. aquatic organisms, microorganisms, and non-target plants such as tomato) and concludes that certain areas of the risk assessment could not be finalized on the basis of the available data, among them effects of glyphosate towards microorganisms, on non-target plants and on biodiversity.

For all uses, the RMS acknowledges that the impacts of glyphosate on biodiversity is a critical area of concern and recommends that member states should pay attention to such potential indirect effects and may consider adequate risk mitigation measures.

Comments

It is not acceptable that glyphosate that is known to negatively impact biodiversity to such an extent should be re-authorized in the EU. Glyphosate exhibits acute and chronic toxicity, in particular, to aquatic species and non-target plants. As stated in the RAR and reported by Kremer & Means (2009), glyphosate leads to significant shifts in bacterial community composition but it also affects some fungal species, e.g. beneficial mycorrhizal fungi (Druille et al. 2013a,b). Previous use of glyphosate has been linked to increased Fusarium infection of wheat and barley (Fernandez et al. 2009). Amphibians, many of which are endangered, have been shown to be affected, possibly both their larval and adult stages (Wagner et al. 2013). Plötner and Matschke (2012) concluded that glyphosate is itself toxic to amphibians, and surfactants such as POEA are even more so causing abnormal behavior, teratogenic effects and developmental failures.

Glyphosate can adversely impact micronutrient uptake in plants as it is a strong metal chelator (Tesfamariam et al. 2009, Cakmak et al. 2009). Even low levels of residual glyphosate in soil can greatly impede the availability and uptake of Mn, Fe, Cu, and Zn by plants and lead to their undersupply with these nutrients. Reduced disease resistance and plant growth may be the result (Johal & Huber 2009). Adverse impacts of (repeated) glyphosate use on the health of non-target plants have to be taken into account, as reduced disease resistance most likely will increase use of other pesticides, e.g. fungicides that may be highly toxic too.

It is well known that weeds offer considerable benefits for the agro ecosystem, as they support a range of organisms, among them decomposers, predators, pollinators, and parasitoids, by providing food and shelter for them (Marshall et al. 2003). The Farm Scale Evaluations performed in the UK showed that broad-spectrum herbicides such as glyphosate impact abundance and diversity of weeds more severely than conventional herbicide regimes (Heard et al. 2003). The quantitative loss of weeds reduces number and diversity of arthropods heavily and interrupts the food chain for farmland birds and mammals. Ample evidence of negative impacts of glyphosate on biodiversity has been collected in areas where glyphosate is used extensively, e.g. in combination with genetically modified glyphosate-resistant crops. The all-time low in the number of monarch butterflies in the winter 2013/2014 has been attributed to the loss of their food plant (*Asclepias syriaca*) in vast areas of the United States where glyphosate-resistant crops are grown (Wade 2014).

As glyphosate is the herbicide most widely used, these massive negative impacts on biodiversity have to be considered and used as reason not to re-authorize the substance. Mitigation measures, such as buffer strips, that would be up to the individual member states could not reduce the risk of impacting

biodiversity to an acceptable level – even if farmers accepted to spare buffer strips from glyphosate application which they often don't.

Subclause: Formulated glyphosate products (Annex B.9.11 Surface-active substances in glyphosate-based formulations)

In the RAR, solely the active ingredient glyphosate is being considered for authorization, although in the field, only formulated products are applied. The final glyphosate products contain high amounts of surfactants that have surface-active properties. According to the German government[1], in addition to the 5000 t of glyphosate used in Germany in 2010, 1700 t of polyethoxylated alkylamines (POEA) had been applied. Therefore, it is of importance to not only test the toxicity of the active ingredient glyphosate but to take into account the toxicity of the various formulated products that are used.

There is ample evidence that formulated products can exhibit higher toxicity. In particular, polyethoxylated alkylamines (POEA) are known to be highly toxic to cells and organisms (Mesnage et al. 2013). The RMS considers several of the observed effects on endpoints regarding genotoxicity, mutagenicity, and development or reproduction of non-target organisms to be mediated by the surfactant included in the formulations. Thus the RMS concedes that "*the toxicity of glyphosate-based products is greatly enhanced if the active substance is formulated with alkylamine ethoxylates"* and "*the authorization of glyphosate-based products with alkylamine ethoxylated surfactants might require the generation of further data"*. But to argue, that the lead formulation MON52276 for the assessment of glyphosate does not contain this surfactant and that nowadays POEA-formulated products "*are not expected to be neither notified nor registered in the future"*, are not comforting statements, as such products are still on the market and data about the nature and toxicity of other surfactants that replace POEA are not provided to the public. In addition, predicted environmental concentrations for glyphosate and its metabolite AMPA are calculated only for these substances, not taking into account the highly toxic surfactants that are released into the environment together with the active ingredient. Therefore, it is important to collect data about environmental concentrations of surfactants and to consider their impact on the environment already during the authorization process.

Conclusions

To make agriculture in Europe more environmentally benign, it is of utmost importance that pesticide use is restricted to a much greater extent than it is actually the case. As herbicides make up the largest share of pesticides and glyphosate, in particular, is the most used herbicide, regulators are obliged to not renew the approval of this chemical.

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2. Mammalian toxicology (B.6)

Toxicokinetics (B.6.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Acute toxicity (B.6.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Short-term toxicity (B.6.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.6.3. Short term studies	Testbiotech: Several recent studies were not assessed in the DAR. Some were published during the preparation of the DAR and were omitted for unknown reasons. Some studies were conducted with the ai and show significant results (like DNA damage or biochemical modifications) like Larsen et al. (2012) or Manas (2014). Most other studies not mentioned in the DAR were conducted with formulations and also show highly significant	Larsen, K., Najle, R., Lifschitz, A., Virkel, G. (2012). Effects of sub-lethal exposure of rats to the herbicide glyphosate in drinking water: Glutathione transferase enzyme activities, levels of reduced glutathione and lipid peroxidation in liver, kidneys and small intestine. Environmental Toxicology and Pharmacology, 34(3): 811–818. http://www.sciencedirect.com/science/article/pii/S1382668912001378 Mañas, F., Peralta, L., Ugnia, L., Weyers, A., García Ovando, H., & Gorla, N. (2013). Oxidative stress and comet assay in tissues of mice administered glyphosate and ampa in drinking water for 14 days. BAG.

Short-term toxicity (B.6.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		results (Tizhe et al., 2013 a,b,c,).	Journal of basic and applied genetics, 24(2), 67-75. http://www.scielo.org.ar/scielo.php?pid=S1852-62332013000300007&script=sci_arttext Tizhe, E. V., Ibrahim, N. D. G., Fatihu, M. Y., Igbokwe, I. O., George, B. D. J., Ambali, S. F., & Shallangwaa, J. M. (2013a). Haematogical changes induced by subchronic glyphosate exposure: ameliorative effect of zinc in Wistar rats. Sokoto Journal of Veterinary Sciences, 11(2), 28-35. http://www.scopemed.org/?mno=36165 Tizhe, E. V., Ibrahim, N. D. G., Fatihu, M. Y., Igbokwe, I. O., George, B. D. J., Ambali, S. F., & Shallangwa, J. M. (2013b) Serum biochemical assessment of hepatic and renal functions of rats during oral exposure to glyphosate with zinc. Comparative Clinical Pathology, 1-8. http://link.springer.com/article/10.1007/s00580-013-1740-6 Tizhe, E. V., Ibrahim, N. D. G., Fatihu, M. Y., Onyebuchi, I. I., George, B. D. J., Ambali, S. F., & Shallangwa, J. M. (2013c). Influence of zinc supplementation on histopathological changes in the stomach, liver, kidney, brain, pancreas and spleen during subchronic exposure of Wistar rats to glyphosate. Comparative Clinical Pathology, 1-9. http://link.springer.com/article/10.1007/s00580-013-1818-1

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Genotoxicity (B.6.4)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.6.4.8., Published data	Testbiotech: Several recent studies were not assessed in the DAR. Some were published during the preparation of the DAR and were omitted for unknown reasons. Several of the studies not mentioned in the DAR show that the ai has genotoxic properties, (Alvarez-Moya et al., 2014; Moreno et al., 2014, Guilherme et al., 2012; Heu et al., 2012a,b;). Other studies not assessed in the DAR show genotoxicity, mutagenicity oder cytotoxicity of formulations (Chaufan et al., 2014; De Souza Filho et al., 2013; Moreno et al., 2014; Guilherme et al., 2012).	Alvarez-Moya, C., Reynoso Silva, M., Valdez Ramírez, C., Gómez Gallardo, D., León Sánchez, R., Canales Aguirre, A., & Feria Velasco, A. (2014). Comparison of the in vivo and in vitro genotoxicity of glyphosate isopropylamine salt in three different organisms. Genetics and Molecular Biology, 37(1), 105-110. http://www.scielo.br/scielo.php?script=sci_arttext&pid=S1415-47572014000100016&lng=es&nrm=iso&tlng=es Chaufan, G., Coalova, I., & de Molina, M. D. C. R. (2014). Glyphosate Commercial Formulation Causes Cytotoxicity, Oxidative Effects, and Apoptosis on Human Cells Differences With its Active Ingredient. International journal of toxicology, 1091581813517906. http://ijt.sagepub.com/content/early/2014/01/14/1091581813517906.abstract De Souza Filho, J., Sousa, C. C. N., Da Silva, C. C., De Sabóia-Morais, S. M. T., & Grisolia, C. K. (2013). Mutagenicity and Genotoxicity in Gill Erythrocyte Cells of Poecilia reticulata Exposed to a Glyphosate Formulation. Bulletin of environmental contamination and toxicology, 91(5), 583-587. http://link.springer.com/article/10.1007/s00128-013-1103-7 George, J., & Shukla, Y. (2013) Emptying of Intracellular Calcium Pool and Oxidative Stress Imbalance Are Associated with the Glyphosate-Induced Proliferation in Human Skin Keratinocytes HaCaT Cells. ISRN

Genotoxicity (B.6.4)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
			dermatology, 2013. http://www.hindawi.com/journals/isrn.dermatology/2013/825180/ Guilherme, S., Santos, M.A., Barroso, C., Gaivão, I., Pacheco, M. (2012) Differential genotoxicity of Roundup® formulation and its constituents in blood cells of fish (Anguilla anguilla): considerations on chemical interactions and DNA damaging mechanisms. Ecotoxicology, 21(5): 1381-1390. http://link.springer.com/article/10.1007%2Fs10646-012-0892-5 Heu, C., Berquand, A., Elie-Caille, C., Nicod, L. (2012a) Glyphosate-induced stiffening of HaCaT keratinocytes, a Peak Force Tapping study on living cells. Journal of Structural Biology, 178(1): 1- 7. http://www.sciencedirect.com/science/article/pii/S1047847712000597 Heu, C., Elie-Caillea, C., Mougeyc, V., Launayd, S., Nicod, L. (2012b) A step further toward glyphosate-induced epidermal cell death: Involvement of mitochondrial and oxidative mechanisms. Environmental Toxicology and Pharmacology, 34(2): 144–153. http://www.sciencedirect.com/science/article/pii/S1382668912000300 Koller, V.J., Fürhacker, M., Nersesyan, A., Mišík, M., Eisenbauer, M., Knasmueller, S. (2012) Cytotoxic and DNA-damaging properties of glyphosate and Roundup in human-derived buccal epithelial cells. Archives of Toxicology, doi 10.1007/s00204-012-0804-8. http://link.springer.com/article/10.1007%2Fs00204-012-0804-8

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Genotoxicity (B.6.4)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
			Moreno, N. C., Sofia, S. H., & Martinez, C. B. (2014). Genotoxic effects of the herbicide Roundup Transorb< sup>®</sup> and its active ingredient glyphosate on the fish< i> Prochilodus lineatus</i>. Environmental toxicology and pharmacology, 37(1), 448-454.http://www.sciencedirect.com/science/article/pii/S1382668913002846

Long-term toxicity and carcinogenicity (B.6.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.6.5.3, Published data an carcinogenicity	Testbiotech: Several recent studies were not assessed in the DAR. These studies show associations of glyphosate with several types of cancer. • B cell lymphoma (Schinasi et al., 2014) • "nearly significant" association between glyphosate and multiple myeloma in Canadian men (Kachuri et al., 2013) • lymphoma subtypes (Cocco et al., 2013) • association between the ai and breast cancer cells.	Schinasi, L., & Leon, M. E. (2014). Non-Hodgkin Lymphoma and Occupational Exposure to Agricultural Pesticide Chemical Groups and Active Ingredients: A Systematic Review and Meta-Analysis. International journal of environmental research and public health, 11(4), 4449-4527. http://www.mdpi.com/1660-4601/11/4/4449/htm Kachuri, L., Demers, P. A., Blair, A., Spinelli, J. J., Pahwa, M., McLaughlin, J. R., ... & Harris, S. A. (2013) Multiple pesticide exposures and the risk of multiple myeloma in Canadian men. International Journal of Cancer. http://onlinelibrary.wiley.com/doi/10.1002/ijc.28191/abstract Cocco, P., Satta, G., Dubois, S., Pili, C., Pilleri, M., Zucca, M., ... & Boffetta, P. (2013) Lymphoma risk and occupational exposure to pesticides: results of the Epilymph study. Occupational and environmental medicine, 70(2): 91-98. http://oem.bmj.com/content/70/2/91.short

Long-term toxicity and carcinogenicity (B.6.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
			Thongprakaisang, S., Thiantanawat, A., Rangkadilok, N., Suriyo, T., & Satayavivad, J. (2013) Glyphosate induces human breast cancer cells growth via estrogen receptors. Food and Chemical Toxicology. http://www.sciencedirect.com/science/article/pii/S0278691513003633

Reproductive toxicity (B.6.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.6.6.12, Published data	Testbiotech: Several recent studies were not assessed in the DAR. Some were published during the preparation of the DAR and were omitted for unknown reasons. One study found an association between pure glyphosate and breast cancer cells (Thongprakaisang et al., 2013). The results indicated that low concentrations of glyphosate possessed estrogenic activity. Further, in another study not mentioned in the DAR, a pesticide mixture containing the ai led to testicular damage at very low doses in rats (Astiz et al., 2013).	Thongprakaisang, S., Thiantanawat, A., Rangkadilok, N., Suriyo, T., & Satayavivad, J. (2013) Glyphosate induces human breast cancer cells growth via estrogen receptors. Food and Chemical Toxicology. http://www.sciencedirect.com/science/article/pii/S0278691513003633 Astiz, M., Hurtado de Catalfo, G. E., García, M. N., Galletti, S. M., Errecalde, A. L., Alaniz, M. J. D., & Marra, C. A. (2013) Pesticide-induced decrease in rat testicular steroidogenesis is differentially prevented by lipoate and tocopherol. Ecotoxicology and environmental safety, 91: 129–138. http://www.sciencedirect.com/science/article/pii/S0147651313000389 Basrur, P. K., 2006. Disrupted sex differentiation and feminization of manand domestic animals. Environ. Res. 100, 18–38. http://www.sciencedirect.com/science/article/pii/S0013935105001234

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Reproductive toxicity (B.6.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		Also other studies with glyphosate formulations have suggested adverse effects on male reproductive performance (Caglar and Kolankaya,2008; de Liz Oliveira Cavalli; Omran et al., 2013). A review by Basrur (2006) showed that glyphosate can act as a sexual differentiation disruptor and an estrogen-like compound in domestic animals and humans. .	Caglar, S., Kolankaya, D., 2008. The effect of sub-acute and sub-chronic exposure of rats to the glyphosate-based herbicide Roundup. Environ. Toxicol. Pharmacol. 25, 57–62. http://www.sciencedirect.com/science/article/pii/S1382668907001135 de Liz Oliveira Cavalli, V. L., Cattani, D., Elise Heinz Rieg, C., Pierozan, P., Zanatta, L., Benedetti Parisotto, E., ... & Zamoner, A. (2013) Roundup Disrupted Male Reproductive Functions By Triggering Calcium-Mediated Cell Death In Rat Testis And Sertoli Cells. Free Radical Biology and Medicine. http://www.sciencedirect.com/science/article/pii/S0891584913003262 Omran, N. E., & Salama, W. M. (2013). The endocrine disrupter effect of atrazine and glyphosate on Biomphalaria alexandrina snails. Toxicology and industrial health, 0748233713506959. http://tih.sagepub.com/content/early/2013/11/05/0748233713506959.abstract

Neurotoxicity (B.6.7)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.6.7.1., Published data on neurotoxicity	Testbiotech: A recent study (Cattani et al., 2014) not presented in the DAR shows that a glyphosate-based pesticide	Cattani, D., de Liz Oliveira Cavalli, V. L., Heinz Rieg, C. E., Domingues, J. T., Dal-Cim, T., Tasca, C. I., ... & Zamoner, A. (2014). Mechanisms

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Neurotoxicity (B.6.7)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		is associated with neurotoxicity. Other studies (older studies which are also not presented in the DAR for unknown reasons) came to the same conclusion (for example El-Shenawy, 2009).	underlying the neurotoxicity induced by glyphosate-based herbicide in immature rat hippocampus: Involvement of glutamate excitotoxicity. Toxicology, 320, 34-45. http://www.sciencedirect.com/science/article/pii/S0300483X14000493 El-Shenawy, N.S., 2009. Oxidative stress responses of rats exposed to Roundup and its active ingredient glyphosate. Environ. Toxicol. Pharmacol. 28, 379–385. http://www.sciencedirect.com/science/article/pii/S1382668909001100

Other toxicological studies & Medical data (B.6.8-B.6.9)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.6.8.3., Studies on farm animals	Testbiotech: The DAR is inconsistent here. In the Annex 6.1 “Toxicology and metabolism”, it is said that the results of a BfR study on the effects of glyphosate on microorganisms in rumen of ruminants are not available. In the Summary report however, it is said that “no adverse effects on animal health are to be anticipated “.	

Section 2 - Mammalian toxicology (B.6)

Summary of mammalian toxicology and setting ADI, AOEL, ARfD (B.6.10)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Toxicity of the product(s) (B.6.11)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Dermal absorption (B.6.12)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Toxicity of non-active substances (B.6.13)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Section 2 - Mammalian toxicology (B.6)

Exposure data (B.6.14)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

3. Residues (B.7)

Storage Stability (B.7.0)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Metabolism in plants (B.7.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.7.1.2., Tolerant crops	Testbiotech: High levels of glyphosate and metabolites were found in glyphosate tolerant soybeans by Bohn et al. (2014) and Testbiotech (2013)	Bøhn, T., Cuhra, M., Traavik, T., Sanden, M., Fagan, J., & Primicerio, R. (2014). Compositional differences in soybeans on the market: glyphosate accumulates in Roundup Ready GM soybeans. Food Chemistry, 153: 207–215. http://www.sciencedirect.com/science/article/pii/S0308814613019201 Testbiotech (2013) High levels of residues from spraying with glyphosate found in soybeans in Argentina. Testbiotech Backgrund http://www.testbiotech.de/en/node/926

Metabolism in livestock (B.7.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>,	<< Identifier >>: <<comment>>	

Section 3 - Residues (B.7)

Metabolism in livestock (B.7.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	<<description>>		

Residue definition (B.7.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Use pattern, critical GAP, residues trials (B.7.4 to B.7.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Processing (B.7.7)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Section 3 - Residues (B.7)

Livestock feeding (B.7.8)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Succeeding/Rotational crops (B.7.9)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

4. Environmental fate and behaviour (B.8)

Route and rate of degradation in soil (B.8.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Adsorption, desorption and mobility in soil (B.8.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

PEC in soil (B.8.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Fate and behaviour in water and impact on water treatment procedures (B.8.4 – B.8.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, Annex B.8.4, Fate and behaviour in	Testbiotech: A recent study by Mercurio et al. (2014) shows that	Mercurio, P., Flores, F., Mueller, J. F., Carter, S., & Negri, A. P. (2014). Glyphosate persistence in seawater. Marine pollution bulletin.

Section 4 - Environmental fate and behaviour (B.8)

Fate and behaviour in water and impact on water treatment procedures (B.8.4 – B.8.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	water	glyphosate and AMPA may persist much longer in water than previously thought.	http://www.sciencedirect.com/science/article/pii/S0025326X14000228

PEC in surface water and ground water (B.8.6)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Fate and behaviour in air and PEC in air (B.8.7 – B.8.8)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Definition of the residues (B.8.9)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Section 4 - Environmental fate and behaviour (B.8)

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

5. Ecotoxicology (B.9)

Birds and mammals (B.9.1 and B.9.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Aquatic organisms (B.9.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.9.2, <<description>>	Testbiotech: Several publications that were not assessed in the DAR show risks for aquatic organisms. For example, the ai was shown to be toxic to several fish species by Avigliano et al., 2014; Fan et al., 2013; Further, toxic effects were found in different glyphosate formulations. For example, Nwani et al. (2013) found genotoxicity damage, Richard et al. (2014) found an impaired immune system. Also other aquatic organisms like mussels (Sandrini et al., 2013) or snails (Mona et al., 2013) were shown to be sensitive to glyphosate.	Avigliano, L., Fassiano, A. V., Medesani, D. A., de Molina, M. R., & Rodríguez, E. M. (2014). Effects of Glyphosate on Growth Rate, Metabolic Rate and Energy Reserves of Early Juvenile Crayfish, Cherax quadricarinatus M. Bulletin of environmental contamination and toxicology, 1-5. http://link.springer.com/article/10.1007/s00128-014-1240-7 Fan, J. Y., Geng, J. J., Ren, H. Q., Wang, X. R., & Han, C. (2013). Herbicide Roundup® and its main constituents cause oxidative stress and inhibit acetylcholinesterase in liver of Carassius auratus. Journal of Environmental Science and Health, Part B, 48(10), 844-850. http://www.tandfonline.com/doi/abs/10.1080/03601234.2013.795841#.UdAVvJwlE9U Mona, M. H., Gaafar, R. M., Helal, I. B., Omran, N. E., & Salama, W. M. (2013). Evaluation of cytotoxic effects of atrazine and glyphosate herbicides on< i> Biomphalaria glabrata</i> snails. The Journal of Basic

Section 5 - Ecotoxicology (B.9)

Aquatic organisms (B.9.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		Several publications that were not assessed in the DAR also show risks for other aquatic organisms, induced by glyphosate or formulations containing glyphosate (see "further explanations" for a list of publications), Most of these studies were not assessed in the DAR.	& Applied Zoology, 66(2), 68-75. http://www.sciencedirect.com/science/article/pii/S2090989613000398 Nwani, C. D., Nagpure, N. S., Kumar, R., Kushwaha, B., Kumar, P., & Lakra, W. S. (2013). Induction of micronuclei and nuclear lesions in Channa punctatus following exposure to carbosulfan, glyphosate and atrazine. Drug and chemical toxicology, (0), 1-8. http://informahealthcare.com/doi/abs/10.3109/01480545.2013.866138 Richard, S., Prévot-D'Alvise, N., Bunet, R., Simide, R., Couvray, S., Coupé, S., & Grillasca, J. P. (2014). Effect of a Glyphosate-Based Herbicide on Gene Expressions of the Cytokines Interleukin-1β and Interleukin-10 and of Heme Oxygenase-1 in European Sea Bass, Dicentrarchus labrax L. Bulletin of environmental contamination and toxicology, 1-6. http://link.springer.com/article/10.1007/s00128-013-1180-7 Sandrini, J. Z., Rola, R. C., Lopes, F. M., Buffon, H. F., Freitas, M. M., Martins, C. D., & da Rosa, C. E. (2013) Effects of glyphosate on cholinesterase activity of the mussel Perna perna and the fish Danio rerio and Jenynsia multidentata: In vitro studies. Aquatic toxicology (Amsterdam, Netherlands), 130, 171. http://www.sciencedirect.com/science/article/pii/S0166445X13000088 Brodeur, J. C., Poliserpi, M. B., & Sánchez, M. (2014). Synergy between glyphosate-and cypermethrin-based pesticides during acute exposures in tadpoles of the common South American Toad< i> Rhinella

Aquatic organisms (B.9.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
			arenarum</i>. Chemosphere, 112, 70-76. http://www.sciencedirect.com/science/article/pii/S0045653514003336 Syedkolaei, S. J. G., Shiri, N., Mirvaghefi, A. R., Rafiee, G. R., & Makhdomi, C. (2013). Toxicity evaluation of Malathion, Carbaryle and Glyphosate in common carp fingerlings (Cyprinus carpio, Linnaeus, 1758). Journal of Veterinary Research, 68(3), 257-267. http://www.cabdirect.org/abstracts/20133405485.html;jsessionid=B09A53378AD3690E177667F021F149A9 Erhunmwunse, N. O., Alohan, F. I., Enuneku, A., Tongo, I., Ainerua, M., & Idugboe, S. (2013). Pathological alterations in the liver of post-juvenile African Catfish (Clarias gariepinus) exposed to sublethal concentrations of the herbicide Glyphosate. Journal of Natural Sciences Research, 3(15), 87-91. http://iiste.org/Journals/index.php/JNSR/article/viewFile/9720/9932 Moreno, N. C., Sofia, S. H., & Martinez, C. B. (2014). Genotoxic effects of the herbicide Roundup Transorb< sup>®</sup> and its active ingredient glyphosate on the fish< i> Prochilodus lineatus</i>. Environmental toxicology and pharmacology, 37(1), 448-454. http://www.sciencedirect.com/science/article/pii/S1382668913002846 dos Santos, K. C., & Martinez, C. B. (2014). Genotoxic and biochemical effects of atrazine and Roundup< sup>®</sup>, alone and in combination, on the Asian clam< i> Corbicula fluminea</i>. Ecotoxicology and environmental safety, 100, 7-14.

Section 5 - Ecotoxicology (B.9)

Aquatic organisms (B.9.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
			http://www.sciencedirect.com/science/article/pii/S0147651313005095 Uren Webster, T. M., Laing, L. V., Florance, H., & Santos, E. M. (2013). Effects of glyphosate and its formulation, Roundup®, on reproduction in zebrafish (Danio rerio). Environmental science & technology. http://pubs.acs.org/doi/abs/10.1021/es404258h Dornelles, M. F., & Oliveira, G. T. (2013). Effect of Atrazine, Glyphosate and Quinclorac on Biochemical Parameters, Lipid Peroxidation and Survival in Bullfrog Tadpoles (Lithobates catesbeianus). Archives of environmental contamination and toxicology, 1-15. http://link.springer.com/article/10.1007/s00244-013-9967-4 Gholami-Seyedkolaei, S. J., Mirvaghefi, A., Farahmand, H., & Kosari, A. A. (2013). Effect of a glyphosate-based herbicide in< i> Cyprinus carpio:</i> Assessment of acetylcholinesterase activity, hematological responses and serum biochemical parameters. Ecotoxicology and environmental safety, 98, 135-141. http://www.sciencedirect.com/science/article/pii/S0147651313003965 Yadav, S. S., Giri, S., Singha, U., Boro, F., & Giri, A. (2013). Toxic and genotoxic effects of Roundup on tadpoles of the Indian skittering frog (< i> Euflictis cyanophlyctis</i>) in the presence and absence of predator stress. Aquatic Toxicology, 132, 1-8.http://www.sciencedirect.com/science/article/pii/S0166445X1300026X

Aquatic organisms (B.9.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
			Janssens, L., & Stoks, R. (2013). Synergistic effects between pesticide stress and predator cues: Conflicting results from life history and physiology in the damselfly< i> Enallagma cyathigerum</i>. Aquatic Toxicology, 132, 92-99. http://www.sciencedirect.com/science/article/pii/S0166445X13000350 De Souza Filho, J., Sousa, C. C. N., Da Silva, C. C., De Sabóia-Morais, S. M. T., & Grisolia, C. K. (2013). Mutagenicity and Genotoxicity in Gill Erythrocyte Cells of Poecilia reticulata Exposed to a Glyphosate Formulation. Bulletin of environmental contamination and toxicology, 91(5), 583-587. http://link.springer.com/article/10.1007/s00128-013-1103-7 Güngördü, A. (2013). Comparative toxicity of methidathion and glyphosate on early life stages of three amphibian species:< i> Pelophylax ridibundus</i>,< i> Pseudepidalea viridis</i>, and< i> Xenopus laevis</i>. Aquatic Toxicology. http://www.sciencedirect.com/science/article/pii/S0166445X13001550 Lanctôt, C., Robertson, C., Navarro-Martín, L., Edge, C., Melvin, S. D., Houlahan, J., & Trudeau, V. L. (2013). Effects of the glyphosate-based herbicide Roundup WeatherMax® on metamorphosis of wood frogs (< i> Lithobates sylvaticus</i>) in natural wetlands. Aquatic Toxicology. http://www.sciencedirect.com/science/article/pii/S0166445X13001331 Wagner, N., Reichenbecher, W., Teichmann, H., Tappeser, B., & Lötters, S. (2013) Questions concerning the potential impact of

Aquatic organisms (B.9.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
			glyphosate- based herbicides on amphibians. Environmental Toxicology and Chemistry. http://onlinelibrary.wiley.com/doi/10.1002/etc.2268/abstract Kumar, A., Jahavar Ali, A. (2013) TOXIC IMPACTS OF TWO ORGANOPHOSPHORUS PESTICIDES ON THE ACETYLCHOLINESTERASE ACTIVITY AND BIOCHEMICAL COMPOSITION OF FRESHWATER FAIRY SHRIMP STREPTOCEPHALUS DICHOTOMUS. International Journal of Pharma and Bio Sciences, 4(2): 966 – 972. https://ijpbs.net/cms/php/upload/2340_pdf.pdf Meza-Joya, F.L., Ramírez-Pinilla, M.P., Fuentes-Lorenzo, J.L. (2013) Toxic, cytotoxic, and genotoxic effects of a glyphosate formulation (roundup®SL–cosmoflux®411F) in the direct-developing frog eleutherodactylus johnstonei. Environmental and Molecular Mutagenesis, DOI: 10.1002/em.21775. http://onlinelibrary.wiley.com/doi/10.1002/em.21775/abstract Akinsorotan, A., Zelibe, S., & Olele, N. (2013) Acute Toxicity And Behavioural Changes On African Catfish (Clarias gariepinus) Exposed To Dizensate (Glyphosate Herbicide). International Journal of Scientific & Engineering Research 4(3). http://www.ijser.org/researchpaper%5CAcute-Toxicity-And-Behavioural-Changes-On-African-Catfish-Clarias-gariepinus-Exposed-To-Dizensate-Glyphosate-Herbicide.pdf

Section 5 - Ecotoxicology (B.9)

Aquatic organisms (B.9.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
			de Castilhos Ghisi, N., & Cestari, M. M. (2012). Genotoxic effects of the herbicide Roundup® in the fish Corydoras paleatus (Jenyns 1842) after short-term, environmentally low concentration exposure. Environmental Monitoring and Assessment, 185(4): 3201-3207. http://link.springer.com/article/10.1007%2Fs10661-012-2783-x?LI=true Cuhra, M., Traavik, T., & Bøhn, T. (2013) Clone-and age-dependent toxicity of a glyphosate commercial formulation and its active ingredient in Daphnia magna. Ecotoxicology, 1-12. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3572389/ Lajmanovich, R. C., Junges, C. M., Attademo, A. M., Peltzer, P. M., Cabagna-Zenklusen, M. C., & Basso, A. (2013). Individual and Mixture Toxicity of Commercial Formulations Containing Glyphosate, Metsulfuron-Methyl, Bispyribac-Sodium, and Picloram on Rhinella arenarum Tadpoles. Water, Air, & Soil Pollution, 224(3), 1-13. http://link.springer.com/article/10.1007/s11270-012-1404-1 Vera-Candioti, J., Soloneski, S., Larramendy, M.L. (2013) Evaluation of the genotoxic and cytotoxic effects of glyphosate-based herbicides in the ten spotted live-bearer fish Cnesterodon decemmaculatus (Jenyns, 1842). Ecotoxicology and environmental safety, 89(1): 166–173. http://www.sciencedirect.com/science/article/pii/S0147651312004484 Yadav, S.S., Giri, S., Singha, U., Boro, F., Giri, A. (2013) Toxic and genotoxic effects of Roundup on tadpoles of the Indian skittering frog (Euflictis cyanophlyctis) in the presence and absence of predator stress.

Aquatic organisms (B.9.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
			Aquatic Toxicology, 132–133: 1–8. http://www.sciencedirect.com/science/article/pii/S0166445X1300026X Guilherme, S., Santos, M.A., Barroso, C., Gaivão, I., Pacheco, M. (2012) Differential genotoxicity of Roundup® formulation and its constituents in blood cells of fish (Anguilla anguilla): considerations on chemical interactions and DNA damaging mechanisms. Ecotoxicology, 21(5): 1381-1390. http://link.springer.com/article/10.1007%2Fs10646-012-0892-5 Hued, A. C., Oberhofer, S., de los Ángeles Bistoni, M. (2012) Exposure to a Commercial Glyphosate Formulation (Roundup®) Alters Normal Gill and Liver Histology and Affects Male Sexual Activity of Jenynsia multidentata (Anablepidae, Cyprinodontiformes). Archives of environmental contamination and toxicology, 62(1): 107-117. http://link.springer.com/article/10.1007%2Fs00244-011-9686-7?LI=true Moore LJ, Fuentes L, Rodgers JH Jr, Bowerman WW, Yarrow GK, Chao WY, Bridges WC Jr. (2012) Relative toxicity of the components of the original formulation of Roundup to five North American anurans. Ecotoxicol Environ Saf;78: 128-33. http://www.sciencedirect.com/science/article/pii/S0147651311004234 Plötner, J. & Matschke, J. (2012) Akut-toxische, subletale und indirekte Wirkungen von Glyphosat und glyphosathaltigen Herbiziden auf Amphibien – eine Übersicht. Zeitschrift für Feldherbologie, 19: 1-20. http://www.researchgate.net/publication/231178416_Akut-

Section 5 - Ecotoxicology (B.9)

Aquatic organisms (B.9.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
			toxische_subletale_und_indirekte_Wirkungen_von_Glyphosat_und_glyphosathaltigen_Herbiziden_auf_Amphibien__eine_bersicht/file/9fcfd5064034fe8016.pdf Relyea, R.A. (2012) New effects of Roundup on amphibians: Predators reduce herbicide mortality; herbicides induce antipredator morphology. Ecological Applications, 22(2), 634-647. http://www.esajournals.org/doi/abs/10.1890/11-0189.1 Glusczak, L., Loro, V.L., Pretto, A., Moraes, B.S., Raabe, A., Duarte, M.F., de Sousa Valladão, D.M. (2011) Acute exposure to glyphosate herbicide affects oxidative parameters in Piava (Leporinus obtusidens). Archives of environmental contamination and toxicology, 61(4): 624-630. http://link.springer.com/article/10.1007%2Fs00244-011-9652-4?LI=true#page-1 Guilherme, S., Santos, M. A., Gaivão, I., & Pacheco, M. (2014). DNA and chromosomal damage induced in fish (Anguilla anguilla L.) by aminomethylphosphonic acid (AMPA)—the major environmental breakdown product of glyphosate. Environmental Science and Pollution Research, 1-10. http://link.springer.com/article/10.1007/s11356-014-2803-1

Section 5 - Ecotoxicology (B.9)

Aquatic organisms (B.9.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
			Armiliato, N., Ammar, D., Nezzi, L., Straliotto, M., Muller, Y. M., & Nazari, E. M. (2014). Changes in Ultrastructure and Expression of Steroidogenic Factor-1 in Ovaries of Zebrafish Danio rerio Exposed to Glyphosate. Journal of Toxicology and Environmental Health, Part A, 77(7), 405-414. http://www.tandfonline.com/doi/abs/10.1080/15287394.2014.880393 Lajmanovich, R. C., Junges, C. M., Attademo, A. M., Peltzer, P. M., Cabagna-Zenklusen, M. C., & Basso, A. (2013). Individual and mixture toxicity of commercial formulations containing glyphosate, metsulfuron-methyl, bispyribac-sodium, and picloram on Rhinella arenarum tadpoles. Water, Air, & Soil Pollution, 224(3), 1-13. http://link.springer.com/article/10.1007/s11270-012-1404-1

Bees and non-target arthropods (B.9.4 and B.9.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Section 5 - Ecotoxicology (B.9)

Earthworms and other soil non-target organisms (macro and micro) (B.9.6, B.9.7 and B.9.8)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Other non-target organisms (flora and fauna), sewage treatment (B.9.9 and B.9.10)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

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Risiken der Anwendung von Glyphosat-haltigen Pestiziden durch bestimmte Beistoffe

Mit dieser Eingabe soll auf das Risiko einer relevanten Gefährdung der öffentlichen Gesundheit und Sicherheit durch bestimmte Beistoffe in Glyphosat-haltigen Pflanzenschutzmitteln (PSM) hingewiesen werden. Es erscheint als sehr fraglich, ob die gültige Rechtslage an diese in letzter Zeit vermehrt sichtbar gewordene Bedrohungslage angepasst ist. Wobei die Diskussion um die POE-Tallowamine ein gutes Beispiel darstellt, dass in diesem Bereich erhebliche Probleme bestehen. Wodurch in der Konsequenz das Vertrauen der Bevölkerung in die staatliche Vorsorge (und Risikominimierung) aufs Spiel gesetzt wird.

Es ist vielfältig deutlich geworden, dass die POE-Tallowamine toxischer sind als andere Netzmittel in PSM. Das wurde auch von den Behörden so dargestellt. So wurden in Deutschland im Jahr 2008 die Zulassungsinhaber von PSM, die diese Netzmittel verwenden, behördlicherseits dringend aufgefordert, diese durch andere zu ersetzen. Was in einer größeren Zahl der Fälle, zumindest in Deutschland, offenbar auch geschehen ist.

Einige Hersteller jedoch haben diesen Austausch nicht vorgenommen, die Zulassungen solcher PSM auf dem deutschen Markt laufen noch bis 2016 bzw. 2018. Dieser Umstand wird zu einem fatalen Signal für die Öffentlichkeit angesichts der Tatsache, dass (unter anderem über die Medien) ja sehr deutlich geworden ist: erstens, dass diese Tallowamine eine gesteigerte Toxizität aufweisen, mithin ein höheres Risiko darstellen; und zweitens, dass es offenkundig weniger toxische Alternativen gibt.[1]

Wenn nun also der als Landwirt bei der Sikkation gerne auf das weniger giftige Produkt zugreifen möchte, dann kann er das nicht, weil er im Dunkeln gelassen wird, welches PSM noch Tallowamine enthält. Er bekommt die Auskunft, dass diese Information als „Betriebs- und Geschäftsgeheimnis“ des Herstellers

[1] Auf dem Behördensymposium am 20.01.2014 in Berlin wurde von Behördenseite vor den anwesenden Medien deutlich herausgestellt, dass bestimmte toxikologische Schadwirkungen (wie ernsthafte Vergiftungen) nicht dem Hauptwirktstoff Glyphosat, sondern bestimmten Beistoffen zugeschrieben werden.

gesetzlich geschützt ist. Ebenso jeder, der ein solches Mittel in seinem Haus- und Kleingartenbereich einsetzen möchte.

Hier wird eindeutig der Grundsatz verletzt, dass die öffentliche Gesundheit Vorrang vor dem Interesse des Pflanzenschutzes haben soll. Eher gilt hier, dass dem Wirtschaftsinteresse des Herstellers, der den von ihm verwendeten Beistoff angesichts neuer Erkenntnisse nicht gegen eine weniger toxische Alternative austauschen möchte, Vorrang vor der öffentlichen Gesundheit eingeräumt wird.

Letztes gilt umso mehr, als Jedem klar sein dürfte, dass alle Bemühungen, eine Risikoeinschätzung für Pflanzenschutzmittel vorzunehmen, die eine Mischung darstellen zwischen einem Wirkstoff (oder auch mehreren) und weiteren mehr oder weniger toxischen Beistoffen, zwangsläufig mit einem hohen Risiko einhergehen. Allein der Wirkstoff wird hinsichtlich chronischer Langzeitfolgen im relativ zuverlässigen Tierversuch getestet, die Mischung dagegen (bzw. das Pflanzenschutzmittel als Ganzes) in der Regel nicht.

Die Bemühungen, eine kumulative Abschätzung der Gesamttoxizität zustande zu bringen ohne eine Langzeittestung des Gemischs wird sicherlich noch für längere Zeit risikobehaftet sein. Denn es gilt ja, sich über den toxikologischen Grundsatz hinwegsetzen, dass sich die Toxizität eines Gemisches nicht aus der Toxizität der Einzelsubstanzen bestimmen lässt.

Am anderen Ende steht bei diesem kritischen Unterfangen das hohe Gut der öffentlichen Gesundheit. Dieses muss dem wirtschaftlichen Interesse des Herstellers weichen, ohne dass dem Bürger auch nur die Chance gegeben wird, die Produkte mit dem (amtlich festgestellten) höheren Risiko zu meiden.

Dabei kommt als Wesentliches hinzu, dass die POE-Tallowamine schwerlich das einzige Beispiel eines solchen Hazardspieles sind. Es liegen bereits wissenschaftliche Studien vor, die darauf hinweisen, dass andere Pflanzenschutzmittel, die kein Tallowamin enthalten, eine ähnlich (gegenüber dem eigentlichen Wirkstoff Glyphosat) gesteigerte Toxizität aufweisen.

So hat die Forschergruppe um Prof. Gilles-Eric Séralini von der Universität Caen in den letzten Jahren eine Reihe von in-vitro-Studien veröffentlicht, in denen es um dieses Thema geht.[2] Gefunden wird eine erheblich gesteigerte

[2] Mesnage, R.; Defarge, N.; Spiroux de Vendomois, J. and Séralini, G.-E. : Major pesticides are more toxic to human cells than their declared active principles, BioMed Research International, vol. 2014, Article ID 179691, 8 pages, 2014. doi:10.1155/2014/179691
http://www.hindawi.com/journals/bmri/aip/179691/
Im Folgenden: **Mesnage et al. 2014**
sowie:
Mesnage, R.; Bernay, B. and Séralini, G.-E. (2013): Ethoxylated adjuvants of glyphosate-based herbicides are active principles of human cell toxicity. Toxicology, 313, no. 2-3, pp.122-128, 2013
Im Folgenden: **Mesnage et al. 2013**

Toxizität der Formulierungen bestimmter Pflanzenschutzmittel gegenüber ihrem jeweiligen Hauptwirkstoff, offenkundig wiederum durch die Wirkung bestimmter Beistoffe / Netzmittel / sonstiger Adjuvantien. Die Toxizität soll bis zum Faktor 10.000 höher sein. Erste behördliche Stellungnahmen gehen eher von einer Plausibilität dieser in vitro-Ergebnisse aus.[3] Wobei die Antwort auf die Frage nach der Übertragbarkeit auf Mensch und Tier aussteht. Doch schon allein die Tatsache, dass diese Frage offenbar offen ist, lässt Vertrauen verloren gehen.

Bemerkenswert an den Ergebnissen der Forschergruppe ist außerdem, dass sich das Präparat „Roundup® GT plus“ in derselben Größenordnung als (im Vergleich zum Hauptwirkstoff) toxischer erwies, wie dies bei jenen untersuchten handelsüblichen Formulierungen der Fall war, die eindeutig ein POE-Tallowamin enthielten. Was bei „Roundup® GT plus“ offenkundig nicht der Fall ist.[4] Das dort verwendete Netzmittel „Ether amine ethoxylate“ entfaltet offenbar ähnliche Wirkungen wie die POE-Tallowamine. Und es wird vermutlich nicht das einzige sein.

Hinzu kommt, dass auch die Antwort auf die Frage, durch welche Stoffe die Tallowamine ersetzt wurden, unter jenes „Betriebs- und Geschäftsgeheimnis“ fällt. Dies ist somit allein den Behörden und den Herstellern bekannt, sonst niemandem. Und damit auch nicht unabhängigen Forschern, universitären Einrichtungen etcetera. Auch dies leistet einem gewaltigen Vertrauensverlust Vorschub.

Die Behörden als alleinige Instanz, von deren Unfehlbarkeit das hohe Gut der öffentlichen Gesundheit abhängt, ist eine Zumutung für jedes demokratische Staatswesen und stellt einen Konstruktionsfehler dar, der mit Sicherheit ungute Folgen haben wird. Soweit nichts Schlimmeres in Gestalt realer gesundheitlicher Folgen eintritt (soweit sie sich dann überhaupt konkret zuordnen lassen), wird wiederum Vertrauensverlust die Folge sein. Zumal auch Behörden sich häufig gegen den Vorwurf zu großer Industrienähe wehren müssen. Dass eine solche Gefahr immer besteht, liegt auf der Hand.

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[3]: http://www.bfr.bund.de/cm/343/bfr-stellungnahme-zu-major-pesticides-are-more-toxic-to-human-cells-than-their-declared-active-principles.pdf

[4] Zum einen ergibt dies eine von der Séralini-Gruppe durchgeführte MALDI-TOF-Analyse. (Mesnage et al. 2013, Fig. 3) Zum anderen sind die Formulierungen von „Roundup®GT plus“ und dem auf dem deutschen Markt vertretenen „Roundup® UltraMax“ offenbar weitgehend identisch. Dies ergibt sich aus einem Sicherheitsdatenblatt zu „Roundup® UltraMax“ (datierend vom 25.07.2011) sowie der entsprechenden „fiche de securitée“ zu „Roundup® GT plus“ (ebenfalls datierend vom 25.07.2011): in beiden Präparaten wird das Netzmittel mit „Ether amine ethoxylate“ bezeichnet, mit in beiden Fällen identischer CAS-Nummer (71486-88-9). Zudem hat Monsanto in einem Dokument (stammend aus 2012) sein Produkt Roundup® UltraMax“ als „POE-T frei“ bezeichnet.

Gerade bei Glyphosat ist das Auseinanderklaffen der behördlichen Einschätzungen und jener von vielfältigen Veröffentlichungen weltweit, die immerhin in den meisten Fällen ebenfalls Peer Review-Prozesse durchlaufen haben, augenfällig. Es stellt sich die dringende Frage, ob hier die unterschätzte Wirkung der Beistoffe einen wesentlichen Hintergrund darstellt.

Wobei gerade im Fall der Beistoffe wohl die Gefahr gegeben ist, dass die derzeitige Rechtslage ein Ungleichgewicht darstellt insofern, als die Anforderungen hinsichtlich Datenanforderungen, bezogen auf die Pflanzenschutzmittel einerseits, und hinsichtlich Wirkstoffen andererseits, in einem Missverhältnis stehen zu den Datenanforderungen, bezogen auf Beistoffe. Wenn die Aussage stimmt, dass es derzeit für die Zulassungs- und Überwachungsbehörden keine Rechtsgrundlage gibt, um über zahlreiche Beistoffe die erforderlichen Daten anzufordern, die eine umfassende Risikobewertung ermöglichen (inklusive Daten über Rückstände in Erntegütern etc.), wird man wohl auch das als einen Konstruktionsfehler werten müssen.

Es ist fraglich, ob das Instrumentarium der Behörden den Anforderungen und der Risikolage entspricht.

Classification and labelling (B.10)

Comments of Society "Competence Center of Ecodesign" on the Renewal Assessment Report on Glyphosate 11. 05. 2014

Classification and labelling (B.2.10.)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
1.	Vol.1, B.2.10.1, Proposals for the classification and labelling of the active substance	Incorrect classification proposed. According to Article 36 of CLP regulation EC Nr. 1272/2008 the plant protection products shall normally be the subject to harmonised classification and labelling. Glyphosate is included in Annex IV of the CLP regulation EC Nr. 1272/2008 with entry 607-315-00-8 and classified as Eye Dam.1, Aquatic Chronic 2 with hazards statements H318, H411.	Disappointment that producers of glyphosate repeatedly ignore the known information on properties of this substance leading to classification. There are court cases reported and warnings by competent authorities, see examples: • Statement of Attorney general of State New York, 1996 http://big.assets.huffingtonpost.com/fraud.pdf • Decision of highest court of France, 2009: http://news.bbc.co.uk/2/hi/europe/8308903.stm • UK Chemicals Regulation Directorate about Aquatic Hazard Classification Issues For Plant Protection Products Containing Glyphosate, 2012: http://www.pesticides.gov.uk/guidance/industries/pesticides/News/Collected-Updates/Regulatory-Updates-

Classification and labelling (B.10)

Comments of Society "Competence Center of Ecodesign" on the Renewal Assessment Report on Glyphosate 11. 05. 2014

Classification and labelling (B.2.10.)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
2.	Vol.1, B.2.10.2, Proposals for the classification and labelling of preparations	Incorrect classification proposed. According to Annex 1 of regulation EC1272/2008 (4.1.3.5.5): if mixture contains substance classified as Aquatic Chronic 2 ≥ 25%, also the mixture has to be classified as Aquatic Chronic 2. If the mixture contains substance classified as Aquatic Chronic 2 more (or equal) 2,5 % but less than 25%, the mixture has to be classified as Aquatic Chronic 3.	Disappointment that producers avoid correct classification of mixtures despite warnings of competent authorities. E.g., see: • UK Chemicals Regulation Directorate about Aquatic Hazard Classification Issues For Plant Protection Products Containing Glyphosate, 2012: http://www.pesticides.gov.uk/guidance/industries/pesticides/News/Collected-Updates/Regulatory-Updates-2012/April/Aquatic-Classification-Glyphosate-ppps Correct classification is very important, since it is a key to consumer and farmer information and helps them to take the correct precautionary measures.

Section 5 - Ecotoxicology (B.9)

1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)

NO COMMENTS.

2. Mammalian toxicology (B.6)

Genotoxicity (B.6.4)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	You discuss this paper and deem it acceptable (apparently), but ignore that the effects occurred at levels of glyphosate everyone is exposed to. New paper but in time for EFSA to modify RAR's conclusions; as it establishes glyph is genotox. across 3 kingdoms (fish: more potent vivo than vitro!), confirms previous academic findings (even as to potency), well-accepted comet assay (DNA breaks). No way can you/notifiers keep insisting glyph. is not genotox!	Benachour N, Séralini GE. Chem Res Toxicol. 2009 Jan;22(1):97-105. Glyphosate formulations induce apoptosis and necrosis in human umbilical, embryonic, and placental cells. Alvarez-Moya et al. 2014 Genet & Molec Biol:37:105-110.

Long-term toxicity and carcinogenicity (B.6.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	Abstract indicates glyphosate tested (unusual if scientists would misname it). It says the protein expression measured is very significant to cancer. The US NTP finds salivary gland lesions after hi dose glyphosate just a year after US EPA classes glyphosate as 'probably not carcinogenic'.	Hedberg D, Wallin M. Toxicol In Vitro. 2010 Apr;24(3):795-802. Chan P, Mahler J. Toxic Rep Ser. 1992 Jul;16:1-D3.

Section 5 - Ecotoxicology (B.9)

Long-term toxicity and carcinogenicity (B.6.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		This prospective study's authors' very specific co-published rebuttal is not even mentioned! In fact it is a meta-study (515 cases, 1141 controls) with validated exposure estimates (always proven to be accurate enough) co-variates as controlled as possible. More important, notifier's own studies found high dose lymphomas at elevated rate if studies using same CD1 mouse strain were summed; supporting the same finding in Swiss albino mice. In support are 3 (here uncited) case-control lymphoma associations (prompting de Roos et al. association with other immune cancer) and Hardell's meta lymphoma finding. In sum, converging if incompletely evidence points to a lymphoma risk.	De Roos et al. '05 Hardell et al. '02

Other toxicological studies & Medical data (B.6.8-B.6.9)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	This in vitro endocrine disruption study is noted, but its low dose findings are not discussed. Therefore you have not dismissed its relevance, and I note that reviews such as Vandenberg et al '12 prove	Thongprakaisang et al. 2013.

Section 5 - Ecotoxicology (B.9)

Other toxicological studies & Medical data (B.6.8-B.6.9)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		both in theory & practice why toxicity happens at low doses that you never tests for any chemical. Again, your alleged ADI is no such thing. Despite your new mandate to find all literature, you missed this important low dose toxicity finding: 0.7 mg/L in water (c. 0.2 mg/kg d-): anti-oxidant enzyme disturbances in rats. You did not discuss a supporting finding (Cavuşoğlu et al. '11).	Effects of sub-lethal exposure of rats to the herbicide glyphosate in drinking water: glutathione transferase enzyme activities, levels of reduced glutathione and lipid peroxidation in liver, kidneys and small intestine. Larsen K, Najle R, Lifschitz A, Virkel G. Environ Toxicol Pharmacol. 2012 Nov;34(3):811-8

Summary of mammalian toxicology and setting ADI, AOEL, ARfD (B.6.10)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	RAR's criticsm this paper is: "..highly artific[i]al routes of exposure [&] excessive doses. Craniofacial malformations were not noted in developmtl. studies in rats or rabbits…" **RAR *fails to discuss author's published response to such claims***. In brief, they *and a review* explain the dose route & level relevance. You cannot dismiss this until your defense is agreed on by majority of independent scientists. That glyphos is teratog. In 3 species in two studies using sensitive methods ((1/5,000th dilution); plus very similar results using RUp, argue it is notifier's insensitive tests that are false negatives; and the ADI is not.	Paganelli A, Gnazzo V, Acosta H, López SL, Carrasco AE. Chem Res Toxicol. 2010;23(10):1586-95. (Antoniou et al. 2012) Marc J, et al. Toxicol Appl Pharmacol. 2005

Section 5 - Ecotoxicology (B.9)

3. Residues (B.7)

NO COMMENTS.

4. **Environmental fate and behaviour (B.8)**

NO COMMENTS.

5. Ecotoxicology (B.9)

Aquatic organisms (B.9.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	Despite your new mandate, you failed to find this important low dose glyphosate aq. ecotox at 0.05 mg/L. Don't MS/notifier failure to obey law mean you have to try again? Does this aquatic ecotox at just 2 ppb matter?! They ID it but fail to discuss it!	Traavik T, Bøhn T Clone- and age-dependent toxicity of a glyphosate commercial formulation and its active ingredient in Daphnia magna. Cuhra M. Ecotoxicology. 2013 Mar;22(2):251-62. Relyea '09

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Comments of Milieudefensie on the Renewal Assessment Report on Glyphosate 11. 05. 2014

1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)

Identity (B.1, Annex C)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Physical and chemical properties of the active substance (B.2.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Physical, chemical and technical properties of the formulation (B.2.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Further information (B.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, Annex B.3 Data	***Milieudefensie***: Worldwide there are at least 28	In Europe, there are more cases of glyphosate resistance than depicted in

Further information (B.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	on application and further information, page 7-8	weed species (not only 24) for which glyphosate-resistance has been documented, comprising more than 200 populations and infesting millions of hectares (Heap 2014). Although countries with RRcrop cultivation are affected most heavily, cases of glyphosate-resistant weed species are increasingly reported from other countries too. As a result, a massive increase in herbicide amounts applied has been documented. To stop the pesticide treadmill, glyphosate use has to be restricted.	the RAR (16 cases instead of 10 and 6 species instead of 5). Contrary to the RAR, glyphosate-resistant weed species have not been found exclusively in orchards, vineyards or olive groves, but also in other crops, e.g. asparagus (Lolium rigidum in France) and alfalfa (Conyza canadensis in Greece). And Northern and Central Europe will also be affected, with Poland being already the second country after the Czech Republic to report glyphosate-resistant weeds. It will be a question of time when glyphosate-resistant weed biotypes will show up in countries such as Germany. Therefore, evolution of glyphosate-resistance will speed up in Europe too, unless use of glyphosate is severely restricted.

Methods of analysis (B.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

5. Ecotoxicology (B.9)

Birds and mammals (B.9.1 and B.9.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Aquatic organisms (B.9.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	B.9.2.2 Summary of aquatic toxicity data Page 132	***Milieudefensie*** : In particular, amphibians, many of which are endangered, have been shown to be affected by glyphosate-based herbicides, possibly both their larval and adult stages (Wagner et al. 2013). Reviewing peer-reviewed studies on glyphosate impacts on amphibian, Plötner and Matschke (2012) concluded that glyphosate is itself toxic to amphibians, and surfactants such as POEA are even more so leading to abnormal behaviour, teratogenic effects and developmental failures. In addition, toxicity of glyphosate and Roundup to aquatic invertebrates such as *Daphnia magna* has been underestimated (Cuhra et al. 2013). Toxicity classification has to be revised.	Cuhra et al. (2013) found EC50 (48) values for glyphosate IPA in *Daphnia magna* that were significantly lower than the values depicted in table B.9.2-59. Testing glyphosate and Roundup for 55 days (instead of only 21 days tested in the long-term studies referred to in table B.9.2-59) led to significant reduction in juvenile size even at the lowest test concentration of 0.05 mg a.i./L. About ten times higher concentrations of Roundup affected fecundity, growth and abortion rate and at1.35 and 4.05 mg a.i./L of both glyphosate and Roundup significant negative effects were seen on most tested parameters, including mortality. Thus even low ambient concentrations of glyphosate will affect aquatic invertebrate ecology.

Section 5 - Ecotoxicology (B.9)

Bees and non-target arthropods (B.9.4 and B.9.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Earthworms and other soil non-target organisms (macro and micro) (B.9.6, B.9.7 and B.9.8)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.9.8 Effects on soil non-target micro-organisms	***Milieudefensie***: As stated in the RAR and reported by Kremer & Means (2009), glyphosate leads to significant shifts in bacterial community composition but it also affects importantfungal species, e.g. beneficial mycorrhizal fungi (Druille et al. 2013a,b). Previous use of glyphosate has been linked to increased Fusarium infection of wheat and barley (Fernandez et al. 2009). Thus impacts of glyphosate use on bacterial and fungal species that are linked to plant health and disease have to be considered too.	

Section 5 - Ecotoxicology (B.9)

Other non-target organisms (flora and fauna), sewage treatment (B.9.9 and B.9.10)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.9.9.1.4 Summary of results on non-target plants	***Milieudefensie***: Glyphosate can adversely impact micronutrient uptake in plants as it is a strong metal chelator (Tesfamariam et al. 2009, Cakmak et al. 2009). Even low levels of residual glyphosate in soil can greatly impede the availability and uptake of Mn, Fe, Cu, and Zn by plants and lead to their undersupply with these nutrients. Reduced disease resistance and plant growth may be the result (Johal & Huber 2009).	Adverse impacts of (repeated) glyphosate use on the health of non-target plants have to be taken into account, as reduced disease resistance most likely will increase use of other pesticides, e.g. fungicides that may be highly toxic too.
	Vol. 3, B.9.9.1.6 Indirect effects via trophic interactions	The Farm Scale Evaluations have shown that the quantitative loss of weeds reduces number and diversity of arthropods heavily and interrupts the food chain for farmland birds and mammals. Ample evidence of negative impacts of glyphosate on biodiversity has been collected in areas where glyphosate is used extensively, e.g. in combination with genetically modified glyphosate-resistant crops. The all-time low in the number of monarch butterflies in 2013/2014 has been attributed to the loss of their food plant (*Asclepias syriaca*) in vast areas of the United States where glyphosate-resistant crops are grown (Wade 2014).	As glyphosate is the herbicide most widely used, these massive negative impacts on biodiversity have to be considered and used as reason not to re-authorize the substance. Mitigation measures, such as buffer strips, that would be up to the individual member states will not reduce the risk of impacting biodiversity to an acceptable level – even if farmers accepted to spare buffer strips from glyphosate application which they often don't.

Section 5 - Ecotoxicology (B.9)

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	B.9.11 Surface-active substances in glyphosate-based formulations	***Milieudefensie:*** There is ample evidence that formulated products can exhibit higher toxicity. In particular, polyethoxylated alkylamines (POEA) are known to be highly toxic to cells and organisms (Mesnage et al. 2013). Glyphosate has endocrine disrupting properties which cannot only be attributed to the surfactants. Paganelli et al (2010) showed that both formulated products and the active substance have adverse effects and that glyphosate acts as an endocrine disruptor. To make agriculture in Europe more environmentally benign, it is of utmost importance that pesticide use is restricted to a much greater extent than it is actually the case. As herbicides make up the largest share of pesticides and glyphosate is the most used herbicide, regulators are obliged to not renew the approval of this chemical.	To argue, that the lead formulation MON52276 for the assessment of glyphosate does not contain POEA and that POEA-formulated products “are not expected to be neither notified nor registered in the future”, is not comforting, as such products are still on the market and data about the nature and toxicity of other surfactants that replace POEA are not provided to the public. In addition, predicted environmental concentrations for glyphosate and its metabolite AMPA do not take into account the highly toxic surfactants that are released into the environment in combination with the active ingredient. Therefore, data about environmental concentrations of surfactants should have been collected and their impact on the environment should have been considered before drafting the RAR .

Milieudefensie: Comments to the Renewal Assessment Report (RAR) – Glyphosate

Introduction

The Renewal Assessment Report (RAR) prepared by the Rapporteur Member State (RMS) has been opened by EFSA to comments from the public. Some parts of the final report have been blackened, presumably names that refer to studies provided by the applicants. Unfortunately, in **Volume 1 Report and Proposed Decision** the very last chapter, **3.2 Proposed Decision,** has been blackened too. This means the public will not get informed about what kind of decision the RMS and the Co-RMS propose. Thus the public can only speculate about details of the proposal.

Milieudefensie is commenting on specific sections of the renewal assessment report (RAR), in particular those that deal with environmental impacts of glyphosate.

Development of resistance

In **Volume 1, Section 2.3.2 Summary of information on the development of resistance**, and **Volume 3 Annex B.3 Data on application and further information**, the topics "development of resistance and appropriate management strategies" are being discussed.

Comments:

The simplicity and effectiveness of weed control through glyphosate will be undermined by shifts in weed communities and populations resulting from the selection pressure of the applied herbicides. Glyphosate has long been considered to be a low risk herbicide in terms of the evolution of resistant weed populations (Beckie 2006), but ever increasing use of glyphosate has favored the development of glyphosate-resistance in weeds. It has taken 8-20 years of glyphosate use in conventional systems until the first glyphosate-resistant weed, rigid ryegrass (*Lolium rigidum*), was found in 1996 in Australia (Pratley et al. 1999). Since then, at least 28 cases of glyphosate-resistant weed species (comprising more than 200 populations) have been recorded worldwide (Heap 2014). The resistant weeds infest millions of hectares at many different places in various countries. Although countries, such as the US, Argentina, Australia, and Brazil, where glyphosate-resistant crops are cultivated are affected most heavily, countries without GM crop cultivation increasingly report cases of glyphosate-resistant weed species.

Glyphosate-resistance in weeds has been found to be based on several mechanisms, such as target site insensitivity, overproduction of the target protein EPSPS (5-enolpyruvylshikimate-3-phosphate synthase), amplification of the EPSPS gene, reduced glyphosate translocation, and increased sequestration of glyphosate in plant cell vacuoles (Perez-Jones & Mallory-Smith 2010). Resistance mechanisms can co-occur, in particular, when related resistant weed species hybridize. In addition, multiple-resistance to other herbicide mode of actions than glyphosate has been reported too (Heap 2014).

In the RAR, reference is made to the development of glyphosate-resistance in Europe. But in reality, the situation is far more severe than depicted in the RAR document (as of September 2012). There are not only 10 cases of resistance known in Europe, but meanwhile the number is 16 and it is not

only five species that have been found, but there are six (Heap 2014). With five resistant species that have infested hundreds of hectares, Spain is the most afflicted country. Contrary to the RAR presentation, glyphosate-resistant weed species have not been found exclusively in orchards, vineyards or olive groves, but also in other crops such as asparagus (*Lolium rigidum* in France) and alfalfa (*Conyza canadensis* in Greece). It is also not quite true, that "*Apart from one case (C. canadensis) in the Czech Republic, Northern and Central Europe are not affected by glyphosate resistance up to now*", since resistant *C. canadensis* has also been reported from Poland railways. This indicates that evolution of glyphosate-resistance will speed up in Europe too, unless use of glyphosate is severely restricted.

In the US, not only the broad adoption of glyphosate-resistant crops but also the continuous rise in the number of resistant species and areas inflicted by resistant weeds has resulted in a massive increase in herbicide amounts applied (Benbrook 2012a). A similar scenario has been depicted for Europe in case genetically modified glyphosate-resistant crops would be authorized for cultivation here too (Benbrook 2012b). Therefore, to stop the pesticide treadmill, glyphosate use has to be restricted.

Environmental effects

In **Volume 1, Section 2.9 Effects on non-target species and Volume 3, Annex B.9 Ecotoxicology),** data on ecotoxicology studies are discussed, evaluated, and summarized.

Environmental impacts on non-target organisms

The risk assessment for birds and mammals is based on the active ingredient glyphosate acid in the product MON 52276 for the intended uses in several crops including pre-planting, pre-emergence, pre-harvest and row-application in orchards and vineyards. From the data provided by the applicants, the RMS comes to the conclusion that after use of the lead formulation MON 52276 in the indications according to the label there is an acceptable acute risk for birds and mammals due to uptake of contaminated food and an acceptable risk resulting from an exposure of small herbivorous mammals, non-target arthropods, and aquatic organisms. Use under the proposed conditions will result in a negligible exposure of honeybees or has no unacceptable acute or chronic effects on colony survival and development. The RMS concludes further, that for the evaluation of the formulation MON 52276 on non-target plants data are still required, in particular, as a valid study with this product to non-target plants is lacking and the formulants in the product may enhance toxicity.

The RMS concedes that, depending on the agricultural and ecological conditions, the use of glyphosate may affect populations of non-target terrestrial arthropods and vertebrate species (especially farmland birds) via trophic interactions and suggests mitigation measures. The RAR reads at this point: *These effects trace back to the intended effect of the herbicides – eliminating competing plants – and the interruption of the food web going along with it*.

In Volume 1, Section 3 Proposed decision, the RMS states: *It is considered that Article 4 of Regulation (EC) No 1107/2009 is complied with. Specifically the RMS considers that authorization in at least one Member State is expected to be possible for at least one plant protection product containing the active substance for at least one of the representative uses*. But the approval should be subject to conditions and restrictions. According to the RMS, glyphosate is not a candidate for substitution.

This statement has been made although the RMS identifies data gaps with regard to the ecotoxicology risk assessment (e.g. aquatic organisms, microorganisms, and non-target plants such as tomato) and concludes that certain areas of the risk assessment could not be finalized on the basis of the available data, among them effects of glyphosate towards microorganisms, on non-target plants and on biodiversity.

For all uses, the RMS acknowledges that the impacts of glyphosate on biodiversity is a critical area of concern and recommends that member states should pay attention to such potential indirect effects and may consider adequate risk mitigation measures.

Comments

It is not acceptable that glyphosate that is known to negatively impact biodiversity to such an extent should be re-authorized in the EU. Glyphosate exhibits acute and chronic toxicity, in particular, to aquatic species and non-target plants. As stated in the RAR and reported by Kremer & Means (2009), glyphosate leads to significant shifts in bacterial community composition but it also affects some fungal species, e.g. beneficial mycorrhizal fungi (Druille et al. 2013a,b). Previous use of glyphosate has been linked to increased Fusarium infection of wheat and barley (Fernandez et al. 2009). Amphibians, many of which are endangered, have been shown to be affected, possibly both their larval and adult stages (Wagner et al. 2013). Plötner and Matschke (2012) concluded that glyphosate is itself toxic to amphibians, and surfactants such as POEA are even more so causing abnormal behavior, teratogenic effects and developmental failures.

Glyphosate can adversely impact micronutrient uptake in plants as it is a strong metal chelator (Tesfamariam et al. 2009, Cakmak et al. 2009). Even low levels of residual glyphosate in soil can greatly impede the availability and uptake of Mn, Fe, Cu, and Zn by plants and lead to their undersupply with these nutrients. Reduced disease resistance and plant growth may be the result (Johal & Huber 2009). Adverse impacts of (repeated) glyphosate use on the health of non-target plants have to be taken into account, as reduced disease resistance most likely will increase use of other pesticides, e.g. fungicides that may be highly toxic too.

It is well known that weeds offer considerable benefits for the agro ecosystem, as they support a range of organisms, among them decomposers, predators, pollinators, and parasitoids, by providing food and shelter for them (Marshall et al. 2003). The Farm Scale Evaluations performed in the UK showed that broad-spectrum herbicides such as glyphosate impact abundance and diversity of weeds more severely than conventional herbicide regimes (Heard et al. 2003). The quantitative loss of weeds reduces number and diversity of arthropods heavily and interrupts the food chain for farmland birds and mammals. Ample evidence of negative impacts of glyphosate on biodiversity has been collected in areas where glyphosate is used extensively, e.g. in combination with genetically modified glyphosate-resistant crops. The all-time low in the number of monarch butterflies in the winter 2013/2014 has been attributed to the loss of their food plant (*Asclepias syriaca*) in vast areas of the United States where glyphosate-resistant crops are grown (Wade 2014).

As glyphosate is the herbicide most widely used, these massive negative impacts on biodiversity have to be considered and used as reason not to re-authorize the substance. Mitigation measures, such as buffer strips, that would be up to the individual member states could not reduce the risk of impacting

biodiversity to an acceptable level – even if farmers accepted to spare buffer strips from glyphosate application which they often don't.

Subclause: Formulated glyphosate products (Annex B.9.11 Surface-active substances in glyphosate-based formulations)

In the RAR, solely the active ingredient glyphosate is being considered for authorization, although in the field, only formulated products are applied. The final glyphosate products contain high amounts of surfactants that have surface-active properties. According to the German government[1], in addition to the 5000 t of glyphosate used in Germany in 2010, 1700 t of polyethoxylated alkylamines (POEA) had been applied. Therefore, it is of importance to not only test the toxicity of the active ingredient glyphosate but to take into account the toxicity of the various formulated products that are used.

There is ample evidence that formulated products can exhibit higher toxicity. In particular, polyethoxylated alkylamines (POEA) are known to be highly toxic to cells and organisms (Mesnage et al. 2013). The RMS considers several of the observed effects on endpoints regarding genotoxicity, mutagenicity, and development or reproduction of non-target organisms to be mediated by the surfactant included in the formulations. Thus the RMS concedes that "*the toxicity of glyphosate-based products is greatly enhanced if the active substance is formulated with alkylamine ethoxylates"* and "*the authorization of glyphosate-based products with alkylamine ethoxylated surfactants might require the generation of further data"*. But to argue, that the lead formulation MON52276 for the assessment of glyphosate does not contain this surfactant and that nowadays POEA-formulated products "*are not expected to be neither notified nor registered in the future"*, are not comforting statements, as such products are still on the market and data about the nature and toxicity of other surfactants that replace POEA are not provided to the public. In addition, predicted environmental concentrations for glyphosate and its metabolite AMPA are calculated only for these substances, not taking into account the highly toxic surfactants that are released into the environment together with the active ingredient. Therefore, it is important to collect data about environmental concentrations of surfactants and to consider their impact on the environment already during the authorization process.

Conclusions

To make agriculture in Europe more environmentally benign, it is of utmost importance that pesticide use is restricted to a much greater extent than it is actually the case. As herbicides make up the largest share of pesticides and glyphosate, in particular, is the most used herbicide, regulators are obliged to not renew the approval of this chemical.

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Ban Glyphosate until many key questions have been answered.
Glyphosate is ubiquitous - present everywhere especially in the USA- water, sea water, soil, animal tissues, human urine, and breast milk in the USA. Many staple foods such as bread have been found to contain glyphosate resulting in the assertion (with no scientific studies) that the levels are far too low to cause significant health effects.
There has been no studies on the low level exposure to glyphosate over the life time of an animal except for the peer-reviewed paper by Seralini that after being accepted and published was withdrawn by the the publisher for reasons that are not acceptable to bona fide scientists. It seems that there was direct interference by corporate interests to protect and remove major health concerns about glyphosate from ever reaching the 'light of day'.
There have been no follow-up studies to those of Dr. Andres Carrasco who found disturbing evidence of damage to developing embryos that modelled the impact of glyphosate exposure in babies and children found in Argentina soy growing areas where GM crops required repeated spraying of glyphosate.
This requires replication and a wider look at genetic and epigenetic effects of glyphosate and roundup - many more studies are needed.
Although many laboratory experiments have only investigated glyphosate it is well established that the formulated product, usually roundup, has increased adverse biological effects compared with glyphosate itself. Many toxicological studies must now be repeated. Roundup contains so-called 'inerts' including tallow amine surfactants. It is naive, in the extreme, to assume that the many 'inerts' used in often complex formulations will have no biological effects. Many of the 'inerts' have had little toxicological investigation and represent an important area where our knowledge is seriously deficient.
Such a lack of knowledge makes ADI values more of a guess than reliable science - a very unsatisfactory state of affairs.
yours sincerely
Malcom Hooper
Emeritus Professor of Medicinal Chemistry
University of Sunderland
UK

Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)

Identity (B.1, Annex C)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Physical and chemical properties of the active substance (B.2.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Physical, chemical and technical properties of the formulation (B.2.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Further information (B.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, Annex B.3 Data on application and further	***Corporate Europe Observatory***: Worldwide there are at least 28 weed species (not only 24) for	In Europe, there are more cases of glyphosate resistance than depicted in the RAR (16 cases instead of 10 and 6 species instead of 5). Contrary to

Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

Further information (B.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	information, page 7-8	which glyphosate-resistance has been documented, comprising more than 200 populations and infesting millions of hectares (Heap 2014). Although countries with RRcrop cultivation are affected most heavily, cases of glyphosate-resistant weed species are increasingly reported from other countries too. As a result, a massive increase in herbicide amounts applied has been documented. To stop the pesticide treadmill, glyphosate use has to be restricted.	the RAR, glyphosate-resistant weed species have not been found exclusively in orchards, vineyards or olive groves, but also in other crops, e.g. asparagus (Lolium rigidum in France) and alfalfa (Conyza canadensis in Greece). And Northern and Central Europe will also be affected, with Poland being already the second country after the Czech Republic to report glyphosate-resistant weeds. It will be a question of time when glyphosate-resistant weed biotypes will show up in countries such as Germany. Therefore, evolution of glyphosate-resistance will speed up in Europe too, unless use of glyphosate is severely restricted.

Methods of analysis (B.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Section 5 - Ecotoxicology (B.9)

5. Ecotoxicology (B.9)

Birds and mammals (B.9.1 and B.9.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Aquatic organisms (B.9.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	B.9.2.2 Summary of aquatic toxicity data Page 132	***Corporate Europe Observatory*** : In particular, amphibians, many of which are endangered, have been shown to be affected by glyphosate-based herbicides, possibly both their larval and adult stages (Wagner et al. 2013). Reviewing peer-reviewed studies on glyphosate impacts on amphibian, Plötner and Matschke (2012) concluded that glyphosate is itself toxic to amphibians, and surfactants such as POEA are even more so leading to abnormal behaviour, teratogenic effects and developmental failures. In addition, toxicity of glyphosate and Roundup to aquatic invertebrates such as *Daphnia magna* has been underestimated (Cuhra et al. 2013). Toxicity classification has to be revised.	Cuhra et al. (2013) found EC50 (48) values for glyphosate IPA in *Daphnia magna* that were significantly lower than the values depicted in table B.9.2-59. Testing glyphosate and Roundup for 55 days (instead of only 21 days tested in the long-term studies referred to in table B.9.2-59) led to significant reduction in juvenile size even at the lowest test concentration of 0.05 mg a.i./L. About ten times higher concentrations of Roundup affected fecundity, growth and abortion rate and at1.35 and 4.05 mg a.i./L of both glyphosate and Roundup significant negative effects were seen on most tested parameters, including mortality. Thus even low ambient concentrations of glyphosate will affect aquatic invertebrate ecology.

Section 5 - Ecotoxicology (B.9)

Bees and non-target arthropods (B.9.4 and B.9.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<< Identifier >>: <<comment>>	

Earthworms and other soil non-target organisms (macro and micro) (B.9.6, B.9.7 and B.9.8)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.9.8 Effects on soil non-target micro-organisms	***Corporate Europe Observatory***: As stated in the RAR and reported by Kremer & Means (2009), glyphosate leads to significant shifts in bacterial community composition but it also affects importantfungal species, e.g. beneficial mycorrhizal fungi (Druille et al. 2013a,b). Previous use of glyphosate has been linked to increased Fusarium infection of wheat and barley (Fernandez et al. 2009). Thus impacts of glyphosate use on bacterial and fungal species that are linked to plant health and disease have to be considered too.	

Section 5 - Ecotoxicology (B.9)

Other non-target organisms (flora and fauna), sewage treatment (B.9.9 and B.9.10)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.9.9.1.4 Summary of results on non-target plants	***Corporate Europe Observatory***: Glyphosate can adversely impact micronutrient uptake in plants as it is a strong metal chelator (Tesfamariam et al. 2009, Cakmak et al. 2009). Even low levels of residual glyphosate in soil can greatly impede the availability and uptake of Mn, Fe, Cu, and Zn by plants and lead to their undersupply with these nutrients. Reduced disease resistance and plant growth may be the result (Johal & Huber 2009).	Adverse impacts of (repeated) glyphosate use on the health of non-target plants have to be taken into account, as reduced disease resistance most likely will increase use of other pesticides, e.g. fungicides that may be highly toxic too.
	Vol. 3, B.9.9.1.6 Indirect effects via trophic interactions	The Farm Scale Evaluations have shown that the quantitative loss of weeds reduces number and diversity of arthropods heavily and interrupts the food chain for farmland birds and mammals. Ample evidence of negative impacts of glyphosate on biodiversity has been collected in areas where glyphosate is used extensively, e.g. in combination with genetically modified glyphosate-resistant crops. The all-time low in the number of monarch butterflies in 2013/2014 has been attributed to the loss of their food plant (*Asclepias syriaca*) in vast areas of the United States where glyphosate-resistant crops are grown (Wade 2014).	As glyphosate is the herbicide most widely used, these massive negative impacts on biodiversity have to be considered and used as reason not to re-authorize the substance. Mitigation measures, such as buffer strips, that would be up to the individual member states will not reduce the risk of impacting biodiversity to an acceptable level – even if farmers accepted to spare buffer strips from glyphosate application which they often don't.

Section 5 - Ecotoxicology (B.9)

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	B.9.11 Surface-active substances in glyphosate-based formulations	***Corporate Europe Observatory:*** There is ample evidence that formulated products can exhibit higher toxicity. In particular, polyethoxylated alkylamines (POEA) are known to be highly toxic to cells and organisms (Mesnage et al. 2013). Glyphosate has endocrine disrupting properties which cannot only be attributed to the surfactants. Paganelli et al (2010) showed that both formulated products and the active substance have adverse effects and that glyphosate acts as an endocrine disruptor. To make agriculture in Europe more environmentally benign, it is of utmost importance that pesticide use is restricted to a much greater extent than it is actually the case. As herbicides make up the largest share of pesticides and glyphosate is the most used herbicide, regulators are obliged to not renew the approval of this chemical.	To argue, that the lead formulation MON52276 for the assessment of glyphosate does not contain POEA and that POEA-formulated products "are not expected to be neither notified nor registered in the future", is not comforting, as such products are still on the market and data about the nature and toxicity of other surfactants that replace POEA are not provided to the public. In addition, predicted environmental concentrations for glyphosate and its metabolite AMPA do not take into account the highly toxic surfactants that are released into the environment in combination with the active ingredient. Therefore, data about environmental concentrations of surfactants should have been collected and their impact on the environment should have been considered before drafting the RAR .

Corporate Europe Observatory*:* Comments to the Renewal Assessment Report (RAR) – Glyphosate

Introduction

Corporate Europe Observatory would like to comment on specific sections of the renewal assessment report (RAR) for glyphosate, in particular those that deal with environmental impacts.

We want to note that parts of the Renewal Assessment Report (RAR) prepared by the Rapporteur Member State Germany have been blackened, including even the proposed decision. This means the public will not get informed about what kind of decision the RMS and the Co-RMS propose. Thus the public can only speculate about details of the proposal.

As Corporate Europe Observatory, we find this lack of transparency unacceptable.

Development of resistance

In **Volume 1, Section 2.3.2 Summary of information on the development of resistance**, and **Volume 3 Annex B.3 Data on application and further information**, the topics "development of resistance and appropriate management strategies" are being discussed.

Comments:

The simplicity and effectiveness of weed control through glyphosate will be undermined by shifts in weed communities and populations resulting from the selection pressure of the applied herbicides. Glyphosate has long been considered to be a low risk herbicide in terms of the evolution of resistant weed populations (Beckie 2006), but ever increasing use of glyphosate has favored the development of glyphosate-resistance in weeds. It has taken 8-20 years of glyphosate use in conventional systems until the first glyphosate-resistant weed, rigid ryegrass (*Lolium rigidum*), was found in 1996 in Australia (Pratley et al. 1999). Since then, at least 28 cases of glyphosate-resistant weed species (comprising more than 200 populations) have been recorded worldwide (Heap 2014). The resistant weeds infest millions of hectares at many different places in various countries. Although countries, such as the US, Argentina, Australia, and Brazil, where glyphosate-resistant crops are cultivated are affected most heavily, countries without GM crop cultivation increasingly report cases of glyphosate-resistant weed species.

Glyphosate-resistance in weeds has been found to be based on several mechanisms, such as target site insensitivity, overproduction of the target protein EPSPS (5-enolpyruvylshikimate-3-phosphate synthase), amplification of the EPSPS gene, reduced glyphosate translocation, and increased sequestration of glyphosate in plant cell vacuoles (Perez-Jones & Mallory-Smith 2010). Resistance mechanisms can co-occur, in particular, when related resistant weed species hybridize. In addition, multiple-resistance to other herbicide mode of actions than glyphosate has been reported too (Heap 2014).

In the RAR, reference is made to the development of glyphosate-resistance in Europe. But in reality, the situation is far more severe than depicted in the RAR document (as of September 2012). There

are not only 10 cases of resistance known in Europe, but meanwhile the number is 16 and it is not only five species that have been found, but there are six (Heap 2014). With five resistant species that have infested hundreds of hectares, Spain is the most afflicted country. Contrary to the RAR presentation, glyphosate-resistant weed species have not been found exclusively in orchards, vineyards or olive groves, but also in other crops such as asparagus (*Lolium rigidum* in France) and alfalfa (*Conyza canadensis* in Greece). It is also not quite true, that "*Apart from one case (C. canadensis) in the Czech Republic, Northern and Central Europe are not affected by glyphosate resistance up to now*", since resistant *C. canadensis* has also been reported from Poland railways. This indicates that evolution of glyphosate-resistance will speed up in Europe too, unless use of glyphosate is severely restricted.

In the US, not only the broad adoption of glyphosate-resistant crops but also the continuous rise in the number of resistant species and areas inflicted by resistant weeds has resulted in a massive increase in herbicide amounts applied (Benbrook 2012a). A similar scenario has been depicted for Europe in case genetically modified glyphosate-resistant crops would be authorized for cultivation here too (Benbrook 2012b). Therefore, to stop the pesticide treadmill, glyphosate use has to be restricted and herbicide-resistant crops should not be authorised for import or cultivation.

Environmental effects

In **Volume 1, Section 2.9 Effects on non-target species and Volume 3, Annex B.9 Ecotoxicology),** data on ecotoxicology studies are discussed, evaluated, and summarized.

Environmental impacts on non-target organisms

The risk assessment for birds and mammals is based on the active ingredient glyphosate acid in the product MON 52276 for the intended uses in several crops including pre-planting, pre-emergence, pre-harvest and row-application in orchards and vineyards. From the data provided by the applicants, the RMS comes to the conclusion that after use of the lead formulation MON 52276 in the indications according to the label there is an acceptable acute risk for birds and mammals due to uptake of contaminated food and an acceptable risk resulting from an exposure of small herbivorous mammals, non-target arthropods, and aquatic organisms. Use under the proposed conditions will result in a negligible exposure of honeybees or has no unacceptable acute or chronic effects on colony survival and development. The RMS concludes further, that for the evaluation of the formulation MON 52276 on non-target plants data are still required, in particular, as a valid study with this product to non-target plants is lacking and the formulants in the product may enhance toxicity.

The RMS concedes that, depending on the agricultural and ecological conditions, the use of glyphosate may affect populations of non-target terrestrial arthropods and vertebrate species (especially farmland birds) via trophic interactions and suggests mitigation measures. The RAR reads at this point: *These effects trace back to the intended effect of the herbicides – eliminating competing plants – and the interruption of the food web going along with it*.

In Volume 1, Section 3 Proposed decision, the RMS states: *It is considered that Article 4 of Regulation (EC) No 1107/2009 is complied with. Specifically the RMS considers that authorization in at least one Member State is expected to be possible for at least one plant protection product containing the*

active substance for at least one of the representative uses. But the approval should be subject to conditions and restrictions. According to the RMS, glyphosate is not a candidate for substitution.

This statement has been made although the RMS identifies data gaps with regard to the ecotoxicology risk assessment (e.g. aquatic organisms, microorganisms, and non-target plants such as tomato) and concludes that certain areas of the risk assessment could not be finalized on the basis of the available data, among them effects of glyphosate towards microorganisms, on non-target plants and on biodiversity.

For all uses, the RMS acknowledges that the impacts of glyphosate on biodiversity is a critical area of concern and recommends that member states should pay attention to such potential indirect effects and may consider adequate risk mitigation measures.

Comments

It is not acceptable that glyphosate that is known to negatively impact biodiversity to such an extent should be re-authorized in the EU. Glyphosate exhibits acute and chronic toxicity, in particular, to aquatic species and non-target plants. As stated in the RAR and reported by Kremer & Means (2009), glyphosate leads to significant shifts in bacterial community composition but it also affects some fungal species, e.g. beneficial mycorrhizal fungi (Druille et al. 2013a,b). Previous use of glyphosate has been linked to increased Fusarium infection of wheat and barley (Fernandez et al. 2009). Amphibians, many of which are endangered, have been shown to be affected, possibly both their larval and adult stages (Wagner et al. 2013). Plötner and Matschke (2012) concluded that glyphosate is itself toxic to amphibians, and surfactants such as POEA are even more so causing abnormal behavior, teratogenic effects and developmental failures.

Glyphosate can adversely impact micronutrient uptake in plants as it is a strong metal chelator (Tesfamariam et al. 2009, Cakmak et al. 2009). Even low levels of residual glyphosate in soil can greatly impede the availability and uptake of Mn, Fe, Cu, and Zn by plants and lead to their undersupply with these nutrients. Reduced disease resistance and plant growth may be the result (Johal & Huber 2009). Adverse impacts of (repeated) glyphosate use on the health of non-target plants have to be taken into account, as reduced disease resistance most likely will increase use of other pesticides, e.g. fungicides that may be highly toxic too.

It is well known that weeds offer considerable benefits for the agro ecosystem, as they support a range of organisms, among them decomposers, predators, pollinators, and parasitoids, by providing food and shelter for them (Marshall et al. 2003). The Farm Scale Evaluations performed in the UK showed that broad-spectrum herbicides such as glyphosate impact abundance and diversity of weeds more severely than conventional herbicide regimes (Heard et al. 2003). The quantitative loss of weeds reduces number and diversity of arthropods heavily and interrupts the food chain for farmland birds and mammals. Ample evidence of negative impacts of glyphosate on biodiversity has been collected in areas where glyphosate is used extensively, e.g. in combination with genetically modified glyphosate-resistant crops. The all-time low in the number of monarch butterflies in the winter 2013/2014 has been attributed to the loss of their food plant (*Asclepias syriaca*) in vast areas of the United States where glyphosate-resistant crops are grown (Wade 2014).

As glyphosate is the herbicide most widely used, these massive negative impacts on biodiversity have to be considered and used as reason not to re-authorize the substance. Mitigation measures, such as buffer strips, that would be up to the individual member states could not reduce the risk of impacting biodiversity to an acceptable level – even if farmers accepted to spare buffer strips from glyphosate application which they often don't.

Subclause: Formulated glyphosate products (Annex B.9.11 Surface-active substances in glyphosate-based formulations)

In the RAR, solely the active ingredient glyphosate is being considered for authorization, although in the field, only formulated products are applied. The final glyphosate products contain high amounts of surfactants that have surface-active properties. According to the German government[1], in addition to the 5000 t of glyphosate used in Germany in 2010, 1700 t of polyethoxylated alkylamines (POEA) had been applied. Therefore, it is of importance to not only test the toxicity of the active ingredient glyphosate but to take into account the toxicity of the various formulated products that are used.

There is ample evidence that formulated products can exhibit higher toxicity. In particular, polyethoxylated alkylamines (POEA) are known to be highly toxic to cells and organisms (Mesnage et al. 2013). The RMS considers several of the observed effects on endpoints regarding genotoxicity, mutagenicity, and development or reproduction of non-target organisms to be mediated by the surfactant included in the formulations. Thus the RMS concedes that "*the toxicity of glyphosate-based products is greatly enhanced if the active substance is formulated with alkylamine ethoxylates"* and "*the authorization of glyphosate-based products with alkylamine ethoxylated surfactants might require the generation of further data"*. But to argue, that the lead formulation MON52276 for the assessment of glyphosate does not contain this surfactant and that nowadays POEA-formulated products "*are not expected to be neither notified nor registered in the future"*, are not comforting statements, as such products are still on the market and data about the nature and toxicity of other surfactants that replace POEA are not provided to the public. In addition, predicted environmental concentrations for glyphosate and its metabolite AMPA are calculated only for these substances, not taking into account the highly toxic surfactants that are released into the environment together with the active ingredient. Therefore, it is important to collect data about environmental concentrations of surfactants and to consider their impact on the environment already during the authorization process.

Conclusions

To make agriculture in Europe more environmentally benign, it is of utmost importance that pesticide use is restricted to a much greater extent than it is actually the case. As herbicides make up the largest share of pesticides and glyphosate, in particular, is the most used herbicide, regulators are obliged to not renew the approval of this chemical.

[1] http://dipbt.bundestag.de/dip21/btd/17/071/1707168.pdf

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Comments on the addendum of September 2015 for glyphosate

1. Exposure data

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
		No comments	

2. Studies of cancer in humans

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	Table 2.2-2, De Roos et al., 2003, p18	BE: It is not very transparent why the study authors considered the result from hierarchical regression model (providing more conservative estimates than logistic regression, according to IARC) as significant, with an OR 1.6, 95% CI 0.9-2.8. Moreover, it is stated that the description of the study design, analysis and results do not allow assessing methodological quality.	
	Table 2.2-2, De Roos et al., 2005, p19	BE: It is unclear why the much bigger study of the prospective AHS cohort was not given a higher weight in the overall assessment of the possible association between glyphosate use and NHL.	
	2.5.2 Conclusions on the classification… (p26)	BE: As regards the choice in categories, some doubts remain, and this should be discussed.It seems that classification as "*Inadequate evidence of carcinogenicity…*" is also defendable. It is agreed that 4 epidemiological studies on 16 are of acceptable quality/power, but overall, the results are far from consistent. On the other hand, stating that there is "*limited evidence of carcinogenicity…for which a causal interpretation is considered credible…*" is not entirely supported by the facts as well. RMS is right in clarifying that it is a matter of expressing the remaining uncertainty, and it seems that the choice was merely driven by the precautionary principle.	

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	2.5.2 Conclusions on the classification… (p27)	BE: concurs with RMS that there could be a problem with the formulation. Since epidemiological data are by definition collected on people who have been in contact with the product and not with the pure a.s. itself, BE re-iterates its request to adopt an EU position in banning suspicious coformulants with glyphosate.	

3. Cancer in experimental animals

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	Animal studies in rats: minor remark	BE:Table 3.1, p33: [redacted] 1981 study: results 3rd column combined adenoma or carcinoma incidence, correct typos (4,4,4,2%)	
	Animal studies in mice and rats: general observation	BE: it is obvious that the overall evaluation by RMS and IARC cannot be the same, since a number of studies in the EU-dossier were not available for the IARC workgroup. An overall assessment is in this case justified to put into perspective the observed (non-statistically significant) elevated tumour incidences at the top-doses.	
	Table 3-1 (p29), mouse studies: renal tumours [redacted]n, 1983)	BE: it is observed that only in one mouse study, both renal tubule adenoma and carcinoma appear at a higher incidence at the top-dose. The increase is not statistically significant (n.s.s.), and is only flagged positive by IARC because of the borderline significant trend test. Although it is observed that there are marginal increases of adenoma but not carcinoma at the top-doses of two other studies ([redacted] 1997 and [redacted] 2001), it seems debatable, in the absence of renal findings in the other mouse studies, if the renal findings are sufficient to classify for carcinogenicity.	
	Table 3-1 (p29), mouse studies: haemangiosarcoma ([redacted] 1993)	BE: increased incidence at top-dose (1000 mkd) considered spurious, in the absence of the same finding in the other mouse studies (except 2 cases in the Sugimoto study at the top-dose). If really compound-related, it is unlikely that the same tumour would not have been detected at higher incidence in the studies in CD-1 mice with top-doses >4000 mkd.	

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	Table 3.6-3.9 (p38-39), mouse studies: malignant lymphoma ; conclusion p44	BE : Except for the [redacted] 2001 study, the slightly elevated incidences of lymphoma in ♂at the top-doses are either within HCD, or display poor dose-response. For the study on Swiss Albino (2001), the rationale on the basis of known high spontaneous background levels in this strain by the RMS is supported. Although the top-dose lymphoma findings in 3/5 mouse studies (where trend-tests or pair-wise comparisons were significant) are the most consistent among the observed malignancies in the mouse, the overall weight of evidence would indicate that it is equivocal for classification.	
	Table 3-2 (p31), rat studies: pancreas,liver, C-cell tumours ([redacted] 1990)	BE: Pancreas: there is definitely no proper dose-respons (5,18,10,15% in ♂; 8,2,7,0% in ♀), and no carcinoma. In two other rat studies, the combined incidences also show no dose-response, or are absent. Overall, pancreatic lesions do not trigger any classification. Liver: only trend in increased adenoma (11,9,8,19%), with a poor dose response, and no carcinoma. C-cell adenoma: slight trend: 3,3,10,10%, but without progression to carcinoma.	
	Conclusions p44	BE: In this DAR, RMS has well elucidated the possible causes of a different classification outcome between the EU and IARC. It was unfortunate that IARC did not take into account 3 guideline studies in both mice and rats, since this could have put the overall conclusions in another perspective. Next, relying on significant trends to declare a finding eligible for classification is a policy decision not supported by the EU. Further, CLP-criteria such as spontaneous incidence and excessive toxicity confounders are key elements in the discussion by the RMS, and supported. One important point, perhaps understressed, is the consistency of outcome, which is poor among the various studies. Finally, IARC's decision is also influenced by itsopinion on glyphosate being genotoxic, inducing oxidative stress and –to a lesser extend- receptor-mediated effects, influencing cell proliferation/death, or affect the immune system. Since the first two key mechanisms are considered unproven, at least fort he a.s., these may not increase the level of concern as regards the	

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
		carcinogenic outcome of glyphosate.	

4. Mechanistic and other relevant data

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	4.2.1 Genetic and related effects, overall conclusions (p49)	BE: concurs with RMS to conclude that, on a WoE basis, glyphosate should not be considered a genotoxic agent. This conclusion is mainly based upon established guideline studies. It was unfortunate that most of the *in-vivo* micronucleus assays submitted in the EU-dossiers were unavailable to IARC, as the result of these could have put into context the few positive published studies, which became decisive in the IARC conclusion. Inconsistent results were obtained in the published studies on indicator genotoxicity endpoints (DNA strand break, DNA adducts). In the IARC monograph, these tests are listed among the other studies on chromosome aberration, without further interpretation.	
	4.2.2 receptor-mediated mechanism (p68)	BE: acknowledges that some studies with some formulations had positive outcomes in mostly *in-vitro* systems targeting hormone production or activity. However, in most cases glyphosate itself was devoid of endocrine activity. Based on negative EPA EDSP Tier 1 testing, it was concluded that for glyphosate there was no convincing evidence of potential interaction with the oestrogen, androgen or thyroid pathways. RMS' conclusion that glyphosate is devoid of endocrine activity is thus supported.	

5. Summary of data reported

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	5.5 further conclusions and recommendations	BE: based upon the many uncertainties regarding key genotoxicity endpoints, some formulations of glyphosate should be further investigated in the frame of the re-registration at zonal level.	

6. Other comments

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
		No further comments	

5. Summary of data reported

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
1	Further considerations and recommandations	DK: Given the documentation and assessment provided for glyphosate and products containing glyphosate we support the recommendation to require data on genetoxicity for the products. In general we recommend that given the current situation where data and evaluations of data are lacking for the vast majority of coformulants, and the implementation of article 27 of regulation 1107/2009 is outstanding, the Commission should urgently initiate the work to establish a negative list for co-formulants and develop criteria and guidance for this area.	

1. Other comments

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	General	We would like to echo the comment of UK on the excellent quality of the addendum. On the specific evaluations and conclusion we will address this at the expert meeting	

Comments on the addendum of September 2015 for glyphosate

1. Exposure data

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
		EFSA: No comments	

2. Studies of cancer in humans

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	Addendum 2.5.2, Conclusions on the classification of the evidence relevant to carcinogenicity from studies in humans into the IARC categories, p. 26-27	EFSA: There seems to be a consensus regarding the conclusion on epidemiological studies in classifying glyphosate in the 3rd IARC category 'limited evidence of carcinogenicity'. It is agreed that carcinogenic effects cannot be ruled out, however as most studies (including the most powerful one (the AHS prospective cohort-study) do not show a positive association of carcinogenicity with glyphosate, the relative weighting of the different studies could be further discussed.	

3. Cancer in experimental animals

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	Addendum 3, Cancer in experimental animals, summary and conclusion, pp. 28-44	EFSA: The statistical analysis methods should be discussed considering that, according to the OECD 451 guideline for carcinogenicity studies, "the statistical method most appropriate for the analysis of results, given the experimental design and objectives, should be established before	

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
		commencing the study".	
	Addendum 3, Cancer in experimental animals, summary and conclusion, pp. 29-31 Addendum 5.3, animals carcinogenicity data, pp. 89-91 and Table 5.3-1	EFSA: In mice positive trends reported in the IARC assessment: renal tubular adenoma and carcinoma ([redacted], 1983), haemangiosarcomas ([redacted]., 1993) and malignant lymphomas ([redacted] 2001 -already discussed during the expert's meeting 125 in February 2015) are limited to high dose levels ≥ 1000 mg/kg bw per day; the background incidence and biological relevance of the findings should be discussed further.	
	Addendum 3, Cancer in experimental animals, summary and conclusion, pp. 32-34	EFSA: In rats, positive trends in adenomas are noted in one out of nine valid studies ([redacted], 1990). While there is no clear dose-response relationship in the incidence of pancreatic islet-cell adenomas, liver cell and thyroid C-cell adenomas appear at high dose levels around the limit dose of 1000 mg/kg bw per day. These findings should be discussed in line with the CLP criteria.	

4. Mechanistic and other relevant data

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	Addendum 4.2.1, genotoxicity	EFSA: A critical difference between the IARC monograph and the RAR relates to the genotoxic potential of glyphosate. It should be confirmed by the experts that the few positive results (*in vitro* DNA damage and *in vivo* tests) in the database can be reliably discounted by the (numerous) negative results.	
	Addendum 4.2.3.1, oxidative stress, pp. 74-79	EFSA: indications of the occurrence of oxidative stress have been observed in one *in vivo* study in combination with cytotoxic/degenerative effects upon intraperitoneal injections to male rats (Astiz *et al*. 2009b). A parallel could be established with slightly increased tumour incidence in some studies at high dose levels.	

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	Addendum 4.2.3.2, Inflammation and immunomodulation, p. 79-82	EFSA: as the evidence from the available data on immunosuppression is insufficient to conclude on the immunomodulatory action of glyphosate, it should be discussed whether a concern remains that should be addressed regarding this endpoint.	

5. Summary of data reported

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
		EFSA: see comments in sections 2, 3, 4	

6. Other comments

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	General	EFSA: The considerable amount of work invested by DE in the production of the addendum (in much reduced timelines) is highly appreciated, thank you.	

Comments of Spain on the addendum of September 2015 for glyphosate

1. Exposure data

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
(1)		ES: No comment.	

2. Studies of cancer in humans

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
(1)	2. Studies of cancer in humans	ES: We agree with the RMS in highlighting the limitations of the epidemiological studies: multiple exposure, low power, very few studies show marginally increased ORs (not always statistically significant), quality criteria not always detailed, literature search and delection of literature done for IARC not described in detail, internal validity not assess due to limitations in the reporting of the study. No measures from biomarkers from the blood are used (Exposure measured through interviews or questionnaires), the number of cases involved and no knowledge of glyphosate or the type of glyphosate formulate used. It is noteworthy that the most powerful study, the AHS (Agricultural Health Study), the prospective cohort-study, which in epidemiological terms is best suited to study the relationship showed no association witn cancer incidence. This study should be given a higher weight in the overall assessment of the possible associtation between glyphosate use and NHL (non-Hodgkin lymphoma). We agree with the RMS that in the epidemiological studies a differentiation between the effects of glyphosate and the co-formulants is not possible.	

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
		Therefore, it is difficult to use the results of epidemiological studies to demonstrate a carcinogenicicty potential of glyphosate, given the very weak, inconsistent (across studies) and in most cases non- statistically significant associations reported.	

3. Cancer in experimental animals

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
(1)	4. Cancer in experimental animals	ES: We agree with the RMS that the large volume of animal data for glyphosate should be evaluated using a weight approach. It should be avoided to base any conclusion only on the statistical significance of an increased tumour incidence identified in a single study, without consideration of biological significance of the finding. In most cases tumours incidence were not statistically significant, no dose dependent and within the range of historical controls. Confounding effect of excessive toxicity cannot be excluded and be the cause of the increased incidence of tumours at the higest dose in life time studies. Consistency and reproducibility are very important factors to take into account in making a decision. Thus, based on the data from six carcinogenicity studies in mice and ten chronic toxicity and carcinogenicity in rats, the weight of evidence suggest that no hazard classification for carcinogenicity is warranted for glyphosate according to the CLP criteria.	

5. Mechanistic and other relevant data

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
(1)	4.2.1 Genenitc and retaled effects/glyphosate	ES: The *in vitro* and *in vivo* studies show that glyphosate is not genotoxic. A classification for mutagenicity is not warranted accorging to the CLP criteria.	
(2)	4.2.1 Genetic and retaled effects/glyphosate-based formulations	ES: There remains an uncertainty about the genotoxicity (comet assay) of glyphosate-based formulation.	

6. Summary of data reported

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	5.5 Further conclusions and recommendations	ES: Based on the results of published data, no firm conclusions can be drawn on the genotoxic potential of the formulations. Further genotoxicity testing of these formulations should be left at MS level at product authorisation as confirmatory information for the authorisation of plant protection products.	

7. Other comments

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	General comment	ES: Spain thanks the thororough analysis provided by Germany.	

Comments on the addendum of September 2015 for glyphosate

1. Exposure data

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
(1)		FR: No comment.	

2. Studies of cancer in humans

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
(1)	2.Studies of cancer in humans	FR: FR agrees that it is difficult to use the results of epidemiological studies in order to demonstrate or not a carcinogenicity potential for glyphosate. In addition, based on the available human data, FR agrees that it is not possible to make a difference between the effects of the active substance and the coformulants.	

3. Cancer in experimental animals

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
(1)	3. Cancer in experimental animals	FR: FR agrees with RMS that a weight of evidence approach, based on all available carcinogenicity studies, has to be adopted. Based on the RMS analysis, the active substance glyphosate does not satisfy the CLP criteria for carcinogenicity classification.	

4. Mechanistic and other relevant data

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
(1)	4.2.1 Genetic and related effects/glyphosate	FR: FR agrees with the RMS that, by weight of evidence, the active substance glyphosate can be considered as devoid of genotoxic properties and that a classification for mutagenicity is not warranted according to the CLP criteria.	
(2)	4.2.1 Genetic and related effects/glyphosate-based formulations	FR: FR agrees with the RMS that based on the results of published data, no firm conclusions can be drawn on the genotoxic potential of the formulations.	

5. Summary of data reported

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
(1)	5.5 Further conclusions and recommendations	FR: In view of the positive results observed in non-regulatory genotoxicity assays conducted with the representative formulation, the RMS concluded that no firm conclusions can be drawn on the genotoxic potential of the formulations.Moreover the RMS recommends *"further genotoxicity studies (…) for the representative formulation as confirmatory information for the authorisation of plant protection products*". In that case, considering uncertainties about the genotoxicity of the representative formulation, would it be possible to identify a safe use in the context of the renewal of approval of glyphosate?	

6. Other comments

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
(1)	General comment	FR: France acknowledges the good quality of the scientific analysis and the huge work provided by Germany on the IARC conclusions.	

Comments on the addendum of September 2015 for glyphosate

1. Cancer in experimental animals

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	Addendum 1 to RAR., Cancer in experimental animals, table 3-1	NO: Due to the application of different statistical approaches selected for the evaluation, IARC and RMS came to diverging conclusions. Why does the RMS consider the statistical evaluation provided with the study reports as more appropriate than the trend test used by IARC? According to the OECD quidance document on the conduct and design of chronic toxicity and carcinogenicity studies, significance in either kind of test is sufficient to reject the hypothesis that chance accounts for the result.	
	Addendum 1 to RAR., Cancer in experimental animals, point iii) differences in decision criteria, page 42	NO: It is stated on page 42 in the addendum that *"Since no consistent significant increase in any of the tumour types was originally reported in the available studies, the apparent effects were not considered sufficient for classification in the RAR."* However, we are of the opinion that effects do not necessarily have to appear in a consistent dose-dependent manner, in order to be considered as a treatment-related effect.	
	Addendum 1 to RAR., Cancer in experimental animals, point iii) differences in decision criteria, additional criteria CLP, page 43	NO: As stated in the addendum, the RMS has also taken into account additional criteria when evaluating the carcinogenic effects. To what extent should these additional criteria and the listed factors which may be taken into consideration, determine the conclusion with respect to a potential carcinogenic effect. In our opinion, too much weight is given to the factors "progression of lesions to malignancy" as well as "whether responses are in single or both sexes". This will for instance implicate that studies, in which a treatment-dependent increase in adenomas in male rats is demonstrated, will not be taken into consideration when evaluating the carcinogenic potential.	

2. Mechanistic and other relevant data

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	Addendum 1 to RAR, 4.2.1., Genetic and related effects	NO: A number of non-regulatory studies both *in vitro and in vivo* investigating glyphosates DNA damaging potential have shown positive results. We suggest that a regulatory *in vivo* mammalian alkaline comet assay (for instance, in the rat liver and kidney) should be conducted according to OECD 489.	
	Addendum 1 to RAR, 4.2.1 Genetic and related effects, tables 4.2-3, 4.2-4, 4.2-5 and 4.2-7	NO: It would be interesting to know which mouse strains are used in the tests for genotoxicity, since it pointed to a possible strain specific effect in mice (in the conclusion from RMS on section 3 Cancer in experimental animals on page 44).	

Comments on the addendum of September 2015 for glyphosate

1. Exposure data

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	Glyphosate Addendum 1 to RAR: 1. Exposure data	No essential comments at this time	

2. Studies of cancer in humans

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	Glyphosate Addendum 1 to RAR: 2. Studies of cancer in humans	We note that the RMS "adopts a more cautious view since no consistent positive association was observed, and the most powerful study showed no effect. The IARC interpretation is more precautionary. It was also noted that in the epidemiological studies a differentiation between the effects of glyphosate and the co-formulants is not possible." It should be noted that the IARC and the CLP criteria for sufficient and limited evidence of cancer in humans are virtually identical, and still the RMS and IARC assessments differ. We believe that the IARC conclusion is admittedly precautionary but still feasible. Furthermore, we agree to the RMS conclusion that a differentiation between the effects of glyphosate and the co-formulants is not possible adding	

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
		further uncertainty to the assessment of glyphosate. We would also like to underline that the final harmonised classification of substances as regards carcinogenicity and other endpoints is decided by the Commission after a RAC Opinon that would include an assessment of the evidence of cancer in humans.	

3. Cancer in experimental animals

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	Glyphosate Addendum 1 to RAR: 3. Studies of cancer in experimental animals	We note that IARC and the RMS have diverging assessments regarding kidney tumours in male CD-1 and Swiss mice, haemangiosarcoma in male CD-1 mice, liver cell adenoma in male SD rats and thyroid C-cell adenoma in female SD rats and malignant lymphoma in CD-1 mice. In these studies statistical analysis with the Cochran-Armitage trend test yielded a significant result, whereas the analysis by pair-wise comparisons indicated no statistically significant differences. It is generally believed that trend tests are more sensitive than e.g. pair-wise compaison methods and from a precautionary assessment point of view trend tests would be preferable. In our view the evidence for carcinogenicity in experimental animals is at least limited as compared to the IARC and CLP criteria. We don´t believe	

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
		that reference to historical control data can abrogate the positive results from the trend tests. Possibly, the high doses and resulting toxicity may have influenced the tumour outcome in the high dose groups in some of the rodent studies. It should be noted that the IARC and the CLP criteria for sufficient and limited evidence of cancer in experimental animals are virtually identical, and still the RMS and IARC assessments differ. We agree that the diverging assessments are mainly due to differences in the choice of statistical assessment methods.. As above we like to underline that the final harmonised classification of substances as regards carcinogenicity and other endpoints is decided by the Commission after a RAC Opinon that would include an assessment of the evidence of cancer in experimental animals.	

4. Mechanistic and other relevant data

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	Glyphosate Addendum 1 to RAR: 4. Mechanistic and Other Relevant Data	We are concerned by the data on genotoxicity of glyphosate. Some in vitro and in vivo studies seems to suggest clastogenic effects. Possibly, a modern Comet assay in relevant target tissues such as kidney, liver and bone marrow should be undertaken. Presently, the genotoxicity data would	

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
		contribute to an increased level of concern in the weight of evidence assessment of glyphosate carcinogenicity.	

5. Summary of data reported

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure

6. Other comments

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure

Comments on the addendum of September 2015 for glyphosate

1. Exposure data

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
		UK (LMC): no comments	

2. Studies of cancer in humans

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
1	Addendum 2.1., Cohort studies – De Roos 2005a	UK (LMC): Agree that there is limited power for the analysis of myeloma although there is a suggestion of a trend, increasing risk with increasing exposure.	
2	Addendum 2.1., Cohort studies – Sorahan 2015	UK (LMC): The re-analysis still seems to show suggestion of a trend of increased risk of multiple myeloma with increasing exposure, regardless of dataset used. There is very little power with so few cases of multiple myeloma, particularly when split into categories of exposure.	
3	Addendum 2.4., meta-analysis	UK (LMC): Case-control studies, while potentially affected by recall, have the benefit of being focussed on specific causes of death and comparing the exposures experienced by the cases to that of the controls. The inclusion of the Hardell study in the meta-analysis will have inflated the resulting RR as this study found the higest RR of all included in the meta-analysis, but also had the widest confidence interval, as there were only 8 cases and controls who had glyphosphate exposure.	
4	Addendum 2.5.2., Conclusions on the	UK (LMC): Overall there is limited evidence of carcinogenicity of glyphosphate in humans – where there is a suggestion of an association the	

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	classification of the evidence relevant to carcinogenicity	cohort studies have limited power to conclude a statistically significant relationship/trend. There is mixed evidence from the case-control studies.	

3. Cancer in experimental animals

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure

4. Mechanistic and other relevant data

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure

5. Summary of data reported

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure

6. Other comments

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure

Comments on the addendum of September 2015 for glyphosate

1. Exposure data

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
1	1.4.1	UK (SB): I agree with RMS that data from supervised trials at maximum application rates results in much more conservative scenarios compared to the monitoring studies considered by IARC.	

2. Studies of cancer in humans

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
1	Introduction	UK (SB): I agree with the limitations of the epi studies highlighted in the second paragraph.	
	Introduction	UK (ID): It would be useful if the document included a brief introduction to epidemiology clarifying that it is not just the headline OR/RR that is important but also the 95% CI range.	
2	Cohort studies	UK (SB): It is evident that the cohort studies show no increased risk of any tumour type. It would be helpful to add that where the risk estimate is >1 but the lower C.I. is below 1, the increased association is not statistically significant.	
3	Case-control studies on NHL	UK (SB): I agree with the conclusions of the RMS that due to a number of limitations (low power, glyphosate or glyphosate formulation), very few studies show marginally increased ORs. In addition, in many studies, these ORs were not statistically significant.	

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	Table 2.3-1	Uk (ID)In the conclusion for Carreon et al, 2005 it is unclear why the risk is reduced. As the CI range extends around 1.0 we consider the conclusion should be no increased risk, as is given for studies with similar CI ranges.	
4	Meta-analysis	UK (SB): A meta-risk ratio of 1.3 (CI 1.03-1.65) for NHL on the basis of 6 studies appears rather weak. It is impossible to exclude that it is due to chance.	
5	Co-formulants	UK (SB): I agree with the RMS that IARC has not taken into account the role that co-formulants play in the toxicity of glyphosate and the PPPs containing them.	
6	Conclusion on human data	UK (SB): I agree with IARC and the RMS that the only possible conclusion is "limited evidence of carcinogenicity in humans" as causality has not been estabilished and the findings could be due to chance, bias or confounding. Given the very weak, inconsistent (across studies) and in most cases non-statistically significant associations reported, it would have been useful for IARC to have performed an analysis of causality according to the Bradford-Hill criteria.	

3. Cancer in experimental animals

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
1	[redacted] 1983	UK (SB): The different results obtained between the original pathologist and the PWG raise a concern about the reliability of this study in CD-1 mice.	
2	[redacted] 1993	UK (SB): It is also a concern that the same strain of mice (CD-1 mice) gives a completely different cancer profile response (renal tumours in the study above and haemangiosarcoma in this study). The reliability of the study is therefore questioned.	

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
3	Kumar 2001	UK (SB): The increase in malignant lymphoma in Swiss albino mice stands against a very high background level in controls and historical controls. In addition, it has not been reproduced in any other strain of mice (or in rats) questioning its relevance to human cancer hazard.	
	Table 3-4 and elsewhere	UK (ID): We would question the suitability of relying on a trend test where the incidence in controls is zero and the only group responding, with no pairwise significance, is the top dose group. The trend test gives an extreme response e.g. compare the p values for [redacted] and [redacted] – intuitively the [redacted] data could be seen as more significnat due to the result at a mid-dose.	
4	[redacted] 1990	UK (SB): Regardless of statistics, the biological plausibility of the reported tumours in SD rats in this study points towards chance. The pancreas adenoma in males was increased only at the lowest dose and did not progress to carcinoma. The liver adenoma in males was increased at the top dose against a very high background in controls and did not progress to carcinoma. The thyroid C-cell adenoma in females showed a very flat response and did not progress to carcinoma.	
4	Overall conclusions	UK (SB): With so many studies (6 in the mouse and 10 in tye rat), consistency and reproducibility are very important factors to take into account in making a decision. The overall WoE indicates that there is no unequivocal evidence of carcinogenicity in animals. Therfore, I agree with the conclusions of the RMS and I disagree with the conclusions of IARC.	
		UK (ID): The document does not mention the extensive discussions at the PRAPeR meeting where the conclsion of the experts based mainly on the animal data was no classification for cancer. We feel this would be a useful addition.	

4. Mechanistic and other relevant data

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
1	Genotoxicity	UK (SB): The conclusion of IARC on genotoxicity is simply wrong. The in vitro and in vivo WoE shows that glyphosate is not genotoxic. I also agree with the RMS that AMPA is not genotoxic in vivo. There remains an uncertainty about the genotoxicity of glyphosate-based formulation, but further genotoxicity testing of these formulations sould be left a MS level at product authorisation.	
		UK(ID): We would be cautious about placing too much reliance on results from new assay types in unusual species (e.g. Comet assay in eels), when there is no indication of a concern from standard regulatory studies.	
2	Receptor-mediated mechanism	UK (SB): Clearly IARC was not aware of the results of the US EPA EDSP which concluded that based on Tier 1 studies and some higher tier studies, it glyphosate is not an ED. In addition, the study by Bailey (2013) confirms that glyphosate is negative in both the male and female pubertal assays.	
3	Oxidative stress	UK (SB): Although there are some indications in vitro of oxidative stress, the in vivo study in rats (Astiz, 2009b) shows effects that cannot be relied upon as the study was conducted by i.p. administration, By this route of exposure, the normal, physiological detoxification mechanisms of glyphosate are bypassed. On this point, I disagree with IARC and RMS that there is significant evidence that glyphosate causes adverse effects through oxidative stress. Further studies by relevant routes of exposure should be performed.	
4	Inflammation and immunomodulation	UK (SB): I agree that there is very little evidence to concluded that glyphosate causes immunosuppression. I also agree that the endpoint has not been evaluated adequately.	

5. Summary of data reported

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
1	Human data	UK (SB): I agree with IARC and the RMS that the only possible conclusion is "limited evidence of carcinogenicity in humans" as causality has not been estabilished and the findings could be due to chance, bias or confounding.	
2	Animal data	UK (SB): With so many studies (6 in the mouse and 10 in tye rat), consistency and reproducibility are very important factors to take into account in making a decision. The overall WoE indicates that there is no unequivocal (sufficient) evidence of carcinogenicity in animals. Therfore, I agree with the conclusions of the RMS and I disagree with the conclusions of IARC.	
		UK (ID): Additional discussion could be useful on the fact that there are no reports of renal or pancreatic tumours in the epidemiology versus the animal findings. In addition the lack of consistency within the animal studies, and within the epidemiology, could be brought out further. Table 5.3-1 is excellent in displaying the variability between similar studies.	
3	Mechanistic data	UK (SB): I agree with RMS that the in vitro and in vivo WoE shows that glyphosate is not genotoxic. Recent evidence shows that glyphosate is not an ED. I disagree with IARC and RMS that there is significant evidence that glyphosate causes adverse effects through oxidative stress. I agree that there is very little evidence to concluded that glyphosate causes immunosuppression. Overall, there is insufficient animal, human and mechansitic data to support the conclusion that glyphosate is carcinogenic.	

6. Other comments

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
1	General	UK (SB, ID): We would like to thank the DE RMS for the addendum and the analysis provided. It is well structured, extremely thorough and of outstanding quality.	

Comments on the addendum of September 2015 for glyphosate

1. Exposure data

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
1	1 Exposure Data 1.3 Measurement and analysis	IE: Thank you for your addendum for glyphosate. IE. Method validation is an essential prerequisite to accurate exposure determination. The omission of the 40 RAR volume 3 studies and dependence on 16 public domain studies demonstrating partial method validation is worrying. Can DE describe the elements of validation missing from the public domain studies?	
	1.4.1.1 Occupational exposure	IE. There are significant flaws in the occupational and para-occupational studies cited in the IARC report for example Centre de Toxicologie du Québec,1988, does not describe either the product used or the rate of application; Jauhiainen et al., 1991, only found 2 air values above 1.25 µg/m^3 and was limited to 5 operators; Johnson etal., 2005, shows air concentrations 1000 times more than the air samplers calibrated range “mg rather than µg ranges”. In the Curwin et al., 2007 study, product applied (1 of 7 various pesticides was used), application rate and application rate were omitted. Also in the Acquavella et al., 2004 study product and application rate not clearly stated. It would appear that none of the cited occupational exposure studies comply with OECD guidance. Can DE comment on this? In addition it is suggested that even accepting the outcomes of the aforementioned deficient studies exposure values were not in excess of those predicted by the German exposure model used in the RAR. Can DE comment on the exposure predicted by the new EFSA OpEx model?	

1. Studies of cancer in humans

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	2., Cancer in humans	In cohort studies no biomarkers from the blood are used. Exposure was measured through interviews or questionnaires. We agree with DE that there is a big recall problem to judge the amount of exposure to chemicals or what substance or product was used over time. We also agree that there may be a recall biases since individuals with cancer are more likely to think about possible reasons for their cancer than healthy individuals.	
	2.2 Case–control studies on non-Hodgkin lymphoma, multiple myeloma, and leukaemia	The 4 medium to high validity epidemiological studies McDuffie et al. 2001, Eriksson et al. 2008, De Roos et al. 2005, Orsi et al. 2009, seem to suffer from the problems of multiple exposures and of the possible effect of Frequently used co-formulants. Are epidemiological studies on products not always hampered by these effects? The fact that glyphosate is routinely formulated with [redacted] creates difficulties as this substance is more irritant and toxic than glyphosate itself. Can DE comment on the carcinogenicity of this substance?	

2. Cancer in experimental animals

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	3., Cancer in experimental animals	IE. It appears that 14 acceptable animal carcinogenicity studies (5 mouse and 9 rat) were available for evaluation. IARC have considered 2 of the 5 mouse studies and 6 of the 9 rat studies. Using trend analysis IARC has	

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
		concluded that there is a positive trend to carcinoma in the mouse and adenoma in the rat. In the rat IARC agree with the DE evaluation of the other 5 studies indicating no concern regarding carcinogenicity. In the rat IARCs failure to evaluate the 3 other studies is not helpful. Compiling the rat data (as evaluated by IARC) we note 5 negative studies and 1 that shows a trend for c Cell adenomas of the thyroid (it is noted in the IARC monograph that there was no apparent progression to carcinoma). We do not consider the aforementioned data sufficient for classification as carcinogenic under CLP criteria. Furthermore, inclusion of the 3 other rat studies not evaluated by IARC adds further weight to this conclusion. In the mouse IARC have noted a positive trend for renal tubule adenoma and carcinoma in 1 study ([redacted] 1983) and a positive trend for haemangiosarcoma in another. DE evaluated 3 other mouse studies of those 2 [redacted], 1997 and [redacted] 2001 showed a positive trend for renal tubular adenomas in mice. We note that doses of 4000-5000 mg/kg bw day were administered in 2 of the studies with 1460mg being the top dose in the 3rd. Again, using the IARC data alone it is difficult to justify a classification for carcinogenicity. There is no pattern of tumours in the studies and the doses are excessive. However, the renal tubular adenomas in the other mouse studies may require further investigation. Can DE comment? Generally it would appear that the use of trend analysis rather than other statistical tools has led to different findings in 3 of the 14 studies. These statistical differences are pivotal to the disparity of conclusions drawn by IARC and DE. Can DE comment on the differences in the 2 statistical methods used? The omission by IARC of the findings of 6 reliable studies has a significant bearing on the conclusions drawn. Were these studies available to IARC?	

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
		It is not clear what historical controls IARC referenced. They do not appear to be date or test house specific but from the open literature. Can DE comment on this?	

3. Mechanistic and other relevant data

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
		IE Not comments	

4. Summary of data reported

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
		IE Not comments	

5. Other comments

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
		IE No comments	

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03	Pesticides peer review meeting reports
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List of all reporting tables:

Date	**Document**
06.08.2014	Glyphosate reporting table_2014-08-06.doc
06.08.2014	Glyphosate reporting table_public consultation_2014-08-06.doc
14.07.2014	Glyphosate_reporting table_Vol 4_Afrasa - INA_CONFIDENTIAL_rev 0__2014-07-14.doc
14.07.2014	Glyphosate_reporting table_Vol 4_AGRIA- AGR_CONFIDENTIAL_rev 0__2014-07-14.doc
14.07.2014	Glyphosate_reporting table_Vol 4_Agrichem - AGI_CONFIDENTIAL_rev 0__2014-07-14.doc
14.07.2014	Glyphosate_reporting table_Vol 4_Agrotrade - AGT_CONFIDENTIAL_rev 0__2014-07-14.doc
14.07.2014	Glyphosate_reporting table_Vol 4_Albaugh UK - ALB_CONFIDENTIAL_rev 0__2014-07-14.doc
14.07.2014	Glyphosate_reporting table_Vol 4_Arysta - AAP_CONFIDENTIAL_rev 0__2014-07-14.doc
14.07.2014	Glyphosate_reporting table_Vol 4_BARCLAY - BCL_CONFIDENTIAL_rev 0__2014-07-14.doc
14.07.2014	Glyphosate_reporting table_Vol 4_Brokden - BRO_CONFIDENTIAL_rev 0__2014-07-14.doc
14.07.2014	Glyphosate_reporting table_Vol 4_Bros S.J. - BSJ_CONFIDENTIAL_rev 0__2014-07-14.doc

Date	Document
14.07.2014	Glyphosate_reporting table_Vol 4_Cheminova - CHE_CONFIDENTIAL_rev 0__2014-07-14.doc
14.07.2014	Glyphosate_reporting table_Vol 4_DOW AgroSciences - DOW_CONFIDENTIAL_rev 0__2014-07-14.doc
14.07.2014	Glyphosate_reporting table_Vol 4_Excel - XLE_CONFIDENTIAL_rev 0__2014-07-14.doc
14.07.2014	Glyphosate_reporting table_Vol 4_Feinchemie - FCS_CONFIDENTIAL_rev 0__2014-07-14.doc
14.07.2014	Glyphosate_reporting table_Vol 4_General information_CONFIDENTIAL_rev 0_2014-07-14.doc
14.07.2014	Glyphosate_reporting table_Vol 4_Helm AG - HEL_CONFIDENTIAL_rev 0__2014-07-14.doc
14.07.2014	Glyphosate_reporting table_Vol 4_Monsanto - MON_CONFIDENTIAL_rev 0__2014-07-14.doc
14.07.2014	Glyphosate_reporting table_Vol 4_Nufarm - NUF_CONFIDENTIAL_rev 0__2014-07-14.doc
14.07.2014	Glyphosate_reporting table_Vol 4_Rotam - RTA_CONFIDENTIAL_rev 0__2014-07-14.doc
14.07.2014	Glyphosate_reporting table_Vol 4_Sabero - SAO_CONFIDENTIAL_rev 0__2014-07-14.doc
14.07.2014	Glyphosate_reporting table_Vol 4_SAPEC - SAP_CONFIDENTIAL_rev 0__2014-07-14.doc
14.07.2014	Glyphosate_reporting table_Vol 4_SFP - SFP_CONFIDENTIAL_rev 0__2014-07-14.doc
14.07.2014	Glyphosate_reporting table_Vol 4_Sinon - SNN_CONFIDENTIAL_rev 0__2014-07-14.doc
14.07.2014	Glyphosate_reporting table_Vol 4_Syngenta - SYD_CONFIDENTIAL_rev 0__2014-07-14.doc
14.07.2014	Glyphosate_reporting table_Vol 4_United Phosphorous - UPL_CONFIDENTIAL_rev 0__2014-07-14.doc
14.07.2014	Glyphosate_reporting table_Vol 4_Wynca - ZXC_CONFIDENTIAL_rev 0__2014-07-14.doc

Commenting table on addendum 1 (September 2015):

Date	Document
16.09.2015	Glyphosate_commenting table_Addendum Sept 2015.doc

0. General

General				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
0(1)		DK: We would like to congratulate Germany and Slovakia on the excellent and comprehensive work done.	RMS: Thank you!	Addressed.

1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(1)				---

Physical and chemical properties of the active substance (B.2.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(2) (1)	Vol. 1, Level 1, 3.1.4, List of studies to be generated, still ongoing or available but not evaluated, page 155	GTF: 3.4.1.2. Physical and chemical properties of the active substance and physical, chemical and technical properties of the formulation. Spectra or relevant impurities. Not relevant. *For further explanation please refer to Column 3 of the original commenting table.*	RMS: The GTF had already mentioned in the first commenting round that a certificate regarding the purity of tested material (100%) is available and could be submitted. This information was accidently not transferred in the RAR that was sent out to the MS and EFSA for comments.	Addressed.

Physical and chemical properties of the active substance (B.2.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(3)	Vol.3, B.2.1 Physical and chemical properties of the active substance	ES (MSSSI): pH value for the active substance glyphosate and its salts (IPA, K, NH4) it's not included. We consider it should be provided.	GTF: The measurement of pH values is not a data requirement for active substances (refer to Regulation (EC) 544/2011) which were in force at the time of the AIR submission. RMS: Unfortunately, the comment is unclear. The pH value of the as is not a data requirement.	Addressed
1(4)	Vol. 3, Annex B.2.1.2, Relative density, page 3	GTF: The result for the relative density of glyphosate technical material with purity 96.9% (Wollerton, Husband, 1997, CHE2001-63) is concluded to be "not acceptable (technical a.s.)". However, the relative density has also been generated using pure glyphosate, the value generated using glyphosate technical may be considered as addition information. *For further explanation please refer to Column 3 of the original commenting table.*	RMS: Due to the fact that these data have been evaluated and accepted without any comment during the original evaluation and no new requirements and/or guidance documents have been developed, a reassessment of these data is not foreseen according to the legal framework.	Addressed

Physical and chemical properties of the active substance (B.2.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(5)	Vol. 3, Annex B.2.1.4.2, Appearance: odour, page 6	GTF: The result for the odour of glyphosate technical material with purity 96.9% (Wollerton, Husband, 1997, CHE2001-63) is concluded to be "not acceptable (technical a.s.)". However, since the odour has also been generated using pure glyphosate, the value generated using glyphosate technical may be considered as addition information. *For further explanation please refer to Column 3 of the original commenting table.*	RMS: Due to the fact that these data have been evaluated and accepted without any comment during the original evaluation and no new requirements and/or guidance documents have been developed, a reassessment of these data is not foreseen according to the legal framework.	Addressed
1(6)	Vol. 3, B.2.1.4.2, Appearance: odour, page 6	GTF: No data on the odour of the NH_4-salt has been submitted.	GTF: It is not considered acceptable to request that laboratory personnel establish the odour of a product, as this involves inhaling the air above a test substance. Nevertheless, if an odour is detected it is recorded. In the case of the NH4 salt no specific odour was reported during the evaluations of the active substance. RMS: Comment noted.	Addressed

Physical and chemical properties of the active substance (B.2.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(7)	Vol 3, B.2.1.6 solubility in water	FR: Indicate the method in which the test of solubility in water was performed for K salt.	GTF: The solubility of K-salt in water was established using method EEC A.6 (flask method). RMS: Flask method. This could be added in a revised RAR.	Addressed
1(8)	Vol 3, B.2.1.6, B.2.1.7 solubility in water and in organic solvents	FR: It is more appropriate to use column elution method when the solubility is $<10^2$g/l.	GTF: The column elution method involves the elution of a test substance with water from a micro-column which is charged with an inert support material, such as glass beads or sand, coated with an excess of test substance. It is not suitable for use with volatile substances and was therefore not considered to be appropriate for establishing the solubility in organic solvents. RMS: The comment is unfortunately unclear. The solubility in water is >10 mg/l. Therefore, the shake flask method is acceptable according to EEC A.6. For the solubility in organic solvents, no particular method is proposed in Reg. (EU) No. 544/2011. The used method is considered acceptable. In addition, due to the fact that these data have been evaluated and accepted without	Addressed

Physical and chemical properties of the active substance (B.2.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			any comment during the original evaluation and no new requirements and/or guidance documents have been developed, a reassessment of these data is not foreseen according to the legal framework.	
1(9)	Vol. 3, B.2.1.11.2, Auto-flammability, page 17	GTF: The auto-flammability of the K salt was considered as a missing study. It was confirmed by the applicant in the reporting table that a study will be available by the end of 2013. *For further explanation please refer to Column 3 of the original commenting table.*	RMS: The results of the study could be evaluated and included in a revised RAR, provided that the study is available to the RMS and it is possible from a procedural point of view to assess the study.	Data requirement: Applicant to submit data for the auto-flammability of the K salt
1(10)	Vol 3 B.2.1.15 Oxidising properties	FR: A statement has been provided to justify that K salt has no oxidising properties. More details concerning the statement should be reported.	GTF: The oxidising properties of the K salt have been established by expert statement in accordance with methods EEC A.17 and UN O.1. Details are provided in report MSL0023950. The molecular structure of the K salt was evaluated. The oxygen atoms that are present in the molecular structure of the test substance are chemically bonded to carbon or hydrogen or phosphorus. Based on this the test substance is considered to pose no function as oxidizing agent. RMS: The comment is unfortunately unclear.	Addressed

Physical and chemical properties of the active substance (B.2.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			In EEC A17 it is clearly stated that "*This test need not be performed when examination of the structural formula establishes beyond reasonable doubt that the substance is incapable of reacting exothermically with a combustible material*". This was provided and the criteria given in "UN Recommendations on the Transport of Dangerous Goods (DSC)" are met and therefore the case has been accepted.	
1(11)	Vol. 3 B.2.2.5.1 Kinematic viscosity	FR: the method in which the test of kinematic viscosity was performed should be reported.	GTF: The method used was OECD 114, with Ubbelohde tube viscometer at 20 °C and 40 °C. RMS: Capillary viscometer. This could be added in a revised RAR.	Addressed.
1(12)	Vol. 3, B.2.2.2.2, Oxidising properties, page 24	GTF: The oxidising properties of MON 52276 have been extrapolated from the results obtained using the active ingredient which is the major component of the formulation (Krips, 1995, CHE9600635). It was confirmed by the applicant in the reporting that a study (expert judgement) would be available. *For further explanation please refer*	RMS: The results of the study could be evaluated and included in a revised RAR, provided that the study is available to the RMS and it is possible from a procedural point of view to assess the study.	Data requirement: Applicant to submit information concerning the oxidising properties of MON 52276

Physical and chemical properties of the active substance (B.2.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		to Column 3 of the original commenting table.		
1(13)	Vol. 3, B.2.2.6.1 Relative density	FR: Relative density has no unity. Please RMS indicates relative density of the formulation.	RMS: The comment is correct. However, in both studies (original Annex I listing and the additional data of the renewal) rather the density than the relative density has been determined. This should have been indicated in the DAR and RAR.	Addressed.
1(14)	Vol 3, B .2.2.7.1 Stability after storage for 14 days at 54°C.	FR: Please RMS indicates methods of the different test reported.	RMS: The French approach behind this kind of comments is not supported by the RMS and seems also not to be in compliance with the legal framework. These are data that have been evaluated and accepted without any comment during the original evaluation and no new requirements and/or guidance documents have been developed, a reassessment of these data is not foreseen according to the legal framework. Nevertheless the methods are: Colour, physical state - Visual assessment Odour - Olfactory assessment As content - HPLC method pH – US EPA 63.12; ASTM method E 70-90 Relative density – OECD 109	Addressed.

Physical and chemical properties of the active substance (B.2.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			Persistent foam – CIPAC MT 47.2 Viscosity – OECD 114 (Brookfield) Dilution storage stability – CIPAC MT 46.1.3	
1(15)	Vol 3, B .2.2.7.1 and B.2.2.7.5	FR: Please RMS indicate if the method for the determination of the active substance in the formulation is validated or not.	RMS: The French approach behind this kind of comments is not supported by the RMS and seems also not to be in compliance with the legal framework. These are data that have been evaluated and accepted without any comment during the original evaluation and no new requirements and/or guidance documents have been developed, a reassessment of these data is not foreseen according to the legal framework.	Addressed.
1(16)	Vol. 3, RAR, B.2.2.7.1 Accelerated storage test, persistent foam, p. 28	EFSA: is there any explanation why the initially already high persistent foam value is increasing during storage from 63 to 75 ml?	GTF: Persistent foam levels are generally higher after accelerated storage. No explanation is evident, but may be related to the impact of elevated temperature on the formulation ingredients. RMS: No. However, the EFSA approach behind this kind of comments is not supported by the DE and seems also not to be in compliance with the legal framework. Due to the fact that these data that have been evaluated and accepted without any	Addressed. See also data requirement 1(20)

Physical and chemical properties of the active substance (B.2.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			comment during the original evaluation and no new requirements and/or guidance documents have been developed, a reassessment of these data is not foreseen according to the legal framework. Consequently, DE has just "copy and paste" it from the DAR.	
1(17)	Vol 3 B.2.2.7.5	FR: The method CIPAC 284/SL/(M)/3 (HPLC) is used for the determination of active substance in the formulation. However, according to the section B.5.1.3, the method is validated in the formulation MON 78043, MON 78044 and MON 2139 (not in the representative formulation MON 52276). Please RMS justify.	GTF: The compositions of MON 78043 and MON 78044 are equivalent to the composition of MON 52276. A full comparison of the formulation compositions can be submitted on request. RMS: The comment is unfortunately unclear. In B.5.1.3 it is stated that the applicant has to confirm whether or not MON78043 is identical with MON52276. If not, further validation data and the applicability of the CIPAC method are necessary (see also GTF comment above).	Data requirement: Applicant to submit a full comparison of the formulation compositions (MON 78043 and MON 78044 vs. MON 52276)
1(18)	Vol. 3, B.2.2.7.5 Shelf life, a.s content, p. 30	EFSA: it is not clear what is meant by % recoveries of glyphosate acid? Is the change in the a.s. content after storage acceptable?	GTF: The % recoveries are based on the comparison of obtained results versus the theoretical glyphosate content based on the nominal concentration of the formulation. RMS: Comment noted. Due to the fact that	Addressed.

Physical and chemical properties of the active substance (B.2.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			the data in question have been evaluated and accepted without any comment during the original evaluation and no new requirements and/or guidance documents have been developed, a reassessment of these data is not foreseen according to the legal framework. Consequently, the data from the DAR have just been copy and paste. The understanding of the RMS is that the percentage value results from a comparison of the found results and the theoretical values (see also comment of GTF above). Concerning the change of the as content in the study of Bates (2001), this is acceptable for DE.	
1(19)	Vol 3 B.2.2.8.2	FR: In the persistent foaming test (CIPAC MT 47), there is 73ml of foam (after 1min) indicating that the formulation is a foaming product. While in the persistent foaming test (CIPAC MT 47.2), there is 0ml of foam (after 1min) indicating that the formulation is not a foaming product. Please RMS clarify.	GTF: The persistent foaming results of 73 ml foam after 1 minute were obtained in 1992. The persistent foaming results of 0 ml after 1 minute were obtained in 2011. The decrease in persistent foaming is attributed to continuous improvement of formulation ingredient quality over the 20 year period; as the formulation composition has not been	Addressed. See also data requirement 1(20)

Physical and chemical properties of the active substance (B.2.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			modified during this time. RMS: Due to the fact that the data in question have been evaluated and accepted without any comment during the original evaluation and no new requirements and/or guidance documents have been developed, a reassessment of these data is not foreseen according to the legal framework. Consequently, the data from the DAR have just been copy and paste. The data from the new study are acceptable for DE (see also comment from the GTF above).	
1(20)	Vol. 3, Annex B.2.2.8.2, Persistent foaming, page 33	GTF: It should be noted that according to the FAO Manual the test concentration should correspond to the highest rate of use. According to the list of representative uses the highest rate is 8%. It was confirmed by the applicant in the reporting that a study will be conducted if requested. *For further explanation please refer to Column 3 of the original commenting table.*	RMS: The results of the study could be evaluated and included in a revised RAR, provided that the study was submitted to the RMS and it is possible from a procedural point of view to assess the study.	Data requirement: Applicant to submit the persistent foam study result using the concentration corresponding to the highest rate of use

Further information (B.3)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point: (if data point not addressed or fulfilled)
1(21)				

Classification and labelling (B.4)
For comments on classification and labelling see the relevant sections.

Methods of analysis (B.5)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(22)	Vol. 3 B.5	FR: It should be specify the number of concentration level tested for linearity.	RMS: Comment noted. This grade of detail is not foreseen in the current harmonised approach to present the data. However, in general 5 levels have been used.	Addressed.
1(23)	Vol.3 B.5.1.2 + B.5.1.4	FR: The confirmation of identity of relevant impurities should be reported.	RMS: Formaldehyde is determined after post-column Hantzsch reaction which can be regarded as specific for formaldehyde. NNG is also determined after post-column reaction. The method is specific for nitroso compounds and nitrite. Nitroso groups can be cleaved via UV degradation. If the signal disappears, there are no interferences. The applicant stated that for technical material MON 77973 and the formulation MON	Addressed.

Methods of analysis (B.5)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			52276 no interferences were observed.	
1(24)	Vol.3 B.5.1.2	FR: The LOQ of NNG is 0.125ppm. However, the lowest validated concentration for formaldehyde is 0.50ppm. How do you set the LOQ? Please RMS clarify.	GTF: The limit of quantification (LOQ) of the method is defined as LOQ = (Lowest target standard level) x (Target sample dilution) The lowest standard level was 0.01 ppm and the sample dilution factor was 12.5 resulting in LOQ of 0.125 ppm RMS: It seems that FR is using the LOQ definition that is stipulated in the regulation for residue analytical methods. As this definition is not applicable for other analytical methods, the approach used in the study has been accepted as long as it is comprehensible.	Addressed.
1(25)	Vol.3 B.5.1.2	FR: The LOQ of formaldehyde is 20ppm. However, the lowest validated concentration for formaldehyde is 52.96ppm. How do you set the LOQ? Please RMS clarify.	GTF: Please see above comment. RMS: It seems that FR is using the LOQ definition that is stipulated in the regulation for residue analytical methods. As is definition is not applicable for other analytical methods, the approach used in the study has been accepted as long as it is	Addressed. See also comment 1(24)

Methods of analysis (B.5)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			comprehensible.	
1(26)	Vol.3 B.5.1.3	FR: The composition of formulations MON 78043, MON 78044 and MON 2139 and MON 52276 should be provided. The specificity of the method CIPAC 284/SL/(M)/3 (HPLC) should be demonstrated in the formulation MON 52276.	GTF: The composition of formulations MON 78043, MON 78044 and MON 2139 is substantially similar to the composition of MON 52276. For compositional comparison please see AIII DOC J RMS: The comment is unfortunately unclear. It is clearly stated that if MON 78043 is not identical with MON 52276 further validation data and the applicability of the CIPAC method are necessary.	See data requirement in comment 1(17)
1(27)	Vol.3 B.5.1.4	FR: The LOQ of formaldehyde is 20ppm. However, the lowest validated concentration for formaldehyde is 155.508ppm. How do you set the LOQ? Please RMS clarify.	GTF: Please see previous responses. [1(20) 1(21)] RMS: It seems that FR is using the LOQ definition that is stipulated in the regulation for residue analytical methods. As is definition is not applicable for other analytical methods, the approach used in the study has been accepted as long as it is comprehensible.	See comment 1(25)
1(28)	Vol.3 B.5.1.4	FR: Determination of 1.4-dioxane As no validation data is reported, the method is not validated.	GTF: Formaldehyde and N-nitrosoglyphosate are stated as the only relevant impurities in the FAO specifications	Addressed.

Methods of analysis (B.5)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			in glyphosate technical material. RMS: Comment noted. It should be noted that this method was just "copy and paste" from the DAR. A reassessment of these data is not foreseen according to the legal framework. Furthermore, it is not stated that the method has been accepted.	
1(29)	Vol. 3 B.5.2 + B.5.3	FR: According to Sanco 825/00 rev 8.1, when an analytical method uses a derivatisation step, the efficiency and precision of the derivatisation step should be demonstrated. Please RMS justify.	GTF: The efficiency and precision of the derivatisation steps are demonstrated by measuring acceptable recovery of analyte(s) found in fortified samples which are derivatised in the untreated control sample matrix. RMS: Disagreed with GTF comment. A demonstration of the efficiency of derivatisation step by recovery and precision is not sufficient. According to SANCO/825/00 rev .8.1 the calibration shall be performed by standard solution of the pure derivative prepared by weighting. Also stability and specifity of the derivatives should be addressed. This approach should be followed by quantification against the pure derivative of the standard. Such questionable studies are discussed in	Data requirement: Additional data to address the efficiency and precision of the derivatisation step of the methods using derivatisation.

Methods of analysis (B.5)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			B.5.2.1.1.3 (Anderson, L. and Ely, S.V., 2001), B.5.2.1.1.4 (Alferness, P.L. and Wiebe, L.A., 2001), B.5.2.2.1.3 (Clarke, D.M. and Robinson, N.J., 1998) and B.5.3.1.1 (Szuter, S.L., 1996). These studies will be moved to the section of studies, which do not fulfill the requirements. Due to the analysis without stable isotope labelled standards the method for soil discussed in B.5.3.1.1 (Szuter, S.L., 1996) will be deleted and a new confirmatory method for residues in soil is required. However, if the analytical procedure use stable isotope labelled internal standards added to the test portion, the efficiency of the derivatization step will be sufficiently considered. In such cases, the demonstration of sufficient efficiency and precision of the derivatisation step seems not important and methods are considered acceptable without additional tests of efficiency and precision of the derivatisation step. Such decision is proposed for the studies discussed in B.5.2.2.1.4 (Schneider, V., 2001), B.5.3.1.1 (Schneider, V., 2001), B.5.3.2 (Knoch, E.,	

Methods of analysis (B.5)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			2010) and B.5.3.3 (Schneider V., 2001). It is proposed to accept these studies..	
1(30)	Vol. 3, B.5.2.1.1.1, Acceptable methods/ reports – Method 1, page 28	GTF: At the bottom of page 29 (Findings), it is incorrectly stated that the proposed residue definition for enforcement purpose in lentils is glyphosate and N-acetyl-glyphosate. The recent import tolerance for lentils (EFSA Journal 2012:10(1):2550) is incorrectly included with GAT genetically modified crops (oilseeds rape, soya beans and maize). The import tolerance was for conventional lentils. The GTF refers to 'Comment (1(48))' and the further explanations under 'Comment (1(48))' *For further explanation please refer to Column 3 of the original commenting table.* *(RMS remark: see Reporting table 1(50))*	RMS: The listing of 'lentils' was incorrect and will be replaced by 'sweet corn' in the revised Vol. 3 B.5 of the RAR and in the List of Endpoints. In Vol. 3 B.5 of the RAR such replacement is necessary in B.5.2.1.1.1, B.5.2.1.1.3, B.5.2.1.1.4, B.5.2.1.2 (two times), and B.5.5.	Open point: RMS to amend Vol. 3 B.5 B.5.2.1.1.1, B.5.2.1.1.3, B.5.2.1.1.4, B.5.2.1.2 (two times), and B.5.5. of the RAR and the LoEP replacing 'lentils' by 'sweet corn'
1(31)	Vol. 3 B.5.2.1.1.1 B.5.2.1.1.2	FR: The method 1 and the ILV used internal standards radio labelled. So, a certificate ensuring that the Notifier can supply internal standard radio labelled in case of control	GTF: Glyphosate and AMPA internal standards used in all of analytical methods are not radiolabelled but rather they are enriched in stable isotopes, such as carbon-	Addressed. See also comments 1(36), 1(37),

Methods of analysis (B.5)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		should be provided and mentioned in the text. In the other case, the method 1 is not taking into account for monitoring purposes.	13 and nitrogen-15 stable isotopes which are not radioactive. Glyphosate and AMPA standards enriched with various stable isotopes are commercially available. RMS: The stable isotope labelled standards 1,2 $^{13}C_2$ ^{15}N-glyphosate and ^{13}C^{15}N-AMPA are commercially available from Ehrenstorfer GmbH (order numbers 14050100 and XA10205100WA), Cambridge Isotope Laboratories and LGC (order number CNLM-4666-10 and CDNLM-6786-1.2).	1(43), 1(44), 1(47)
1(32)	Vol. 3 B.5.2.1.1.2	FR: The ILV method is validated on high acid content (grape) and high oil content (soybean seed) commodities. So, the ILV of the method 1 is acceptable only for soybean seed (no data validation in grape in method 1).	GTF: The primary validation of the method included limes which is a high acid content crop comparable to grape. RMS: Agreement with GTF.	Addressed
1(33)	Vol. 3 B.5.2.1.1.3 B.5.2.1.1.4	FR: The method 2 and its ILV have the same test facility. Please RMS clarify. If they are the same test facility, the method reported in B.5.2.1.1.4 cannot be accepted as ILV of method 2.	GTF: The technical letter (Crook, S.J. (2007) Glyphosate: Provision of independent laboratory validation data to support analytical methods RAM 328/01 and RAM 308/01) was written to explain the status of the ILV situation and is not an ILV report in itself – hence why they both come from	Addressed

Methods of analysis (B.5)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			Syngenta. It includes details of published data which provide independent validation of the Syngenta methods RAM 328/01 and RAM 308/01. RMS: The studies discussed in B.5.2.1.1.3 (Anderson, L. and Ely, S.V., 2001) and B.5.2.1.1.4 (Alferness, P.L. and Wiebe, L.A., 2001) will be moved to the section of studies, which do not fulfill the requirements. See point 1(27).	
1(34)	Vol. 3, B.5.2.1.1.3, Acceptable methods/ reports – Method 2 (part of Section B.5.2.1 Plant matrices), page 37	GTF: At the top of the page 39 (Conclusion) it is stated that the study of Anderson and Ely (2001, ASB2012-12364) does not allow the determination of the second component N-acetyl-glyphosate (NAG) of the proposed residue definition for enforcement purposes in lentils, oilseeds rape, soya beans and maize. The GTF does not agree and refers to 'Comment (1(48))' and the further explanations under 'Comment (1(48))' *For further explanation please refer to Column 3 of the original commenting table.*	RMS: The listing of 'lentils' was incorrect and will be replaced by 'sweet corn' in the revised Vol. 3 B.5 of the RAR and in the List of Endpoints. In Vol. 3 B.5 of the RAR such replacement is necessary in B.5.2.1.1.1, B.5.2.1.1.3, B.5.2.1.1.4, B.5.2.1.2 (two times), and B.5.5.	See Open point: in comment 1(30)

Methods of analysis (B.5)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		(RMS remark: see Reporting table 1(50))		
1(35)	Vol. 3, Annex B.5.2.1.4, Studies which do not fulfil the requirements (part of Section B.5.2.1 Plant matrices), page 50	GTF: Page 51 - Additional validation data at the limit of quantification level in oranges and sunflower are available and are ready for submission upon request from EFSA.	RMS: In the study of Gemrot (2010), the efficiency and precision of the derivatisation step was not demonstrated as required in accordance to SANCO/825/00 rev. 8.1. Therefore, the extent of validation of the derivatisation is not sufficient. Additional validation data would be required to address this point.	See data requirement in comment 1(29)
1(36)	Vol. 3 B.2.2.1.1	FR: The method 1 and the ILV used internal standards radio labelled. So, a certificate ensuring that the Notifier can supply internal standard radio labelled in case of control should be provided and mentioned in the text. In the other case, the method 1 is not taking into account for monitoring purposes.	GTF: Internal standards used in all of glyphosate and AMPA analytical methods are not radiolabelled but rather they are enriched in stable isotopes, such as carbon-13 and nitrogen-15 stable isotopes which are not radioactive. Glyphosate and AMPA standards enriched with various stable isotopes are commercially available. RMS: The stable isotope labelled standards 1,2 $^{13}C_2$ ^{15}N-glyphosate and ^{13}C^{15}N-AMPA are commercially available from Ehrenstorfer GmbH (order numbers 14050100 and XA10205100WA), Cambridge Isotope Laboratories and LGC	Addressed See also comments 1(31), 1(37), 1(43), 1(44), 1(47)

Methods of analysis (B.5)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			(order number CNLM-4666-10 and CDNLM-6786-1.2)	
1(37)	Vol. 3 B.2.2.1.4 method 3	FR: The method 3 used internal standards radio labelled. So, a certificate ensuring that the Notifier can supply internal standard radio labelled in case of control should be provided and mentioned in the text. In the other case, the method 3 is not taking into account for monitoring purposes	GTF: Internal standards used in all of glyphosate and AMPA analytical methods are not radiolabelled but rather they are enriched in stable isotopes, such as carbon-13 and nitrogen-15 stable isotopes which are not radioactive. Glyphosate and AMPA standards enriched with various stable isotopes are commercially available. RMS: The stable isotope labelled standards 1,2 $^{13}C_2$ ^{15}N-glyphosate and ^{13}C^{15}N-AMPA are commercially available from Ehrenstorfer GmbH (order numbers 14050100 and XA10205100WA), Cambridge Isotope Laboratories and LGC (order number CNLM-4666-10 and CDNLM-6786-1.2)	Addressed See also comments 1(31), 1(36), 1(43), 1(44), 1(47)
1(38)	Vol. 3, B.5.2.2.1.3, Method 2, (part of Section B.5.2.2 Animal matrices), page 63	GTF: Report RJ2585B (BVL-2309039, ASB2012-12398 page 63 - GTF has already conducted additional work on the appropriate analytical methods for glyphosate in matrices of animal origin generating additional method validations data and confirming the method of analysis	RMS: The efficiency and precision of the derivatisation step was not demonstrated as required in studies RJ2585B (BVL-2309039, ASB2012-12398), TO11644-06 (ASB2012-7837) and CEMR-3532 (ASB2012-12417) in accordance to SANCO/825/00 rev. 8.1. Therefore, the extent of validation of the	Data requirement: Applicant to submit the additional validation data for the analytical methods for glyphosate in matrices of animal origin.

Methods of analysis (B.5)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		via inter lab validations. The reports are ready for submission upon request from EFSA. *For further explanation please refer to Column 3 of the original commenting table.*	derivatisation is not sufficient. Additional validation data would be required to address this point also. The same statement applies to page 69 reference to Report TO11644-06, ASB2012-7837 and page 70 reference to Report CEMR-3532, ASB2012-12417	
1(39)	Vol. 3, B.5.2.3.1 Extraction efficiency, p. 72	EFSA agrees with the RMS on the acceptability of the extraction efficiency of plant methods	GTF agrees. RMS: Agreement noted. Thank you.	Addressed
1(40)	Vol. 3, B.5.2.3.2 Extraction efficiency, p. 73	EFSA agrees with the RMS on the acceptability of the extraction efficiency of methods for animal matrices	GTF agrees. RMS: Agreement noted. Thank you.	Addressed
1(41)	Vol. 3, B.5.3.1.1 Soil methods, Method 2, p. 76 and B.5.3.1.2, p.78	EFSA: small typo in the formula of the derivatise d AMPA (F_{17})	GTF agrees. RMS: The formula $C_{11}H_7F_{14}NO_4P$ was incorrect and will be replaced by $C_{11}H_7F_{17}NO_4P$ in the revised Vol. 3 B.5 of the RAR (eight times noticed).	Addressed

Methods of analysis (B.5)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(42)	Vol. 3, B.5.3.1.1 and B.5.3.1.2 Soil methods, Method 2 (Szuter), p. 76, and method Alferness, p.78	EFSA: RMS considered the method of Alferness as not acceptable because of the number of the validation experiments, however this method validated in 1994 is practically identical with the accepted 'Method 2' validated in 1996.	GTF agrees. RMS: The study discussed in B.5.31.1 (Szuter, S.L., 1996) will be moved to the section of studies, which do not fulfill the requirements. See point 1(27). In addition, the methods are not identical because of an additional cleanup with graphitized carbon black is made in the method of Szuter.	See data requirement in comment 1(29)
1(43)	Vol. 3 B.5.3.1.1 method 1	FR: The method 1 used internal standards radio labelled. So, a certificate ensuring that the Notifier can supply internal standard radio labelled in case of control should be provided and mentioned in the text. In the other case, the method 1 is not taking into account for monitoring purposes	GTF: Internal standards used in all of glyphosate and AMPA analytical methods are not radiolabelled but rather they are enriched in stable isotopes, such as carbon-13 and nitrogen-15 stable isotopes which are not radioactive. Glyphosate and AMPA standards enriched with various stable isotopes are commercially available. RMS: The stable isotope labelled standards 1,2 $^{13}C_2$ ^{15}N-glyphosate and ^{13}C^{15}N-AMPA are commercially available from Ehrenstorfer GmbH (order numbers 14050100 and XA10205100WA), Cambridge Isotope Laboratories and LGC (order number CNLM-4666-10 and CDNLM-6786-1.2)	Addressed See also comments 1(31), 1(36), 1(37), 1(44), 1(47)

Methods of analysis (B.5)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(44)	Vol. 3 B.5.3.2	FR: The method (Knoch E 2010) used internal standards radio labelled. So, a certificate ensuring that the Notifier can supply internal standard radio labelled in case of control should be provided and mentioned in the text. In the other case, the method is not taking into account for monitoring purposes.	GTF: Internal standards used in all of glyphosate and AMPA analytical methods are not radiolabelled but rather they are enriched in stable isotopes, such as carbon-13 and nitrogen-15 stable isotopes which are not radioactive. Glyphosate and AMPA standards enriched with various stable isotopes are commercially available. RMS: The stable isotope labelled standards 1,2 $^{13}C_2$ ^{15}N-glyphosate and ^{13}C^{15}N-AMPA are commercially available from Ehrenstorfer GmbH (order numbers 14050100 and XA10205100WA), Cambridge Isotope Laboratories and LGC (order number CNLM-4666-10 and CDNLM-6786-1.2)	Addressed See also comments 1(31), 1(36), 1(37), 1(43)
1(45)	Vol. 3 B.5.3.2	FR: As validation data has been provided for two transitions for glyphosate and AMPA, the method (Knoch E 2010) and its ILV (Gesscke.S 2011) are considered as highly specific.	GTF agrees. RMS: The words “highly specific” are added to the conclusions regarding the method (Knoch E 2010) and its ILV (Geschke.S 2011) in the revised Vol. 3 B.5 of the RAR.	Addressed
1(46)	Vol. 3, B.5.3.2 Water methods,	EFSA: small typo: the unit of electric conductance (siemens) is S (s is second)	GTF agrees. RMS: The typo will be corrected in the	Addressed

Methods of analysis (B.5)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
	p.81		revised Vol. 3 B.5 of the RAR.	
1(47)	Vol. 3 B.5.3.3	FR: The method (Schneider V (2001)) used an internal standard radio labelled. So, a certificate ensuring that the Notifier can supply internal standard radio labelled in case of control should be provided and mentioned in the text. In the other case, the method is not taking into account for monitoring purposes.	GTF: Internal standards used in all of glyphosate and AMPA analytical methods are not radiolabelled but rather they are enriched in stable isotopes, such as carbon-13 and nitrogen-15 stable isotopes which are not radioactive. Glyphosate and AMPA standards enriched with various stable isotopes are commercially available. RMS: The stable isotope labelled standards 1,2 $^{13}C_2$ ^{15}N-glyphosate and $^{13}C^{15}$N-AMPA are commercially available from Ehrenstorfer GmbH (order numbers 14050100 and XA10205100WA), Cambridge Isotope Laboratories and LGC (order number CNLM-4666-10 and CDNLM-6786-1.2)	Addressed See also comments 1 (31), 1(36), 1(37), 1(43), 1(44)

Methods of analysis (B.5)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(48)	Vol. 3, Annex B.5.5.2, Residue analysis, page 87	GTF: At the bottom of the page 89 it was concluded that the following methods for monitoring are missing: "A confirmatory method for N-acetyl-glyphosate in dry plant materials and those with high water and high fat content. A confirmatory method for N-acetyl-glyphosate in all kinds of animal matrices." The GTF disagrees with this conclusion and refers to 'Comment (1(48))' and the further explanations under 'Comment (1(48))' *For further explanation please refer to Column 3 of the original commenting table.* *(RMS remark: see Reporting table 1(50))*	RMS: The enforcement of MRLs in crops like sweet corn, oilseed rape, soya beans and maize shall be possible without the knowledge of glyphosate tolerance. Therefore, matrices with high water content (sweet corn), high oil content (oilseed rape, soya beans) and dry matrices (maize grain) require analytical methods, which allow the determination of N-acetyl-glyphosate.	Data requirement: Applicant to submit a confirmatory method for *N*-acetyl-glyphosate in dry plant materials and those with high water and high fat content and a confirmatory method for *N*-acetyl-glyphosate in all kinds of animal matrices. See also comment 3(18)
1(49)	Vol. 3, B.5.5.2 Residue methods, p.89	EFSA agrees with the data gaps identified by the RMS concerning the residue monitoring methods	RMS: Agreement noted. Thank you.	See data requirement in comment 1(48)

Methods of analysis (B.5)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(50)	List of endpoints, Analytical methods for residues	GTF: Residue definition for monitoring purposes in food of plant origin and food of animal origin should not include N-acetyl-glyphosate as described in Column 3. *For further explanation please refer to Column 3 of the original commenting table.*	GTF: In 2009 EFSA issued a reasoned opinion (RO) on the Modification of the residue definition of glyphosate in genetically modified maize grain and soybeans, and in products of animal origin (EFSA Journal 2009; 7(9): 1310). This RO proposed a residue definition for risk assessment in all plant commodities, (including soybean and maize) and all food commodities of animal origin. In addition three (3) possible options were proposed regarding the residue definition in maize and soybeans for enforcement purposes. In the Summary report (SANCO-D(2011) 353285) of the Standing Committee meeting on the Food Chain and animal health; section Pesticide residues + plant protection products-legislation of February 3-4 2011, the committee concluded that the residue definition for enforcement should not change (option 1 in the EFSA reasoned opinion; it is residue = **glyphosate only**) but that for the definition for the purpose of risk assessment the complete residue definition with all metabolites would need to be used. Given the fact that no GM uses are included	See comment 3(18)

Methods of analysis (B.5)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			in the representative GAP of the joint submission and given the argumentation above, no analytical methods for enforcement purposes are needed to cover N-acetyl glyphosate. The primary and confirmatory methods provided in the joint submission (with additional validation data that will be submitted where appropriate) are adequate to cover the residue definition for monitoring and post registration purposes. Also in the context of risk assessment, the uses listed in the representative GAP do not yield N-acetyl Glyphosate as a residue (no GM uses included). The residues (including N-acetyl Glyphosate) related to imported commodities are regulated under EU Regulation 369/2005 and not Regulation 1107/2009 nor regulation 1141/2010. These data have recently been submitted by the data owner and considered for risk assessment. RMS: please refer to RMS comment 1(46).	

Other comments				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(51)	Vol. 1, 1.5.1 Details of representative uses, p. 16	EFSA: it is not clear to what refers the ** in the first two rows of the GAP table	RMS: ** refers to crops including but not restricted to: root & tuber vegetables, bulb vegetables, stem vegetables, field vegetables (fruiting vegetables, brassica vegetables, leaf vegetables and fresh herbs, legume vegetables), pulses, oil seeds, potatoes, cereals, and sugar- & fodder beet; before planting fruit crops, ornamentals, trees, nursery plants etc.	Addressed.
1(52)	Vol. 1, 1.5.1 Details of representative uses, p. 16	EFSA: probably it would be useful to insert the name/code of the representative formulation, too in the GAP table	RMS: The name of the representative formulation (i.e. MON 52276) can be included in a revised GAP table.	Addressed.

Other comments				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(53)	Vol. 3, B.5.6 References relied on, p.89-100	EFSA: all the studies that are not part of the dossier for renewal (highlighted in yellow) and were evaluated in the RAR should be submitted to the COM, MSs and EFSA for transparency reasons and to have access to the raw data evaluated. Art. 10(3) of Reg. (EU) No 1141/2010 states that the supplementary complete dossiers shall contain the full text of **each** test and study report.	RMS: Request to be addressed by the applicant, i.e. the GTF.	Data requirement: According to Art. 10(3) of Reg. (EU) No 1141/2010 the supplementary complete dossiers shall contain the full text of **each** test and study report, as a consequence all the studies that are not part of the dossier for renewal (highlighted in yellow) and were evaluated in the RAR should be submitted to the COM, MSs and EFSA for transparency reasons and to have access to the raw data evaluated.
1(54)	Spectzra of relevant impurities –			Data requirement: Spectra of relevant impurities. The data requirement has already been identified in the RAR

Other comments				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(55)	Confirmatory method			Data requirement: A confirmatory method for glyphosate in animal fat and kidney/liver. Relevant, basic data set for all active substances! The data requirement has already been identified in the RAR

2. Mammalian toxicology

Toxicokinetics (B.6.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
2(1)		BE: BE agrees with the estimation of the oral absorption, which should be revised downwards from 30 % to 20 %.	RMS: Agreement	Addressed The oral absorption for glyphosate is 20%.
2(2)	Vol. 3, B.6.1 Absorption, distribution, excretion and metabolism (toxicokinetics)	EL: The oral absorption value of 20% proposed by the RMS taking into account only the radioactivity detected in urine, cage wash and tissues/carcass, as low biliary excretion has been proven, is considered acceptable. This value has been resulted considering the excretion pattern in female rats as a worst case. The concluded oral absorption value is clearly mentioned only in Vol. 1 in the part for the setting of reference values. For clarity reasons it is proposed to include at the end of this section an overall conclusion for the oral absorption end point giving a detailed rational for this proposal.	RMS: Agreement, an explanatory statement will be included in a revised RAR.	Addressed RMS to consider in a revised RAR
2(3)	Vol. 3, B.6.1 Oral absorption	EFSA: the proposed oral absorption of 20% is agreed with.	RMS: Agreement	Addressed See 2(1)

Acute toxicity (B.6.2)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
2(4)	Vol. 3, B.6.2.1	NL: Minor comment, typo: under RMS comment (August 2013) "Glyphosate" should be replaced by "glyphosate".	RMS: Agreement, will be replaced in a revised RAR.	Addressed RMS to consider in a revised RAR
2(5)	Vol. 3, B.6.2	NL: Minor comment: throughout the document the Magnusson & Kligman test for skin sensitisation is inconsequently referred to as "Magnusson Kligman", "Magnusson-Kligman", "Magnusson and Kligman", or "Magnusson & Kligman".	RMS: Agreement, a consistent nomenclature will be used in a revised RAR.	Addressed RMS to consider in a revised RAR
2(6)	Vol. 1, Level 1, 2.6.3.1, Acute oral toxicity, page 42	GTF: The GTF respectfully restates their position, that oral LD50 values are noted above 2000 mg/kg/day. The data presented for oral LD50 values are more precisely described as greater than 5000 mg/kg/day. *For further explanation please refer to Column 3 of the original commenting table.*	GTF: Please refer to comments on 2(7) and 5(22) RMS: The LD50 values in one study with glyphosate (salts) in rats and in two studies in mice are between 2000 and 5000 mg/kg bw. Furthermore, not all different batches were tested up to 5000 mg/kg bw. Therefore, an overall LD50 of >2000 mg/kg bw is proposed.	Addressed
2(7)	List of endpoints, Acute toxicity	GTF: The GTF respectfully restates their position that the rat LD50 oral and Rat LD50 dermal values are listed as >2000 mg/kg bw, whereas the data presented concludes LD50-values above 5000 mg/kg. This would also be consistent with the values presented in summary Table B.6.2-1 and Table B.6.2-6 in	GTF: As previously pointed out, acute mammalian toxicity endpoints are applicable to other sections of the dossier, such as wildlife risk assessment and therefore the data (LD50 > 5000 mg/kg) rather than EU classification limit dose (2000 mg/kg) should be stated. Please refer to France's comment	Addressed

Acute toxicity (B.6.2)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		Volume 3 B6. All test materials meeting specifications should be deemed appropriate as representative of the substance undergoing Annex I Renewal. *For further explanation please refer to Column 3 of the original commenting table.*	5(22) in the ecotoxicology section, wherein the MS states "The lowest limit LD50 of 2000 mg/kg bw/d was used in the risk assessment however there is evidence that it would be likely over 5000 mg/kg bw/d.". RMS: See comments on 2(6) and 2(8).	
2(8)	Vol. 1, Level 1, 2.6.3.2, Acute dermal toxicity, page 42	GTF: The GTF respectfully restates their position that dermal LD50 values are noted above 2000 mg/kg/day. The data presented for dermal LD50 values are more precisely described as greater than 5000 mg/kg/day. *For further explanation please refer to Column 3 of the original commenting table.*	RMS: Not all different batches were tested up to 5000 mg/kg bw. Therefore, an overall LD_{50} of >2000 mg/kg bw is proposed.	Addressed

Short-term toxicity (B.6.3)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
2(9)	Vol. 1, level 2, 2.6.4.2 Rat 90d studies	BE: RMS proposed an 'overall' NOAEL for the subchronic rat studies, of 300-400 mg/kg b.w./d, but specifies a more precise value	GTF: When the NOAEL / LOAELs from all relevant 90-day toxicity studies in rodents are plotted (Figure 5.11-2, page 1027 of	Addressed The relevant NOAEL of the 90-day

Short-term toxicity (B.6.3)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		which would be 414 mg/kg b.w./d, which compares with the LOAEL of 569 mg/kg b.w./d. BE would propose to choose the NOAEL of the [redacted] study (1991), i.e. 300 mg/kg b.w./d, which seems more appropriate in order to maintain a sufficient margin of safety. This compares well with the overall dog NOAEL at the same dose-level. It is acknowledged that this does not impact on the establishment of a short-term RfD. The LoEP should then be amended accordingly.	Annex II Doc M, Section 3 Point 5) it is clear that 414 mg/kg b.w./d is an appropriate NOAEL. No change to the LoEP is required. RMS: In contrast to most other active substances in plant protection products, several studies with glyphosate are available to address each of the different toxicological endpoints. Therefore, we decided to give a range rather than a single figure for an ”overall NOAEL”. However, for different purposes, a precise values might be needed, that will depend, of course, very much on dose spacing. For selecting the most appropriate one, the NOAELs/LOAELs in the valid 90-day studies were compared. As shown in Tables 2.6-3a and -3b in Volume 1, the lowest LOAEL in any of the studies was 569 mg/kg bw/day ([redacted] 1995). Thus, it seems reasonable to use the NOAEL of 414 mg/kg bw/d from the study by [redacted] (1996) as the most relevant. In the study by [redacted] (1991) that was suggested by BE, the NOAEL was indeed lower but the LOAEL was much higher (1000 mg/kg bw/day).	studies in rats is 414 mg/kg bw per day
2(10)	Vol 3, B.6.3,	BE: has some reservations as regards the	GTF: Statistically significant changes	Addressed

Short-term toxicity (B.6.3)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
	90d dog ([redacted] 1999)	determination of the study NOAEL at the top-dose, taking into account interim and/or final significant modifications in clotting time, GGT activity, and total bilirubin rise at the top-dose level. The worrying fact is that all these modifications are dose-dependent. It was questioned whether 2000 ppm (52.8 mkd) would not be a more appropriate (conservative) NOAEL. It is recognised that exact the same parameters were unaffected in other dog studies, but on the other hand adverse hepatic effects were observed.	observed in clotting time and GGT activity were minor and only observed at the interim bleed (Day 45) and not the final bleed (Day 90) at the end of the treatment period. Total bilirubin was higher in females in the interim bleed and in both sexes at the terminal bleed. However, there was no correlating effect on liver weight and no histopathological changes were observed in the liver. Therefore, 10000 ppm (252.6 mg/kg b.w./d) is the proposed NOAEL for this study. RMS: The occasional clinical chemistry findings, in the absence of concomitant liver toxicity and not occurring in studies of longer duration, are rather due to statistical variability (if many parameters are measured, some of them can be expected to be changed in a significant way) than to test substance administration. We suggest to keep the NOAEL as it is.	
2(11)	Vol. 1, level2, 2.6.4.2 Dog 90d-1yr studies	BE: agrees with the proposed overall NOAEL, taking into account all dog studies. The NOAEL of 300 mkd is sufficiently protective, taking into account the 2/8 deaths in the [redacted] (2007) study at the top-dose of	RMS: Agreement noted, thank you.	Addressed

Short-term toxicity (B.6.3)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		1000 mkd.		
2(12)	Vol. 1, Level 1, 2.6.4.2, Oral subchronic (90 days and longer) studies, page 48	GTF: It is unlikely that clearly local (irritation) effects have huge interspecies-differences. Addition of the following underlined wording takes this into account. *For further explanation please refer to Column 3 of the original commenting table.*	RMS: The local effects in these studies have no impact on the evaluation including derivation of reference doses.	Addressed
2(13)	LoEP	BE: In the critical short-term effects, the consistent increase of alkaline phosphatase could be explicitly mentioned when reference is made of 'clinical chemistry findings'.	GTF: The short term dog data set reflects general changes in clinical chemistry (including increased or decreased alkaline phosphatase), sometimes in conjunction with reduced liver weight, suggesting weak liver toxicity or general toxicity in dogs at high doses. RMS: More than one clinical chemistry parameter was affected in rodents and dogs.	Addressed

Genotoxicity (B.6.4)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
2(14)	B.6.4.8.	DK: Could you please include and evaluate the following study Mesnage R, Defarge N, Spiroux de Vendômois J, Séralini G-E. Major pesticides are more toxic to human cells than their declared active principles. Biomedical Research International, 2014.	GTF: Comparable to other in vitro publications by Seralini et al., reviewed in the RAR (Volume 3, p. 658 and pp. 666 - 673. Similar publications by Seralini have been widely refuted and are considered irrelevant to human tissue exposures and are not applicable to human health risk assessment. This specific study suffers from the unrealistic exposure conditions (i.e. exposing organ cells directly to detergent-containing formulations). Similar effects would be observable with any detergent if the skin as a protective barrier is removed, but detergents are used for centuries as human hygiene products and are of no health concern if the physiological condition (i.e. barrier function of the skin) is retained. The authors state that the in vitro system represents an underestimation of what is observed in vivo. They argue that while metabolism may reduce the toxic effects, this reduction is compensated for by bioaccumulation and the combined effects of the AP (e.g. glyphosate) with adjuvant. The basis for this statement is the in vivo long-	Data requirement Applicant to submit the study by Mesnage R, Defarge N, Spiroux de Vendômois J, Séralini G-E. Major pesticides are more toxic to human cells than their declared active principles. Biomedical Research International, 2014

Genotoxicity (B.6.4)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			term toxicity observed in the highly publicized but now retracted rodent study by Seralini et al., 2012. Clearly the authors are unwilling to acknowledge the overwhelming data demonstrating that glyphosate is essentially not metabolized in mammals and that it is rapidly eliminated in urine. It is clear from the previous work of Seralini and others that surfactants can injure or kill cells following the direct application of surfactants to cells in vitro. Surfactants in general, including POEAs, can impair the integrity of cellular membranes at high concentrations in culture. Injured cells will demonstrate the expected activation of injury-response systems and suffer from a general decline in a wide variety of cellular functions. The concentrations of surfactant applied in these experiments are much higher than those achieved in living humans or animals, and are not relevant to real world human exposures to glyphosate-surfactant products. Such in vitro systems are not considered relevant for evaluating the toxicity of surfactants and are not translatable to whole animal outcomes	

Genotoxicity (B.6.4)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			(Levine et al., 2007). Seralini and colleagues at the University of Caen in France and CRIIGEN have six prior publications on the results of exposing unprotected cells in culture to glyphosate, AMPA (aminomethylphosphonic acid, the primary environmental degradate of glyphosate), glyphosate- based formulations or a surfactant used in some formulated products. The results from the current study offer nothing new. RMS: The study will be commented in a revised RAR.	
2(15)	B.6.4.5 Genotoxicity – in-vivo MN ([redacted] 2006) p357	BE: the explanation for the equivocally positive response at 24h sampling time is plausible, given the HCD, and also the negative finding at the 48h sampling time. Conclusion of the RMS supported.	RMS: Agreement.	Addressed
2(16)	Genotoxicity – in-vivo MN ([redacted] 2007) p359	BE: finds it is surprising that the dose of 30 mg/kg would constitute the highest tolerable one. However, positive effects were observed and the sole criticism of low dose is not sufficient to disregard the study *per se*.	TECAM (CRO on behalf of Helm): Although it is surprising that the dose of 30 mg/kg would constitute the highest tolerable one, mortality was observed at 2000 mg/kg; 320 mg/kg and 50 mg/kg body weight (bw)	Addressed

Genotoxicity (B.6.4)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		More detailed information should be provided with the range-finder. HCD are cited but not represented. Are there batch details from the Helm source possibly explaining a casual pve result?	as presented in Table 1 of the final report. Item 2.5 presents the signs and symptoms observed at the toxic doses. Two dosed animals at 2000 mg/kg showed prostration, ataxia and died on day 3 after dosing. The three animals dosed at 320 mg/kg bw showed prostration and ataxia on day 1 and died on day 2. Three animals were dosed at 50 mg/kg bw and one died on day 1. Considering mortality and toxicity at 2000 mg/kg bw; 320 mg/kg bw and 50 mg/kg bw. Although statistically significant results were observed at the highest dose when compared to the concurrent negative control group, these results have no biological relevance when compared to historical control and published data. Published negative control data (Salamone & Mavournin, 1994) suggest that the historical negative control frequency for a mouse stock should fall between 1 and approximately 3.4 MNPCE/1 ,000 to accommodate all commonly used strains. Therefore, the frequency of micronuclei observed at 30 mg/kg bw of 1.39 MNPCE/1000 was considered to be within the historical control and published data.	

Genotoxicity (B.6.4)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			Considering the findings of this study and that the active ingredient Glyphosate is reported in the literature not to be mutagenic (Tomlin, 2006), we consider Glyphosate Technical Grade from HELM DO BRASIL MERCANTIL LTDA did not induce an increase of micronucleus number in mouse bone marrow erythrocytes. RMS: The result of high mortality at 2000, 320 and 50 mg/kg bw is strongly contradictory to the results of all acute oral toxicity studies. Obviously, in this study a substance was used which was much more toxic than other batches of glyphosate. The reasons of this extreme difference are unknown and a discussion may be speculative. Therefore, on this basis the study is not considered acceptable.	
2(17)	Genotoxicity – in-vivo MN ([redacted] 2008) p361	BE: again, the low dose of 30 mg/kg is probably not representing the highest tolerable one, but this is on itself an insufficient reason to declare the GLP-study unreliable. Positive effects were observed at the top-dose of Glyphosate. More detailed information should be provided with the range-finder. HCD are not represented. Are	RMS: Unfortunately, there are mistakes in table B.6.4-16 (lines are dislocated). The increased values in this table are caused by the positive control CPA and not by glyphosate. There was no evidence of a mutagenic activity of glyphosate in this study. Sorry for this confusion. The table	Open point: RMS to amend table B.6.4-16 in a revised RAR

Genotoxicity (B.6.4)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		there batch details from the HAG source possibly explaining a casual pve result? In addition, contrarily to the text, CPA positive control displays a 0 value in the table B.4-16.	will be corrected in a revised RAR.	
2(18)	Genotoxicity - Vol 1	BE: agreement with DE that overall, glyphosate is devoid of genotoxic properties.	RMS: Agreement	Addressed
2(19)	B.6.4.1 In vitro genotoxicity testing – Bacterial assays for gene mutation, p. 303	EL: In the text it reads: *Some of the studies mentioned in Table B.6.4-1 are considered supplementary because either the plate-incorporation method or the pre-incubation method was performed but not both.* According to the guideline B.13/14 "*Either of them* (pre-incubation or plate incorporation methods) *is acceptable for conducting experiments both with and without metabolic activation.* Therefore, all these studies must be considered as fully acceptable. Please amend.	RMS: The text and table will be corrected in a revised RAR.	Open point: RMS to amend B.6.4.1 In vitro genotoxicity testing – Bacterial assays for gene mutation, p. 303, in a revised RAR

Genotoxicity (B.6.4)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
2(20)	B.6.4.2 In vitro genotoxicity testing – Tests for gene mutation in mammalian cells B.6.4.3 Tests for DNA damage and repair in mammalian cells and bacteria B.6.4.4 *In vitro* genotoxicity testing – Tests for clastogenicity in mammalian cells	EL: Pls provide the results of the following assays in tabulated form to enable their independent evaluation: Clay, 1996, TOX2000-1994; Jensen (1991, TOX9552372) Rossberger (1994, TOX9400697) 2nd new clastogenicity study *in vitro* (Wright, 1996) 3d new clastogenicity study *in vitro* (Fox, 1998)	GTF: Tabulated data for industry sponsored glyphosate genotoxicity studies are easily accessible on-line and searchable electronically after downloading via open access in the supplemental materials to Kier and Kirkland (2013), Review of genotoxicity studies of glyphosate and glyphosate-based formulations, *Critical Reviews in Toxicology* 43(4): 283-315. DOI:10.3109/10408444.2013.770820. http://informahealthcare.com/doi/abs/10.3109/10408444.2013.770820 RMS: The studies are described in detail in the old DAR (1998) or in the new RAR. Further information see comment of GTF above.	Addressed

Long-term toxicity and carcinogenicity (B.6.5)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
2(21)	Vol. 1, Level 2.6.6 Summary of long-term toxicity and carcinogenicity	ES (MSSSI): An increase in malignant lymphoma incidence is observed in the carcinogenicity studies in mice. We consider the increased incidence of these tumours in Cr1:CD-1 strain mice ([redacted]*l*, 2009; [redacted] 1997; [redacted]., 1993) is not relevant because it is within the historical controls published for this strain. Nevertheless, to evaluate the results of the carcinogenicity study with the strain HsdOLA: MF1 (swiss albino) (kumar, 2001), we deem necessary the historical controls of this strain.	GTF: The test system used (HsdOla: MF1, Hooded Swiss Albino Mice) is rarely used in carcinogenicity testing (not in Europe or US at all) and thus historical control data are very difficult to obtain. Limited historical control data is given in the report. However, as the incidence in control is already outside historical control, it is of very limited use and indicative that the background variation on this most predominant tumour type in mice is significant. RMS: See comment of GTF, no additional information available.	Addressed
2(22)	Rat carcinogenicity studies (Vol 1)	BE: agreement with the approach of the RMS to establish an overall NOAEL of 100 mg/kg b.w./d, for the totality of 9 rat carcinogenesis studies.	GTF: The chronic rat NOAEL of 100 mg/kg b.w./d is for chronic toxicity, not carcinogenicity. Glyphosate is not carcinogenic. RMS: The overall NOAEL of long term toxicity studies in rats is 100 mg/kg bw/day.	Addressed
2(23)	Mouse carcinogenicity studies (Vol 1)	BE: agreement with the approach of the RMS to establish an overall NOAEL of 150 mg/kg b.w./d, for the totality of 7 mouse	GTF: The chronic mouse NOAEL of 150 mg/kg b.w./d is for chronic toxicity, not carcinogenicity. Glyphosate is not	Addressed

Long-term toxicity and carcinogenicity (B.6.5)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		carcinogenesis studies.	carcinogenic. RMS: The overall NOAEL of long term toxicity studies in mice is 150 mg/kg bw/day.	
2(24)	List of endpoints, Long term toxicity and carcinogenicity	GTF: Carcinogenicity: the indication "very limited evidence in mice..." may give an erroneous and overly conservative indication of glyphosate's carcinogenicity potential. The notifier suggests removing this indication. The conclusion should read "Not carcinogenic in rats and mice at relevant doses". *For further explanation please refer to Column 3 of the original commenting table.*	GTF: The extraordinarily large database on glyphosate is considered a sufficient basis to clearly conclude that glyphosate is not carcinogenic in rats at mice at relevant doses. RMS: It is proposed to mention the lymphoma in male mice in the LOEP for reasons of transparency. However, it is clearly indicated that a classification and labelling is not required.	Addressed
2(25)	Vol. 1, Level 1, 2.6.1, Overall Summary, page 35	GTF: See paragraph 7 of this section. Further rationale is requested to clarify the basis for the lack of carcinogenicity concern for glyphosate in humans. Propose the additional underlined text. "At the highest dose level of 1460 mg/kg bw/day (10 000 ppm), in one of five studies there was an increase in the incidence of malignant lymphoma in male mice. This type of tumour is quite common	RMS: We assume that all relevant information of the underlined text is already contained in the summary.	Addressed

Long-term toxicity and carcinogenicity (B.6.5)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		in aging mice and was also found in a high incidence in the control group of this study. There was no significant increase in the incidences of malignant lymphoma in 4 other studies even in the higher dose range up to 40000 ppm (4348 mg/kg bw/day). Considering that the described effect was not reproducible in studies even at higher doses, and that high incidences of malignant lymphoma were found in the untreated control, it is concluded that a true tumorigenic response in the mouse is highly unlikely. Together with the absence of genotoxicity, glyphosate was considered unlikely to be carcinogenic in humans. It is relevant to note that the slight elevation of malignant lymphoma in males at 1460 mg/kg bw/day is well in excess of the current OECD 453 Test Guideline (OECD, 2009) limit dose of 1000 mg/kg bw/day.		

Long-term toxicity and carcinogenicity (B.6.5)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
2(26)	Vol. 3, Annex B.6.5.3, Published data on carcinogenicity, page 518	GTF: Regarding the RMS review of Hardell and Eriksson (1999, ASB2012-11838) and Hardell et al. (ASB2012-11839). *For further explanation please refer to Column 3 of the original commenting table.*	RMS: The mentioned studies are considered to be not reliable. Therefore, neither a positive relation nor the absence of a relation between glyphosate and NHL is evidenced by these studies.	Addressed

Reproductive toxicity (B.6.6)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
2(27)	Vol. 1, Level 2.6.7 Summary of reproductive toxicity	ES (MSSSI): In the developmental toxicity study in rabbits ([redacted] 1991-TOX9552391), there was an increase in interventricular septal defects (4.2%), at high dose (450 mg/kg b.w./d). At this dose this effect was outside the historical controls range (0.66%) and it occurs without maternal toxicity. Therefore a classification for glyphosate due to developmental toxicity shall be considered.	GTF: The cited cardiac endpoints have been thoroughly analysed and were found unrelated to treatment. The results of the analysis have passed rigorous scientific peer review in a highly regarded, quality Toxicology Journal [Kimmel GL, Kimmel CA, Williams AL, DeSesso JM (2013) Evaluation of developmental toxicity studies of glyphosate with attention to cardiovascular development. Crit. Rev. Toxicol. 43(2):79-95]. Citing page 89 of the expert summary of Brooker et al. (1991) in	See 2(41)

Reproductive toxicity (B.6.6)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			the above review reinforces expert opinion that glyphosate does not display selective developmental toxicity. "Based on clinical signs and decreased food consumption at 150 and 450 mg/kg/day, the NOAEL for maternal toxicity is considered to be 50 mg/kg/day. There was a slight increase in fetuses with malformations at 450 mg/kg/day. Several of the cardiovascular malformations that were observed, particularly in the high dose group, occurred in the same animals (Table A4) and are related to a single morphogenetic mechanism (i.e. displacement of the developing aorticopulmonary septum), which may adjust during the postnatal period as some of these improve during the first few months of life in humans (Hoffman and Kaplan, 2002). These mechanistically related findings, which often cluster together, include dilated/narrow aorta and narrow/dilated pulmonary artery; IV septal defect and disproportionately sized right and left ventricles. These malformations and the associated morphogenetic mechanism are discussed in greater detail in the integrated assessment	

Reproductive toxicity (B.6.6)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			below. These findings in the heart were also observed (often in clusters) in the historical control data provided by [redacted] (1991a). Overall, the malformation data showed an increase at 450 mg/kg/day (not statistically significant) and all findings in the glyphosate-treated groups were within historical control ranges." RMS: Maternal toxicity (lethality, clinical signs) and fetal malformations occurred at highest dose level of 450 mg/kg bw/d. A classification seems to be not necessary.	
2(28)	Vol 3, B.6.6.1 Two-generation studies ([redacted] 2007)	BE: agrees with the RMS to establish the parental, reproductive and offspring toxicity NOAEL at 5000 ppm. The 23% reduction of spermatids and +3d preputial separation delay in F_1 should not be disregarded.	RMS: Agreement	Addressed

Reproductive toxicity (B.6.6)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
2(29)	Vol 3, B.6.6.1 Two-generation studies ([redacted] 1997)	BE: it is not entirely clear why the 20% decrease of fertility index in the F_1 was considered non-treatment-related (the next-lower dose showed a decrease too, thus there was a trend). The reason to disregard this finding (a re-meeting with untreated males restored a normal fertility index) is not considered valid (the test methods foresees re-mating with treated males of the same dose-group). BE would take the top-dose effect into account to establish the fertility NOAEL for this study. Agreed that the effect was not observed in the other multigeneration studies. Are there historical control data?	Historical control data were not available at the time of the study because this was the first study of this type conducted with this strain of rat, IGS, at the Institute of Environmental Toxicology (IET), Japan. The data owner has requested control data for subsequent studies conducted at IET. The F1 fertility indices in [redacted] (1997) are not consistent with the most recent multigenerational study in the same strain of rat by [redacted] (2007), with the following F1 fertility indices. 0 ppm 95.8% (23/24) 1500 ppm 95.8% (23/24) 5000 ppm 100% (24/24) 15000 ppm 95.8% (23/24) If the reported F1 effects in [redacted] (1997) were test substance induced, the results would have been reproducible in [redacted] (2007). RMS: Agreed. The NOAEL should be set at 6000 ppm (417 mg/kg bw/d), although the decreased fertility index at 30000 ppm	Addressed RMS to consider the information in a revised RAR

Reproductive toxicity (B.6.6)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			(>2000 mg/kg bw) was statistically not significant. The RAR will be revised accordingly.	
2(30)	Vol 1, Level 1, 2.6.6.2, Summary of long-term toxicity and carcinogenicity - Mouse, page 61	GTF: In the table 2.6-8 b we suggest revised wording all three studies under "Targets / Main Effects". Suggested changes in **bold**. [redacted] (2009): **No evidence of test substance related cancer.** [redacted] (2001): Higher incidence of malignant lymphoma at top dose level (outside **limited** historical control range for males) **at excessively high doses**; cytic glands in stomach in m[ales]↑ (equivocal toxicological relevance) [redacted] (1997): Bw gain, food consumption and efficiency↓, loose stool, caecum distended and organ wt↑, prolapse and ulceration of anus in m[ales]. **No evidence of test substance related cancer.**	RMS: The headline of this column in table 2.6-8 b is: targets/main effects. Therefore, only targets and main effects are reported here.	Addressed
2(31)	Vol 1, 2.6.7, LoEP evaluation reproductive toxicity	BE: agrees with the establishment of the overall parental and offspring NOAEL= 197 mkd and the reproductive NOAEL= 351 mkd, taking into account all one- and two-generational studies.	RMS: Thank you. However, according to the comment by El 2(37)] we propose to revise the parental NOAEL in the LOEP: As stated in the RAR (please refer to Vol. 1) the overall parental (&offspring) NOAEL is considered to be 300 mg/kg bw/d, despite the	Addressed

Reproductive toxicity (B.6.6)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			lowest observed NOAEL of 197 mg/kg bw/d ([redacted] *1992*,LOAEL 668 mg/kg bw/d) which resulted from dose selection.	
2(32)	Vol 1, 2.6.7.2.2, LoEP evaluation developmental toxicity	BE: agreement with the approach of the RMS to establish an overall rabbit maternal and developmental NOAEL of 50 mg/kg b.w./d.	GTF: Overall rabbit developmental toxicity study NOAEL for maternal effects is believed to be 75 mg/kg/day, based on [redacted] (1980, TOX2552390) and supported by the maternal NOAEL of 100 mg/kg/day in 2 robust developmental toxicity studies ([redacted] 1995, ASB2012-11498; & [redacted] 1996, TOX2000-2001). See comment 2 (33 & 34). RMS: Thanks to BE!	Addressed
2(33)	Vol. 1, Level 1, 2.6.7.2.2, Developmental toxicity and teratogenicity – Rabbit, page 73	GTF: The GTF again questions the reliability and utility of this study for establishing a LOAEL for maternal toxicity in rabbits. The GTF respectfully suggests that the additional safety margin for risk assess-ment (disregarding the 75 mg/kg/day NOAEL in [redacted] 1980, TOX2552390) as proposed by the RMS, is not necessary. *For further explanation please refer to Column 3 of the original commenting table.*	RMS: Again not agreed. According to the study report, one gavage error was reported in the control group, but not at 100 and 500 mg/kg bw/d. Assuming technical incompetency as the main reason for lethality at mid and high dose level, one would expect the same observations at lowest dose level. Furthermore, at highest dose level 3 out of 8 animals died post-treatment, which can not be related to administration procedure, definitely.	Addressed

Reproductive toxicity (B.6.6)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
2(34)	Vol. 1, Level 1, 2.6.7.2.2, Developmental toxicity and teratogenicity – Rabbit, page 74	GTF: Overall rabbit developmental toxicity study NOAEL for maternal effects is believed to be 75 mg/kg/day, based on [redacted] (1980, TOX2552390) and supported by the maternal NOAEL of 100 mg/kg/day in 2 robust developmental toxicity studies ([redacted] 1995, ASB2012-11498; & [redacted] 1996, TOX2000-2001). Further discussion of observations indicating GI effects in rabbits warrant discussion. *For further explanation please refer to Column 3 of the original commenting table.*	RMS: Again, the multitude of developmental toxicity studies in rabbits revealed a heterogeneous picture regarding the tolerance towards Glyphosate expressed in differing NOAELs and LOAELs. The overall NOAEL is proposed to be 50 mg/kg bw/d instead of 75 mg/kg bw/d, because the latter was too close to a dose causing maternal lethality in another study in rabbits and therefore considered to be supportive.	Addressed
2(35)	Vol. 1, Level 1, 2.6.7.2.2, Developmental toxicity and teratogenicity – Rabbit, page 75	GTF: The GTF respectfully disagrees with the RMS and restates their opinion that the developmental NOAEL in [redacted] (1996, ASB2012-11499) is 400 mg/kg/day, with no evidence to test substance related dose-response and citing the following published expert review which was included in the RAR literature review; Kimmel et al., 2013, Evaluation of developmental toxicity studies of glyphosate with attention to cardiovascular development, *Crit Rev Toxicol*, 2013; 43(2): 79–95	RMS: As already stated, the NOAEL is considered to be 50 mg/kg bw/d due to significantly increased post-implantation loss at 200 mg/kg bw/d. The statement, that this increase was caused by a slight rise in early foetal deaths and not in late foetal deaths, as seen at the high dose level and therefore considered not to be treatment-related, cannot be followed, because there is no information given regarding the mechanism behind this foetal deaths.	Addressed

Reproductive toxicity (B.6.6)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		For further explanation please refer to Column 3 of the original commenting table.		
2(36)	Vol. 1, Level 1, 2.6.7.2.2, Developmental toxicity and teratogenicity – Rabbit, page 76	GTF: Further discussion of observations indicating GI (non-systemic) effects in orally dosed rabbits. *For further explanation please refer to Column 3 of the original commenting table.*	RMS: These further explanations were already noted in the original Commenting Table (2013).	Addressed
2(37)	Vol. 1, Level 2, 2.6.7.1 Multi generation studies	EL: Although it was concluded that the 'overall' parental NOAEL is in the magnitude of 300-400 mg/kg b.w./day, based on the overall database for reproductive toxicity, the NOAEL = 197 mg/kg b.w./day was eventually included in the LoEP as relevant parental NOAEL. The reasoning for not using the highest parental NOAEL as most relevant should be presented by the RMS.	RMS: Agreed. The NOAEL given in the LOEP will be adapted according the 'overall' parental NOAEL of 300 mg/kg bw/d (when the LOEP will be revised).	Open point: RMS to amend the list of end points with regard to the reproductive toxicity NOAELs
2(38)	Vol. 1, Level 2, 2.6.7 Summary of reproductive toxicity	EL: The RMS has presented quite a comprehensive review of the available data on the endocrine disrupting properties of glyphosate and glyphosate based formulations. The available data are suggestive of potential endocrine disrupting	GTF: Literature relating to endocrine disruption, dominated by in vitro publications from the Seralini research group, has been evaluated in detail in the RAR; much of the endocrine disruption literature was considered in the RAR as	Addressed.

Reproductive toxicity (B.6.6)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		properties. The outcome of this review and the endocrine disrupting potential of glyphosate should be discussed in a meeting of experts.	unreliable for human health risk assessment. The comprehensive subchronic, developmental and reproductive toxicology data set does not trigger concerns about an endocrine toxic potential of glyphosate. Data from the US EPA Endocrine Disruptor Screening Program Tier 1 Screening Studies have also been documented and presented at public scientific meetings (Society of Toxicology 2012 [ASB2012-12016], 2013 [ASB2013-3464]; American College of Toxicology, 2012; Society of Environmental Toxicology and Chemistry, 2012; SETAC Focus Topic Meeting on Endocrine Disruptors, February 2014). These study data clearly demonstrate a lack of potential for glyphosate to interact with the androgen, oestrogen and thyroid pathways. The RMS concludes in Volume 3, page 661; "Therefore, on basis of this comprehensive and high quality data package the active substance glyphosate is not considered to be an endocrine disruptor or a teratogenic substance". Further discussion in Volume 3, pages 661-663 sufficiently summarize to scope of relevant literature on the topic of	

Reproductive toxicity (B.6.6)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			endocrine disruption, and should be considered adequate to warrant no further discussion on this topic at an expert meeting. RMS: Glyphosate is not considered to be an endocrine disruptor.	
2(39)	B.6.6.11 Teratogenicity test by oral route in the rabbit,	FR: In several developmental studies in rabbit suspected occurrence of heart malformations were observed. Indeed, in the study by [redacted] (1995) cardiac malformation mainly intraventricular septal defect was observed at 450 mg/kg/d, higher tested dose. This heart finding was slightly outside of the historical background. Moreover, post implantation losses and late embryonic death were also observed in the high-dose group (450 mg/kg/d). In the study by [redacted] (1993), the percentage of fetuses with "dilated heart" was increased in the high dose group despite a low number of fetuses and litters included in the high-dose group. Moreover, in the study by [redacted] (1989), ventricular septal defects as in the study by [redacted] (1991) were also noted in the high dose group. A higher number of further visceral malformations at	GTF: The cited cardiac endpoints have been thoroughly analysed and were found unrelated to treatment. The results of the analysis have passed rigorous scientific peer review in a highly regarded, quality Toxicology Journal [Kimmel GL, Kimmel CA, Williams AL, DeSesso JM (2013) Evaluation of developmental toxicity studies of glyphosate with attention to cardiovascular development. *Crit. Rev. Toxicol.* 43(2):79-95]. Citing page 89 of the expert summary of [redacted] (1991) in the above review reinforces expert opinion that glyphosate does not display selective developmental toxicity. "Based on clinical signs and decreased food consumption at 150 and 450 mg/kg/day, the NOAEL for maternal toxicity is considered to be 50 mg/kg/day. There was a slight	See 2(41)

Reproductive toxicity (B.6.6)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		the top dose level were due to kidneys defects. The relevance of the heart and kidney findings observed in several studies should be discussed at an expert meeting.	increase in fetuses with malformations at 450 mg/kg/day. Several of the cardiovascular malformations that were observed, particularly in the high dose group, occurred in the same animals (Table A4) and are related to a single morphogenetic mechanism (i.e. displacement of the developing aorticopulmonary septum), which may adjust during the postnatal period as some of these improve during the first few months of life in humans (Hoffman and Kaplan, 2002). These mechanistically related findings, which often cluster together, include dilated/narrow aorta and narrow/dilated pulmonary artery; IV septal defect and disproportionately sized right and left ventricles. These malformations and the associated morphogenetic mechanism are discussed in greater detail in the integrated assessment below. These findings in the heart were also observed (often in clusters) in the historical control data provided by [redacted] (1991a). Overall, the malformation data showed an increase at 450 mg/kg/day (not statistically significant) and all findings in the glyphosate-treated groups were within	

Reproductive toxicity (B.6.6)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			historical control ranges." RMS: Agreed	
2(40)	B.6.6.11 Teratogenicity test by oral route in the rabbit,	FR: These effects on cardiovascular development (described above) were discussed in the published review of Kimmel et al. (Crit Rev Toxicol. 2013 Feb;43(2):79-95). The analysis of this review concluded that the observed cardiac malformations were not related to treatment. This article could be more detailed allowing this statement.	RMS: The study of Kimmel et al. (2013) is mentioned in B.6.6.12, page 661. More details of this analysis will be reported in a revised RAR.	Addressed RMS to consider in a revised RAR
2(41)	Vol. 3, B.6.6.11, IIA, 5.6.11/05 The Effect of Glyphosate on Pregnancy of the Rabbit [redacted] 1991a)	NO: The NOAEL for developmental toxicity in this study should be set at 50 mg/kg/day based on the increase in the occurrence of the retroesophageal right subclavian artery at 150 mg/kg/day. Based on the increase in the occurrence of the cardiovascular malformations and in the post- implantation loss in this study, glyphosate should be considered for a classification as a developmental toxicant. The developmental toxicity study in the rabbit ([redacted], 1991a) shows a treatment-related increase in a variety of	GTF: See GTF comments to 2(39) and France comments 2(40). The appropriate developmental toxicity point of departure based on the rabbit developmental toxicology data set should be set at the highest relevant developmental NOAEL of 175 mg/kg b.w./day, as outlined below. Pooling data for developmental effects in rabbits clearly demonstrates that 175 mg/kg bw/day is the NOAEL for developmental toxicity. Dose (mg/kg bw/d); Developmental Effects; Study (AIR Ref.)	Expert consultation The developmental toxicity potential of glyphosate to be discussed in a meeting of experts.

Reproductive toxicity (B.6.6)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		malformations of the heart and great vessels (interventricular septal defects, retroesophageal right subclavian artery and other malformations) at 450 mg/kg/day. An increase, above the historical control data, in the retroesophageal right subclavian artery was also seen at 150 mg/kg/day. The increase in the occurrence of this malformation did not follow a clear dose-response. However a possible dose-response relationship for this effect may have been masked by the limited number of fetuses at the highest dose level. A treatment-related increase in the post-implantation loss was seen at 450 mg/kg/day. This parameter was also statistically significant increased at 50 and 150 mg/kg/day, but without a clear dose-response. The developmental toxicity was observed in the presence of maternal toxicity. One death occurred at 450 mg/kg/day. However, the maternal toxicity observed in the remaining dams consisted of a slight reduction in the body weight gain associated with a reduction in food	10; No Adverse Effects; [redacted] (1995, ASB2012-11498) 20; No Adverse Effects; [redacted] (1993, TOX9551106) 50; No Adverse Effects; [redacted] (1996, ASB2012-11499) 50; No Adverse Effects; [redacted] (1991, TOX9552393) 75; No Adverse Effects; [redacted]. (1980, TOX9552392) 100; No Adverse Effects; [redacted] (1995, ASB2012-11498) 100; No Adverse Effects; [redacted] (1996, TOX2000-2001) 100; No Adverse Effects (insufficient number of adults and litters); [redacted] (1993, TOX9551106) 125; No Adverse Effects; [redacted] (1989, TOX9551960) 150; No Adverse Effects; [redacted] (1991, TOX9552393) 175; No Adverse Effects; [redacted] (1996, TOX2000-2001) 175; No Adverse Effects (supplementary data due to insufficient number of litters);	

Reproductive toxicity (B.6.6)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		consumption. An increase in the occurrence of soft/liquid faeces was also observed, but gross-examination at necropsy did not identify any treatment-related findings. The NOAEL for developmental toxicity in this study should be set at 50 mg/kg/day based on the increase in the occurrence of the retroesophageal right subclavian artery at 150 mg/kg/day Based on the increase in the occurrence of the cardiovascular malformations and in the post- implantation loss in this study, glyphosate should be considered for a classification as a developmental toxicant. This is in accordance with the guidance on the application of the CLP criteria (guidance to regulation (EC) No 1272/2008 on classification, labelling and packaging (CLP) of substances and mixtures, version 4, 2013): Annex I: 3.7.2.4.2 *`Based on pragmatic observation, maternal toxicity may, depending on severity, influence development via non-*	[redacted] (1980, TOX9552392) 200; Increased post-implantation loss (early foetal death); [redacted] (1996, ASB2012-11499) 250; No Adverse Effects; [redacted] (1989, TOX9551960) 300; Abortion/premature delivery; [redacted] (1995, ASB2012-11498) 300; Reduced foetal body weight and reduced ossification; [redacted] (1996, TOX2000-2001) 350; No Adverse Effects (insufficient number of surviving dams and thus litters); [redacted]. (1980, TOX9552392) 400; Increased post-implantation loss (late foetal death); [redacted] (1996, ASB2012-11499) 450; Late embryonic death/post-implantation loss [redacted] (1991, TOX9552393) 500; No Adverse Effects (insufficient number adults and litters); [redacted] (1993, TOX9551106) 500; failed to produce viable litters (aborted or no live fetuses); [redacted] (1989, TOX9551960)	

Reproductive toxicity (B.6.6)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		specific secondary mechanisms, producing effects such as depressed foetal weight, retarded ossification, and possibly resorptions and certain malformations in some strains of certain species. However, the limited number of studies which have investigated the relationship between developmental effects and general maternal toxicity have failed to demonstrate a consistent, reproducible relationship across species. Developmental effects which occur even in the presence of maternal toxicity are considered to be evidence of developmental toxicity, unless it can be unequivocally demonstrated on a case-by-case basis that the developmental effects are secondary to maternal toxicity. Moreover, classification shall be considered where there is a significant toxic effect in the offspring, e.g. irreversible effects such as structural malformations, embryo/foetal lethality, significant post-natal functional deficiencies.´	With regards the with the guidance on the application of the CLP criteria (guidance to regulation (EC) No 1272/2008 on classification, labelling and packaging (CLP) of substances and mixtures, version 4, 2013) the GTF does not believe the trigger for classification is met. Given that the proposal for the overall maternal NOAEL for glyphosate is 50 mg/kg bw/day any developmental effects related to glyphosate treatment were only observed at doses that were considered to be in well within the range of maternal toxicity. Many of these effects, such as reduced foetal bodyweight, reduced ossification and increased post-implantation lost (reduced fetal litter size) can be related to the degree of maternal toxicity observed (Tyl, 2012). Review of all the developmental toxicity studies in the rabbit indicates that there is no correlation between cardiovascular malformations and treatment with glyphosate. Tyl, R. W., 2012. Commentary on the Role of Maternal Toxicity on Developmental Toxicity. Birth Defects Research (Part B) 95: 262-266.	

Reproductive toxicity (B.6.6)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			RMS: In any case, the overall NOAEL for developmental toxicity is considered to be 50 mg/kg bw/d. But a classification as a developmental toxicant seems not to be necessary.	
2(42)	Vol. 3, Annex B.6.6.11, Teratogenicity test by the oral route in the rabbit, IIA, 5.6.11/02, [redacted] 1996, (ASB2012-11499), page 607	GTF: The GTF respectfully disagrees with the RMS and restates their opinion that the developmental NOAEL in [redacted] (1996, ASB2012-11499) is 400 mg/kg/day, with no evidence to test substance related dose-response and citing the following published expert review which was included in the RAR literature review. Kimmel et al., 2013, Evaluation of developmental toxicity studies of glyphosate with attention to cardiovascular development, *Crit Rev Toxicol*, 2013; 43(2): 79–95 *For further explanation please refer to Column 3 of the original commenting table.*	RMS: As already stated, the NOAEL is considered to be 50 mg/kg bw/d due to significantly increased post-implantation loss at 200 mg/kg bw/d. The statement, that this increase was caused by a slight rise in early foetal deaths and not in late foetal deaths, as seen at the high dose level and therefore considered not to be treatment-related, cannot be followed, because there is no information given regarding the mechanism behind this foetal deaths. Furthermore, the published expert review by Kimmel et al. was already available when preparing the first draft of the RAR.	Addressed
2(43)	Vol. 3, Annex B.6.6.11, Teratogenicity test by the oral route in the rabbit, IIA, 5.6.11/04, [redacted]	GTF response to RMS comment (August 2013): *What is the idea behind this comment? It is only a summary of the conclusion/comment given by the RMS in the*	RMS: It remains still unclear. Only the NOAELs for maternal and developmental toxicity in this supplementary study were described by GTF. However, these values	Addressed

Reproductive toxicity (B.6.6)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
	al., 1980 (TOX9552392), page 607	*Draft RAR.* page 635 *For further explanation please refer to Column 3 of the original commenting table.*	have already been suggested by the RMS in the first Draft of the RAR..	
2(44)	Vol. 3, Annex B.6.6.11, Teratogenicity test by the oral route in the rabbit, IIA, 5.6.11/06, [redacted] 1993 (TOX9551106), page 607	GTF: The GTF again questions the reliability and utility of this study for establishing a LOAEL for maternal toxicity in rabbits. The GTF respectfully suggests that the additional safety margin for risk assessment (disregarding the 75 mg/kg/day NOAEL in [redacted] 1980, TOX2552390) as proposed by the RMS, is not necessary. *For further explanation please refer to Column 3 of the original commenting table.*	RMS: Not agreed. According to the study report, one gavage error was reported in the control group, but not at 100 and 500 mg/kg bw/d. Assuming technical incompetency as the main reason for lethality at mid and high dose level, one would expect the same observations at lowest dose level. Furthermore, at highest dose level 3 out of 8 animals died post-treatment, which can not be related to administration procedure, definitely.	Addressed
2(45)	Vol. 3, B.6.6.12 (page 662)	NL: The publication by Mesnage et al. (in press, ASB2012-13917) is published in 2013 in its final form (Toxicology 313(2-3): 122-128, 2013). Please also correct in reference list.	RMS: The reference will be completed in an revised RAR.	Addressed RMS to consider in a revised RAR

Reproductive toxicity (B.6.6)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
2(46)	Vol. 3, B.6.6.12 (page 536)	NL: The paper discussed, by Seralini et al. (ASB2012-15514), has meanwhile been retracted. This could be reason to remove it from the RAR, or it should at least be mentioned. NB there is also a reference to it on page 621.	GTF: Agreed RMS: see comment 2 (89)	Addressed
2(47)	Vol.3, Annex B.6.6.12, Published data, Page 687, 688	GTF: Aris et Leblanc 20011 "Maternal and fetal exposure to pesticides associated to genetically modified foods in Eastern Townships of Quebec, Canada." Monsanto's letter to the editor which was submitted in the dossier is not referenced. *For further explanation please refer to Column 3 of the original commenting table.*	RMS: All available original studies have been reported in the RAR. However, it is not possible to include additionally all opinions and unshortened letters of notifiers.	Addressed

Neurotoxicity (B.6.7)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
2(48)	B.6.7.1	DK: Could you please include and evaluate the reference "Malhotra RC, Ghia DK, Cordato DJ, Beran RG. Glyphosate surfactant herbicide-induced reversible encephalopathy. *J Clin Neurosci* 2010; **17:** 1472–73."	GTF: This is case report of a 71 year old male's attempted suicide via ingestion of a formulated glyphosate product. He was found unresponsive, in cardiac shock with severe metabolic acidosis. He was initially misdiagnosed and treated for OP poisoning with intravenous atropine and pralidozime for 48 hours. This unfortunate report of extreme intentional exposure is confounded by misdiagnosis/treatment to restore pharmacological balance and brings little to bear on the human health risk assessment of glyphosate and Annex I Renewal. The reported prolonged encephalopathy is not consistent with other case reports or the glyphosate toxicology data base. RMS: The reference will be reported in a revised RAR.	Data requirement: Applicant to submit the study by Malhotra RC, Ghia DK, Cordato DJ, Beran RG. Glyphosate surfactant herbicide-induced reversible encephalopathy. *J Clin Neurosci* 2010; **17:** 1472–73.
2(49)	Vol. 3 B.7 Neurotoxicity	EFSA: the delayed neurotoxicity study in chicken by [redacted] (1996 ASB2013-9828) needs to be submitted.	GTF: This study has been submitted to the RMS. RMS: This study is reported in Vol. 3, B7, page 701-704.	Addressed

Other toxicological studies & Medical data (B.6.8-B.6.9)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
2(50)	Vol. 3, Annex B.6.8.2.1, Studies on mechanisms of salivary gland findings, page 729	GTF: This section repeats the previous DAR position under "*Copy from the previous DAR: Possible explanation for salivary gland alterations",* without consideration of the evaluations by Williams et al. (2000) and the 2004 JMPR review of this endpoint. *For further explanation please refer to Column 3 of the original commenting table.*	RMS: It is repeated because we have maintained our previous position. RMS is aware of the Williams paper and of the JMPR review. The comment has not impact on general assessment of glyphosate and no revisions are needed.	Addressed
2(51)	Vol. 3, Annex B.6.8.2.1, Studies on mechanisms of salivary gland findings, Effects of citric acid ([redacted] 2010), page 729	GTF: Regarding RMS comments on [redacted] (2010), "*However, in principle, severe organ weight and histological changes may become adverse even if they are adaptive by nature."* *For further explanation please refer to Column 3 of the original commenting table.*	RMS: The study of [redacted] (2010) investigated effects of citric acid and not of glyphosate. In the comment of the RMS to this study a general statement to the observed effects and to the conclusions of the notifiers was included. No further comments are considered necessary.	Addressed

Other toxicological studies & Medical data (B.6.8-B.6.9)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
2(52)	Vol. 3, Annex B.6.8.2.1, Studies on mechanisms of salivary gland findings, Comparison of sensitivity of different rat strains to salivary gland lesions ([redacted] 1996), RMS comments page 740	GTF: The GTF is of the opinion that changes in salivary glands result from constant exposure to a low pH diet. *For further explanation please refer to Column 3 of the original commenting table.*	RMS: The study of [redacted] (1996) is commented by the RMS in the RAR. No further comments are considered necessary.	Addressed
2(53)	Vol. 3, Annex B.6.8.2.1, Studies on mechanisms of salivary gland findings, Comparison of sensitivity of different rat strains to salivary gland lesions ([redacted] 1996), RMS comments page 740	GTF: The incidence of basophilia of parotid acinar cells in F344 rats in the control group was 7/8, 0/8 & 1/8 at different time points throughout this study. This suggests that there is a large variation in the background incidence of this finding in this strain of rat. Basophilia of parotid acinar cells was observed in 6/8 and 5/8 animals after 4 and 13 weeks recovery respectively. This incidence is well within the control incidence of this finding observed in this strain in this study. *For further explanation please refer to Column 3 of the original commenting table.*	RMS: Agreement that the high incidence in the control group suggests a large variation in the background incidence of this finding in this strain.	Addressed

Other toxicological studies & Medical data (B.6.8-B.6.9)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
2(54)	B.6.8.3.3.	DK: Krüger *et al.* (2013, ASB2013-11599). We support the assessment of the aforementioned study. It could be further added that the positive correlation (if indeed there is one – we agree that this has not been properly shown due to unknown origin of the reference-values) between urea and glyphosate lacks plausibility. If urea was indeed above the reference value, indicating some kind of renal dysfunction, a lower clearance of glyphosate would be the consequence and therefore *lower* urine glyphosate. Such a negative correlation was seen in relation to creatinine. In conclusion, two so divergent findings of markers of renal function suggest that these are random.	RMS: The additional comment will be considered in a revised RAR.	Addressed
2(55)	B.6.8.3.3.	DK: Could you please include and evaluate the reference Samsel et Seneff « Glyphosate's Suppression of Cytochrome P450 Enzyme and amino acid biosynthesis by the gut microbiome : Pathways to modern diseases » *Entropy* **2013**, *15*, 1416-1463; doi:10.3390/e15041416	GTF: Published in the physics journal *Entropy*, this paper attempts to outline possible causal connections between glyphosate and numerous diseases, including autism, Alzheimer's, obesity, anorexia nervosa, liver disease, reproductive and developmental disorders, and cancer. The author's choice to publish in a journal of	Data requirement Applicant to submit the study by reference Samsel et Seneff « Glyphosate's Suppression of Cytochrome P450 Enzyme and amino acid biosynthesis by the gut microbiome : Pathways to modern diseases » *Entropy* **2013**, *15*, 1416-

Other toxicological studies & Medical data (B.6.8-B.6.9)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			physics most likely would not have subjected the paper to appropriate peer review by experts in relevant fields of biology and medicine. On the surface, this paper appears to have a high level of scientific content and a large number of references (relevant citations are reviewed in the RAR); however the authors' approach is based on weakly-supported hypothetical relationships. The paper provides no new data and is of insufficient scientific quality to provide any useful information related to the safety of glyphosate. This paper does not meet the criteria as relevant glyphosate toxicology or epidemiology literature for consideration in the RAR. On-line critique available at http://pipeline.corante.com/archives/2013/04/30/is_glyphosate_poisoning_everyone.php RMS: The study will be reported in a revised RAR.	1463
2(56)	B.6.5.3 Published data on carcinogenicity -	BE: The overall lack of association between potential glyphosate exposure and specific	RMS: The review will be reported in a revised RAR.	Data requirement Applicant to submit *Mink et al,*

Other toxicological studies & Medical data (B.6.8-B.6.9)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
	Epidemiological studies	cancer incidence is considered sufficiently demonstrated in the open literature. A further recent systematic review on this topic (*Mink et al, Regulat Toxicol Pharmacol, 63, 440-452, 2012*) further supports this evaluation.		*Regulat Toxicol Pharmacol, 63, 440-452, 2012*
2(57)	B.6.5.3 Published data on carcinogenicity - animal studies	BE: supports the RMS evaluation on the existing open literature. The Seralini study is pointless, and moreover withdrawn. The skin tumour promoting study of George et al. indicates a certain activity of the product, where it is unknown what the influence is of the coformulant. Given the known toxicity profile of Glyphosate itself, it seems highly unlikely that the latter would have any tumour promoting activity. The study is not entirely conclusive, as no proper negative control is present, is not in favour of the maintenance of the coformulant!	GTF: Given the conclusion of the additional comments on this publication in Volume 3, page 536, the comment that this "is not in favour of the maintenance of the coformulant!" is not justifiable. "The up-regulation / down-regulation of protein expression reported after a single dermal dose of a glyphosate formulated product (proteomics experiment, group II), while interesting, does not demonstrate any toxicological endpoint. Rather, perturbations may well represent normal homeostatic fluctuations and be a natural response to insult." RMS: Agreement that the study is not entirely conclusive. A commercial formulation was used. However, the results	Addressed

Other toxicological studies & Medical data (B.6.8-B.6.9)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			are discussed as glyphosate effects by the authors. There is no evidence if observed effects are caused by glyphosate or co-formulants. Therefore, no conclusion on the toxicity of the active substance or any co-formulant can be based on this study.	
2(58)	B.6.6.12 Published data on endocrine perturbation	BE: concurs with the RMS evaluation of all published papers on alleged *in-vivo* or *in-vitro* endocrine effects of glyphosate.	RMS: Agreement	Addressed

Summary of mammalian toxicology and setting of ADI, AOEL and ARfD (B.6.10)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
2(59)	Vol. 1, Level 2.6.12 Toxicological end point for assessment of risk following long-term dietary exposure - ADI	ES (MSSSI): Erratum: The study code of the development toxicity study in rabbit is [redacted] 1991, TOX9552391. Therefore, where it says `TOX9552393´ it should say `TOX9552391´.	RMS: The study code will be corrected in a revised RAR.	Addressed RMS to consider in a revised RAR
2(60)	Vol. 1, Level 1, 2.6.12,	GTF: The notifiers agree with the RMS that [redacted] (1980, TOX9552392) is not	RMS: Agreement was noted since this is exactly the approach that we have taken. The	Addressed

Summary of mammalian toxicology and setting of ADI, AOEL and ARfD (B.6.10)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
	Toxicological end point for assessment of risk following long-term dietary exposure – ADI, page 91	compliant with current guidelines for establishing developmental toxicity due to insufficient numbers of litters produced. However, this study is acceptable for establishing a maternal toxicity NOAEL, as a maximum tolerated dose was attained with a dose-response and NOAEL demonstrated with sufficient numbers of adult rabbits. *For further explanation please refer to Column 3 of the original commenting table.*	downgrading of the study quality to "supplementary" (in contrast to the former EU evaluation) was triggered by the fact that investigating developmental toxicity and teratogenicity of a test substance is the principal reason to perform such a study. Maternal toxicity is also of interest, of course, but not the main objective.	
2(61)	Vol. 1, Level 1, 2.6.12, Toxicological end point for assessment of risk following long-term dietary exposure - ADI, page 91	GTF: The notifiers suggest that findings of maternal toxicity in rabbits reported by [redacted] (1993, TOX9551106) are not consistent with the six other studies of the same design and therefore the lower NOAEL of 100 mg/kg bw/day should be considered unreliable. *For further explanation please refer to Column 3 of the original commenting table.*	RMS: Not agreed. For further explanation please refer to 2(44).	See 2(44)
2(62)	Vol. 1, Level 1, 2.6.12, Toxicological end point for assessment of risk	GTF: The appropriate point of departure for developmental effects in rabbits in the overall NOAEL value of 175 mg/kg bw/day. Therefore the endpoint for developmental	RMS: Not agreed. The justification for deriving the ADI as given under 2.6.12 in Vol. 1 of the DRAR is still considered	Addressed

Summary of mammalian toxicology and setting of ADI, AOEL and ARfD (B.6.10)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
	following long-term dietary exposure - ADI, page 91	toxicity is not a driver for risk assessment purposes. *For further explanation please refer to Column 3 of the original commenting table.*	convincing.	
2(63)	Vol. 1, level 1, 2.6.13 ARfD	FR: Based on the study by [redacted] (1991), the developmental NOAEL of 50 mg/kg bw/d due to post implantation losses is considered acceptable. This effect could be considered as a consequence of cardiac malformation observed in fetuses. The observed post implantation losses could be considered as an acute adverse effect occurring within the first days of treatment. As a consequence, an ARfD could be derived based on this effect on the development and the resulting ARfD for glyphosate would be of 0.5 mg/kg bw/d (with a safety factor of 100).	GTF: Comments to 2(41) provide rationale for a rabbit developmental NOAEL of 175 mg/kg b.w./d. Given the absence of adverse cardiac effects at non-maternally toxic doses, and no pattern of dos-response for these endpoints across the seven rabbit developmental toxicity studies, there is not a sound basis for proposing an ARfD. Regarding the evaluation of cardiac effects, please refer to the expert review cited in comments to 2(39); Kimmel GL, Kimmel CA, Williams AL, DeSesso JM (2013) Evaluation of developmental toxicity studies of glyphosate with attention to cardiovascular development. Crit. Rev. Toxicol. 43(2):79-95. RMS: Necessity for deriving an ARfD should be discussed at expert meeting.	Experts' consultation Necessity for deriving an ARfD to be discussed in a meeting of experts
2(64)	Setting Acute reference	EFSA: can the RMS please confirm that deaths in rabbits, recorded in different	GTF: Nearly all mortality occurred towards	Addressed

Summary of mammalian toxicology and setting of ADI, AOEL and ARfD (B.6.10)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
	dose	studies, do not occur in the first days of exposure?	study end, not near study start. [redacted] all deaths that were not proven acute consequences of gavaging errors occurred between day 7 and 19 [redacted] three, gestation day (GD) 16, 19 & 20. [redacted] one, GD 20 [redacted] four, GD 20-25 [redacted] one at GD 20. Two other deaths unrelated to treatment (broken hind leg and congenital abnormality). [redacted] one each at GD 3, 12, 14, 17, 22, 25 and 26. Three each at GD 18 and 21. RMS: The available data do not reveal any evidence for maternal deaths in rabbits in the first days of treatment.	
2(65)	Vol. 1, Level 2.6.14 Toxicological end point for assessment of occupational and	ES (MSSSI): Erratum: The study code of the development toxicity study in rabbit is [redacted]. 1991, TOX9552391. Therefore, where it says `TOX9552393´ it should say `TOX9552391´.	RMS: The study code will be corrected in a revised RAR.	Addressed

Summary of mammalian toxicology and setting of ADI, AOEL and ARfD (B.6.10)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
	bystander risks - AOEL			
2(66)		BE: RMS agrees with the establishment of the ADI and the AOEL.	GTF: The GTF believes that if both the ADI and AOEL are to be based on the rabbit data then the relevant NOAEL for maternal toxicity (not developmental toxicity) should be taken from the [redacted] study (9552392). The RMS confirmed 75 mg/kg bw/day as the NOAEL for this study. RMS: Agreeement with BE.	Addressed
2(67)	Vol. 1, Level 1, 2.6.14, Toxicological end point for assessment of risk following long-term dietary exposure - AOEL, page 94	GTF: The notifiers do not believe that the overall NOAEL for maternal toxicity in rabbit developmental toxicity studies reflects systemic toxicity in these rabbits. Rather effects were a consequence of gavage dosing of acidic technical glyphosate and local gastrointestinal effects consequent of this route of dosing. The GTF investigated dermal absorption in rabbit skin to estimate systemic exposures for the highest dose tested in repeat dose dermal toxicity studies rabbits. *For further explanation please refer to Column 3 of the original commenting table.*	RMS: The justification for deriving the ADI as given under 2.6.12 in Vol. 1 of the DRAR is still considered convincing	Addressed

Summary of mammalian toxicology and setting of ADI, AOEL and ARfD (B.6.10)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
2(68)	Vol. 1, Level 1, 2.6.14, Toxicological end point for assessment of risk following long-term dietary exposure - AOEL, page 94	GTF: Given the questionable relevance of the rabbit model for establishing a point of departure from systemic toxicity, the GTF proposes the overall NOAEL for chronic rat studies of 100 mg/kg bw/day. *For further explanation please refer to Column 3 of the original commenting table.*	RMS: The allocation of this comment is not entirely clear. It seems that it deals with ADI rather than AOEL setting. The RMS suggests to keep it as proposed with the arguments given in Vol. 1 of the DRAR (2.6.12).	Addressed

Toxicity of the product(s) (B.6.11)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
2(69)	Vol 3, B.6.11- Vol 1, 2.6.15	BE: noted that MON52276 is the representative formulation not containing any ethoxylated [redacted] which have been proven of higher toxicity than the a.s. itself. However, as the inhalative AOEL of another frequently used surfactant CAS [redacted] is 0.016 mg/kg b.w./d. Has it been demonstrated that a safe use exists for products with this coformulant? Is a restriction necessary?	GTF: Toxicology of the representative formulation has been adequately characterized in the Annex III submission, as required. Data gaps have not been identified and communicated to the GTF. RMS: Although there is no data gap in the context of this DAR on glyphosate, it is well known that PPP with both glyphosate and POE-[redacted] gave rise to major concerns with regard to mammalian toxicity in the past. Since some products containing both glyphosate and POE-[redacted] are still on the market the following reply is given to BE: Full risk assessments for glyphosate herbicides containing POE-[redacted] surfactants (CAS No 61791-26-2) have been carried out for the active substance as well as for the above mentioned co-formulants in the context of national authorisation in Germany for more than four years. In any case the AOEL inhalative for POE-[redacted] was not exceeded without using RPE at usual application rates up to now (exposure estimations according to the German model, worst case) so that application has been considered safe from	Addressed The assessment of the toxicological properties of [redacted] does not fall under the glyphosate peer review process. In addition, the representative formulation presented for the renewal process does not contain this surfactant. Further actions might be undertaken by COM for the specific assessement of co-formulants.

Toxicity of the product(s) (B.6.11)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			this perspective. Presentation of respective risk assessments would be beyond the scope of this DAR, since the representative formulation MON52276 does not contain any POE-[redacted]	
2(70)	Vol 3, B.6.11	BE: it may indeed be expected that the ban of irritant and toxic surfactants like POEA's will reduce the risk of severe health effects and death following intentional or accidental ingestion of glyphosate products containing them. A case should be made at the EU- and not only at the zonal level to reach such a restriction.	GTF: Annex 1 Renewal is not a forum for regulating PPPs against mis-use contrary to labelled directions, such as intentional ingestion. Guidance on ARfD setting by Solecki et al. [Guidance on setting of acute reference dose (ARfD) for pesticides, Food and Chemical Toxicology 42 (2005) 1569-1593], notes that specific endpoints relevant to acute effects should be identified to justify an ARfD, and that acute toxicity observed in repeat dose studies should be considered potentially relevant, with weight given to adverse effects noted at the beginning of repeat dose studies. The basis for a POEA ARfD in line with Solecki et al. (2005) has not been presented. RMS: The proposal by BE is supported.	See 2(69)

Toxicity of the product(s) (B.6.11)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
2(71)	Vol. 1, Level 1, 2.6.1, Overall Summary, page 37	GTF: The assessment of POE-[redacted] is not considered to fall under the review of glyphosate. *For further explanation please refer to Column 3 of the original commenting table.*	GTF: The basis for assessing and regulating a single component of one formulation based on having greater toxicity than the active ingredient is not within the scope of glyphosate Annex 1 Renewal. Given that glyphosate has a more favourable toxicological profile than almost all agricultural and industrial chemicals in Europe, this sets a new precedent for the Commission to request evaluation of all coformulants at the EU level when a PPP contains lesser toxicity than an active ingredient. RMS: In the public discussion on the toxicity of glyphosate and even in many scientific studies and papers there is a confusion between glyphosate and preparations like Roundup. Many of the effects which are described for glyphosate are obviously caused by co-formulants. Especially many of the older studies used preparations which contained POE-[redacted] instead of the actives substance. However, the observed effects are often described as substance related effects. For clarification of the very	See 2(69)

Toxicity of the product(s) (B.6.11)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			controversial and confuse discussion it was urgently necessary to submit information on the toxicity of POE-[redacted] and further surfactants.	

Dermal absorption (B.6.12)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
2(72)	Vol. 3, B.6.12.1 Dermal absorption of glyphosate from MON 52276 *in vitro* (Human epidermis)	EL: The dermal absorption values proposed are considered acceptable. The approach that the RMS has followed is in line with the general approach that has been followed even before the EFSA Guidance has come into force. Therefore, the RMS should have no concerns on the validity/applicability of the proposed values.	RMS: Agreement	Addressed
2(73)	B.6.12 Dermal absorption	FR: The preparation MON 52276 is the representation formulation of the Glyphosate Task force. This formulation does not contain any POE-[redacted] For the representation formulation MON 52276, dermal absorption was assessed in vitro on human skin. We agreed	RMS: Agreed. In particular cases in which comparability of formulations can be shown the use of the dermal absorption value (3% for concentrate and dilution) for glyphosate determined using Roundup that contained POE-[redacted] during the first Annex I-inclusion procedure might be taken into	Addressed

Dermal absorption (B.6.12)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		with the dermal absorption rates of 0.1, 0.2 and 0.3% for the high, mid and low concentration. However, for the other formulations the new European Guidance document on dermal absorption (EFSA 2012) should be considered to determine dermal absorption values of glyphosate used for exposure calculation and risk assessment.	account as well.	
2(74)	Vol. 3, Annex B.6.12.2, Dermal absorption of glyphosate active substance *in vitro* (abraded rabbit skin), page 827	GTF: This study was originally submitted in Section B.6.3.1.3 to supplement the repeat dose dermal toxicity study, [redacted] (1982, TOX9552366), in order to calculate the systemic NOAEL from the rabbit repeat dose dermal NOAEL of 5000 mg/kg/day by Johnson. The RMS apparently did not address the purpose of this study in linking this with the [redacted] study to calculate the systemic dose and NOAEL in rabbits, as stated in the opening paragraph of the study summary. *For further explanation please refer to Column 3 of the original commenting table.*	RMS: The dermal study of [redacted] (1982, TOX9552366) was reviewed during the 2001 EU evaluation in the original DAR (1998) and is not repeatedly reported in the RAR. However, the study of Hadfield (2012) was not available for the DAR and is therefore reported now in the RAR. The purpose of this study and the links between the two studies (according to the GTF comment in column 2) have been reported in the RAR in chapters B.6.3.1.3 and B.12.2.	Addressed

Toxicity of non-active substances (B.6.13)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
2(75)	Vol 3, B.6.13	BE: it is obvious that the consumer reference doses from the common POEA coformulant are estimated at a lower level than those of Glyphosate itself. The toxic effects are generally also much more severe. On the basis of this evaluation, a safe use of products containing this coformulant is uncertain. In the estimation of the AOEL, it is assumed that the oral absorption is 100%, which is not supported by facts. The comparison of critical endpoints in table B.6.13-2 for reprotoxicity are not in line (too high) with those listed in the LoEP.	GTF: Given the fact that glyphosate has a robust low toxicity profile, almost any substance added to a formulated product, other than water, will be more toxic than glyphosate alone. Given the lack of numerous significant case reports of non-self-inflicted poisonings after 35 years of widespread use of glyphosate based formulations containing POEA, the basis for evaluating POEA under the scope of glyphosate Annex I Renewal does not appear to be science driven. POEA evaluation is outside the scope of the join submission as per comment 2(80). AOELs are established to be protective of systemic toxicity. The study cited (Velasquez, 1983) reports respiratory effects, considered local irritation effects rather than systemic and is therefore an inappropriate study for establishing a point of departure for AOEL setting. RMS: It was noted that three different issues have been addressed in this comment. (1) We agree that the POE-[redacted] surfactant for which a separate risk	See 2(69)

Toxicity of non-active substances (B.6.13)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			assessment was performed is more toxic than glyphosate. The question if there is a safe use of PPP containing this co-formulant is of no concern for re-evaluation of glyphosate since the representative formulation is different. We have included this appendix into the DRAR to ensure that this information will be taken into consideration throughout the EU when applications for products with this co-formulant will be made. (2) The whole database for the surfactant is much weaker than for the well-investigated glyphosate. A toxicokinetic study is lacking, as for most co-formulants. The proposals for reference values result from pragmatic use that was made of the existing data. (3) The remark on the Table B.6.13-2 is correct. This assessment was made in 2010 and the comparison to glyphosate data was based on the previous EU evaluation (see also our response to 2 (79)). It will be amended in the revised RAR but after the PRAS meeting since the new glyphosate endpoints should be agreed first.	

Toxicity of non-active substances (B.6.13)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
2(76)	Vol. 3, B.6.13.2 Available toxicological data for each formulant	EL: Considering the available data it is highly appreciated that a toxicological evaluation for POE-[redacted] has been included in the RAR for glyphosate. The establishment of EU agreed reference values is supported.	Specific formulation components are outside the scope of the active ingredient Annex I Renewal. The GTF does not agree with the basis of this undertaking or the endpoint selection in the POEA proposed risk assessment. RMS: Agreement, no further comment.	Addressed
2(77)	Vol. 3, B.6.13.3.1 Toxicological evaluation of the POE-[redacted] surfactant (CAS no. 61791-26-2)	EL: An inhalative AOEL of 0.0166 mg/kg b.w./day is proposed by the RMS. Since no toxicokinetic data are available for the examined the POE-[redacted] surfactant, a justification should be provided for the establishment of a higher systemic AOEL (0.1 mg/kg b.w./day).	GTF: AOELs are established to be protective of systemic toxicity. The study cited ([redacted] 1983) reports respiratory effects, considered local irritation effects rather than systemic and is therefore an inappropriate study for establishing a point of departure for AOEL setting. RMS: It was noted that two different issues have been addressed in this comment. (1) A route-specific AOEL may become needed if there is evidence that toxicity by inhalation (as it is the case here) or dermal contact might be higher than by oral ingestion. To derive it, local (irritation) effects may and should be taken into account. However, it should be discussed on the expert meeting, if it was more	See 2(69)

Toxicity of non-active substances (B.6.13)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			appropriate to give an AOEC to make it more clear that this is an ”external” value. (2) The whole database for the surfactant is much weaker than for the well-investigated glyphosate. A toxicokinetic study is lacking, as for most co-formulants. The proposals for reference values result from pragmatic use that was made of the existing data.	
2(78)	Vol. 3, B.6.13.3.1, page 836	NL: Under ‘conclusion’ is mentioned “(Xi, R43, corresponding to “Skin sens. 1, H302)” – this should be Skin sens. 1, H317	RMS: Agreement, will be corrected in a revised RAR.	Addressed RMS to consider in a revised RAR
2(79)	Vol. 3, B.6.13.3.1, page 850	NL: Under ‘Impact of POE-[redacted] on the toxicity of Roundup formulations is stated that the oral absorption of glyphosate is about 30% only. Should be decreased to 20%, the newly suggested value.	RMS: Thank you for the correction! When the separate risk assessment on the POE-[redacted] was prepared in 2010, an oral absorption rate of 30% for glyphosate was still assumed. The rate was decreased during the current evaluation, based on studies that were not available before. The figure will be corrected in the revised RAR.	Addressed RMS to consider in a revised RAR
2(80)	Vol. 3, Annex B.6.13.3.1, [redacted] evaluation of the POE-[redacted] surfactant [redacted]	GTF: The assessment of POE-[redacted] is not considered to fall under the review of glyphosate Annex I Renewal. *For further explanation please refer to Column 3 of the original commenting table.*	RMS: See comment on 2(71)	See 2(69)

Toxicity of non-active substances (B.6.13)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
	page 835			

Exposure data (B.6.14)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
2(81)	Vol. 3, B.6.14 Exposure data Table B.6.14-2	EL: From the summary of supported uses of MON 52276 only the maximum in-use concentration is given. It should be clarified whether a combination of e.g. 0.36 kg a.s./ha application rate and 400 L/ha spray volume is supported. If this is the case the resulted in-use dilution (0.9 g/L) is not covered by the dermal absorption value for the dilution (tested concentration 2.5 g/L).A justification should be given for using the 0.3% value that based on the results of the available *in vitro* study with human skin, dermal absorption is not dose depended and a pro rata approach is not necessary.	RMS: Accepted, proposed justification to be included into revised RAR.	Open point: RMS to amend the RAR with regard to the use of 0.3% value dermal absorption for exposure assessment
2(82)	Vol. 3, B.6.14.1.2	NL: Minor comment: first paragraph, please do not abbreviate “according “ into “acc.”.	RMS: Agreement, will be corrected in a revised RAR.	Addressed RMS to consider in a revised RAR

Exposure data (B.6.14)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		And one dot too many at the end of the first paragraph.		

Other comments				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
2(83)		BE: the clear and transparent evaluation of the vast amount of studies and public literature is highly appreciated.	RMS: Thank you.	Addressed
2(84)	List of Endpoints. Impact on Human and Animal Health). Acute toxicity (Annex IIA, point 5.2) Eye Irritation	ES (MSSSI): In the proposal for classification and labelling according to Regulation (EC) nº 1272/2008, category Eye Dam. should be included.	RMS: In the List of Endpoints the proposal for classification and labelling: "Cat. 1, H318 causes serious eye damage" is indicated.	Addressed
2(85)	List of Endpoints. Impact on Human and Animal Health).	ES (MSSSI): It should be indicated that the values LD_{50} oral and dermal in rat, LC_{50} inhalation rat, skin irritation and skin sensitisation have been obtained for	RMS: This information will be added in a revised RAR.	Addressed RMS to consider in a revised RAR

Other comments				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
	Acute toxicity (Annex IIA, point 5.2)	glyphosate acid and for its salts.		
2(86)	Volume 1, Level 1; 2.6 Effects on human and animal health B.6 Toxicology and metabolism	EL: In Volume 1, 2.6 Effects on human and animal health, it is stated that «*A huge amount of more than 900 scientific publications (published since 2000 until August 2013) and other relevant information was additionally considered*». Notwithstanding, in B.6 it reads: *With rather few exceptions in the areas of genotoxicity and human data, mainly scientific literature published since 2000 was assessed*. Pls revise/correct Vol.1 to be consistent with B.6.	RMS: Consistent information will be submitted in a revised RAR.	Addressed RMS to consider in a revised RAR
2(87)	Vol. 1, 2.6.3.6 (page 45)	NL: In the conclusion glyphosate acid is classified as H318: "irreversible effects on the eye / serious damage to eyes" - should cat. 1 not just read "causes serious eye damage"?	RMS: Agreement, will be corrected in a revised RAR.	Addressed RMS to consider in a revised RAR

Other comments				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
2(88)	Vol. 1, 2.6.7.2.2 (page 79)	NL: The publication by Mesnage et al. (in press, ASB2012-13917) is published in 2013 in its final form (Toxicology 313(2-3): 122-128, 2013). Please also correct in reference list.	RMS: This new information will be added in a revised RAR.	Addressed RMS to consider in a revised RAR
2(89)	Vol. 1, 2.6.7.2.2 (page 64)	NL: The paper discussed, by Seralini et al. (ASB2012-15514), has meanwhile been retracted. This could be reason to remove it from the RAR, or mention this work in this context.	GTF: Agreed. RMS: The paper was in the mean time already in the public discussion. For reasons of transparency the study should be mentioned in the paper with the information that it was retracted.	Addressed
2(90)	Vol. 3, B.6	NL: The title page of the Toxicology and metabolism section reads “Annex B.6.1”, this should be “Annex B.6”.	RMS: Agreement, will be corrected in a revised RAR.	Addressed RMS to consider in a revised RAR
2(91)	Vol. 3, B.6.15	NL: The reference Krüger et al. (ASB2013-8527) is not in press anymore; published in Anaerobe 20: 74-78, 2013.	RMS: This new information will be corrected in a revised RAR.	Addressed RMS to consider in a revised RAR
2(92)	Specification and toxicological data	EFSA: considering the comment 62 in the section Identity (based on RMS’s evaluation of the confidential volumes it seems that there is no supported reference specification. Clarification is needed whether there would be two proposed reference specifications	RMS: Based on the data submitted up to now it can not be evaluated whether the specification is covered by the tox. batches.	Data requirement Applicants to demonstrate the compliance of the batches tested in the mammalian toxicology data package with the proposed specifications

Other comments				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		representing the two main processes and covering all manufacturers or one overall specification?) it is not possible to confirm whether the batches tested in the mammalian toxicology section adequately represent the reference specification; however, based on the huge amount of available data, including batches likely having lower purity than the most recent ones, it seems quite unlikely that the purer batches would bring additional toxicological burden compared to what has been tested so far and carefully presented in the RAR.		
2(93)	Vol. 1, Level 1, 2.6, *Introductory remarks to the evaluation in Volume 1*, bullet point #3	GTF: The notifiers wish to ensure the statement "Where possible, on the basis of all reliable studies and information, it was tried to establish "overall" NOAELs/LOAELs for a specific toxicological endpoint taking dose spacing into account" is applied consistently for the NOAEL used for ADI and AOEL calculations". The notifiers believe the NOAEL selected by the Rapporteur for ADI and AOEL calculations, 50 mg/kg bw/day, does not	RMS: The experimental basis and appropriate point of departure for deriving the ADI and AOEL will be discussed on an expert meeting. For the time being, we keep the arguments given in Vol. 1, sections 2.6.12 and 2.6.14. In addition, we would like to stress that our intention to establish "overall NOAELs/LOAELs was driven by the fact that so many studies were submitted by different companies. If an "overall" NOAEL/LOAEL for an endpoint is given, it is mostly a range or magnitude. For setting reference values, however, a more precise	Expert consultation ADI and AOEL of glyphosate to be confirmed in a meeting of experts.

Other comments				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		reflect an accurate overall NOAEL/LOAEL for the separate toxicological endpoints of maternal toxicity and offspring effects, as discussed below. An overall NOAEL for maternal toxicity of 75 mg/kg bw/day is reflected in the rabbit maternal data set.	figure will be needed.	
2(94)	Historical control data			Data requirement: In the carcinogenicity studies in mice by [redacted] (1997, ASB2012-11493, notifier: Arysta) and by [redacted] (2009, ASB2012-11492, notifier: Nufarm), a certain increase in the incidence of malignant lymphoma in high dose males (6/50 as compared to 2/50 in the control in the first and 5/51 vs. 0/51 in the second study) was noted. The differences did not gain statistical significance. However, for more reliable assessment, historical control data from the performing laboratories should be provided. The data requirement has already been identifies in the RAR.

3. Residues

Storage Stability (B.7.0)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
3(1)		FR: agreed	RMS: Comment noted.	Addressed.
3(2)	1. Vol. 3, B.7.0, table B.7.6-13	NL: Storage stability of AMPA in barley straw is really low in month 6 and 12. Please reconsider these data, since in the conclusion of this study storage stability of 18 months is suggested in all matrices studied. In particular for barley straw, this conclusion is questionable.	GTF: Analysis at 18 months indicates storage stability is acceptable indicating potential analytical variability at earlier time points. The final time point is considered to verify stability. RMS: The intermediate results for AMPA are below the typical trigger of "70% remaining". However, the 18 month value was acceptable. RMS also took into account the corresponding data for glyphosate in the same samples, which showed the same decline for 6 and 12 months and an increase for 18 months samples, suggesting side effects like poor fortification or analytical problems to be responsible for the lower recoveries. Under consideration of other straw matrices, a true degradation of AMPA during storage is not evident.	Addressed. AMPA residues in straw are concluded to be stable under frozen conditions up to 18 months. Low recoveries after 6 and 12 months are assumed to result from analytical variability.

Metabolism in plants (B.7.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
3(3)		FR: agreed	RMS: Comment noted.	Addressed.
3(4)	Vol. 3, B.7.1.1, Conclusion non-tolerant crops	NL: Since glyphosate is considered to be a systemic herbicide, how is it possible that translocation to untreated parts of the plants is limited?	GTF: The metabolism studies of glyphosate in non-tolerant crops referenced here were conducted to support uses where glyphosate was not directly applied to the crop (preemergence and directed spray) and so uptake and translocation would be limited in the crop (while extensive in the directly-treated weeds). Efforts to increase uptake through hydroponics and direct leaf or stem application, while not significantly damaging the crop, resulted in some uptake and subsequent translocation. The amount varied by crop type. RMS: Designation as “systemic” may be discussed in view of the data. It is undeniable that glyphosate shows systemic properties related to phytotoxicity. It should be kept in mind that the translocation only occurs from treated leaves into roots and not vice versa. However, from a residue perspective the residue behaves non-systemic. The amounts taken up by the leaves which are sufficient to kill the plant are negligible compared to surface residues	Addressed. The amounts of glyphosate taken up from leaves and translocated to roots (and sufficient to kill the plant) are negligible, compared to surface residues remaining (typical ratios are >80% in favour of surface residues), might explain the apparent "non-systemic" behaviour of the active substance in the metabolism studies conducted on non-tolerant plants.

Metabolism in plants (B.7.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			remaining. Typical ratios are >80% in favour of surface residues, which does not qualify for a "systemic" pesticide in terms of residue assessment. Other kinds of treatment (hydroponic, soil, trunk etc.) required large gradients to identify at least minimum residues in plant parts, also showing a non-systemic behaviour.	
3(5)	Vol. 3, B.7.1.1, Conclusion non-tolerant crops	NL: Glyphosate is considered to kill the plant, however, the plants in the metabolism studies are not being killed. How is that possible?	GTF: The studies were conducted at sub-lethal application rates. RMS: Agreement with GTF. In addition many metabolism studies involve soil or hydroponic treatment, showing incorporation of 14CO2 into the plants at sublethal doses. However, the metabolism study on wheat for desiccation purposes showed the expected phytotoxicity on the target crop.	Addressed. Metabolism in non-tolerant crops was investigated using sub-lethal doses and therefore, plants were not killed.
3(6)	Vol. 3, B.7.1, Metabolism in GAT maize	EFSA: Figure for un-extracted residues in table B.7.1-68 in GAT maize forage (42.9% TRR) is probably wrong and need to be corrected (4.29% ??).	GTF: Uses of glyphosate in GAT-modified crops are not within the scope of the submission. The GTF does not have access to this study and can't comment on the correction. RMS: correct number is 4.3% TRR. To be	Open point: RMS to correct in Table B.7.1-68, the unextracted residue value (4.3% instead of 42.9%).

Metabolism in plants (B.7.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			amended.	
3(7)	Vol. 3, B.7.1.1.3, Pulses and oilseeds. Report No. 304, (RIP9600099), page 20	GTF: This report was not conducted under GLP.	RMS: correct. To be amended.	Open point: RMS to considerer in a revised RAR, GTF comments 3(7) to 3(9) on sections B.7.1.1.3 and table B.7.1.1.4 in Vol.3
3(8)	Vol. 3, B.7.1.1.3, Pulses and oilseeds, Report RR 91-029B (RIP9500015), page 19	GTF: In Table 7.1-20, several values differ from those presented in the study report: Total extracted from both green and yellow seeds should be 53.1% TRR Total extracted from hay should be 48.5% TRR	RMS: Correct. Values switched. To be amended.	See Open point: 3(7)
3(9)	Vol. 3, B.7.1.1.4, Cereal grains, Report A1 (RIP95012109), page 31	GTF: Report RIP9501209 is provided in the plant metabolism section, under B.7.1.1.4 – Cereal grains. It is a residue study, not a metabolism study.	RMS: correct. To be deleted.	See Open point: 3(7)
3(10)	Vol. 3, B.7.1.1.5, Miscellaneous crops, Report RD93 (RIP9501198), page 37	GTF: Report RIP9501198 is provided in the plant metabolism section, under B.7.1.15 – Miscellaneous Crops. It is a residue study, not a metabolism study.	RMS: This study is considered as additional information. It was conducted with radiolabel and investigates glyphosate and AMPA in sugar cane and its processed products. Interconversion, if it would occur, should have been observed making it a useful information in the metabolism section.	Addressed Study on sugar cane is reported under the plant metabolism section as conducted with ^{14}C-labelled components and providing additional useful information on metabolism in plant.

Metabolism in livestock (B.7.2)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
3(11)		FR: agreed	RMS: Comment noted.	Addressed
3(12)	Vol.3, B.7.2., Metabolism, distribution and expression of residues in livestock	LV: Table B.7.2-5 "Identification of radioactive residues in urine, faeces, liver and kidney of lactating goats following administration of 14C-glyphosate to lactating goats at nominal feed levels of 200 mg/kg feed", shows that unknown substances represent as much as 22.34% of TRR. However, according to SANCO 7030/VI/95 Rev.3 all components of the residue which exceed 10% or 0.05 mg/kg of TRR need to be characterised and identified.	GTF: The unknown compounds were only reported for excreta. As discussed in report RIP9501207, the radioactivity listed as 'unknown' in the TLC analyses for urine and faeces was attributed to nonspecific binding of glyphosate to the cellulose sorbent on the TLC plates and retention of radioactivity at the origin, and not an unidentified metabolite. This was demonstrated by the variability in the percent 'unknown' between TLC systems, and in the reduction in amount by co-spotting with glyphosate standard. As confirmed in Table B.7.3-8 (p130) no unknown TRR was observed in edible tissues or milk with AMPA being the only metabolite observed in kidney. Regarding excreta, SANCO 7030/VI/95 Rev 3 states that "Excreta should be collected so that the overall recovery of radioactivity can be judged and as source for metabolites likely to be present in edible tissues." It does not require characterization and identification	Addressed Unknown compounds above 10% were only reported for urine and not in edible commodities, and therefore further identification is not requested. Moreover, as mentioned by applicant, analytical difficulties attributed to binding to the TLC plates may explain these proportions (15% to 22%), as lower amounts were measured by HPLC techniques.

Metabolism in livestock (B.7.2)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			of excreta metabolites. RMS: As described by GTF, the analytical methods involve some technical difficulties due to adsorption in the TLC systems. Therefore several techniques were used in parallel. For the interpretation RMS is in favor of using the radio-HPLC results over TLC data, which have a higher recovery rate of the TRR.	
3(13)	Vol. 3, B.7.2.1, Lactating goats, Report RR 93-062B (RIP9500022), page 76	GTF: In Table 7.2-14, the following reported value appears to be incorrect: The amount of glyphosate found in milk was 0.005 mg eq/kg, not 0.004. These difference also affects Table 7.3-8	RMS: correct. To be amended.	Open point: RMS to considerer in a revised RAR the value for milk in table 7.2-14 (0.005 mg eq./kg instead of 0.004).

Metabolism in livestock (B.7.2)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
3(14)	Vol. 3, B.7.3, Residue definition for plant commodities	NL: The different glyphosate-salts are shortly mentioned. It would be appreciated if the results obtained with different salt can be shortly discussed on their comparability and whether they are exchangeable.	GTF: See related comment under 3(27). Due to the ready dissociation in water of the glyphosate salts used in formulations, metabolism of the glyphosate anion is comparable across the different salts. RMS: Under B.7.3.1 the following text was amended: "The metabolism data does not show differences in the behaviour of the glyphosate-anion related to the cations used, making all variants of the active substance equivalent.". For a full comparison of formulations all residue data on glyphosate-trimesium submitted in 2002 would be required, which is out of the scope of the current assessment.	Addressed The following text was amended under section B.7.3.1"*Metabolism data do not show differences in the behaviour of the glyphosate-anion related to the cations used, making all variants of the active substance equivalent.*"
3(15)	Vol. 3, B.7.3.1.2.2, GOX ("glyphosate oxidoreductase") modified crops, page 122	GTF: Table 7.3-5 (Overview of glyphosate residues and its metabolites in CP4-EPSPS and GOX modified crops), Maize values for fodder and grain are reversed in Cols 5-7 and Col 9. In Column 4, fodder and its value are listed first and grain second. In columns 5-7 and 9, the grain value is listed above the fodder value. Grain values are lower than fodder values for all metabolites	RMS: correct. To be amended.	Open point: RMS to reconsider Table 7.3-5 (Overview of glyphosate residues and its metabolites in CP4-EPSPS and GOX modified crops) in a revised RAR, according to applicant comments in column 2.

Metabolism in livestock (B.7.2)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
3(16)	Vol 3, Annex B.7.3.1.3, Conclusions for plant matrices. Table B.7.3-7, page 127	GTF: In the comment under Current evaluation (proposal), it mentions pending import tolerances for GAT modified lentils. The import tolerance is for conventional lentils, not GAT modified lentils.	RMS: Correct – should have be been deleted already.	Open point: RMS to amend Table B.7.3-7 in a revised RAR, with the deletion of "lentils" in column "comments". See also comment 3(20)
3(17)	Vol 3, Annex B.7.3.2 Residue definition for animal commodities, page 131	GTF: The following value for AMPA in Table 7.3-8 (for hen studies Bodden, 1988, RIP9501205 & Patanella et al,1988, RIP9501206) is incorrect based on revisions to the summary table on page 86: Hen kidney, Group 4 (49.9 mg glyphosate + 5.3 mg AMPA per kg bw), AMPA should be 4.4% TRR, not 4.2%.	RMS: Correct. To be amended.	Open point: RMS to correct AMPA value for hen kidney in Table 7.3-8, in a revised RAR (4.4% TRR instead of 4.2%).

Residue definition (B.7.3)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
3(18)	Vol. 3, B.7.1.3, Plant and animal residue definitions [GTF: This appears to be referring to section B.7.3.1.3]	EFSA agrees the residue definition proposals made by the RMS for plant and animal commodities.	GTF: The GTF disagrees with the proposed residue definition for enforcement, and believes it should be **glyphosate only** for all crop and animal commodities. In 2009 EFSA issued a reasoned opinion (RO) on the Modification of the residue definition of glyphosate in genetically modified maize grain and soybeans, and in products of animal origin (EFSA Journal 2009; 7(9): 1310). This RO proposed a residue definition for risk assessment in all plant (including soybeans and maize) and animal commodities. In addition three (3) options were proposed regarding the residue definition in maize and soybeans for enforcement purposes. In the Summary report (SANCO-D(2011) 353285) of the Standing Committee meeting on the Food Chain and animal health; section Pesticide residues + plant protection products-legislation of February 3-4 2011, the committee concluded that the residue definition for enforcement should not change (option 1 in the EFSA reasoned opinion; it is residue = **glyphosate only**) but that for the definition for the purpose of	Addressed The residue definition for enforcement proposed by the RMS is agreed, considering all scientific information made available for the peer review of the active substance (including information on GMO glyphosate tolerant plants). 1) sweet corn, oilseeds rape, soya bean and maize (non-tolerant and tolerant, all modifications): sum glyphosate and N-acetyl-glyphosate, expressed as glyphosate 2) Other plant commodities glyphosate See also comment 3(21), 3(22)

Residue definition (B.7.3)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			risk assessment the complete residue definition with all metabolites would need to be used. RMS: In view of the RMS the current proposal reflects the state of scientific knowledge.	
3(19)	Vol. 3, B.7.3, Residue definition for plant commodities	NL: The different glyphosate-salts are shortly mentioned. It would be appreciated if the results obtained with different salt can be shortly discussed on their comparability and whether they are exchangeable.	GTF: See comment under 3(14). RMS: See comment to 3(14).	see comment 3(14)
3(20)	Vol.3, B.7.3.1.3 Conclusion for plant matrices; p125 and Table B.7.3-7; p127	FR: it is not clear if the GAT modified crop included oilseed rape and/or lentil.	GTF: GAT-modified crops include oilseed rape, but not lentils. See related comments 1(30) and 3(16) regarding lentils. RMS: Oilseed rape only. Lentils were wrongly included in the first draft and not completely deleted in the current version.	See open point: 3(16)
3(21)	Vol.3, B.7.3.1.3 Conclusion for plant matrices; p126	FR: France agrees with the new proposed residue definition for monitoring for plant commodities that could be tolerant crops (GAT modified).	GTF: The GTF disagrees with the proposed residue definition for enforcement, and believes it should be **glyphosate only** for all crop commodities including those that could be from tolerant crops. See additional comments under 3(18).	see comment 3(18)

Residue definition (B.7.3)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			RMS: Noted.	
3(22)	Vol.3, B.7.3.2 Residue definition for animal commodities; p132	FR: France agrees with the new residue definition for monitoring for animal commodities that could be fed with tolerant crops (GAT modified)	GTF: The GTF disagrees with the proposed residue definition for enforcement, and believes it should be **glyphosate only** for all animal commodities including those that could be fed with tolerant crops. See additional comments under 3(18). RMS: Noted.	see comments 3(18)

Use pattern, critical GAP, residues trials (B.7.4 to B.7.6)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
3(23)	Vol. 3; B.7.4 Use pattern and LoEP	EFSA: In table B.7.4-1 and LoEP, representative use for olive cannot be defined without PHI as proposed for Orchard. As MRL for olive is based on the residue levels observed in fruits fallen on ground and exposed to the direct spray of the treatment, a minimum PHI has to be defined (length of time between the application and	GTF: It is our understanding that the current MRL for olives is based on a critical GAP with a 7 day PHI for „ground fallen“ olives, based on the previous review of 4 trials in Spain, 7 in Greece and 1 in Italy, all with 7 days PHI. The purpose of the treatment is to clear ground to allow easy harvest of olives which have fallen to the ground or where	Data requirement A PHI should be provided to define the GAP for olive for oil production, based on the ground fallen fruits (since fruits fallen onto ground are directly exposed to the treatment spray).

Use pattern, critical GAP, residues trials (B.7.4 to B.7.6)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		the harvest of the fruits fallen on the ground).	nets are used to catch falling olives. So 7 days is correct agronomic practice for a minimum interval, and thus relevant for the GAP. However, ground-picked olives are used only for oil production and the processing studies clearly show that residues in oil are always <LOQ. RMS: No PHI was provided in the representative uses. However, in combination with Comment 3(26), the data will be limited to 4 trials collected at PHI 7 anyway. The final GAPs should be reconsidered.	
3(24)	Vol. 3, Table B.7.4-1: List of representative uses (glyphosate); p 138 Table B.7.5-1: Critical GAPs for glyphosate; p 144 Vol 1, Level 1 ; List of representative uses evaluated (Glyphosate);	FR: in the column „growth stage &season "should refer to the BBCH GS **of the treated crop** and not **to weeds growth stage**. So „Post emergence of weeds "should be précised with ranges of crops growth stages according to the selected trials to support uses in orchards (BBCH 70-75). If not a PHI should be proposed. For the use in orchard, could you please precise all the commodities	GTF: No PHI is required for tree crops except olives. The application timing is driven by the need to treat weeds and is independent of the growth stage of the crop. This is because glyphosate is applied as a directed spray, in established trees, avoiding contact with green leaves and shoots, and there is no uptake through matured bark. The majority of trials have been conducted at a crop growth stage around 7 (fruit development) to provide a worst-case	Addressed Olives: see data requirement 3(23) "**All crops****" in table B.7.4-1 has to understood as "Pre-planting application on all seeded crops in the list above [including but not restricted to: root & tuber vegetables, bulb vegetables, stem vegetables, field vegetables (fruiting vegetables, brassica vegetables, leaf vegetables

Use pattern, critical GAP, residues trials (B.7.4 to B.7.6)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
	p16	concerned. For the use on "all crop **", could you precise to what referred "**"in Vol 3 tables.	situation for potential residues. The data show that when applied around these timings, there are no glyphosate residues in edible portions (fruit, nuts, and olives picked from the tree). Therefore it is clear that there will be no residues at any timing (of the crop). It is therefore appropriate to define the application according to the growth of the weeds. For the same reason, no PHI is required. For the same reason, that no detectable residues have been found in a wide range of tree crops (pome and stone fruit, nuts, olives [other than ground-picked]), it is not appropriate to define the commodities; the use pattern applies to all orchard crops. The interpretation of the GAP was not questioned by the RMS at the time of the application for renewal and therefore it does not seem appropriate to change the GAP at this late stage. The '**' was described in the submitted GAP table as '** all seeded crops in the list above [including but not restricted to: root & tuber vegetables, bulb vegetables, stem	and fresh herbs, legume vegetables), pulses, oil seeds, potatoes, cereals, and sugar/fodder beet; before planting fruit crops, ornamentals, trees, nursery plants…]

Use pattern, critical GAP, residues trials (B.7.4 to B.7.6)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			vegetables, field vegetables (fruiting vegetables, brassica vegetables, leaf vegetables and fresh herbs, legume vegetables), pulses, oil seeds, potatoes, cereals, and sugar- & fodder beet; before planting fruit crops, ornamentals, trees, nursery plants etc.] RMS: This comment affects orchards only. Here the growth stage of the crop is irrelevant, since the ground is treated. Under practical conditions the treatment may occur directly before harvest, since the crop itself is not affected. The term *all crops* can not be further clarified. The specific property of glyphosate of showing no root uptake allows general seed-bed preparation. The range of crops to be planted afterwards is unlimited, hence representative crop groups were evaluated in B.7.6 and extrapolated to all major and minor crops within the groups.	
3(25)	Vol. 3, 7.6, Table B.7.6-2 residues in orchards	EFSA: Data for apple and pear have to be pooled together, since according to EU guideline, trials on pome fruits may be performed either on apple or pear (LoEP should be corrected accordingly)	GTF: This is a question of data interpretation and this approach could be considered RMS: Addressed.	Addressed An MRL of 0.05* mg/kg is derived for the "pome fruit group" based on the residue trials conducted on apple and pear: NEU: <0.02, 3x <0.05

Use pattern, critical GAP, residues trials (B.7.4 to B.7.6)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
				SEU: 17x <0.05
3(26)	Vol.3, B.7.6, Table B.7.6-2	EFSA: For olive, contrary to what is reported in the table B.7.6-2, only 4 trials are available to derive MRL from the ground picked fruits. The trials conducted in Spain and reported from page 405 to 408 of the DAR, are **4 reverse decline studies** conducted in 4 locations (Chartaojal, La Carlota, Villa del Rio, Ubeda). It is therefore not appropriate to consider the residues observed in the same location at 3 different time PHIs (7, 14 and 28 days) as separate trials. Therefore, in each location, EFSA proposes to consider only, the highest level observed at 7, 14 or 28 day PHI (0.11, 0.14, 0.53 and 0.93 mg/kg). As olive is a major crop in SEU, additional trials have to be requested (see also comment in 3(3), the selection of the values for MRL calculation is pending the setting of a PHI for olive). Olive trials	GTF: The data from the EFSA MRL review are being considered in the Renewal of Approval. In our view the proposed data requirement should be addressed in that review and not repeated in this procedure. Four further residue decline trials on olives could be performed in order to verify the residue. In the meantime a provisional MRL could be proposed since there is no perceived consumer risk based on processing trials showing no transfer of residues to oil. RMS: Agreed. Reverse decline studies may not be considered as independent trials, leaving 4 trials for group-picked olives. Olives for oil production are a major crop in SEU, while table olives are minor (rev.9). The MRL proposal will be changed to table olives only and a data gap for olives for oil production is identified.	Data requirement Four additional trials on ground-picked olives are requested to derive MRL for olives (oil production). A PHI should be proposed to support this uses (see data requirement 3(23)) See also comment 3(53)

Use pattern, critical GAP, residues trials (B.7.4 to B.7.6)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
3(27)	Vol 3, B.7.6 Residues resulting from supervised trials	FR: in this section it is mentioned: "The formulation and the active ingredient (salt) are not expected to influence the residue for glyphosate." Could you please argue and give elements to support this position?	GTF: Formulations of glyphosate all contain the same active ingredient, the glyphosate anion. Different counter-ions are used (historically and currently) to aid in the formulation of the glyphosate anion into acceptable commercial products. When the formulated product is diluted in the spray tank, the counter-ion quickly dissociates. Thus the crop and weed plants are exposed only to glyphosate anion, irrespective of the original counter ion. Within the plants, the glyphosate anion binds to the active site in the enzyme and so a counter-ion can have no effect. In reality there are no significant differences between the products except for their concentrations and whether they contain surfactants or not. Residues arising from different glyphosate counter-ions and formulations are comparable. RMS: The position is based on OECD TG-509 (33): "Some active ingredients (e.g., phenoxy herbicides) can be applied as one or more salts and/or esters. Different salts of an active ingredient may be considered	Addressed It is concluded that formulations and different glyphosate salts are not expected to have an impact on final residue levels (See also comment 3(14)).

Use pattern, critical GAP, residues trials (B.7.4 to B.7.6)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			equivalent for residue purposes in most cases regardless of the timing of the application. However, examples for which additional data may be needed for a new salt include the presence of counter ions that impart surfactant properties, significantly change the degree of dissociation, or chelate with the active ingredient ion." Both sodium and isopropylamine salts of glyphosate do not affect surfactant properties, are fully dissociated and do not chelate the PMG ion. Concerning the formulation type itself, OECD TG-509 (25-28) describe the criteria for equivalence. Water dissociated formulations are generally comparable for PHI above 7 days. The desiccant uses in the RAR, which are the only uses with a 7 day PHI, are nearly completely performed with a "SL" formulation or designed as side-by-side trials with an "SL" formulation.	
3(28)	Vol. 3, B.7.6, table 7.6-1	NL: Since it is presented that levels of AMPA are very minor compared to parent glyphosate, wouldn't calculation number 2 from this table (0.05 mg/kg glyphosate +	GTF: Clear guidance is required from EFSA on how residue data should be interpreted in order to avoid different evaluations. But the NL approach seems very reasonable from a	Addressed The summing of glyphosate and AMPA residue levels is agreed as

Use pattern, critical GAP, residues trials (B.7.4 to B.7.6)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		<0.05 mg/kg AMPA, calculated as 0.13 mg/kg total residues) still be an overestimation? Could you consider to calculate such cases as 0.05 mg/kg total residues (so no addition of AMPA in this case)?	scientific standpoint. RMS: The line 2 of the table is just one example how residues >LQO for glyphosate and <LOQ for AMPA are calculated. RMS agrees, that for the listed value of 0.05 mg/kg the total residue is probably overestimated. However, for higher levels of glyphosate, AMPA could be present near the LOQ, demanding such addition for the total residue. Unfortunately, no clear glyphosate level could be identified from which AMPA needs to be taken into account. For consistency purposes it was therefore decided to add AMPA always when glyphosate was detected. Unless it is decided that AMPA is generally irrelevant for the RD for risk assessment, the current calculation follows the practice used in previous DARs, RARs and EFSA documents.	proposed by the RMS in Table B.7.6-1, considering that the sum "*0.05 mg/kg glyphosate + <0.05 mg/kg AMPA = 0.13 mg/kg total residue level*," is probably an overestimated. See also comment 3(83)
3(29)	Vol. 3, B.7.6.2	NL: Is it acceptable to extrapolate to all other crops, based on the number of trials and the selected crops (e.g. only 2 trials on carrots and 2 trials on potato)?	GTF: The approach taken is considered to be consistent with SANCO 7525/VI/95 Rev.9 section 2.6 in order to show a no residue situation across a full range of crop groups. Results are consistent with the available metabolism data. It has been clearly shown	Addressed Based on the EU guidance "SANCO 7525/VI/95 - rev.9, where it is stated that 2 trials are sufficient in case of a nil-residue situation, and considering that residues were all <LOQ in a wide

Use pattern, critical GAP, residues trials (B.7.4 to B.7.6)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			across a very wide range of crop types that no residues of glyphosate occur in crops at harvest from applications made pre-planting or pre-emergence. No further data are therefore required. RMS: For the evaluation of the residues the new data requirements defined in COMMISSION REGULATION (EU) No 283/2013 do not apply since the dossier was presented before the Regulation entered into force. Based on the old EU guidance two trials are sufficient in case of a nil-residue situation: "SANCO 7525/VI/95 - rev.9 (2.5): When the residues of an active substance are foreseen to be under the LOD and at least 2 residue trials confirm this then no further trials are normally necessary." In view of the numerous plant metabolism data involving soil treatment, no uptake via the roots is expected and therefore a nil-residue situation can be assumed. Since no significant difference in the residue behaviour was identified between crops, a broader extrapolation within crop groups is considered acceptable to confirm	range of crops, extrapolations to all other crops, as proposed by the RMS, are agreed.

Use pattern, critical GAP, residues trials (B.7.4 to B.7.6)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			the nil-residue situation.	
3(30)	Vol. 3, Annex B.7.6.3, Linseed, mustard seed and rape seed, page 151	GTF: Trials involving a PHI of 14 days and an application rate > +25% (2.8 - 2.9 kg as/ha) should be accepted as they represent a worst case scenario. In this case, sufficient data to defend the pre-harvest use in linseed, mustard seed and oilseed rape is available. If the proportionality principle is adopted, then additional trials will also be available to fill the data gap.	RMS: no agreement. After completing the RAR, the proportionality principle was generally excluded for herbicides by both OECD and CODEX. Without proportionality, the utilisation of trials with exaggerated application rates is against the ALARA principle in MRL setting.	Data requirement Additional residue trials on rapeseed conducted according to the supported GAP are requested. Only 3 trials conducted according to the representative uses (2160 g/ha ± 25% tolerance) are available. As the use of the proportionality has not been yet agreed at EU level and since proportionality principle was generally excluded for herbicides by both OECD and CODEX, trials out of the 25% tolerance are not considered.
3(31)	Vol. 3, B.7.6.4	NL: Since the PHI is an important factor in the level of residues concerning the GAPs for desiccation of the crops (see text: longer PHI are also acceptable, since drying of the crops generally results in higher residues), shouldn't trials be conducted with longer PHIs included? If residues still increase after a PHI of 7 days, it is important to monitor the residue level at longer PHIs as well. It is known that there is no data	GTF: Residues have been monitored across a range of PHIs and worst case residues have already been taken into account. The cereal grain tables assembled by EFSA (see comments 3(33) and 3(34)) list the range of PHIs that have been included in existing studies, and show the overall decline with residues by PHI. The one instance where a longer PHI resulted in significantly higher residues was noted by EFSA and proposed to	See expert consultation 3(33)

Use pattern, critical GAP, residues trials (B.7.4 to B.7.6)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		requirement to study residues at longer PHIs than the PHI of the critical GAP, however, regarding this particular situation with glyphosate it might be of importance.	be disregarded (see comments 3(36) and 3(55)). RMS: The impact on the residues by higher PHIs is generally expected to be <25%. In contrast to most uses, where higher PHIs result in a significant decrease of residue levels mainly due to plant growth and metabolism, the application of glyphosate for desiccation has an opposite effect. Crops near harvest dryness (normally 70-80% DM) are desiccated to a preferred DM content of ~88%. In parallel the plant dies, not being able to metabolize glyphosate. In combination, the residue concentration remains stable or shows a slight increase due to drying – however the impact is considered minor to justify specific trial data. The statement was included to show that the PHI itself is no sensitive parameter in the selection of field trial data compared to the application rate itself.	
3(32)	Vol. 3, Table 7.6.5, Glyphosate and AMPA residues after application to rape and	GTF: In Table B.7.6-5, the HR value for Rape Seeds is incorrect and should be reduced from 30.35 to 11.9 mg/kg to reflect the residue data presented.	RMS: agreement. To be amended	See data requirement 3(30)

Use pattern, critical GAP, residues trials (B.7.4 to B.7.6)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
	linseed with application rates deviating more than 25 % to the cGAP, page 153			
3(33)	Vol.3, B.7.6, Table B.7.6-6, Residue trials on barley and oats	EFSA: For Barley grain in NEU, it is difficult to understand how mean values (referenced as [f]) have been calculated. Residue levels observed in plots conducted in the same location with different application rates seems have been averaged (EFSA is of the opinion that values resulting from plots covered by different application rates have not to be averaged, but the highest value taken into account). In addition, in some locations, 2 residue values (related to 2 different application rates) have been selected for MRL calculations, while only one figure has to be selected in each location (e.g. UK trial, Neston, variety Igri, reported from page 660 to 668), To select the relevant residue trials, EFSA proposes the following approach (see excel file embedded): - When different dose rates are available in one location (within ±25%, 1620 to 2700 g/ha), the closest dose to the	GTF: Clear guidance is required from EFSA on how residue data should be interpreted in order to avoid different evaluations. The proposed approach looks reasonable. RMS: The RMS applied the following reasoning to the calculation of residues: 1) Same location, same crop, same variety, same application rate, same PHI, different plot: The trials are considered highly dependent and indistinguishable from a replicate sample from one plot. The mean of all plots is taken as representative residue. 2) When several set of plots were conducted at one location, but with different application rates, the use pattern is considered different and each set is used individually. Regarding the EFSA approach the RMS acknowledges its idea. In summary the	Expert consultation A general approach for the selection of the residue trials relevant for the MRL calculations on cereals, should be discussed in an expert meeting. See also comment 3(31), 3(34), 3(36), 3(52), 3(54), 3(55) and 3(82)

Use pattern, critical GAP, residues trials (B.7.4 to B.7.6)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		supported dose (2160 g/ha) is first considered, - If, higher residue levels are observed in one of the other dose rates (within ±25%), this highest residue value is finally selected for MRL calculation. - If, replicates or several plots are available at the selected dose rate, values are averaged. - Only one value is selected for MRL calculation in each location. Moreover, since residue levels in barley and oats grain and straw (NEU and SEU) are not significantly different, it is proposed to pool all data to derive MRL, STMR and HR values. Barley Oats Trials	proposal by EFSA is close to the RMS approach, except for the decision of one or two values to be selected at deviating application rates: 1) Replicate plots shall be averaged (bullet point 3) 2) Either pick closest set to GAP or higher one within ±25% RMS is fine with both approaches (the outcome does not change significantly). A general decision for future RARs should be made by an Expert Meeting Concerning the pooling of NEU and SEU data the RMS is of the opinion that the minimum data requirements should be fulfilled before statistical testing is applied to justify extrapolations beyond the commonly accepted cases described in SANCO 7525/VI/95 - rev.9. Barley is a major crop in SEU, demanding 8 trials. The data for barley+oats from SEU with 4 trials is not	

Use pattern, critical GAP, residues trials (B.7.4 to B.7.6)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			considered sufficiently representative to conclude on the same residue pattern as in NEU, irrespective on the applicability of statistical testing.	
3(34)	Vol.3, B.7.6, Table B.7.6-7, Residue trials on wheat and rye	EFSA: Similar comments as for barley. In addition, it is difficult to understand why in the German trials reported from pages 832 to 839, values at 14 day PHI have been selected, while data at PHI 7 days are available and higher than at day 14. The same approach as for barley is proposed (see excel file embedded). As residue population for rye is significantly different from NEU + SEU wheat populations (H-test, 5%), it is not appropriate to merged wheat and rye data as done in table B.7.6-7. Separate MRLs have to be derived for wheat and rye. Wheat Rye trials	GTF: Clear guidance is required from EFSA on how residue data should be interpreted in order to avoid different evaluations. The GTF agrees with the overall approach, but questions whether it is appropriate to compare residue populations for wheat and rye given the differences in size of the respective residue databases. Under the residue guidelines SANCO 7525/VI/95 - rev.9, wheat residue data can be extrapolated to rye. RMS: Handling of replicate plots see barley (3(33)). In the trials on page 832-839 the DAT was 6 days, which is less than the minimum PHI of 7 days. The earlier harvest is not within GAP. The data set for rye is not sufficient for a separate evaluation (major crop in NEU). Extrapolation from wheat to rye close to	See Expert consultation 3(33)

Use pattern, critical GAP, residues trials (B.7.4 to B.7.6)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			harvest is commonly accepted according to SANCO 7525/VI/95 - rev.9. If desired, the MRL for both commodities can be based on wheat data only, however the HR from rye would be lost. RMS prefers combination of the data for mutual support.	
3(35)	Vol. 3, Annex B.7.6.7, Storage stability, Crop, Report MSL-10843 (RIP9501332), page 163	GTF: For report RIP9501332 it is noted that there is a deviation: 'original guideline not provided'. The study was conducted under the current guideline at the time, which was referenced in the report (and noted in the DAR), and therefore this is not concluded to be a deviation. The same comment applies to additional studies on the following pages: 177, 220, 222, 223, 243, 253, 264, 267 and 274.	RMS: agreed. To be amended.	Open point: RMS to amend section B.7.6.7 on storage stability in a revised RAR, considered applicant comment (not deviation to current guideline).
3(36)	Vol.3, B.7.18, Appendix, Table B.7.18-22, page 742	EFSA: The results reported in table B7.18-22 (Wheat trials NEU) page 754 (DE trial, Bad Segeberd, variety Kraka) are questionable. Residues in grain and straw are listed as: following: **PHI 10 14 26 days** - grain: 8.8 7.4 **15**	GTF: Data have been verified as correct from the original report. RMS: Apart from the odd results the study is well reported (including sample date, sample IDs etc.) and does not involve any deviations. Grain and straw samples	See expert consultation 3(33)

Use pattern, critical GAP, residues trials (B.7.4 to B.7.6)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		- Straw:- 12 **4.9** I should be verified if results for grain and straw at 26 day PHI have not been inverted. Such an inversion would have a significant impact on the MRL proposal for wheat, since the 15 mg/kg value observed in this trial is the highest value observed for wheat grain. As the next highest value for wheat grain is 9.5 mg/kg only, MRL proposal for wheat would be 10 mg/kg, if residues in the Bad Segeberd trial are only 4.9 mg/kg in grain.	involved different extraction techniques. In the sample set the respective grain sample was in two other samples were re-analysed for confirmation using peak addition with glyphosate confirming the concentrations measured in the first run. However, the respective grain sample was analysed only once. In summary no information are available supporting an invalid sample or analysis. The only option RMS sees to exclude the sample is Expert Judgement based on the overall residue pattern by an Expert Meeting. In the 2002 DAR the trial was considered acceptable.	

Use pattern, critical GAP, residues trials (B.7.4 to B.7.6)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
3(37)	Vol.3, B.7.6, Residue trials, Conversion Factor for risk assessment (CF)	EFSA: For most of the crops, AMPA residue levels are <LOQ and therefore, as proposed by the RMS, the setting of CFs is not relevant. In contrast, for barley and wheat, significant AMPA residues were measured and CFs have therefore to be proposed. However, these CFs were derived at the intended PHIs only. EFSA is of the opinion that CF proposals should not be based on the values observed at the intended PHI only. CFs may be time dependent and the ratio parent/metabolites subject to significant changes over time. Therefore, the possible variations in the CF values at the different PHI time points should be considered and CF values have to be proposed considering all PHIs investigated in the different residue trials. According to EFSA assessment (cf. table in Column 3), an overall CF of 1.1 would be appropriate to cover the cereal group (for grain and straw).	GTF: This is a question of data interpretation and this approach could be considered RMS: CFs are presented in the RAR when possible (e.g. for the cereal grains Vol.3 Tables B.7.6-6 & -7). A general conclusion on a CF of 1.1 for cereals (to be put in the LoEP), based on desiccation uses, is not supported: - In terms of metabolic formation desiccation is the least favourable GAP compared to early applications - Cereal grains should be limited to barley, rye, oats, triticale and wheat, since maize is a GMO - GMO cereal grains (e.g. wheat MON 71800) are currently under development Besides, it should be discussed whether a CF of 1.1 is a “significant change” or not.	Expert consultation The setting of a conversion factor (CF) for risk assessment on cereals (maize excluded) should be discussed in an expert meeting.

Use pattern, critical GAP, residues trials (B.7.4 to B.7.6)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		Plant part / **Crop** / **PHI (days)**: 0 / 1 / 3~5 / 6~8 / 9~12 / 14~15 / 20~24 / **Total samples** **Grain** — Barley & Oats — Ber: 67 / 5 / 55 / 139 / 43 / 88 / 25 — 422 **Grain** — Barley & Oats — **CF**: **1.01** / **1.01** / **1.01** / **1.03** / **1.02** / **1.03** / **1.06** **Grain** — Wheat & Rye — Ber: 77 / 0 / 8 / 214 / 30 / 54 / 35 — 418 **Grain** — Wheat & Rye — **CF**: **1.04** / **1.09** / **1.23** / **1.10** / **1.10** / **1.11** **Straw** — Barley & Oats — Ber: 32 / 5 / 12 / 118 / 8 / 51 / 24 — 250 **Straw** — Barley & Oats — **CF**: **1.01** / **1.01** / **1.04** / **1.02** / **1.03** / **1.03** / **1.02** **Straw** — Wheat & Rye — Ber: 57 / 0 / 4 / 130 / 20 / 51 / 31 — 293 **Straw** — Wheat & Rye — **CF**: **1.01** / **1.02** / **1.02** / **1.02** / **1.04** / **1.05**		
3(38)	Vol. 1, LoEP, Conversion factor for plant commodities.	EFSA disagrees RMS statement in the LoEP on the Conversion factor for plant commodities: "*not applicable, CF dependent on point of application (pre-emergence ↔ desiccation) and crop (non-tolerant* ↔	GTF: See above RMS: see 3(37)	See expert consultation 3(37)

Use pattern, critical GAP, residues trials (B.7.4 to B.7.6)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		tolerant". Up to now, GMO cereals are not on the market, and AMPA residues are present in cereals (grain and straw) when glyphosate is applied as desiccant. EFSA is therefore of the opinion that a CF of 1.1 should be proposed on cereals (see comment 3(9)), when positive residues of glyphosate are observed.		
3(39)	Vol. 1, LoEP. Table on Summary of the residue trials	EFSA: The Column "*Comments/ Recommendations*" is missing in the summary table and would be useful to explain the grouping of the crops and the setting of group MRLs. Residue data according to the residue definition for monitoring (Mo) and for risk assessment (RA) should be reported in the same column.	RMS: LoEP amended	Open point: RMS to include a column "Comment/ Recommendations" in the LoEP summary table on residue trials.
3(40)	Vol.3, B.7.6.7, Storage stability	EFSA: As mentioned in the current EU guideline 7032/VI/95, "individual results should not be corrected to 100% yield…". This recommendation is indeed taken over in the OECD 506 guideline "…results not adjusted by recoveries….". Therefore, columns "corrected %" in tables B.7.6-9, B.7.6-11, B.7.6-13, B.7.6-14, B.7.6-15,	GTF: Disagree, procedural recovery at the time of analysis can provide important information in evaluation of data especially for complex methodology where variability can be observed over long term studies. Therefore these correction columns provide a useful additional element when evaluating the data and should be considered relevant	Expert consultation: MSs to discuss the recoveries after storage under frozen conditions. Note: EFSA remains of the opinion that concurrent recoveries (= fresh or procedural recoveries) **have not** to be

Use pattern, critical GAP, residues trials (B.7.4 to B.7.6)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		B.7.6-16, B.7.6-18, B7.6-21 and B.7.6-22 should be deleted and the rational concerning the stability of the residues reconsidered, based on uncorrected recoveries.	when concluding on overall stability. RMS: Both cited documents refer to the generation of studies and their reporting. In all cases the uncorrected values were presented in the studies and given in the RAR. The "% corrected" column was included by the RMS to ease interpretation in spite of OECD 506 (35): "Any decline should take into account the uncorrected residues in stored commodities and procedural recoveries." Especially for analytes difficult to analyse like glyphosate and AMPA identification of a true decline demands consideration of the procedural recoveries to get an impression of the overall picture. The impact of the analytical performance was therefore included to help the reader in its assessment.	used to correct the recovery values observed after storage under frozen conditions and therefore, that the columns "corrected %" should be deleted from the different tables in the RAR. Concurrent recoveries should be used only to confirm that the analytical method has been correctly implemented at the different control time points and that, low storage recovery observed at a certain control point, may be explained by a low procedural recovery. Considering that the rational to support the stability was based on the nominal spiking rates (and not the residue level measured at T0), the RMS conclusion on stability are agreed.

Processing (B.7.7)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
3(41)		FR: agreed	RMS: Comment noted.	Addressed
3(42)	Vol. 3, B.7.7.2.1, Citrus fruit	NL: Since the initial residue level (before processing) in many cases is already low (often <0.05 mg/kg), how relevant is it to use these studies?	GTF: A comprehensive set of processing studies has been provided. In the case of citrus, many initial residues were <LOQ but the studies are included for completeness and serve to demonstrate that no unacceptable or extreme concentration of residues occurs in processing. Processing factors have been derived only from those studies with significant initial residues. RMS: PFs were only derived when the RAC contained residues >LOQ for at least one of the metabolites. Most of the data was below LOQ and is only reported for consistency reasons.	Addressed PF factors for citrus were only derived from studies where residues above the LOQ were measured in the raw fruit (RAC).
3(43)	Vol. 3, B.7.7-8, Processing studies on Soya bean	EFSA: In table B.7.7-8, It is unclear how AMPA residues are expressed (as mg AMPA/kg or as mg glyphosate equivalent/kg). This point should be clarified. Moreover, since significant AMPA residues are expected in some processed fractions, conversion factor for risk	GTF: The AMPA values in Table B.7.7-8 are expressed as mg AMPA/kg. They are not converted to glyphosate equivalents. The CF calculation procedure is a question of data interpretation and this approach could be considered We do not agree that the possible inclusion of acetyl-glyphosate and acetyl-	Expert consultation: MSs to discuss the results of the processing studies in soya bean. AMPA residue levels are expressed as AMPA equivalent. Note: In absence of data on acetyl-glyphosate and acetyl-AMPA, EFSA remains of the opinion that PF and CF

Processing (B.7.7)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		assessment should be proposed. **Note:** CF for processed fraction calculated as the ration of (*Residue level in processed fraction, expressed according to RD-RA*)/(*Residue level in processed fraction, expressed according to RD-Mo*). It should be highlighted that PFs and CFs for oilseed rape and soybean, as derived in the DAR, should be considered as a best case, since GMO varieties are present on the market and therefore, N-acetyl-glyphosate residues are expected to be present in seeds (RAC) and significant levels of AMPA and N-acetyl AMPA expected to be present in the processed fractions.	AMPA necessarily means that PFs and CFs derived in the DAR are best-case. The behaviour of acetyl-glyphosate and acetyl-AMPA during processing is outside the scope of this submission and may lead to higher or lower factors. RMS: AMPA is generally presented as AMPA unless noted to be calculated otherwise. CFs for soya bean processed products is not supported. It is unclear whether the GAP used for treating the soya beans is in compliance to US practice. Since no interconversion from glyphosate to AMPA was observed, the initial levels in the RAC dictate the ratio in the processed product. In summary the data is not considered appropriate to derive CFs without GAP compliance. An additional comment on the PFs is not supported by the RMS. As explained above CFs based on the presented studies are not reliable, since no information on GAP compliance are available. The derived PFs are analyte-specific (glyphosate or AMPA).	should be considered as a "best case" in term of residue transfer in processed commodities

Processing (B.7.7)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			The transfer into processed products is independent on the crop being GMO or not but on physico-chemical conditions, the solubility in water/fat and the removal of significant plant parts. When processed in the same manor, an identical amount of residue from conventional or GMO soya beans should be transferred into the processed product. The only difference is the starting concentration and the ratio of metabolites in the conventional and GMO RAC, which is GAP dependent.	

Processing (B.7.7)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
3(44)	Vol. 3, B.7.7-10, Processing studies on Barley	EFSA: It is unclear in table B.7.7-10, how AMPA residues are expressed (as mg AMPA/kg or as mg glyphosate equivalent/kg). This point should be clarified. As AMPA residues are present in significant levels, Conversion factors for risk assessment have to be proposed.	GTF: The AMPA residues are expressed as mg AMPA/kg. They are not converted to glyphosate equivalents. Proposal of AMPA conversion factors is a question of data interpretation and this approach could be considered RMS: AMPA is generally presented as AMPA unless noted to be calculated otherwise. At GAP compliance (2.15 kg as/ha) only one trial (RIP9501248, France, Charest (Trial 41294)) contained detectable residues both for glyphosate and AMPA in the processed products: Malt: 3.35 mg/kg glyphosate, 0.05 mg/kg AMPA (= 0.075 mg/kg glyphosate eq.) → CF: 1.02 Calculation of CFs based on LOQ results or one single trial is not applicable in view of the RMS.	Expert consultation: MSs to discuss the results of the processing studies in barley. Note: Processing studies conducted at higher application rates (4300 and 8600 g/ha) and with PHI ≥ 7 days should indeed be taken into account to derive PF and CF (and not only studies conducted at application rates in compliance with the cGAP). A sufficient number of processing studies is therefore available to derive PF and CF for barley malt.

Processing (B.7.7)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
3(45)	Vol. 3, B.7.7-11, Processing studies on Wheat	EFSA: It is unclear in tables B.7.7-16, B.7.7-18 and B.7.7-19 if AMPA residues are expressed as mg AMPA/kg or as mg glyphosate equivalent/kg,	GTF: For B.7.7-19 it is confirmed that residues are expressed as mg AMPA/kg RMS: AMPA is generally presented as AMPA unless noted to be calculated otherwise.	Addressed AMPA levels in Tables B.7.7-16 to B.7.7-19 (pp. 231 to - 237) are expressed as AMPA equivalent.

Livestock feeding (B.7.8)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
3(46)		FR: agreed	RMS: Comment noted.	Addressed
3(47)	Vol. 3, B.7.8, Livestock feeding studies	EFSA: In table B.7.8-1, it is unclear if the AMPA feeding levels are expressed as "*mg AMPA/kg bw*" or as "*mg glyphosate equivalent/kg bw*". In the same way, in table B.7.8-2, are the AMPA residue levels expressed as "*mg AMPA/kg*" or as "*mg glyphosate equivalent/kg*"? This point should be clarified.	GTF: The AMPA feeding levels are expressed as mg AMPA/kg bw, and AMPA residue levels are expressed as mg AMPA/kg. The same is true for the hen feeding study (Tables B.7.8-13, -14 and -15) and the swine feeding study (Tables B.7.8-24 and -25). RMS: AMPA is generally presented as AMPA unless noted to be calculated	Addressed AMPA levels in Tables B.7.8-1 and B.7.8-2 (pp. 241 and 242) are expressed as AMPA equivalent.

Livestock feeding (B.7.8)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			otherwise.	
3(48)	Vol. 3, B.7.8, Livestock feeding studies	EFSA: Feeding dose levels in the Graham study (1987) are reported as 0.012, 0.13, 1.44, 7.38 and 19.4 mg eq/kg bw/d on page 243, while reported as 0.012, 0.0053, 0.13, 03.78 and 19.4 mg eq/kg bw/d in tables B.7.8-3 and B.7.8-4. Clarification is requested.	GTF: We agree that it is unclear how these values are derived. The values on p 243 may be correct, the values in the tables must be incorrect. RMS: Table header are a left-over from a previous draft and wrong. Correct feed levels are 0.012, 0.13, 1.44, 7.38 and 19.4 mg eq/kg bw/d as used for MRL estimation. RAR to be amended.	Open point: RMS to amend in a revised RAR, the feeding levels reported in Tables B.7.8-3 and B.7.8-4 (correct values: 0.012, 0.13, 1.44, 7.38 and 19.4 mg eq/kg bw/d)
3(49)	Vol.3, B.7.8.1., Livestock feeding studies	LV: Please clarify if any unusual health and behaviour of animals was observed during these studies.	GTF: The MON and SYN livestock feeding studies were reviewed. MON studies: Cow study (RIP9501250) – Nodules (apparent hepatic abscesses) were observed in one cow, and kidney lesions in another. Both were retained in the study. No observations were considered treatment related. Hen study (RIP9501252) – all findings were normal and no treatment-related observations were made. Swine study (RIP9501251) – one animal (lowest treatment group) was sacrificed early due to gastric ulcers. Examinations of all other	Open point: RMS, to insert in a revised RAR (section B.7.8.1 on animal feeding) a statement related to observations on animal health and behaviour.

Livestock feeding (B.7.8)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			animals were normal. SYN studies: Cow study (RIP9500024) and hen study (RIP9500025) - There were no apparent treatment-related effects on the general condition of the animals, their behaviours, body weights, feed consumption or egg/milk production. RMS: Observations as described by GTF will be checked and implemented in the respective study results. For the N-acetly-glyphosate studies included in the RAR the following observations from the study reports will be included: Cows (McLellan, ASB2008-2653): Concerning animal health during the study post-mortem histology showed pyometra in one animal and moderate multifocal hepatic abscesses and a mild bile duct hyperplasia in another animal. Both effects were not related to the dose rates administered. Hens (Dibb-Fuller, ASB2008-2652):	

Livestock feeding (B.7.8)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			no observations	

Succeeding/Rotational crops (B.7.9)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
3(50)		FR: agreed	RMS: Comment noted.	Addressed

MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
3(51)	Vol. 1, Level 1, 2.7.9, Proposed MRLs and compliance with existing MRLs, page 103 Also relevant for Vol. 3, Annex B.7.12,	GTF: In Vol.1 it is indicated 'In comparison to established MRLs for glyphosate (according to Reg. (EC) 396/2005) the MRLs for barley and oats (20 mg/kg), wheat and rye (10 mg/kg), olives (1 mg/kg) and bovine kidney (2 mg/kg) are lower than the values estimated in this document.' It should be noted that the increase in	RMS: noted. Following amendment included: "Higher MRL proposals for plant commodities result from the implementation of the harmonized OECD MRL Calculator procedure."	Addressed MRL proposals in the RAR might differ from the MRL values currently established under Reg. (EC) 396/2005 since: 1) MRL proposals in the RAR are based on the GAPs supported as representative uses for the renewal of

MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
	Proposed EU MRLs and justification for the acceptability of those residues (Annex IIA 6.7; Annex IIIA 8.7)	MRL reflects a change in calculation methodology and does not reflect new data/higher residues.		the approval. Other existing uses (not supported in the RAR) might be authorised at EU level and/or different residue datasets might have been submitted to derive the MRL values currently published under Reg. (EC) 396/2005. 2) In addition, the OECD MRL calculator often results in higher MRL proposals compared to the previous approach based on the Rber/Rmax calculations. All existing MRLs will be reconsidered further, in the framework of the MRL review under Art. 12 of Reg. (EC) 396/2005.
3(52)	Vol. 3, B.7.12, Proposed EU MRLs and justification for the acceptability of those residues	NL: It appears that not all residue data (e.g. barley and oats grain) are supported by the current MRL. Will there be any continuation regarding these MRLs?	GTF: See 3(51), It should be made clear in the RAR that the increase in MRL reflects a change in calculation methodology (OECD calculator) and does not reflect new data/higher residues. RMS: After Annex I re-inclusion a MRL review is foreseen in Reg. (EC) 396/2005.	See expert consultation 3(33)
3(53)	Vol. 3, B.7.12.3,	EFSA: EFSA is of the opinion that an insufficient number of trials has been	GTF: Refer to 3(23) and 3(26) for a discussion of PHI. A provisional MRL can	See data requirement 3(26)

MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
	MRL proposal for olive.	submitted to derive MRL for olive and that GAP for olive have to be reconsidered (a PHI has to be defined for the treatment on olives fallen to the ground). (see comments in 3(23) and 3(26))	be considered. RMS: Agreed, see 3(26).	
3(54)	Vol. 3, B.7.12.5, MRL proposal for barley and oats	EFSA: As mentioned under comment 3(33), selection of the data for MRL calculation has to be reconsidered. NEU and SEU data sets are not significantly different (U-test, 5%) and therefore, can be merged to propose MRL, HR and STMR.	GTF: This is considered to be a broader question concerning data interpretation not specifically related to glyphosate. RMS: see 3(33)	See expert consultation 3(33)

MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
3(55)	Vol. 3, B.7.12.6, MRL proposal for wheat and rye	EFSA: As mentioned under comment 3(34), selection of the data for MRL calculation has to be reconsidered. Moreover, separate MRL proposals have to be done for wheat (NEU+SEU) and rye, since wheat and rye data sets are significantly different (H-test, 5%). Moreover, the highest value in wheat grain is questionable (possible inversion values grain/straw in DE trials on variety Kraka, see comment in 3(8)). If this value has to be disregarded, a MRL of 10 mg/kg for wheat is sufficient. At least, this inconsistent trial should be disregarded. NEU and SEU data sets are not significantly different (U-test, 5%) and can therefore be merged to propose MRL, HR and STMR.	GTF: This is considered to be a broader question concerning data interpretation and selection not specifically related to glyphosate. Refer to 3(36) RMS: see 3(34)	See expert consultation 3(33)
3(56)	Vol. 3, B.7.12.8, MRL proposal for animal products.	EFSA: The changes in the selection of the residue values to be taken into account for MRL, STMR and HR calculations, as proposed by EFSA in comments 3(6) and 3(7), are of no significant impact on the animal burden calculations presented in tables B.7.12-7, B.7.12-8 and B.7.12-9, and EFSA agrees on the MRL values proposed	RMS: acknowledged.	Addressed MRLs for products of animal origin proposed by the RMS in the RAR are agreed.

MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		by the RMS for products of animal origin.		
3(57)	Vol3, B.7.12.8 Animal commodities ; p296	FR: It is noted that "N-acetyl-glyphosate can also not be taken into account, since no information in residues in imported feed items were evaluated within this document". However, some residue data on GAT modified crop from USA (maize and soybean) are presented p 306.	GTF: The GTF agrees that the proposed MRLs for animal commodities are appropriate and that consideration of changes needed to accommodate GAT modified crops should be handled separately. RMS: GMO and import tolerances are not within the scope of this RAR. A complete consideration of all uses, including imported commodities, is foreseen after Annex I re-inclusion.	Addressed GMO import tolerances are not in the scope of the RAR and no residue trials conducted on GMO crops have been submitted. Therefore, residues resulting from the use of glyphosate on GMO crops are not taken into account in the animal burden calculations. Residues in GMO crops will be considered further under Article 12 review or, in the framework of Article 10 of Reg. (EC) 396/2005.
3(58)	Vol3, B.7.12.8 Animal commodities; p296	FR: It is noted that "N-acetyl-glyphosate can also not be taken into account, since no information in residues in imported feed items were evaluated within this document". It could be then concluded that the proposed MRL for animal commodities should be revised as soon as new data on GAT modified feed would be available. Awaiting for these data, it could be more accurate to precise that "no feed	GTF: The GTF agrees that the proposed MRLs for animal commodities are appropriate and that consideration of changes needed to accommodate GAT modified crops should be handled separately. RMS: This proposal is management based and outside the scoop of the RAR. However, since import tolerances have been granted for GAT crops and CXLs exist, the	See comment 3(57)

MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		commodities issued from GAT modified crops should be fed to livestock".	enforcement of such a suggestion is unlikely.	
3(59)	List of endpoints, Residues (Annex Point IIA 6.7) Also relevant for: Vol. 3, Annex B.7.16, Summary and evaluation of residue behaviour, page 312	GTF: Residue definition for monitoring does not include N-acetyl Glyphosate or N-acetyl AMPA but is defined as Glyphosate only for foods of both plant and animal origin. *For further explanation please refer to Column 3 of the original commenting table.*	RMS: Comment unclear. New RD including N-acetyl-glyphosate proposed in RAR. To be discussed.	Addressed Enforcement residue definition for products of animal origin is proposed as "*sum glyphosate and N-acetyl-glyphosate, expressed as glyphosate*", considering all scientific information made available for the peer review of the active substance (including information on GMO glyphosate tolerant plants).
3(60)	Vol 3, B.7.12.8 Animal commodities ; p298	FR: It is surprising to see that the mean DB for chicken is higher than max DB. This is clearly linked to the addition of AMPA residue level. It could be helpful to precise that Max DB is calculated with regard to enforcement residue definition when mean DB is calculated according to RA residue definition and then avoid any misunderstanding.	RMS: The basis for the calculation is presented in the text and in each table header except for Table B.7.12-9, which will be amended.	Open point: RMS to reconsider in a revised RAR, the maximum and median animal dietary burdens reported in Table B.7.12-9.
3(61)	Vol 3, B.7.12.8 Animal commodities ; p302	FR: the MRL proposed for bovine commodities could be extrapolated to the ruminant group. So MRL on sheep and goat	GTF: We agree. EU guidance allows MRLs, STMRs and HRs for bovine commodities to be extrapolated to all terrestrial livestock.	Open point: RMS to propose in a revised RAR, extrapolation to the ruminant group,

MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		commodities could be proposed in accordance with MRL proposed for bovine commodities.	Since separate values are proposed for swine, the MRLs and STMRs for bovine commodities should be extrapolated to sheep and goat commodities. RMS: agreement, to be amended	considering the values derived for bovine (values to be added in the consumer risk assessment)..
3(62)	Vol. 3, Annex B.7.13, Proposed EU Import tolerances and justification for the acceptability of those residues, page 303	GTF: Table B.7.13-1 title should be 'Summary of import tolerances on CP4-EPSPS and GOX modified crops', not just 'GOX modified crops'. Soya beans are modified only with CP4-EPSPS, and the maize included in the first DAR was modified with both CP4-EPSPS and GOX.	RMS: agreed, to be amended	Open point: RMS to reconsider in a revised RAR, the title of Table B.7.13-1 (should include CP4-EPSPS modification, since relevant for maize).
3(63)	Vol. 3, Annex B.7.13, Proposed EU Import tolerances and justification for the acceptability of those residues, page 303	GTF: The section under 'GAT modified crops' should reflect the Standing Committee decision of February 3-4 2011 and therefore only present OPTION 1. Refer to further explanations provided under Point (3(59))	RMS: The newly proposed RD for enforcement purposes will probably be discussed. Therefore a complete overview of the option are helpful within one document. The history of RDs for glyphosate is presented under B.7.3.	Addressed Information on residues in GMO plants reported in section B.7.13 are informative only, as import tolerances and uses of glyphosate on GMO plants are not in the scope of the renewal process.
3(64)	Vol 3, Annex B.7.14, Basis for differences with Codex MRLs, page 307	GTF: The JMPR 2011 review included glyphosate tolerant (CP4 EPSPS only) sugar beets and sweetcorn, and conventional lentils, in addition to the GAT crops.	RMS: yes, but these commodities had - in contrast to GAT crops - no impact on the RD. The level of the MRL itself is not considered relevant at this stage.	Addressed CP4-EPSPS tolerant sugar beet and sweet corn crops were considered in the 2011 JMPR review, but with no

MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
				impact on the proposed residue definition.
3(65)	Vol. 3 B.7.15.1 Long-term dietary intake assessment; p309	FR: the potential presence of GAT modified commodities is not taken into account in risk assessment, although some residue data on GAT modified crop from USA (maize and soybean) are presented p 306. It could be then concluded that the consumer risk assessment should be revised as soon as new data on GAT modified crops(lentils, soya, rapeseed, maize, corn) would be available. Awaiting for these data, it could be more accurate to precise that "no food commodities issued from GAT modified crops should be authorized for human alimentation".	GTF: The GTF agrees that the current dietary assessment is appropriate and that consideration of residues from GAT modified crops should be handled separately. RMS: The proposed phrase is a management restriction and outside the scoop of the RAR. The assessment is normally based on the representative uses applied for by the notifier. The RMS included the complete information on GMO crops to achieve a complete basis for setting a residue definition. Assessment of residues and the dietary intake is limited to the representative uses.	Addressed Chronic consumer risk assessment is conducted considering the representative uses supported in the framework of the renewal only (import tolerances and uses on GMO plants are not in the scope of the peer review).
3(66)	Vol. 3, Annex B.7.18, Appendix – Supervised field trials, page 353	GTF: Discrepancies were noted in the 'Applicant' and 'Commercial Product' listed in a number of the tables. Each instance is listed below on a separate line with the page number(s) in Column 1 and comment in Column 2.	RMS: acknowledged	See Open point:s/comments 3(67) to 3(79)

MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
3(67)	Vol. 3, Annex B.7.18, Appendix – Supervised field trials, pages 354, 358, 370, 374, 380, 405, 410, 413, 422, 427, 441, 445, 448, 522, 525, 531, 533, 751, 931	GTF: The content of a.i. is listed as 355.7 g/l. The value should be 360 g/l.	RMS: agreed. Amended in RAR	Open point: RMS to corrected active substance content in Appendix B.7.18 (360 g/l instead of 355.7),
3(68)	Vol. 3, Annex B.7.18.2, Pome fruit, page 370	GTF: The commercial product should be Glistar, not Roundup.	RMS: no agreement. In the study side-by-side trials using Glistar and RoundUp were conducted. The table with Glistar results is presented at page 371+372.	Addressed Table pages 370-371 refers to Roundup. Results for Glistar are pages 372-373
3(69)	Vol. 3, Annex B.7.18.3, Stone fruit, page 382	GTF: This study was generated by Monsanto using a Monsanto formulation but Cheminova A/S has joint access. Applicant should also include Cheminova A/S	RMS: Tables are generated from the Germany study database used for authorisation of plant protection products. The first submission of the study was by Monsanto, therefore the company is listed as applicant. Addition of further companies with joint access does not provide helpful information for the assessment.	Addressed Applicant who submitted the study is Monsanto. Addition of further companies with joint access to the study is no relevant.
3(70)	Vol. 3, Annex B.7.18.3, Stone fruit, page 383	GTF: This study was generated by Monsanto using a Monsanto formulation but Cheminova A/S has joint access. Applicant should also include Cheminova A/S	RMS: see 3(69)	see comment 3(69)

MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
3(71)	Vol. 3, Annex B.7.18, Appendix – Supervised field trials, pages 555, 692, 757, 942	GTF: The formulation (MON 78568) is listed as SG. It should be listed as WG.	RMS: Study report R A1157 (RIP2005-200) lists MON 78568 as SG formulation. 4 - Test items Name / Formulation / Batch N° / Active ingredient / CAS N° / C.A. name / Nominal content [1] / Actual content [1] MON 2139: SL / A0C2701102 / Glyphosate / [1071-83-6] / *N*-(phosphonomethyl)glycine / 360 g/l / 361 6 g/l MON 78273: SL / GLP-0102-10984-F / Glyphosate / [1071-83-6] / *N*-(phosphonomethyl)glycine / 540 g/l / 541 g/l MON 78568: SG / GLP-0102-11014-F / Glyphosate / [1071-83-6] / *N*-(phosphonomethyl)glycine / 65 % / 65 6 % [1] Acid equivalent The test items were supplied by MONSANTO EUROPE	Open point: RMS to corrected PPP formulation pages 555, 692, 757 and 942 (WG instead of SG),
3(72)	Vol. 3, Annex B.7.18, Appendix – Supervised field trials, pages 401, 412, 417, 419, 420, 426, 429, 430, 432, 433, 434, 435, 436, 438, 439, 447, 451, 453, 454, 585, 586, 592, 592, 594, 599, 601, 607, 610, 615, 619, 623, 627, 650, 653, 660, 662, 669, 674, 676, 707, 814, 844, 871, 892, 894, 914, 916, 946, 960	GTF: The formulation is listed as SC. It should be listed as SL. In some instances the formulation type is also listed as SC in Column 10.	RMS: agreed. Amended in RAR	Open point: RMS to corrected PPP formulation pages 401, 412, 417, 419, 420, 426, 429, 430, 432, 433, 434, 435, 436, 438, 439, 447, 451, 453, 454, 585, 586, 592, 592, 594, 599, 601, 607, 610, 615, 619, 623, 627, 650, 653, 660, 662, 669, 674, 676, 707, 814, 844, 871, 892, 894, 914, 916, 946 and 960 (SL instead of SC),

MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
3(73)	Vol. 3, Annex B.7.18.18, Barley (Northern Europe), page 563	GTF: Applicant is Cheminova A/S and not Monsanto	RMS: see 3(69)	see comment 3(69)
3(74)	Vol. 3, Annex B.7.18.18, Barley (Northern Europe), page 574	GTF: The commercial product is missing. It should be MON 52276. The formulation is listed as SC. It should be listed as SL (both in the header and in Column 10).	RMS: agreed. Amended in RAR	Open point: RMS to add PPP name and to correct formulation type in page 574 (MON 52276 and SL formulation).
3(75)	Vol. 3, Annex B.7.18.18, Barley (Northern Europe), page 578	GTF: The commercial product is missing. It should be MON 44068.	RMS: agreed. Amended in RAR	Open point: RMS to add PPP name in page 578 (MON 44068).
3(76)	Vol. 3, Annex B.7.18.20, Oats, page 704	GTF: Commercial Product is CHE 3607	RMS: agreed. Amended in RAR	Open point: RMS to add PPP name in page 704 and 711 (CHE 3607).
3(77)	Vol. 3, Annex B.7.18.20, Oats, page 711	GTF: Commercial Product is CHE 3607	RMS: agreed. Amended in RAR	See comment 3(76)
3(78)	Vol. 3, Annex B.7.18.22, Wheat (Northern Europe),	GTF: The formulation (MON 44068) is listed as SG. It should be listed as WG.	RMS: agreed. Amended in RAR	Open point: RMS to corrected PPP formulation page 771 (WG instead of SG),

MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
	page 771			
3(79)	Vol. 3, Annex B.7.18.22, Wheat (Northern Europe), page 894	GTF: The commercial product is not listed. It should be MON 14478.	RMS: agreed. Amended in RAR	Open point: RMS to add PPP name in page 894 (MON 14478).
3(80)	Vol. 1, LoEP,; Conversion factor for animal commodities.	EFSA: RMS' statement on CF for animal commodities "*not applicable, ratio of metabolites strongly depends on the amount of GMO-feedstuff in the diet*" is right and supported by EFSA. However and since significant levels of AMPA are expected to be present in kidney, EFSA is of the opinion that a CF of 1.2, derived from the Cowell and Graham (1987) feeding studies, has to be proposed as a default CF value for kidney, having in mind that additional intakes of AMPA and N-acetyl-AMPA resulting from the consumption of GMO plants may request a higher CF value.	RMS: No agreement. The study by Cowell et al involved administration of a 9:1 mix of glyphosate and AMPA. In goat metabolism studies conducted with ^{14}C-glyphosate the formation of AMPA was negligable (<10%). In addition N-acetyl-glyphosate, which is also included in the RD for enforcement purposes of animal commodities, gave no or negligable residues of AMPA or N-acetyl-AMPA in goat metabolism and feeding studies. On the other hand GOX GMOs contain much higher AMPA levels than other crops. Therefore the composition of the feed itself is relevant for the final CF in the animal tissue. Since the current assessment may not cover all option (conventional burden, high GOX burden, high NAG burden) the CF may be variable in both directions (near 1 for high NAG, much higher for high GOX). The only option the	Expert consultation: Setting of conversion factors for risk assessment in animal matrices, based on the representative uses, should be discussed in an expert meeting/

MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			RMS sees is limiting the CF to European uses without GMO, where the ratio of Glyphosate and AMPA in the feed should pass through the animals approximating the CF of 1.2. However, the practical use in not seen by the RMS and a general consensus should be met at an Expert Meeting.	

Other comments				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
3(81)	Vol.3, B.7.17 References relied on; p 353	FR why some studies (highlighted in yellow) were not “part of the dossier for the renewal”? Could you please precise the meaning of this sentence?	RMS: The owner of the GAT-modification (and all studies related to it) is no member of the GTF. The data was included in the RAR by the RMS based on the knowledge from applications for import tolerances. It is open how the ownership of the data will be handled concerning data protection issues.	Addressed Studies highlighted in yellow in the reference list, refer to the owner of the GAT modification, not part of the GTF.

Other comments				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
3(82)	Vol.3, B.7.18 Appendix – Supervised field trials	FR: 1 trial treated at BBCH 69 is underlined for pome fruits p375 – The selection in field trials is not "fully" clear, could you please give some precisions?	GTF: See 3(24). The GAP for tree crops is driven by the need to treat weeds and is independent of the growth stage of the crop, and no PHI is required. The majority of trials have been conducted at a crop growth stage around 7 (fruit development) to provide a worst-case situation for potential residues. The data show that when applied around these timings, there are no glyphosate residues in edible portions (fruit, nuts, olives). Therefore it is clear that there will be no residues at any timing (of the crop) and trials treated at BBCH 69 are equally applicable. In fact trials treated at any stage could be included and serve to demonstrate that residues are <LOQ in every case for tree crops. RMS: The mode of application for glyphosate is ground directed soil treatment. Since glyphosate is not significantly metabolized in plants, a longer period between treatment and harvest is considered acceptable, since more time for the residues to be taken up via the roots and translocated into the fruits has passed.	See expert meeting 3(33)

Other comments				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
3(83)	Vol.3, B.7.18 Appendix – Supervised field trials	FR: Even if it could be discussed how LOQ where "managed" FR considers the approach as consistent: When compound 1 and compound 2 < 0.05* then "total residue" noticed as 0.05* When compound 1 = 0.05 and compound 2 < 0.05* then "total residue" noticed as 0.10 (if "close" molar mass) This point could be a general point of discussion (other compounds could be concerned)	GTF: Refer to 3(28) RMS: For the RAR the approach used by JMPR was taken as a basis. For both compound <LOQ, their individual ratio in plant metabolism studies should be considered.	See comment 3(28) Expert consultation: MSs to discuss this general aspect in an expert meeting.
3(84)	List of Endpoints	NL: In the LoEP it is stated that the TMDI (consumer risk assessment) is not calculated, while in Volume 1 and Volume 3 part B7 a calculation of the TMDI is provided.	RMS: Only NEDI was calculated taking into account STMR values and PF/CF, when applicable. Since no GMOs were taken into account for consumer exposure, calculation of a TMDI is futile.	Addressed TMDI calculation using MRL values has not been performed and is not requested.

Other comments				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
3(85)	Vol 3, B.7, Residue data	NL: In the toxicology section, the surfactant POE-[redacted] is being evaluated. Shouldn't this surfactant be considered in the residue section as well, since it appears to be more toxic that the active substance (in accordance with article 27 of Regulation 1107/2009)?	GTF: The representative formulation used in the submission does not contain POE [redacted] Any discussion of POE [redacted] surfactants or residues is out of scope of this renewal evaluation. RMS: The formulation use for the Annex I Renewal does not contain POE-[redacted] For an assessment of the residues neither data nor a legal basis are available.	Addressed The representative formulation for renewal of the approval does not contain POE-[redacted] and therefore, this surfactant is not considered in the residue section.
3(86)	Metabolism in GAT modified crops			Data requirement: Metabolism in GAT-modified crops, metabolism in livestock animals with N-acetyl-glyphosate, hydrolysis stability of N-acetly-glyphosate and N-acetyl-AMPA. The data requirement has already been identified in the RAR

4. Environmental fate and behaviour

Route and rate of degradation in soil (B.8.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
4(1)	Vol. 3, B.8.1.1.1 Aerobic degradation.	EFSA: RMS indicates that studies Galicia and Morgenroth, 1993, BVL no 1932059 and Matla and Vonk, 1993, BVL no 2151389 in the glyphosate monograph were considered acceptable during the first EU review of glyphosate in 2001 based on evaluation criteria and guidance at that time. As expressed, it is not clear here if the studies are still considered acceptable; however this is clarified later and in the LoEP. If fully valid it would have been helpful to reproduce the summary of the studies in the new RAR in order to have all relevant information in a single document.	RMS: RMS understands that it would be helpful having all relevant information in one document, however sufficient study summaries of Galicia and Morgenroth, 1993, BVL no 1932059 and Matla and Vonk, 1993, BVL no 2151389 can be found in the first DAR for Glyphosat from 1998. Since providing all study summaries of acceptable studies even when there are actually already available in the first DAR again in the new RAR would mean considerable extra work, RMS would prefer to not provide these study summaries but to continue referring to the first DARs of Glyphosate and Glyphosate Trimesium where possible	Addressed
4(2)	Vol. 3, B.8.1.1.1 Aerobic degradation.	EFSA: According to the RMS Kesterson & Atkins, 1991 and Honeger, 1992 were not considered valid in the first review for reasons that do no longer apply and that they may be considered valid now (except for sandy loam soil in Kickapoo). New study summary and assessment needs to be produced for these studies to update the	RMS: Agrees with EFSA. Since Kesterson & Atkins, 1991 were considered not valid in the previous RAR and is now considered acceptable, a new study summary of Kesterson &Atkins, 1991 together with the additional information that can be found in Honegger (1992) will be provided in a revised RAR	Open point: RMS to provide a transparent summary and evaluation of the studies Kesterson & Atkins, 1991 and Honegger (1992) in a revised RAR.

Route and rate of degradation in soil (B.8.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		assessment to current evaluation criteria.		
4(3)	Vol. 3, B.8.1.1.1 Aerobic degradation. Table B.8.1-2.	EFSA: Table B.8.1-2 is a helpful overview of the route of degradation in soil studies considered acceptable by the RMS. An apparent pH dependence of mineralization is noted. This may be the result of differential degradation route or just be caused be the pH dependent solubility of CO_2 in water.	GTF: In the aerobic soil degradation studies, $^{14}CO_2$ is trapped in gaseous form by sweeping air into each soil unit which is then passed through a series of sodium hydroxide trapping reagent. The pH dependent solubility of CO_2 in water should be inconsequential because of the experimental setup employed in the laboratory aerobic soil degradation studies reported in the glyphosate renewal dossier. Differential rate of mineralization does not necessarily support the notion that the route of degradation of glyphosate differs in various soils. Co-RMS: agrees with GTF. RMS: There seems to be indeed a relationship between mineralization and pH. The study duration varies greatly between the different studies and different temperature and moisture conditions were applied, however the pH dependency remains when plotting the CO_2 production at similar days (56 – 70 d) against the pH value of the soil and a trend can also be seen for soils incubated at the same temperature and	Data requirement Applicant to provide a document that sets out the different information available and discusses the pH dependency of biodegradation and adsorption of glyphosate and AMPA. In particular the document should discuss the apparent pH dependence of mineralisation and the likelihood of differential degradation route(s) depending on pH. Note the document cited in column 3 of the reporting table at comment 4(3) (pdf icon only present, but not the actual document), may be sufficient to address this request. See reporting table comment 4(3).

Route and rate of degradation in soil (B.8.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			moisture. The general discussion about pH dependency of biodegradation and adsorption of glyphosate and AMPA took place between GTF and RMS in 2013 and the argumentation of GTF (see enclosed pdf document) was considered plausible and was accepted by RMS. Comment of GTF on the first draft oft the	
4(4)	Vol. 3, B.8.1.1.1 Aerobic degradation. Goodyear, A 1996.	EFSA: the exclusion of soil A to derive end points for exposure assessment of Europeans agricultural soils is agreed.	RMS: noted	Addressed
4(5)	Vol. 3, B.8.1.1.1 Aerobic degradation. Esser, 1996.	EFSA: The exclusion of study Esser, T. 1996 is agreed.	RMS: noted	Addressed
4(6)	Vol. 3, B.8.1.1, Rate of degradation (Dorn, 2012)	SE: For transparency, please include visuals fits i.e. graphs of the kinetic fits from study Dorn, 2012 so the visual assessment is clear.	RMS: From our point of view, the results of the kinetic fits are sufficiently presented in the Tables presenting the kinetic evaluations of the studies. The optimized kinetic parameters together with standard errors, results of the t-test and of the χ^2 error are provided here. Results of the quantitative visual assessment of kinetic fits and the residual plots are provided in the column	Addressed

Route and rate of degradation in soil (B.8.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			'visual assessment'. The validation of the visual fits was performed according to the recommendations of FOCUS 2006, 2011 for persistence and modelling endpoints. RMS does not see further information gain by presenting all graphical fits. It will have no impact on the chosen endpoints but will unnecessarily enlarge the document and making it less easy to read. In general, one of the advantages of the EU-assessment procedure should be that in-depth validation of the assessment approach of the Notifier will be performed only by the RMS and other MS can benefit from his work. If there are special and reasonable questions to decisions of RMS, these special points (e.g. visual fits of individual kinetic modelling) should be discussed. However, it seems to be not constructive and necessary to provide all primary study information, if the provided assessment in the DAR/RAR by RMS is sufficiently documented and plausible.	

Route and rate of degradation in soil (B.8.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
4(7)	Vol. 3, B.8.1.1, Rate of degradation (RMS Comment and recalculation, kinetic analysis)	SE: On page 75 studies that have been data processed and kinetically recalculated by the RMS is discussed. However the Lewis and Turnball study (1992) has not been discussed in the text which also was recalculated by the RMS. Please include this study in the text and clarify why a new kinetic analysis was performed for this study.	GTF agrees. Lewis and Turnball (1992) study should be added to the list of other studies mentioned in the last Paragraph of page 75. RMS: Agrees with EFSA and Notifier.	Open point: RMS to add information on the study Lewis and Turnball (1992) missing from the last paragraph on page 75 of the RAR in an addendum. An explanation is necessary why a new kinetic analysis was performed by the RMS for this study
4(8)	Vol. 3, B.8.1.1, Rate of degradation (RMS Comment and recalculation, kinetic analysis)	SE: For transparency, please include visuals fits i.e. graphs of the re-evaluated kinetics conducted by the RMS so the fits to the visual assessment is clear.	RMS: see our reply to comment 4(6)	Open point: RMS to provide the visual fits i.e. graphs of the re-evaluated kinetics conducted by the RMS, so the fits to the visual assessment statements presented are clear. Note applicants fits are available to competent authorities as they have access to the complete dossier. Fits completed by the RMS cannot be retrieved from the dossier.
4(9)	Vol. 3, B.8.1.1, Rate of degradation, Table B.8.1-77, p.76	SE: There seems to be a typo in Table B.8.1-77 in regards to the optimised value of the DFOP fit. The k_2 value in the table indicates that DT_{50} is faster in the k_2 compartment than in the k_1 compartment. Furthermore the DT_{90}	RMS: Agrees, k1 (fast) and k2 (slow) were actually confused with each other here. In the summary Tables B.8.1-91, 8.1-93 and 8.1-94, they were allocated correctly. However, as the Notifier pointed out in	Open point: RMS to perform a kinetic re-evaluation of the Arrow soil (study Dean, 1995) using correctly 'processed' data including presenting

Route and rate of degradation in soil (B.8.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		seems to have the same value as $DT_{50,\ slow\ phase}$. Is this correct?	comment 4(29), the original residue data were used for kinetic re-evaluation of the Arrow soil (Dean, 1995) instead of the processed data. Thus, a new kinetic re-evaluation for this soil needs to be performed by the RMS	the visual fits in an addendum. see reporting table comments 4(9), 4(26) and also the related Open point: for another soil at 4 (29))
4(10)	Vol. 3, B.8.1.1, Rate of degradation, Table B.8.1-79, p.77	SE: In Table B.8.1-79 the $DT_{50,\ slow\ phase}$ for the DFOP fit seems to have the same value as DT_{90}, is this correct?	RMS: $DT_{50,slow}$ and DT_{90} had indeed the same value. However, a new kinetic evaluation needs to be performed for the Arrow soil. For details see answers to comment 4(9) and 4(29)	Addressed
4(11)	Vol. 3, B.8.1.1, Rate of degradation, Table B.8.1-85, p.80	SE: For transparency, please clarify what PMG stands for.	GTF: PhosphonoMethyl-Glycine (PMG)	Addressed RMS to consider proving the clarification in column 3 in a corrigendum or amended RAR
4(12)	Vol. 3, B.8.1.1, Rate of degradation, last paragraph, p.81	SE: According to the last sentence on page 81 "the residue data of PMG in soils Speyer 2.1 and Beedon Manor can be used without further processing". However the residue data of the Beedon Manor soil and the kinetic analysis is not provided in the kinetic re-analysis of the RMS. Please include the data and kinetic analysis of the Beedon Manor soil in the RAR.	GTF: The sentence highlighted by SE should be removed from RAR. Early draft RAR version initially contained kinetic re-evaluation data for TMS = trimesium salt (^{14}C- labelled at the TMS cation) of glyphosate trimesium test substance. The salt disassociates upon application leaving the active ingredient glyphosate anion. The TMS cation is not active and quickly degrades and its fate is independent from glyphosate's fate	Open point: RMS to remove the last sentence on page 81 "the residue data of PMG in soils Speyer 2.1 and Beedon Manor can be used without further processing" and the DT_{50} value related to TMS in the soil Beedon Manor from the Tables B.8.1-91 to and B.8.1-95 in an addendum. and update the DT

Route and rate of degradation in soil (B.8.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			in the environment. Therefore, RMS removed the TMS radiolabelled study raw data (Beedon Manor soil) from the Lewis and Turnball (1992) study but unfortunately the sentence highlighted by SE and the Tables B.8.1-91 to and B.8.1-95 were not revised accordingly. The DT_{50} values reported in Tables B 8.1-91 to B 8.1-95 for Beedon Manor clay loam is related to TMS. Co-RMS: agrees with GTF. RMS: Agrees with Notifier. The sentence needs to be removed	entries in the list of endpoints consequently.
4(13)	Vol. 3, B.8.1.1, Rate of degradation, Table B.8.1-94, p. 87 (Dean , 1995)	SE: In Table B.8.1-94 for study Dean (1995) the recalculated SFO DT_{50} actual is 300.7 days from DFOP slow phase. However according to table B.8.1-77 on page 76 FOMC fit seems to be a better fit (statistically) and would give a worst case recalculated DT_{50} actual of 412 days. Please explain why DFOP was chosen as a better fit than FOMC.	GTF believes deriving modelling endpoint from the FOMC fit in this case is not appropriate because 10% of the initial glyphosate concentration were not reached within the experimental period for the study. Extrapolation of the FOMC model beyond the duration of the study generally results in unrealistically long DT_{90} value and exactly for this reason FOCUS does not recommend deriving modelling endpoints from FOMC fit when 90% degradation of parent has not occurred. GTF believe DFOP fit is more appropriate for this soil. Co-RMS: agrees with GTF.	Addressed

Route and rate of degradation in soil (B.8.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			RMS: Agrees with Notifier, 10% of initial concentration was not reached during study duration, thus either DFOP or HS fit should be used to derive modelling endpoints	
4(14)	Vol. 3, B.8.1.1, Rate of degradation, Table B.8.1-94, p. 87 (Galicia & Morgenroth, 1993)	SE: In Table B.8.1-94 for study Galicia & Morgenroth, 1993 the recalculated SFO DT_{50} actual is 48.46 days from DT_{90} FOMC/3.32. However according to Table B.8.1-79 the DT_{90} from the FOMC fit is 347 days which would give a recalculated SFO DT_{50} actual of 104.5 days. Please explain the discrepancy.	GTF agrees that DT_{50} value of 48.46 is not supported by the data. However, it appears that DFOP is a better fit statistically than FOMC. Therefore, DT_{50} should be calculated from the slow phase of DFOP which should be 83.9 days. Co-RMS: agrees with GTF. RMS: also agrees that 48.46 d is not correct. However, since 10% of initial concentration was reached during the study, the DT_{90} FOMC/3.32 which is indeed 104.51 d should be used according to FOCUS kinetic recommendations.	Open point: RMS to correct DT_{50} value of the study Galicia & Morgenroth, 1993 in Table B.8.1-94 in an addendum. To do this they should present the FOMC and DFOP fits in the addendum (so it is transparent whether the FOMC or DFOP fit is better (current statement on visual fit would indicate that DFOP should be selected (good is better than acceptable) as proposed by applicant where they quote the lower chi2 to justify DFOP.)) Whichever kinetic gives the better fit should be selected resulting in a not normalised endpoint of 83.9 days (DFOP slow phase) or 104.5 days (FOMC DT90/3.32). The list of endpoints to be updated consequently.
4(15)	Vol. 3, B.8.1.1, Rate of degradation, Table B.8.1-94,	SE: In Table B.8.1-94 for study Galicia & Flückiger, 1993/Mamouni, 2002 for soil Speyer 2.2 the recalculated SFO DT_{50} actual	GTF believes deriving modelling endpoint from the FOMC fit in this case is not appropriate because 10% of the initial	Open point: RMS to delete DT_{50} and DT_{90} values of the soil Speyer 2.2 (study Galicia &

Route and rate of degradation in soil (B.8.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
	p. 87 (Galicia & Flückiger, 1993/Mamouni, 2002) Speyer 2.2, sand	is 45.4 days from DT_{90} FOMC/3.32. According to the study author of the kinetic analysis (Dorn, 2012) no acceptable fit could be derived for modelling endpoints. SE disagrees with the study author and agrees with the RMS that the Speyer 2.2 soil can be used in the kinetic analysis. However the DT_{90} FOMC/3.32 of 45.4 seems to be an error. According to Table B.8.1-63 the FOMC DT_{90} is >1000 days which would result in a recalculated SFO DT_{50} actual of 301 days. Furthermore the $\chi 2$ error is presented as 1.59 %. However $\chi 2$ error of 1.59 % does not correspond with the $\chi 2$-values presented in Table B.8.1-63. Please clarify where $\chi 2$ error of 1.59 % comes from.	glyphosate concentration was not reached within the experimental period for the study. FOCUS does not allow deriving modelling endpoints from FOMC fit when 90% degradation of parent has not occurred (please see decision flow diagram for deriving degradation parameters for modelling fate of parent compound, page 116 of FOCUS 2011). HS and DFOP models should be rejected based on the t-test results which showed great variations in confidence intervals for both models. Based on the FOCUS guidance highlighted above, GTF believes that the original conclusion of the study author of the kinetic analysis (Dorn, 2012) is correct and the conclusion should be that no acceptable fit could be derived for the modelling endpoints for this soil. Co-RMS: agrees with GTF. RMS: agrees with MS that neither the DT_{50} value nor the $\chi 2$ error is correct. However, when re-assessing the statistical parameter, it becomes clear, that none of the derived parameters are actually statistically reliable as can be seen by the standard errors and the high p-values of the t-test. Thus, the RMS	Flückiger, 1993/Mamouni, 2002) from the Tables B.8.1-93 and Tables B.8.1-94 in an addendum and update the list of endpoints consequently.

Route and rate of degradation in soil (B.8.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			agrees with the conclusion of the Notifier that no acceptable fit could be derived for this soil	
4(16)	Vol. 3, B.8.1.1, Rate of degradation, Table B.8.1-94, p. 88 (Lewis & Turnball, 1992)	SE: The residue data of the Beedon Manor soil and the kinetic analysis is not provided in the kinetic re-analysis of the RMS. Please include the data and kinetic analysis of the Beedon Manor soil in the RAR so it is clear where the modelling endpoints for this soil come from.	GTF: The DT_{50} values reported in Tables B 8.1-91 to B 8.1-95 for Beedon Manor clay loam is related to trimesium (TMS) salt (^{14}C-labelled at the TMS cation) of glyphosate trimesium test substance and its fate is independent from glyphosate's fate in the environment. The data for this soil should be removed from Tables. Co-RMS: agrees with GTF. RMS: agrees with GTF, see also answers to comment 4(12)	See Open point: at comment 4(12)
4(17)	Vol. 3, B.8.1.1, Rate of degradation, Table B.8.1-96, p. 90 (McLaughlin &, Schanne, 1996)	SE: In Table B.8.1-96 for study McLaughlin &, Schanne, (1996) for soil Speyer 2.3 the presented recalculated SFO DT_{50} actual is 42.14 days from DFOP_SFO and χ2error of 9.41. Firstly there seems to be a typo from which fit 42.14 days is derived from. According to Table B.8.1-72 the fit should be FOMC_SFO and not DFOP_SFO. Secondly, it is not clear where χ2 error of 9.41 comes from as the χ2 error of this study in Table B.8.1-72 is >15% (16.23%, DFOP_SFO and 16.48%,	GTF: In soils speyer 2.1 and speyer 2.2, mainly due to the continuous formation of AMPA from the degradation of glyphosate, the decline phase of AMPA was not reached during the study period (120 days), according to FOCUS (2006, 2011) no DT_{50} value could be derived for the metabolite AMPA from this study which was dosed with the parent substance glyphosate. RMS: the DT_{50} value for AMPA was indeed taken from the FOMC-SFO kinetic model and the correct χ2 error should be 16.48%.	Open point: RMS to correct kinetic model in Table B.8.1-96 to 'FOMC_SFO' and correct χ2 error for soil Speyer 2.3 of the study McLaughlin &, Schanne, (1996) in an addendum and update the list of endpoints consequently

Route and rate of degradation in soil (B.8.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		FOMC_SFO). Finally, it is not clear why soil Speyer 2.3 was included and not Speyer 2.1 or Speyer 2.2. According to the footnote under Table 9.1-96 "no statistically fit could be obtained (high chi2 error and/or t-test not passed at 0.05) for parent and metabolite". This statement is also applicable to soil Speyer 2.3 as the $\chi 2$ error is >15%. Please explain why soil Speyer 2.3 was included and not Speyer 2.1 or Speyer 2.2.	Regarding the reliability of the derived DT_{50} values for AMPA in the three soils, RMS agrees with Notifier, that a decline phase of AMPA was only observed in soil speyer 2.3. This is reflected in the high standard error and the failed t-test for the AMPA degradation constants of the soils Speyer 2.1 and speyer 2.2 as well as in the DT_{50} and DT_{90} values being >1000 d. For the soil Speyer 2.3, the standard error and the t-test of the AMPA degradation constant are acceptable. The t-test for the FOMC parameter β is not passing at level 0.05 but still at 0.1 and the $\chi 2$ error for the metabolite is with 16.48% only slightly >15%. Thus, it was decided that the derived DT_{50} value of AMPA is still reliable enough to be used for modelling	
4(18)	LoEP, Route of degradation (Annex IIA, point 7.1.1.1.1, mineralization after 100 days. Volume 1, level 1 point 2.8.1.1 Aerobic soil degradation (p 105 top).	DK: The rate of mineralization was 16.9 – 79.6 % AR. It was achieved after 60 – 180 days according to Volume 1, level 1. But in the LOEP the period is stated as 210 – 364 days. Please clarify and list corresponding time period.	GTF believes that 60-364 days should be the correct time period RMS: the correct days are 60 – 366 days	Open point: RMS to correct the days that refer to measured mineralisation days in the LoEP and consider in a corrigendum or amended RAR Volume 1, Level 1 point 2.8.1.1

Route and rate of degradation in soil (B.8.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
4(19)	Vol. 3, B.8.1.1.1 aerobic degradation	NL: RMS states that several studies (Kesterson & Atkins (1991, BVL no 1932061)/ Honegger (1992, BVL no 2325652)) that were deemed unacceptable in the first DAR are now considered acceptable (temperature deviation is no problem anymore). For these studies microbial activity was tested at the beginning of the incubation. However no measurement after the end of the experiment is described. Were the soils viable throughout the experiments (NB study duration 1 year)? See later remark of the RMS itself on page 9: "rate and pathway studies should normally not exceed 120 days, because thereafter a decrease of the soil microbial activity with time would be expected in an artificial laboratory system isolated from natural replenishment. Longer incubation periods should *[be]* accompanied by biomass measurements during and at the end of these periods." In Table B.8.1-33 further on it was acknowledged that the microbial biomass was not known at the end. NL doubts if these studies should now be considered reliable when such data	RMS: In study in question is Kesterson & Atkins (1991). Honegger (1992) is a review of the study that contains some additional information regarding the field sampling and storage of the investigated soil systems. The reasons (incubation temperature 25°C instead of 20°C) for excluding the study in the first DAR do not hold anymore. Thus a re-evaluation on the acceptability of the study was required. The microbial activity of the soil systems tested at the beginning of the study by determining of the number of microorganismen (aerobic bacteria, Actinomycetes and Fungi) indicated a viable soil. This is also supported by the derived DT_{50} values for glyphosate and AMPA in the soil Dupo, both being in the lower range of the determined DT_{50} values of all soils. From the residues of glyphosate and AMPA in the soils a continuous decline could be observed until the end of the study at 365 days, thus also indicating microbial viability of the soil. The RMS did now another kinetic re-evaluation to test how an exclusion of the residue data >120 days would affect the derived DT_{50} values of glyphosate and	Addressed

Route and rate of degradation in soil (B.8.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		are not available.	AMPA. The resulting DT_{50} value of glyphosate would be slightly longer with 3.06 d instead of 2.8 days, but for AMPA resulting DT_{50} value would be shorter with 43.32 days instead of 48.32 days. Thus, the RMS still considers the study Kesterson & Atkins acceptable for the soil Dupo and also regards an exclusion of the residue data >120 days as not sufficiently justified	
4(20)	Vol 3. B.8.1.1.2 Anaerobic degradation.	EFSA: Only the new study Lowrie et al 2003 is summarized in the RAR. From the LoEP it seems that the RMS has also maintained the results of the old studies Keir & Mackie, 2000 and McBain, 1987. If fully valid, it would have been helpful to reproduce the summary of the studies in the new RAR in order to have all relevant information in a single document. If not fully in accordance with current guidelines a new summary and evaluation would be needed to assess the acceptability of the end points derived from them.	GTF: The only study which is fully compliant with the requirements of the OECD guideline no. 307 (OECD, 2002) for anaerobic transformation in soil is Lowrie et al., 2003. According to the OECD 307 guideline, the anaerobic route and rate of degradation is investigated in a flooded soil maintained under anaerobic conditions following an aerobic aging period equivalent to one half-life. All other studies (Keir & Mackie, 2000; McBain, 1987; McEwen 2004; and Knoch 2003) were conducted according to the old SETAC anaerobic soil test guideline. In these studies degradation of glyphosate was investigated when applied directly to topsoil that had been flooded and converted to anaerobic conditions during a	Addressed

Route and rate of degradation in soil (B.8.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			pre-incubation period resulting in complete anoxic conditions. The SETAC anaerobic soil test guideline method uses a completely anaerobic/anoxic system which does not reflect the circumstances of the use of glyphosate for weed control. Prolonged and fully anaerobic conditions are expected to be rare throughout the surface soil zone where glyphosate occurs due to its limited mobility in soil. Co-RMS: agrees with GTF. RMS: RMS understands that would be helpful having all relevant information in one document. However, sufficient study summary of Keir & Mackie, 2000 is provided in the Addendum to the monograph, volume 3 for glyphosate and glyphosate trimesium. A study summary of McBain, 1987 can be found in the glyphosate trimesium monograph. Since providing all study summaries of acceptable studies even when there are actually already available in the first DAR again in the new RAR would mean considerable extra work. RMS would therefore prefer to not provide these study summaries but to continue	

Route and rate of degradation in soil (B.8.1)				
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			referring to the first DARs of Glyphosate and Glyphosate Trimesium where possible. However, RMS does not agree with the Notifier, that results from anaerobic studies performed according to SETAC anaerobic soil test guideline method should not provided anymore. Instead, the differences resulting from the different study designs of studies performed according to OECD, 307 and to SETAC should be discussed accordingly as has been done in the RAR under B.8.1.1.2. Since the results of anaerobic studies are not used for exposure assessment both the degradation in a completely anaerobic system as well as under semi-anaerobic conditions are regarded as additional information	
4(21)	Vol 3. B.8.1.1.2 Anaerobic degradation.	EFSA: Why studies McEwen (2004) and Knoch (2003) were not submitted to the RMS in the dossier? Have these studies been submitted to other national authorities? Does any new anaerobic metabolite is identified in these studies? It is stated that the OECD guidance 307 is not exactly followed, what are the deviations?	GTF: Please refer to the above comment. No new metabolites were identified in the mentioned studies and the overall results from these studies are consistent with results from Lowrie et al., 2003. GFT believes only one fully compliant anaerobic study (Lowrie et al., 2003) should be required for glyphosate renewal, however, GTF will provide final reports for the above non-	Data requirement Applicant to submit final reports of the anaerobic soil incubation studies studies of McEwen (2004) and Knoch (2003).

Route and rate of degradation in soil (B.8.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			compliant studies upon request. RMS: The studies of McEwen (2004) and Knoch (2003) were neither submitted for glyphosate renewal nor in the national authorisation procedure of plant protection products in Germany. The RMS agrees with EFSA and supports the submission of the studies for glyphosate renewal. The studies can then be evaluated by the RMS in an updated RAR or addendum.	
4(22)	Vol 3. B.8.1.1.3. Soil photolysis	EFSA: No results from the dark control are presented for the McGahen 1983 study. An evaluation of available photolysis studies according current guidance would be needed.	GTF: This study was submitted as part of the 2001 Annex I inclusion. The dark control data are presented in the original study report. GTF believes this study is not acceptable according to the current guidelines; therefore, it was not included in the GTF renewal dossier. Co-RMS: agrees with GTF. RMS: All of the studies submitted for the previous EU evaluation of glyphosate and glyphosate trimesium mainly demonstrated that photolysis on soil surfaces is not a significant degradation pathway for glyphosate. For this reason, the notifier did not submit a new photolysis study with glyphosate according to current guidance.	Open point: RMS to provide missing information of the study McGahen, 1983 (in particular results of the dark control)and revise the soil photolysis section in an addendum to the RAR.

Route and rate of degradation in soil (B.8.1)				
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			Since a re-evaluation of the studies according to current guidance or re-calculation of the derived degradation rates according to FOCUS kinetics would not provide additional information to be actually used for environmental risk assessment, the RMS considers it sufficient to only present the results of the soil photolysis studies previously considered acceptable without re-calculation. However, information that is missing in the study summaries of the monographs will be added in a revised RAR and errors in the section will be corrected when the study summary of the study Esser (1996) is added (see comment below)	
4(23)	Vol 3. B.8.1.1.3. Soil photolysis	EFSA: Why soil photolysis study of Esser (1996) has not been submitted to the RMS? If not available in the dossier it cannot be considered additional information.	GFT believes only one fully compliant soil photolysis study (Shepler & McGovern, 1989) should be required for glyphosate renewal, however, GTF will provide final report for Esser (1996) upon request. No new metabolites were identified in the mentioned study and the overall results from this study are consistent with results from Shepler & McGovern, 1989 study. Co-RMS: agrees with GTF.	Data requirement Applicant to submit the studies of Esser (1996) and to provide a final report

Route and rate of degradation in soil (B.8.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			RMS: Agrees with EFSA comment. The study of Esser (1996) should be submitted for glyphosate renewal and can then be evaluated by the RMS in an revised RAR in order to get a complete picture regarding soil photolysis.	
4(24)	Vol 3. B.8.1.2. Rate of degradation in soil. Laboratory studies.	EFSA: For studies presented in the first review of the substance individual data on measured amounts of parent and metabolite at the different sampling points is neither available in the original monograph not in the new RAR. This data is needed for the peer review. **Note:** the data is already available for Kesterson & Atkins 1991, Honegger, 1992, Runalls 1991 and Lewis & Turnbull 1992 studies for which RMS has done their own kinetic analysis.	GTF: The residues data for all other studies were provided in the GTF renewal dossier but are not summarised in RAR. RMS: The residues of the studies Galicia & Morgenroth (1993, BVL no 1932059) and of Matla & Vonk (1993, BVL no 2151389) can be found under the kinetic re-evaluation study Dorn (2012, BVL no 2315991). The residue data of the Galicia & Morgenroth (1993, BVL no 1932059) can be found under the study summary of the addendum Mamouni (2002, BVL no 2437068) and the remaining residue data for the studies for Kesterson & Atkins 1991, Honegger, 1992, Runalls 1991 and Lewis & Turnbull 1992 are available under the kinetic re-evaluation of the RMS. Thus all residue data of the studies considered acceptable are available in the RAR	Addressed

Route and rate of degradation in soil (B.8.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
4(25)	Vol 3. B.8.1.2. Rate of degradation in soil. Laboratory studies.	EFSA: Graphical representations of the fittings of laboratory study data are not available in the RAR. These may be needed for a proper peer review of the kinetic assessment.	RMS: Please see our reply to comment 4(6)	See Open point:s at comments 4(8) 4(9) and 4(14)
4(26)	Vol. 3, Annex B.8.1.2.1, Laboratory studies, page 74 and 87	GTF: The modelling DT_{50} value of 300.7 days reported in Table B.8.1-94 for glyphosate from the Dean, 1995 Arrow soil appears to be in error and it appears that this value corresponds to the DT_{90} value as reported in Table B.8.1-76. We note that the RMS re-calculated endpoint from the Dean, 1995 study is clearly an outlier among all the modelling endpoint reported in Table B.8.1-94 for glyphosate. Visual inspection of the residue data presented in column 3 for this soil highlight the fact that a DT_{50} of 300.7 days could not fit the experimental data. In other words, a DT_{50} of 300.7 days does not make any sense if the experimental data show glyphosate degradation had occurred nearly for two half-lives (75% degradation) during the 180 days of incubation. *For further explanation please refer to Column 3 of the original commenting table.*	RMS: The DT_{50} value of 300.7 days was derived from the rate constant k_slow phase= 2.305e-03 d^{-1} of the DFOP kinetic. However, as pointed out in comment 4(29), the original residue data were used for kinetic re-evaluation of the soil Arrow (Dean, 1995) instead of the processed data. Thus, a new kinetic re-evaluation needs to be performed by the RMS. However, the DT_{50} value was derived according to FOCUS kinetics guidance - since 10% of the initial concentration was not reached at the end of the study and the degradation showed biphasic behaviour, DFOP and HS kinetics were applied. The microbial biomass of the soil was determined at day 120 and 217. It was still 256 µgC/g dry weight shortly after the end of the study, thus indicating that the soil was still microbial viable. This will also apply after kinetic re-evaluation of the kinetics of the Arrow soil.	See Open point: at comment 4(9) and related Open point: at comment 4 (29).

Route and rate of degradation in soil (B.8.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
4(27)	Vol. 3, Annex B.8.1.2.1, Laboratory studies, page 75, " RMS Comment and re-calculation"	GTF: GTF disagrees with the RMS decision to include data points beyond study duration of 120 days for the studies of Dean, 1995 and Galicia & Morgenroth, 1993. Soil microbial biomass clearly declined in both studies. In addition, total microbial biomass measurement does not guarantee a proportional microbial diversity and activity, ensuring abundance of glyphosate/AMPA-degrading microorganisms in soil. We note that the RMS re-calculated endpoint from Dean, 1995 study appears to be an outlier in the modelling endpoint Table B.8.1-94 for glyphosate. This observation may suggest that inclusion of data points beyond 120 days resulted in endpoints that are not consistent with the weight of evidence. *For further explanation please refer to Column 3 of the original commenting table.*	RMS: understands the arguments of the Notifier for excluding data points >120 days from kinetic re-evaluations. However, as already pointed out in the RAR, RMS does not regard them sufficient enough to actually apply an approach that will lead to shorter and thus less conservative DT_{50} values. In OECD 307, that was cited by the Notifier for to justify its decision, no approach to actually exclude data points after 120 days is described. Here it is only recommended to accompany studies longer than 120 days with biomass measurements, as was done in both studies Dean, 1995 and Galicia & Morgenroth, 1993. Also in FOCUS guidance on kinetics, such an approach is neither described nor recommended. While the DT_{50} value derived from Dean, 1995 is longer than the remaining DT_{50} values for glyphosate, this is not true for the soil Les Evouettes of the study Galicia & Morgenroth (1993). Besides, a correction of the kinetics of the Arrow soil (Dean, 1995) by the RMS is required - see comment 4(29)- that will result in a shorter DT_{50} of 159.6 d for modelling, which is in the same range as the	Addressed

Route and rate of degradation in soil (B.8.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			DT_{50} value of the soil 18-Acres of the new study Ponte 2010, BVL no 2310255. Additionally, the degradation of glyphosate shows biphasic degradation behaviour in almost all investigated soils including the newly submitted studies performed according to OECD 307. For the remaining arguments against exclusion of the data points >120 days please refer to the RAR. Overall, the RMS is still convinced, that the evidence for excluding the data points >120 days is not strong enough and thus choose the more conservative approach of including all data points in the calculation.	
4(28)	Vol. 3, Annex B.8.1.2.1, Laboratory studies, page 75	GTF: On page 75, RMS states: "The approach of the study author, to use the overall mass balance as initial glyphosate concentration is not exactly according to FOCUS (2006, 2011) where it is only suggested to convert the initial metabolite concentration to mass parent and to add it to the value measured for the parent". GTF respectfully disagree with this conclusion for the reasons described in Column 3.	RMS: agrees with the argumentation of the Notifier. The paragraph will be deleted in the revised RAR	Open point: RMS to delete the paragraph cited in reporting table comment 4(28) on page 75 or the RAR in an addendum.

Route and rate of degradation in soil (B.8.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		For further explanation please refer to Column 3 of the original commenting table.		
4(29)	Vol. 3, Annex B.8.1.2.1, Laboratory studies, page 76	GTF: page 76, Table B.8.1-76, Dean, 1995 kinetic re-evaluation for glyphosate - The DFOP rate constants k_1 and k_2 values as reported in Table B.8.1-76 appear to be in error. The DT_{90} value of 300.73 cannot be reproduced by GTF. It appears that RMS re-calculations presented on page 76 (Table B.8.1-76), for Time 0 values (based on the M0 optimized values of about 90%) were not corrected for metabolites and bound residues as described in comment # 3 above.	RMS: Unfortunately, this is true. Not the processed residue data but the original residue data were used for the kinetic re-evaluation of the soil Dupo performed by the RMS. This needs to be corrected and a new kinetic re-evaluation needs to be performed. RMS double checked the kinetic re-evaluations of the other soil studies, however this mistake only appeared to have happened for this soil	Open point: RMS needs to re-do the kinetic re-evaluation of the soil Arrow (soil study Dean, 1995), see Open point: at comment 4(9) and to correct the Tables B.8.1-89, Tables B.8.1-90 and the summary Tables B.8.1-91, B.8.1-93 and B.8.1-94 in an addendum and update the list of endpoints consequently.
4(30)	Vol. 3, Annex B.8.1.2.1, Laboratory studies, page 79	GTF: page 79, Table B.8.1-82 – Kesterson & Atkins processed residue data – Day 0 residue data for glyphosate is not correct. This study was conducted with radiolabeled glyphosate and quantitation of AMPA was based on applied radioactivity which is independent of the relative mass of AMPA or glyphosate. AMPA % of applied on Day 0 should be added to glyphosate and should not be corrected for the molecular weight ratio of AMPA to glyphosate. *For further explanation please refer*	RMS: agrees with Notifier. The concentration of AMPA at day 0 should have been added to the concentration of glyphosate without correction for the molecular weight. This would have led to a concentration of 100.9 % AR instead of 94.48% for day 0. However, the effect on the resulting kinetic fit for Glyphosate is small: The resulting FOMC DT_{50} and DT_{90} values would be 0.96 and 9.45 d instead of now 1.01 and 9.31 d and the DT_{50} for modelling would change from now 2.80 to 2.84 d. RMS	Addressed

Route and rate of degradation in soil (B.8.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		to Column 3 of the original commenting table.	thus considers the current kinetic evaluation sufficient to describe glyphosate degradation in the soil Dupo.	
4(31)	Vol. 3, Annex B.8.1.2.1, Laboratory studies, page 83ff	GTF: The RMS has re-calculated the half-life of a number of studies and provided the χ^2 and t-test values for testing the goodness of fit; however, the visual assessment cannot be reviewed as no graphs have been included. Please provide the graphs in addition to other statistics such as confidence intervals so that the fits can be assessed.	RMS: please refer to our reply to comment 4(6)	See Open point:s at comments 4(8), 4(9) and 4(14).
4(32)	Vol 3, B.8.1.2.1 page 46	NL: it is not clear why DT50 and fit information is provided here, already before the description of the rate of degradation in soil studies. It is not clear if this refers to the Dorn kinetic results which are only described pages away. It seems that RMS has provided the reader with a certain kind of summary on beforehand. (Also for the route studies section in which studies are rejected first and then evaluated – this is a bit confusing).	RMS: The introductory part at the beginning of B.8.1.2.1 intends to provide an overview on the performed rate degradation studies in soil submitted for the first DAR as well as the current RAR together with information on their acceptability and the results. The same was provided for the route studies in B.8.1.1.1. Just above the paragraph with the DT_{50} and fit information of glyphosate and AMPA, the final result Tables selected by the RMS were cited. Thus it was thought apparent that the next paragraph refers to these values not the values of the Dorn (2012) study	Addressed RMS to consider if a corrigendum or amended RAR might adapted to provide the clarity provided by the response in column 3.

Route and rate of degradation in soil (B.8.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
4(33)	Vol 3, B.8.1.2.1, KIIA 7.2.1/03 Dorn study	NL: it is stated in Dorn that „The exclusion of sampling intervals beyond the typical duration of 120 days is justified when taking into account that viability of soil microbes is known to suffer during prolonged storage of soils under laboratory conditions". However for the earlier commented study of Kesterson/ Honegger (duration 12 months) no data points seem to have been left out. In Table B.8.1-26 the footnote 1) is missing (not tested?). Figures of all kinetic fits are missing. (also in RMS refitting) In Table B.8.1-75 correction factors for normalisation for tem and moisture would be appreciated. (also for later summarizing tables by RMS i.e. B.8.1-92-B.8.1-94) Page 80: PMG is mentioned (non labelled study Runnals), this means phosphonomethylglycine Anion but this is only mentioned on the next page. The best fit should be used for determination of the P criterion, not a back-calculated value. This only comes in place as a second tier: when the substance is indeed	GTF: Kesterson/ Honegger study was not part of GTF renewal dossier since GTF assumed that the study was not acceptable based on the EU 2001 Annex I inclusion evaluation of glyphosate. However, This study was kinetically evaluated by RMS. RMS: As described in the RAR on page 75 of the RAR and additionally in our answer to comment 4 (27), we disagree with the approach applied in the study Dorn, 2012 and re-calculated the kinetics for the studies where the data points >120 days were excluded. Thus, these data points were also included in the kinetic re-evaluation of the study Kesterson & Atkins, 1991, BVL no 1932061/ add. Honegger, 1992, BVL no 2325652 performed by the RMS RMS: can't find a footnote in Table B.8.1-26. Maybe a different Table was meant? Regarding the inclusion of figures for all kinetic fits please refer to our reply to comment 4(6) RMS: The DT_{50} values derived by Dorn, 2012 as well as the DT_{50} values derived by	Addressed Addressed Addressed

Route and rate of degradation in soil (B.8.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		PBT (but not toxic not bioacumulating), the DT90/3.32 approach can be followed as a second tier for candidates for substitution (CFS) alone. This approach is only intended for active substances as only they can be designated as candidates for substitution. (DG SANCO Working Document on "Evidence Needed to Identify POP, PBT and vPvB Properties for Pesticides" (version 3): The kinetic model that gives the best description of the chemical's behaviour should be selected. Guidance provided in FOCUS Degradation Kinetics Guidance (Sanco/10058/2005, ver 2.0, June 2006) on how to derive best fit DT50 should be applied. As regards the initial establishment of a list of CFS, if a DT50 value based on single first order kinetics is available in the list of endpoints, the cut-off value should be compared to it directly. Otherwise, the cut-off value should be compared to the DT90 value in the list of endpoints divided by 3.32, provided the DT90 value is calculated and not estimated.)	the RMS were temperature and moisture normalized according to FOCUS guidance (2006, 2011) applying a Q_{10} value of 2.58 and a moisture exponent of 0.7. It is not clear why the actual correction factors would be required in Table B. 8.1-75 and in the summary Tables of the RAR GTF agrees with the MS comment in regard to "The best fit should be used for determination of the P criterion, not a back-calculated value". RMS: disagrees with MS and Notifier. It appears that the respective paragraph of the DG SANCO Working Document is not precise enough and can be interpreted differently: We understand this paragraph in the way that a SFO DT_{50} should be used directly if available, but that a DT_{90} value/3.32 should always be used if the substance exhibits biphasic degradation behaviour and not only as higher tier. Not considering a second slower degradation rate would strongly underestimate real persistence of a substance in the environment and would also be unjust for substances that	Addressed

Route and rate of degradation in soil (B.8.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			degrade following SFO kinetics. Besides, it should be noted that the DG SANCO Working Document on "Evidence Needed to Identify POP, PBT and vPvB Properties for Pesticides" is not finalised yet since it was subject to a lot of criticism by several Member States among them Germany. Among other things, Germany pointed out that metabolites should be included in the assessment against the criteria laid down in point 3.7 of Annex II to Regulation (EC) No 1107/2009, in particular when they are more effective as the active ingredient. Thus, so far the SANCO working document was only used by the Commission to establish an initial list of candidates for substitution, but is not yet intended for the cut-off criteria. Thus, RMS recommends showing the persistence endpoints for the metabolite AMPA in the RAR as additional information in case metabolites will be included in the final PBT- assessment (the information is currently not used for the proposed decisions regarding CfS and cut-off in Volume 1, Level 3)	

Route and rate of degradation in soil (B.8.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
4(34)	Vol 3, B.8.1.2.1, Summary of persistence & modelling endpoints by RMS	NL: Please indicate why the geomean is taken even when n=17 (see e.g. Table B.8.1-94). What is trigger for median used by Germany?	CoRMS: In Slovakia the trigger is n=7, median should be used RMS: The approach to use the median instead of the geometric mean, if enough degradation data are available for endpoint selection, might be statistical reasonable and was often proposed by DE during EU assessments of other substances. However, in our experience, the selection of the geometric mean became more and more the standard approach for endpoint selection in the EU irrespective of the number of available data. Furthermore, the effect of using the median compared to geometric mean on the modelling results of PECgw and PECsw/sed would probably be marginal: Using the current data, the geometric mean is 21.03 d and the median is 18.97 d; however some DT_{50} values for glyphosate need to be corrected according to previous comments by Notifier and MS; after correction the geometric mean is 20.77 d and the median is 16.00 d. Thus, the RMS proposes to use the geometric mean as modelling endpoint.	Addressed
4(35)	Vol 3. B.8.1.2.2 Field studies.	EFSA: Are separated data by horizons available? Are residues above LOQ found in	GTF: In all of soil dissipation studies, soil cores were sectioned into 0-l0, 10-20 and 20-	Addressed RMS to consider including the

Route and rate of degradation in soil (B.8.1)				
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	Tables B.8.1-98, B.8.1-99	the deeper horizon (3 or 2)?	30 cm segments, which were separately analysed for residual glyphosate and AMPA and the results were reported in the final reports of the studies. The measured residues (mg/kg) of the different soil layers were converted into residues expressed in kg/ha (considering the layer depth and bulk density) and then summed up for kinetic analysis. Virtually in all field dissipations studies glyphosate and AMPA residues were limited to the top 0-10 cm soil layers and were not found above LOQ at the lowest segments, with one exception where the residues in soil cores were attributable to inadvertent contamination during sampling. RMS: RMS agrees with the explanation of GTF and doesn`t see need for action.	clarification in column 3 in a corrigendum or amended RAR.
4(36)	Vol 3. B.8.1.2.2 Field studies.	EFSA: Graphical representations of the fittings of field dissipation data are not available in the RAR. These may be needed for a proper peer review of the kinetic assessment	RMS: In our opinion the assessment of the visual fits of the kinetic modelling of field dissipation data was sufficiently presented in the Tables B.8.1-100 to B 8.1-118. The validation of the visual fits was performed according to the recommendations of FOCUS 2006 for persistence and modelling endpoints and relevant information about	Open point: RMS to present the kinetic fitting of parent glyphosate and AMPA from the field dissipation studies in an addendum , to support the expert discussion proposed at reporting table comment 4(37).

Route and rate of degradation in soil (B.8.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			kinetic and statistic parameters just as differentiated visual assessment is provided in the very detailed tables mentioned above. RMS does not see an improvement of information by general presentation of all graphical fits and no impact on the derivation of endpoints. General comment: One of the advantages of the EU-assessment procedure should be the in-depth validation of the assessment approach of the Notifer only by the RMS, so the other MS should benefit from the well done work. If there are special and reasonable questions to decisions of RMS, these special points (e.g. visual fits of individual kinetic modelling) should be discussed. In general it seems to be not constructive and necessary to provide all primary study information in the DAR/RAR (e.g. in general all available graphical representations of fittings), if the provided assessment in the DAR by RMS is sufficiently documented and plausible.	
4(37)	Vol 3. B.8.1.2.2 Field studies. Table B.8.1-101 AMPA	EFSA: If visual fitting suggest AMPA to be persistent in this field a default DT50 = 1000 may need to be incorporated to the data set,	GTF: The apparent persistence could also be due to the continuous replenishment of AMPA from the degradation of glyphosate	Expert consultation Member state experts to discuss the field dataset and kinetic fitting for

Route and rate of degradation in soil (B.8.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
	in Shultz 1992.	even if the calculated fitted parameters are not statistically reliable to avoid the bias towards more favourable situations.	so that the decline phase of AMPA was not reached during the study period. If the rate of formation of AMPA from glyphosate degradation were to be equal to the rate of degradation of AMPA in soil, this will result in an apparent steady state AMPA concentration in soil but it does not mean that AMPA is persistent and is not degrading. RMS: We agree with the statement of GTF. The observed residues of AMPA will be the result of similar formation and degradation of AMPA during the shorter study duration. Above all it was shown in the study of Hill 1992 that AMPA is degrading with half lives between 284 and 633 d. The study period in Shultz is too short to derive reliable half lives compared with the study of Hill, in which a similar residue situation at corresponding sample points like in Shultz 1992 was observed. The default values of 1000 d would lead to an overestimation of the persistence of AMPA in the field. This approach is supported by results of laboratory studies, which show clear biological degradation with maximum half	glyphosate and AMPA and agree the way to interpret AMPA dissipation rates from experiments where no decline of AMPA is observed.

Route and rate of degradation in soil (B.8.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			life of 301 d for AMPA. According to experience studies with the metabolite as parent result in significant lower half lives of metabolites compared with half lives from degradation studies with parent. Therefore the approach of RMS in the RAR should be assessed as conservative.	
4(38)	Vol 3. B.8.1.2.2 Field studies. Shultz 1992 studies	EFSA: Separated references should be given to the Shultz 1992 studies (i.e. Shultz 1992, Shultz 1992a etc…)	RMS: The references given to Shultz studies can be separated by BVL numbers and by the soil names. It is not belike to mistake one soil for another. For citation the criticism is accepted.	Addressed RMS to consider in a corrigendum or amended RAR.

Route and rate of degradation in soil (B.8.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
4(39)	Vol 3. B.8.1.2.2 Field studies. Persistence en points of glyphosato and AMPA selected by the RMS	EFSA: By excluding the soils where no degradation of AMPA is observed the overall data set becomes biased towards to the best case soils. To avoid this, a 1000 d half-life should be assumed for those soils where it is not possible to derive reliable kinetic parameters due to lack of apparent degradation. If this would result in a too conservative assessment, applicant has the option of obtaining refined degradation parameters with studies in which the metabolites are applied as parent.	GTF: please refer to the previous comment in this regard [comment 4 (37)]. Additionally, FOCUS 2011 suggests a "case-by-case" decision scheme for instances that a reliable degradation rate for a metabolite cannot be derived from modelling of the parent/metabolite soil residues data. Although FOCUS recommends that the degradation rate "could" be set to a conservative default DT_{50} value of 1000 days when a reliable decline rate cannot be obtained, however, FOCUS 2011 document also states in the next paragraph of the same document that this worst-case estimate should always be compared to available information from other studies in order to make sure it is consistent with the weight of evidence (FOCUS 2011, page 155). The weight of evidence in regard to degradation rate of AMPA clearly supports much shorter DT_{50} value than 1000 days (i.e. mean DT_{50} for degradation of AMPA under laboratory aerobic conditions is 89 days). Above discussions are also applicable to the DT_{50} value of 633 days that RMS calculated for the Unzhurst, Germany site. There are other	See expert consultation at reporting table comment 4(37).

Route and rate of degradation in soil (B.8.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			field dissipation studies capable of providing valid DT_{50} values for AMPA in which clear decline of AMPA was achieved during the study periods. There is no reason to bias the data for the failure of kinetic models to derive DT_{50} values for cases that the decline phase of AMPA was not reached during the study period. As mentioned before, the lack of change in the concentration of AMPA does not necessarily mean that AMPA is persistent and is not degrading as stated before AMPA could be degrading as it is continuously forming from glyphosate degradation. RMS: We support the statement of GTF (see RMS comment under 4(37))	
4(40)	Vol 3, B.8.1.2.2, field studies	NL: when no fit could be derived for AMPA due to no decline, a value of 1000 days should be taken for those trials (i.e. in 3 out of 8 field studies) RMS states: *If there was no acceptable pathway fit or a clear decline phase for the metabolite AMPA during the study duration, it seems not appropriate to use a default DT50 value of 1000 days, because it could demonstrated in other field*	GTF disagrees and believes RMS approaches for AMPA soil degradation DT_{50} derivation are correct for reasons discussed in details in comments 4(37) and 4 (39). RMS: Please see RMS comments under 4(37)	See expert consultation at reporting table comment 4(37).

Route and rate of degradation in soil (B.8.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		trials, that a slow degradation of AMPA takes place under field conditions and that reliable half-lives could provided in more than four cases. In soils without a decline phase it is only shown, that the formation of the metabolite is higher than its degradation during the duration time of the study, but no information can provided on the rate of degradation of AMPA in these soils. Therefore in the opinion of RMS it is more proper to exclude soils without a clear decline phase from further assessment. This is not agreed.		
4(41)	Vol. 1, Level 1, 2.3.4, Summary of observations on other undesirable or unintended side-effects, page 28	GTF: On page 28, it is stated that the soil (field), DT_{50} value for glyphosate "varies from 3 to 174 days depending on edaphic and climatic conditions". However, in Vole. 3, Annex B.8.1.2.2 Field studies, page 111, Table B.8.1-117, the DT_{50} values of all available field soil dissipation studies of glyphosate were reported to be in the range of 5.7 to 40.9 days.	RMS: We assume that the mentioned range of $DT50_{field}$ values for glyphosate on page 28 includes all available data to demonstrate in general the variability of degradation behaviour of glyphosate in connection with climatic and soil conditions. The used kinetics are unknown and not important in this context. The values in the Table B.8.1-117 include only the EU-relevant trials and the evaluation of degradation behaviour was done according to FOCUS (2006) to derive persistence endpoint (best fit kinetics) for the	Addressed

Route and rate of degradation in soil (B.8.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			further risk assessment of glyphosate. Because of biphasic degradation in six of eight trials the comparison of only DT_{50} values between both chapters of RAR are not meaningful. The complete degradation process can only be described by the kinetic parameters. Therefore in our opinion the both data ranges are not inconsistent with one another und have to be seen in the different contexts.	
4(42)	Volume 3, B.8.1.2 Points considered for kinetics	FR: It is not clear whether modelling endpoints for glyphosate were calculated taking points over 120 days into account from the different laboratory studies. Some clarification might be needed. It seems the notifier chose not to take the points over 120 days into account for estimating the degradation rate of glyphosate in soil, but that the RMS considered some of the points above 120 days could be used.	Co-RMS: agrees with FR RMS: The data points >120 days for all studies are included. For justification see paragraph regarding the acceptability of the kinetic study Dorn, 2012 on page 75. Additionally see reply of RMS to comment 4(27)	Addressed

Route and rate of degradation in soil (B.8.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
4(43)	Volume 3, B.8.1.2 Table B.8.1-75 and B.8.1-94 LoEP, p31 (of pdf)	FR: it seems the recommended kinetics for Les Evouettes was DFOP for modelling endpoints in Table B.8.1-75, but then in Table B.8.1-94 and in the LoEP, p31 (of pdf) the FOMC kinetics were reported. Some clarification might be needed.	RMS: please refer to reply of RMS to comment 4(14)	See Open point: at comment 4(14).
4(44)	Volume 3,B.8.1.2 Table B.8.1-76 LoEP p 34	FR: FR questions the approach used for modelling endpoints of AMPA of excluding some soils because of the lack of decline and the absence of acceptable fit. New modelling endpoints (DT50 and ffm) may therefore have to be calculated, LoEP and PEC calculation may need to be updated. According to FOCUS kinetics guidance (updated 2011), p155, in case of no decline for the metabolite, a DT50 of 1000 days should be considered, along with a formation fraction of 1. FR recommends following the guidance and considering the couple DT50 (=1000 days)/ffm (=1) for the six soils where no decline in the formation of AMPA could be observed.	GTF: FOCUS 2011 suggests a "case-by-case" decision scheme for instances that a reliable degradation rate for a metabolite cannot be derived from modelling of the parent/metabolite soil residues data. It is true that FOCUS recommends that the degradation rate "could" be set to a conservative default DT_{50} value of 1000 days when a reliable decline rate cannot be obtained. However, FOCUS 2011 document also states in the next paragraph of the same page (FOCUS 2011, page 155) that this worst-case estimate should always be compared to available information from other studies to make sure it is consistence with the weight of evidence. The weight of evidence in regard to the soil degradation rate of AMPA supports much shorter DT_{50} value than default 1000 days (i.e. mean DT_{50} for degradation of AMPA under laboratory	See expert consultation at reporting table comment 4(37).

Route and rate of degradation in soil (B.8.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			aerobic soil conditions is 89 days, n= 9) RMS: The RMS agrees with argumentation of the GTF and does not see the need for further action.	
4(45)	Volume 3, B.8.1.2 laboratory studies B.8.6 PEC calculations in groundwater and surface water LoEP, p 32	FR: Since 17 half-lives are available for glyphosate and according to FOCUS recommendations, the median should be considered instead of the geometric mean for modelling endpoints. LoEP and PEC calculation may need to be updated.	CoRMS: Median values DT_{50} 18,97 days for glyphosate and 106,2 days for AMPA should be used for modelling endpoint, but it will not change the risk assessment RMS: see reply to comment 4(34)	Addressed
4(46)	Volume 3, B.8.1.2.2 Field studies	FR: it seems that results from the Oppenhuizen et al. (1993) study are not reported in this part of the RAR when they seem to be used for calculation of PECsoil for glyphosate. Please clarify.	RMS: We refer to the explanations of RMS in the RAR Vol 3, B.8.1.2.2 page 92: "The study of Danhaus (1983) with the addendum of Mueth (1988) and the studies of Oppenhuizen et al. (1993a-d) are excluded and not provided in the summary table because the study by Danhaus (1983) was not considered acceptable for the updated kinetic analyses due to missing soil characterisation (e.g. cation exchange capacity, particle size distribution, water holding capacity and microbial biomass) and the illegible pesticide history of the field plots. Although the studies of Oppenhuizen at al. (1993) conducted in USA (Tennessee, California, Georgia) and Canada, were	Addressed Note the decline rate and pattern used to calculate PECsoil originate from a German field study (Kleinzecher sandy loam).

Route and rate of degradation in soil (B.8.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			included in the assessment of persistence endpoints by the Notifier, in the opinion of RMS the climatic conditions in the mentioned regions are not representative for Europe. The Notifier has not provided additional information on the comparability of weather conditions during the duration of field dissipation studies in USA and Canada and the studies conducted in Europe. Apart from that there are enough half live values from European locations to derive reliable persistence endpoints for glyphosate and its metabolite AMPA.	
4(47)	Volume 3, B.8.2.1 Adsorption/desorption B.8.6 PEC calculations in groundwater and surface water LoEP, p 37	FR: similarly to comment (7), the Kfoc of both glyphosate and AMPA recommended for modelling should be a median since 24 data are available for glyphosate and 16 for AMPA. LoEP and PEC calculation may need to be updated.	CoRMS: Median values Kfoc 9743 for glyphosate and Kfoc 6285 for AMPA should be used for modelling endpoint, but it will not change the risk assessment RMS: see reply to comment 4(34). In addition, it has to be pointed out that both glyphosate and AMPA are strongly adsorbing to soil particles. Therefore, the effect of the median selection compared to arithmetic mean selection on the modelling results would probably be marginal.	Addressed

Adsorption, desorption and mobility in soil (B.8.2)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
4(48)	Vol. 3, B.8.2.1	NL: The RMS proposes to use 1/n default values of 0.9 in cases where no reliable 1/n value could be derived in the study and 1.0 in cases where no investigations of the relationship between soil solution concentration and adsorption behaviour were conducted in the study. Reference is made to: ´Clarification note from EFSA concerning data requirements, study guideline, guidance and consensus of member state fate and behaviour experts on soil adsorption measurements and selection of the slope (1/n value) that describe the Freundlich coefficient (2010)´. The meant clarification note states that the use of 0.9 is only allowed when there are experimental difficulties (for example a labile active substance). The clarification note is not specific on what to do when the data set is mixed i.e. reliable 1/n values are available but complemented with default values. NB for example in the case of imazamox the LoEP clearly states different number of KOC and 1/n. hence it could also	RMS: The Freundlich slope values were assessed according to the ´Clarification note from EFSA concerning data requirements, study guideline, guidance and consensus of member state fate and behaviour experts on soil adsorption measurements and selection of the slope (1/n value) that describe the Freundlich coefficient (2010)´. Values for 1/n are typically in the range from 0.7 to 1.1, though in some valid experiments values outside this range do sometimes occur. FOCUS guidance indicates that an expected average 1/n when looking at a database of a large number of different compounds is 0.9. The RMS considers that the recommendation of the FOCUS guidance to use the often referred to 'FOCUS default' Freundlich slope of 0.9 (average value) is applicable when the experiments attempted to investigate the effect of concentration on adsorption, but a reliable 1/n value could not be derived. In cases where no investigations of the relationship between soil solution concentration and adsorption behaviour were conducted by the Notifier, the RMS is of the opinion to use the default 1/n value of 1.0	Expert consultation Member state experts to discuss the batch adsorption results where calculated 1/n values were <0.7. Experts to conclude on which of the following options to follow with this data set. Should the lower than 1/n values be retained or should the adsorption experiments be considered unreliable and excluded or should a default 1/n of 0.9 be ascribed to soils where 1/n was <0.7? Note the same conclusion does not have to be reached for every soil, it might be dependent on the results in each batch experiment.

Adsorption, desorption and mobility in soil (B.8.2)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		be an option to only use the measured and valid 1/n endpoints. In this case the use of default 0.9 concerns the data of Table B8.2-5 (old study of Van Noorloos & Slangen) for which in three out of four soils the 1/n was < 0.7. These values are now replaced with 0.9. This does not seem logical. NL considers that either the 1/n values as measured should be used (when considered reliable) or the experiments should be left out due to „unrealistic/unexpected“ (low) 1/n values. NL considers that if there is a sufficiently robust number of data for which a 1/n was determined, it may be more correct to leave out 1/n values than to introduce a certain bias towards Freundlich behaviour (or linear behaviour, in case of 1/n = 1 in case of KD studies)In this case there is plenty of reliable data and therefore NL suggests to remove the less reliable values (KOC with 1/n 0.9 and KD values with 1/n of 1)	according to the above mentioned clarification note. Due to the fact that the clarification note is not specific on what to do when the data set is mixed, i.e. only some reliable 1/n values are available, and therefore an established harmonised approach does not exist, the RMS decided not to leave out experimental results (kd values), but to use default 1/n values. Besides the effect of the 1/n value selection on the modelling results, particularly on PECgw, would probably be marginal as glyphosate and AMPA are strongly adsorbing to soil particles.	
4(49)	Vol. 3, B.8.2, The Freundlich adsorption coefficients	SE: There is an error in the reference to Table B.8.2-5 on page 124.	RMS: Thank you. The reference error will be corrected in an updated RAR.	Addressed RMS to consider in a corrigendum or amended RAR.

Adsorption, desorption and mobility in soil (B.8.2)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
4(50)	Vol. 3, Annex B.8.2.2, Adsorption and desorption of all relevant metabolites, page 122	GTF: Page 122, Table B.8.2.1 – Waring 1992 study investigated the adsorption properties of glyphosate in 5 soils and one sediment at single concentrations. No isotherm data were provided by the study. GTF believes that a 1/n default value of 1 applied to the soils and sediment from this study should **not** be included in the arithmetic mean calculation considering that numerous valid data are available from other submitted studies.	RMS: See reply to comment 4(48)	Addressed In this situation agreed evaluation practice is to ascribe a 1/n value of 1 where only a screening test has been completed.
4(51)	Vol. 1 level 2 LoEP sorption	NL: Please indicate in the LoEP the locality of the soil sample as now it is not easy to see which endpoint belongs to which study (only textural class is given) to improve cross-reading of LoEP and Volume 3.	RMS: Agrees with NL comment. The locality of the soil sample was added in the LOEP.	Addressed The list of endpoints was updated as proposed in the version dated 14 July 2014.

PEC in soil (B.8.3)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
4(52)	Vol. 3, B 8.3	NL: mistake in table B.8.3-12: 2x 2160 does not equal 1x1080. (“indication 2”) AMPA calculation approach is	RMS: In the indication 00-002 only 1 x 1080 g ai/ha are applied. Unfortunately there is a copy mistake in the headline of Table B.8.3-	Addressed RMS to consider in a corrigendum or amended RAR.

PEC in soil (B.8.3)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		acceptable since only one application is made. If not then please use dose rate correction instead of PEC correction.	12 and instead of 2 x 2160 the correct application rate has to be written with 1 x 1080 gai/ha. The PECsoil calculation was done with a single application with 1080 g ai/ha. The PECsoil calculation for AMPA was done after the maximal application rate of glyphosate with 4320 g ai/ha corrected by molweight-ratio and maximal observed formation of AMPA in field studies. There was no risk for terrestrial organisms and all other indication are covered because of lower application rates.	
4(53)	Vol. 3, B 8.3, PECsoil Table B.8.3-7 p. 168	SE: We agree with the RMS comments regarding the Notifier's derivation of the input parameters for the PECsoil calculations. However there seems to be an error in Table B.8.3-7 on page 168. The degradation parameter used in the ESCAPE 2.0 is k:0.0013 which represents a DT_{50} of 533 days and not 633 days. Please confirm that DT_{50} soil used in the PECsoil calculations is 633 days.	RMS: Unfortunately there is a copy mistake in the mentioned table. The half life of 633 d for AMPA is correct and was used in the PECsoil calculation of AMPA. Instead of k = 0.0013 the right value is k = 0.0011. But because there is no influence on PEC results no need of action seems to be necessary.	Addressed RMS to consider in a corrigendum or amended RAR.

Fate and behaviour in water and impact on water treatment procedures (B.8.4-B.8.5)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
4(54)	Vol. 3, B.8.4, KIIA 8.3.1/01	SE: The amounts of AMPA in the sediment reported in the text differ from the amounts in the tables. RMS concludes in the study comment (p. 199) that the amounts reported in the table are assumed to be correct. Why are the values in the tables more likely to be correct than the values in the text? Please clarify the comment.	RMS: In the study report of Knoch (2003), amounts of AMPA in the sediment reported in the text (p. 30 of the study report) differ from amounts reported in the tables (p. 51 of the study report). On page 30 only the values of AMPA as percent of applied radioactivity for 6 h and 104 d are given in text form: "AMPA could be found at the 6 hours sampling time in the processed sediment extractable radioactivity with average values of 11.1 (Bickenbach) and 13.7 % AR (Unter-Widdersheim). It's level accounted for 14.0 and 18.3 % AR for Bickenbach sediment and 36.3 and 44.2 % AR for the sediment of location Unter-Widdersheim by the final samplings at day 104." On page 51 of the study report the course of AMPA in the test system on basis of TLC chromatographie results (percent of applied radioactivity) is shown in a table. According to page 51 of the study report the values of AMPA in sediment are: 6 hours: Bickenbach: 11.0 and 10.1 % AR, Unter-Widdersheim: 13.7 and 13.2 % AR 104 days: Bickenbach: 17.7 and 14.2 % AR, Unter- Widdersheim: 37.0 and 43.2 % AR	Open point: RMS to show the values from the text as well as the values from the table and to exclude the sediment systems Bickenbach and Unter-Widdersheim from further evaluation in an addendum and update the list of endpoints consequently.

Fate and behaviour in water and impact on water treatment procedures (B.8.4-B.8.5)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			The amounts reported in the table are more likely to be correct than the values in the text since it is assumed that values listed in a table of a study report are derived from the original laboratory protocol and that the text was written after preparing the tables. Of course, this must not necessarily be true. However, the values are very similar and they are only used to derive DisT50 values for AMPA in sediment. Thereby, no reliable fit was achieved (for none of the water/sediment studies). However, in an updated RAR both, the values from the text as well as the values from the table could be shown. The sediment systems Bickenbach and Unter-Widdersheim could then be excluded from further evaluation, even though this would not change risk assessment.	
4(55)	Vol. 3, B.8.4.4 Water sediment studies. Table B.8.4-2	EFSA: In this table (Table B.8.4-2) the study Heintze, 1996 is listed as pertaining to the 2001 evaluation but it is not summarized neither in the original DAR nor in the Addenda available to EFSA. However it is summarized in new RAR in pg 204. Therefore, it seems the study has been	RMS: The study of Heintze (1996) is mentioned in the COMISSION WORKING DOCUMENT "Review report for the active substance glyphosate - Glyphosate 6511/VI/99-final" (2002), Appendix III, List of studies. However, it is reviewed neither in the original DAR nor in the Addenda.	Data requirement Applicant to provide the final study report Heintze (1996). Note an evaluation of the study is already included in the RAR, Vol 3, B.8.4.4 and the RMS physically has the

Fate and behaviour in water and impact on water treatment procedures (B.8.4-B.8.5)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		submitted in the updated dossier.	Regarding the updated dossier the Notifier did not provide a final report for this study. However, the study of Heintze (1996) was already evaluated by the RMS during the national authorisation procedure of plant protection products in Germany. An evaluation of the study is given in the RAR, Vol 3, B.8.4.4.	study. However the dossier should be updated with the study as all competent authorities may not have the study. The study is not available to EFSA.
4(56)	Vol. 3, B.8.4.4 Water sediment studies. Feser-Zuegner, W.	EFSA: There has been any attempt to identify metabolite M.3.3 that reaches up to 22.8 % AR in Feser-Zuegner, W AMPA water/sediment study?	GTF: Page 191 of RAR states metabolite M3.3 was characterised as 1-oxo-AMPA. Also pages 180 to 181 of RAR provide detail information on the structures and possible identities of metabolite M3.3, and other minor metabolites M2.5, and M7 observed in this study. RMS: Agrees with GTF reply. In addition, within the study evaluation of Feser-Zügner (2002) it is also pointed out that metabolite M3.3 could be characterised as 1-oxo-AMPA (page 191).	Addressed
4(57)	Vol. 3, B.8.4.4 Water sediment studies. McEwen, A. 2004.	EFSA: There has been any attempt to identify metabolite P1a that reaches up to 53 % AR in McEwen, A. AMPA water/sediment study?	GTF believes that unknown P1 is not a distinct metabolite rather it is caused by chromatographic anomalies. In addition to analytical method problems the study contains several deviations from OECD Guidelines for Testing of Chemicals No. 308	Addressed RMS to consider providing the clarifications in column 3 in a corrigendum or amended RAR

Fate and behaviour in water and impact on water treatment procedures (B.8.4-B.8.5)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			and insufficient reporting of important water/sediment parameters. Exactly for these reasons GTF decided to exclude the study from kinetic evaluation. However, RMS kinetically evaluated water/sediment system A and obtained reliable fit for only water phase of the system. RMS: In McEwen (2004) two unidentified metabolites were detected and accounted for 53 % AR (P1a) up to 14 days in Sediment A and 33 % AR (P3) up to 103 days in Sediment B. In the study it is only indicated that the major radioactive component P1a was more acidic in the chromatographic system employed than AMPA. Metabolite P3 was observed as a broad peak and could well be composed of several components that were unresolved due to chromatographic interference from endogenous material. However, the RMS believes that no risk assessment is necessary for the potential minor transient degradation products named above since they were only seen in a AMPA water/sediment study and were never detected in any of the available glyphosate water/sediment studies.	

Fate and behaviour in water and impact on water treatment procedures (B.8.4-B.8.5)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			Due to problems analysing extracts obtained from Sediment B, believed to be caused by endogenous co-extracted material disrupting the ion-exchange chromatography, the RMS excluded Sediment B and the total system B from kinetic evaluation. Apart from that, the study can be accepted and the endpoints may be used for further risk assessment.	
4(58)	Vol. 3, B.8.4.4 Water sediment studies. \\Heintze, A. 1996.	EFSA: Please, clarify what NCR stands for in tables B.8.4-26 to B.8.4-29 of water sediment study Heintze, A. 1996. . Is it a single fraction or is it multi-component? If such, what is the maximum amount found of any single component in it?	RMS: NCR stands for non-chromatographable residues.	Addressed RMS to consider providing the clarifications in column 3 in a corrigendum or amended RAR
4(59)	Vol. 3, Annex B.8.4.4, Water/sediment study and also in list of endpoints, page 282	GTF: page 282 Persistence endpoints for AMPA (Table B.8.4-70) according to the DG SANCO Working Document on “Evidence needed to identify POP, PBT and vPvB Properties for Pesticides” (rev. 3, 25.09.2012), metabolites should not be included in the assessment against the P-criteria laid down in point 3.7 of Annex II of Regulation (EC) no 1107/2009.	RMS: In the present RAR the persistence endpoints for AMPA are only considered as additional information. It should be noted that the DG SANCO Working Document on "Evidence Needed to Identify POP, PBT and vPvB Properties for Pesticides" is not finalised yet since it has been subject to a lot of criticism by several Member States. Among other things, Germany pointed out that metabolites should be included in the assessment against the criteria laid down in point 3.7 of Annex II to Regulation (EC) No	Addressed

Fate and behaviour in water and impact on water treatment procedures (B.8.4-B.8.5)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			1107/2009, in particular when they are more effective as the active ingredient. Thus, so far the SANCO working document was only used by the Commission to establish an initial list of candidates for substitution, but is not yet intended for the cut-off criteria. Thus, RMS recommends showing the persistence endpoints for the metabolite AMPA in the RAR as additional information in case metabolites will be included in the final PBT-assessment (the information is currently not used for the proposed decisions regarding CfS and cut-off in Volume 1, Level 3) See also reply of RMS to comment 4(33).	
4(60)	Vol. 3, Annex B.8.10.6.2, Literature Review, Monitoring data, pages 188 and 232	GTF: Pages 188 and 232 - Augustin (2003) is not a peer-reviewed publication.	RMS: Agrees with GTF comment. The RMS suggests adding this aspect in the presentation/evaluation table of the publication in an updated RAR, Literature review.	Addressed RMS to consider adding this aspect in the presentation/evaluation table of the publication in corrigendum / updated RAR, Literature review
4(61)	Vol. 3, Annex B.8.10.6.2, Literature Review, Monitoring data, pages 230 and 236	GTF: Pages 230 and 236 - Malaguerra et al. (2010) is not a peer reviewed publication.	RMS: Agrees with GTF comment. The RMS suggests adding this aspect in the presentation/evaluation table of the publication in an updated RAR, Literature review.	Addressed RMS to consider adding this aspect in the presentation/evaluation table of the publication in corrigendum / updated RAR, Literature review

Fate and behaviour in water and impact on water treatment procedures (B.8.4-B.8.5)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
4(62)	Vol. 3, Annex B.8.10.7, Literature Review, Other studies, pages 298 and 316	GTF: Pages 298 and 316 - The Watts (2009) citation is not peer-reviewed.	RMS: Agrees with GTF comment. The RMS suggests adding this aspect in the presentation/evaluation table of the publication in an updated RAR, Literature review.	Addressed RMS to consider adding this aspect in the presentation/evaluation table of the publication in corrigendum / updated RAR, Literature review
4(63)	Vol 3 B.7.4 (1998 monograph). Kesterson, A. and Jackson, S.B., 1990	EFSA: Details of Kesterson, A. and Jackson, S.B., 1990 water sediment study in 1998 monograph do not allow a proper peer review of the study.	RMS: In the monograph it was pointed out that the study is not acceptable because the method does not comply the test conditions specified in Annex II and Annex III (25°C instead of 20°C, duration of test only 30 days instead of 100 days). Due to these deviations the study does also not fulfil the current requirements on water /sediment studies. Therefore, the study of Kesterson and Jackson (1990) was not considered in the EU renewal.	Addressed Accepted that the study duration is too short. Note sediment water studies carried out at 25°C are often accepted by the peer review.
4(64)	Vol 3 B.7.4 (1998 monograph). Moellerfeld, J. Roembke, J. 1993.	EFSA: Table with percentage of radioactivity of glyphosate and metabolites states that there is an unknown metabolite but in the text it is stated that the metabolite is actually (hydroxymethyl)-phosphonic acid.	RMS: As described in the RAR, Vol.3, B.8.4.4, in the water/sediment study of Möllerfeld and Römbke (1993) an unknown metabolite was detected in the water phase with maximum amount of about 10 % of the dose after 61 days. This metabolite was identified as hydroxymethylphosphonic acid (HMPA) in an additional study (Steginsky and Powell, 1995).	Addressed

Fate and behaviour in water and impact on water treatment procedures (B.8.4-B.8.5)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
4(65)	Vol. 3, B.8.4.4 Water sediment studies. Table B.8.4-69	EFSA: It would be very helpful to have an overview table with the properties (pH water and sediment, OC, clay etc.) of all the water /sediment systems tested and found acceptable by the RMS.	RMS: An overview table with reference, guideline, application rate, duration of the test, sediment characteristics (oc, pH, water /sediment ratio) and metabolites of all the water /sediment systems found acceptable by the RMS is given in Table B.8.4-2 and Table B.8.4-3. Information on pH water, clay content etc. can be added in an updated RAR or addendum.	Open point: RMS to add information on pH water, clay content etc. in Table B.8.4-2 and Table B.8.4-3 in an addendum.
4(66)	Vol 3. B.8.5.1 Information on drinking water treatment procedures.	EFSA: it is assumed that the applicant has provided this information to address the approval criteria for active substances Art 4.3 (b) of Reg No 1107/2009. Therefore, the information provided should be considered essential and not supplementary. It is noted that main emphasis of the studies presented by the applicant is given to the reduction of glyphosate and AMPA during drinking water treatment procedures. However, also the reaction products would need to be identified (for chemical treatments as oxidation with Cl_2). Taking into account the structure of these substances it is not expected that reaction products will result on an increase of the risk.	GTF: The products from chlorination of glyphosate have all been identified and have been reported in a peer-reviewed article. (Mehrsheikh, et al., 2006. Investigation of the mechanism of chlorination of glyphosate and glycine in water. Water Research 40:3003-3014). This publication was part of the GTF literature review of glyphosate and was mentioned in our submission for glyphosate renewal dossier, literature review Section. The terminal glyphosate chlorination products reported are not unique to glyphosate and would also be expected as products from chlorination of other natural organic matter present in raw water. RMS: The peer-reviewed study of Mehrsheikh et al. (2006) mentioned by GTF	Addressed RMS to consider adding in a corrigendum or amended RAR Vol 3. B.8.5.1 a cross reference to the literature review assessment that has been made. Open point: EFSA to indicate in the conclusion that the approval criteria for active substances Art 4.3 (b) of Reg No 1107/2009 has been appropriately addressed in respect of chemical oxidation of glyphosate and AMPA with Cl_2.

Fate and behaviour in water and impact on water treatment procedures (B.8.4-B.8.5)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			was also part of the RMS literature review (B.8.11.5). There, the glyphosate chlorination products are reported. The conclusion of GTF that terminal glyphosate chlorination products are not unique to glyphosate and would also be expected as products from chlorination of other natural organic matter present in raw water is supported by the RMS and given in Vol.3, B.8, where reference is made to the RMS literature review: "The chlorination products of glyphosate are similar to those expected from chlorination of amino acids, proteins, peptides, and many other natural organic matters present in drinking water."	

PEC in surface water and in ground water (B.8.6)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
4(67)	Vol. 3, B.8.6, PECsw and PECsed calculations by the RMS, Table B.8.6-24	SE: The max. occurrence in soil used by the RMS for the Step 2 calculations of PECsw and PECsed for AMPA is 50.1%, according to Table B.8.6-24. This is the max. occurrence recommended to be used by the Notifier. The RMS concludes on page 168, 176 and 341 that the max. occurrence that should be used is 53.8 % (Schulz 1992, BVL no 1932133, trial Menslage/Germany). Please explain the discrepancy.	RMS: In the MII document of GTF (Table 7.3-1) the maximal occurrence of AMPA was stated with 53.78 % detected in the study of Schulz 1992 in the soil Menslage. In the study itself the maximal concentration of AMPA (as glyphosate equivalents) was 1.299 mg/kg. The applied concentration of glyphosate was 2.659 mg/kg, so the maximal occurrence comes to 48.9 % AR. Disregarding the value in the Table 7.3-1 the PECsw/sed calculation was done with the correct input value. In the PECsoil calculation of AMPA, done conservatively with the higher value of GTF, no risk for terrestrial organisms was shown. Therefore, no action seems to be necessary.	Addressed RMS to consider providing the clarification in column 3 in a corrigendum or amended RAR.
4(68)	Vol. 3, B8.6, PECgroundwater/non-relevance of AMPA	NL: PEARL calculations are not provided by the RMS. (see opinion (2013) to FOCUS 2009 accepted guidance that two models are required) For AMPA a non-relevance assessment was available in the DAR. As the substance is not expected to leach this is no longer present in the current RAR. However on a national level we use the non-relevance assessment also to show non-relevance for	Co-RMS: Comment accepted, FOCUS PEARL modelling should be done with median DT_{50} and Kfoc values, but it is not expected that the resuls of PECgw will be different from PELMO results RMS: FOCUS (2009): “One of the specific details in the remit of the work group was that the revision of the scenarios would include harmonisation of the models (dispersion length, water balance, etc.). This effort was largely	Open point:. RMS to include a groundwater non-relevance assessment for AMPA in an addendum. to the RAR. This assessment should cover consumer exposure as well as risk to aquatic plants. Note that this assessment is only triggered by groundwater monitoring

PEC in surface water and in ground water (B.8.6)				
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		drinking water made from surface water. This is sustained by the Guidance Document (GD) on non-relevant metabolites where it is stated in the introduction that: "*This guidance document focuses on groundwater, though the general approach may also be applicable for the* ***regional management of surface water resources intended for the abstraction of drinking water*** *in Member States.*" In monitoring programmes AMPA is frequently determined above 0.1 µg/L. Therefore it would be welcomed if the non-relevance assessment would still be included in the dossier. (see also remark at page 331 concerning the surface water intake for drinking water in NL)	successful and the Steering Committee recommends that the groundwater assessments can now be performed with any of the models (PEARL, PELMO, and PRZM) and there is no need to perform the assessments with more than one model." In our opinion, the recommendation in the EFSA opinion (2013) to use more than one model is only needed for substances with a potential to exceed the trigger value of 0.1 µg/L. With regard to glyphosate and its metabolite AMPA the exclusive use of FOCUS Pelmo 4.4.3 is justified because it is clearly shown that the 80th percentile PECgw values of glyphosate and AMPA at 1 m soil depth were very much below the groundwater threshold value of 0.1 µg/L or more precisely < 0.001 µg/L. Thus, there is no risk to groundwater via direct leaching. We agree to add a non-relevance assessment, because AMPA was determined in monitoring programmes above 0.1 µg/L. Moreover results from column leaching studies (B 8. 2.4.2) in open literature show that glyphosate and AMPA can be found in groundwater under exceptional cases, usually in	results, that it cannot be excluded result from uses other than the representative uses being assessed in the RAR. It should also be questioned whether AMPA in monitoring might originate from sources other than glyphosate. In the literature, it has been documented that AMPA might be also be a degradation product of other phosphonates, particularly ethylene-diamine-tetra-methylenephosphonic acid (EDTMPA) and diethylene-triamine-penta-methylene-phosphonic acid (DTMTPA), that can be components of domestic detergents?

PEC in surface water and in ground water (B.8.6)				
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			soil prone to preferential flow. The active substance glyphosate belongs to the group of the phosphonate herbicides and has a high toxicity towards aquatic higher plants and algae (EbC50 *Myriophyllum aquaticum* = 4.4 mg/l and EbC50 Anabaena flos-aquae = 8.5 mg/l). For the metabolite AMPA the toxicity to algae (EbC50 *Desmodesmus subspicatus* = 89,9 mg/l) and aquatic higher plants (EbC50 *Myriophyllum aquaticum* = 31.1 mg/l) are summarized in B9.2-66 (Maximum PECSW values and TER values for AMPA). The toxicity for aquatic organisms (especially to algae and aquatic higher plants) shows that the metabolite AMPA is less toxic than the active substance glyphosate. The risk for aquatic organisms is considered to be addressed by the assessment of the parent glyphosate. AMPA is not expected to be $\geq$ 0.1 µg/L by use of FOCUS Pelmo 4.4.3 in groundwater and is not considered as relevant as a result of the hazard assessment. Therefore, the ecotoxicological risk assessment leads to TER values far above the trigger value of 10 for algae and aquatic higher plants indicating low	

PEC in surface water and in ground water (B.8.6)				
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			risk for ground water ecosystems by exposure of the metabolite AMPA.	
4(69)	Vol. 3, B8.6.3.2	NL: it seems that not all available information from The Netherlands was used/provided. The VEWIN (Board for the Dutch drinking water companies) maintains a database in which for nine abstraction points substances are monitored (most recent data 2008-2012). Glyphosate exceeds the 0.1 µg/L on the basis of 90th percentile values for two of the eight locations. The 90th percentile concentration for AMPA exceeds the limits at 7 out of 8 drinking water abstraction points. In assessments the NL uses the non-relevance assessment from the DAR to address the risk – see earlier comment.	RMS: The information from the VEWIN (Board for the Dutch drinking water companies) was not provided by the Notifier and not known to the RMS. Thank you very much for pointing this out. The information will be summarised in an updated RAR Vol. 3, B.8.6.3.2 or in an addendum.	Open point: RMS to summarise information from the VEWIN (Board for the Dutch drinking water companies) in an addendum
4(70)	Volume 3 B.8.6 PEC calculations in groundwater and surface water B.8.6.3 Monitoring data Annex B.8 (Appendix)	FR: When summarizing feedbacks on monitoring programs and glyphosate occurrence in water resources, RMS indicates in most cases that "results are valid for that particular place and time". Referring to PPR opinion, this statement may be acceptable but one has to admit that most if not all monitoring results in EU point out glyphosate occurrence in water resources.	CoRMS agrees with France RMS: Agrees with the comment of France. A statement indicating that monitoring in EU indicated occurrence in water resources will be added in the conclusion of PECgw results in an updated RAR.	Open point: RMS to add a statement indicating that monitoring in EU indicated occurrence in water resources in the conclusion of PECgw results in an addendum.

PEC in surface water and in ground water (B.8.6)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
4(71)	Volume 3, B.8.6.3 Monitoring data Annex B.8 (Appendix) Volume 1, 3.1.6 Critical areas of concern	FR: FR would strongly support to account for the feedbacks from "control and inspection programs" and national datasets. FR fully agrees with the statement provided by RMS on non-professional uses, desiccant use, non-agricultural uses, urban uses and application to time harvest (see below) and strongly believes that such a key point has to be delivered to risk managers and reported in Critical area of concern identified in the RAR and future EFSA conclusions. "Member States might consider the appropriateness of additional herbicide uses especially when addressing sustainable use of plant protection products according to Directive 2009/128/EC" As indicated by RMS, "In addition, control and inspection programs at local authority level in Germany show high rates (35 % in 2009 and 36 % in 2010 during controls that were not event-related) of noncompliance regarding the application of plant protection products on walks and places in housing areas, foot-walks, traffic islands	RMS: Noted and agreed that this key point should be delivered to risk managers and reported in Critical area of concern identified in the RAR and future EFSA conclusions.	Open point: RMS to consider adding a statement on non-professional uses, desiccant use, non-agricultural uses, urban uses and application to time harvest in Critical areas of concern identified in a revised RAR (Volume 1, 3.1.6) Please note: The EFSA conclusion will only identify critical areas of concern relating to the representative uses applied for (D1 of the dossier).

PEC in surface water and in ground water (B.8.6)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		and paved surfaces in private properties (Anonymous, 2011, BVL no 2537364 and Anonymous, 2012, BVL no 2537365). This indicates that misuses of plant protection products on paved surfaces, which often contain glyphosate as active ingredient, by non-professional users occur to a relatively large extent. Therefore, current discussions in Germany are focusing on whether the findings of glyphosate and its metabolite AMPA in surface waters originate to some extent from these misuses of plant protection products containing glyphosate on paved surfaces by non-professional users. In any event, the other EU Member States should be aware of this problem and, if necessary, take appropriate risk management measures at the national level. Next to the use of glyphosate based products by non-professional users, we point to the environmental risks associated with the intended uses of glyphosate as desiccant. An herbicide application to time harvest poses additional ecological risks for surface waters and for non-target species (please refer also to chapter 2.9.6).		

PEC in surface water and in ground water (B.8.6)				
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4(72)	LoEP, Monitoring data, if available (Annex IIA, point 7.4), Groundwater, 6th study (Member states of European Union plus Norway and Switzerland, 2012). Vol. B.8.6.3.1, Groundwater and surface water, page 311 (Horth 2012, BVL no 2310291) and page 329 – 335 (KIIA 7.12/06 Horth, 2012).	DK: The literature study of Horth, 2012 summarises the results of 9908 Danish ground water samples analysed for glyphosate, mainly from the National Danish Groundwater Monitoring Program. The results seem plausible but the conclusion given: « - Denmark: Findings in Denmark appear due to rapid transfer of surface water from nearby surfaces not agricultural use, investigations still ongoing« is not correct. Please delete the above mentioned conclusion in the LoEP and in volume B.8.6.3.1. (The explanation comes from a minor study with few samples from small private digged and/or drilled wells typically in courtyards, which are not representative for the ground water and have nothing to do with the National Ground Water Monitoring Program. Please delete the explanation in the LoEP and in volume B.8.6.3.1.	RMS: The conclusion given in the RAR, Vol. B.8.6.3.1 and in the LOEP is taken from the study of Horth (2012), where it is indicated that the conclusion was derived from other investigations in Denmark. (Unfortunately, the name of the author of these investigations is not mentioned). Thus, the RMS will delete the conclusion in an updated RAR or addendum. The conclusion was deleted in the LOEP.	Open point: RMS to remove the conclusion « - Denmark: Findings in Denmark appear due to rapid transfer of surface water from nearby surfaces not agricultural use, investigations still ongoing« in an updated RAR or addendum .

PEC in surface water and in ground water (B.8.6)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		For your information the annual reports of the Danish National Groundwater Monitoring Program are available at: http://www.geus.dk/DK/publications/groundwater_monitoring/Sider/1989_2012.aspx. Unfortunately the report is in Danish but you can see the results for ground water in appendix 2 (bilag 2). The results of the Danish Pesticide Leaching Assessment Programme (PLAP) can be reached at http://pesticidvarsling.dk/publ_result/2012.html.)		

PEC in surface water and in ground water (B.8.6)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
4(73)	Vol. 1, Level 1, 2.8.4, Summary of monitoring data concerning fate and behaviour of the active substance, metabolites, degradation and reaction products, page 112	GTF : on page 112, RMS concludes: ".....that misuses of plant protection products on paved surfaces, which often contain glyphosate as active ingredient, by non-professional users occur to a relatively large extent. Therefore, current discussions in Germany are focusing on whether the findings of glyphosate and its metabolite AMPA in surface waters originate to some extent from these misuses of plant protection products containing glyphosate on paved surfaces by non-professional users." The use of glyphosate based products by non-professional users or even professional users on paved surfaces is not part of the representative GAP supporting the glyphosate Annex I renewal submission. Therefore comments, suggestions and recommendations regarding this use are not relevant in the context of the European re-authorisation of the active substance glyphosate. Since this use is out of scope of the joint renewal submission, the GTF has not submitted any data proactively as part of the initial submission and is in no position to do so in the rebuttal of the above claim. The	RMS: The Notifier argues that "the use of glyphosate based products by non-professional users or even professional users on paved surfaces is not part of the representative GAP supporting the glyphosate Annex I renewal submission. Therefore comments, suggestions and recommendations regarding this use are not relevant in the context of the European re-authorisation of the active substance glyphosate." Furthermore, "comments regarding this use in the RAR should not influence the EFSA opinion nor the provisions of the Commissions' review report". According to the list of representative uses evaluated the first two uses are defined for all crops (all seeded or transplanted crops and all seeded crops, respectively). Thus, the use of glyphosate based products by non-professional users or even professional users on paved surfaces is not excluded in the representative GAP supporting the glyphosate Annex I renewal submission. Moreover, the RMS has used all information available regarding environmental fate and behaviour of glyphosate and its	Data requirement Applicant to provide information on the possible runoff of glyphosate and consequent concentrations of glyphosate and AMPA in surface water, that might result when application occurs indirectly on hard man made surfaces, consequent to the representative uses of 'all seeded or transplanted crops' and 'all seeded crops' (first two rows of the GAP table).

PEC in surface water and in ground water (B.8.6)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		GTF refers to the re-authorization process of individual company's PPPs containing glyphosate under Article 43 to defend this use at zonal/national level. Therefore comments regarding this use in the RAR should not influence the EFSA opinion nor the provisions of the Commissions' review report.	metabolites in order to perform an adequate risk assessment and therefore, has also taken into account the results of control and inspection programs at local authority level in Germany showing high rates (35 % in 2009 and 36 % in 2010 during controls that were not event-related) of noncompliance regarding the application of plant protection products on walks and places in housing areas, foot-walks, traffic islands and paved surfaces in private properties. This indicates that misuses of plant protection products on paved surfaces, which often contain glyphosate as active ingredient, by non-professional users occur to a relatively large extent. In any event, the RMS is of the opinion that the other EU Member States should be aware of this problem and, if necessary, take appropriate risk management measures at the national level. Furthermore, this statement was fully agreed by FR (see comment 4(71) and FR proposed "that such a key point has to be delivered to risk managers and reported in Critical area of concern identified in the RAR and future EFSA conclusions", which is supported by the RMS.	

PEC in surface water and in ground water (B.8.6)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
4(74)	Vol. 1, Level 1, 2.8.4, Summary of monitoring data concerning fate and behaviour of the active substance, metabolites, degradation and reaction products, page 113	GTF: on page 113, RMS concludes the following in regard to bank filtration of glyphosate into groundwater: "Within a study from Spain (Sanchís et al., 2012, BVL no 2537361), it is described that surface waters exist in 10 out of 11 sampling sites where glyphosate was (at least partly) detected. Due to this fact, surface run-off and/or drainage into these waters with subsequent bank filtration into groundwater cannot be excluded as pathway. During the EU evaluation of the active substances the pathway surface run-off and drainage into an adjacent ditch with subsequent bank filtration into groundwater is not considered until now." The GTF does not concur with the assertion related to the possibility of the movement of glyphosate/AMPA from surface run-off and drainage into groundwater through bank filtration. Conservative experimental data summarized in RAR (Vol.3, Annex B.8.5. Impact on water treatment procedures) show glyphosate and AMPA are removed from water by bank filtration to a large extent (20-50% and 25-95% for glyphosate and AMPA,	RMS: The removal efficiencies mentioned by the GTF (20-50 % and 25-95 % for glyphosate and AMPA, respectively) were taken from the study of Jönsson and Camm (2010): "Removal of glyphosate and AMPA by water treatment" as described in the RAR Vol. 3 B.8.5. The RMS does not agree with the GTF, that glyphosate and AMPA are removed by bank filtration to a large extent. The removal efficiencies are showing that there is a potential of bank filtration to partly eliminate glyphosate and AMPA from water, but to a varying extent. In particular, the RMS considers removal efficiencies of 20, 25 or 50 % as rather low. Furthermore, in the study of Jönsson and Camm (2010) it is concluded that other processes commonly used in water treatment (bankside or dune infiltration, coagulation/ clarification/ filtration and slow sand filtration) would each contribute some removal, but each process in isolation is unlikely to provide a secure barrier in relation to meeting a 0.1 µg l^{-1} standard. Referring to the study of Sanchís et al. (2012), in the RAR Vol.3 B.8.6.3 it is pointed out that the pathways of glyphosate into groundwater are not investigated by the authors.	Addressed

PEC in surface water and in ground water (B.8.6)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		respectively).	Nevertheless, due to the fact that surface waters exist in 10 out of 11 sampling sites, surface run-off and/or drainage into these waters with subsequent bank filtration into groundwater cannot be excluded.	

Fate and behaviour in air and PEC in air (B.8.7-8.8)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point: (if data point not addressed or fulfilled)
4(75)				

Definition of the residues (B.8.9)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
4(76)		NL: it seems the RMS follows a deviating approach to determine whether a substance should be included in the residue definition for further assessment. To our opinion, major soil metabolite AMPA should be assessed for its risk to groundwater and hence included in the definition. The fact that in the end there is no risk does not mean it should not be in the definition. See (many) earlier EU dossiers. It could be questioned whether it should be in the definition for monitoring. However in view of the many detections in EU countries it seems logical to include it in the definition for monitoring as well.	RMS: We agree that AMPA has to be included in the residue definition for further assessment because of its maximal occurrence in biodegradation studies in soils and water-sediment systems. Beside AMPA shows no entry in groundwater > 0,1 µg/L, the metabolite was frequently detected in monitoring studies above the trigger of 0.1 mg/L and this fact justifies the inclusion of AMPA also in residue definition for monitoring. The LoEP will be actualised. Thanks for the support.	Open point: RMS to update the list of endpoints residues requiring further assessment to update the left hand text to: 'Environmental occurring residues requiring assessment by other disciplines (toxicology and ecotoxicology) and or requiring consideration for groundwater exposure.' and to add in the box glyphosate to the Air definition. Note AMPA was already added regarding groundwater to the list of endpoints 'definitions requiring further assessment' section in the revisions dated 14 July 2014. It is unclear how specific AMPA might be to glyphosate. Monitoring result might have other origins? In the literature, it has been documented that AMPA might be also be a degradation product of other phosphonates, particularly

Definition of the residues (B.8.9)				
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				ethylene-diamine-tetra-methylenephosphonic acid (EDTMPA) and diethylene-triamine-penta-methylene-phosphonic acid (DTMTPA), that can be components of domestic detergents.
4(77)	List of endpoints, Page 30, In Section "Residues requiring further assessment"	GTF: AMPA should be included in addition to the glyphosate that has been listed for Groundwater.	RMS: AMPA was added in the LoEP, Section "Residues requiring further assessment" for the compartment groundwater.	Addressed
4(78)	Vol. 1, Level 3, 3.1.1.4, Criteria for the approval of an active substance, page 152	GTF: Page 152 under the "Definition of residues for monitoring" glyphosate, AMPA, and HMPA are listed for surface water and sediment compartments. This is not correct and HMPA should not be included in the list since as described correctly on page 131 of the same document and the "List of Endpoints" the residue definitions for monitoring purposes should be glyphosate and AMPA for surface water and sediment.	RMS: It is correct, that HMPA has to be deleted under "Definition of residues for monitoring" in Vol.1.	Addressed RMS to consider in a corrigendum or amended RAR.

Other comments				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
4(79)	Volume 3 Volume 1	FR: FR acknowledges the huge work performed by RMS in providing a comprehensive AIR dossier with up to date risk-assessment and feedbacks on extensive monitoring programs / databases / experiments on glyphosate occurrence in water resources.	RMS: Thank you.	Addressed
4(80)	Volume 3 Annex B.8 (Appendix) Volume 1, 3.1.6 Critical areas of concern	FR: RMS has provided key messages in its draft-AIR dossier regarding glyphosate occurrence in water resources that may not be addressed at risk assessment level but have to be undoubtedly delivered to the risk manager. FR strongly recommends making this point visible to risk managers, by being reported in vol 1 section: Critical area of concern identified in the RAR and future EFSA conclusions.	RMS: We agree with FR comment and will report key messages regarding glyphosate occurrence in water resources in an updated RAR, Vol. 1, section: Critical areas of concern.	Addressed RMS to consider reporting key messages regarding glyphosate occurrence in water resources in an updated RAR, Vol. 1, section: Critical areas of concern.
4(81)	Vol 3. B.8	EFSA: A literature search on peer reviewed scientific literature has been performed and transparently reported and assessed by the RMS in the RAR (B.8 and B.10 appendices). It is acknowledged that the search of the literature was performed before the EFSA guidance (2011) was released and therefore this guidance has not been followed. For example further details on the search	RMS: In EFSA (2011) guidance is given on how to compile publicly accessible data bases to design searches, and to evaluate the obtained data for further use. As mentioned by EFSA, since articles were already available and no further data base search was performed, EFSA (2011) was not taken into consideration. However, RMS can provide more details on the search strategy and data bases used as described	Open point: RMS to provide more details on the search strategy and data bases used for the literature search in an updated RAR or addendum

Other comments				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		strategy and data bases used would need to be provided and some aspects of the Klimish scheme used to evaluate the reliability of papers submitted scheme are not supported by EFSA guidance. Besides this the search presented seems to comply with the principles of EFSA guidance with respect to exhaustiveness and transparency and can be considered equivalent to a search that had been performed under the EFSA guidance for literature search.	by GTF in Document M in an updated RAR, Literature review or in an addendum.	

Other comments				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
4(82)	Vol 3. B.8	EFSA: A number of the studies from the previous peer review have been accepted by the RMS to support the annex I renewal. Cross references in the RAR to the monograph of 1998 and subsequent addenda are made. However, information nowadays considered essential for a proper peer review by EFSA and MSs is missing in the summary of some of the reports found in these old documents. An update summary will help for the renewal peer review of these studies.	RMS: In our opinion the old studies were generally sufficiently presented in the monograph of 1998 and subsequent addenda, especially since they have already undergone a peer review process. Besides, studies considered 'not valid' and/or 'not plausible' during the first review, would not be accepted nowadays, for the simple reason that studies must meet higher requirements today. Therefore, the RMS decided to give cross references in the RAR to the monograph of 1998 and to the addenda. The RMS does not see an improvement of information by giving updated summaries for old studies and no impact on the derivation of endpoints used for risk assessment.	See open points at comments 4(2), (7), (8), (9), (14), (22), (29), (36), (54) and (65).

5. Ecotoxicology

Birds and mammals (B.9.1 and B.9.3)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
5(1)	Vol. 3, Annex B.9.1.3, Subchronic toxicity and reproduction, Study KIIA 8.1.4/01, page 10	GTF: We believe this study on bobwhite quail was done properly according to the GLP requirements at the time (1999) and that these data are valid for use in the ecological risk assessment. There appears to have been some confusion with the guideline specification from the original 0.25 ft2 floor area of the cages. 6 mortalities occurred in the control group and 2 mortalities occurred in each of the treatment groups in week 17. These are considered incidental as they were linked to likely hysteria, not diseases or toxic effects. The study should therefore not be invalidated. A detailed explanatory report is available and can be submitted upon request. *For further explanation please refer to Column 3 of the original commenting table.*	Co-RMS: GTF should submit A detailed explanatory report. Column 3 of the original commenting table should be pasted into the actual reporting table to simplify further discussion. *Column 3 of the original commenting table* The main concern in this 20 week study, where essentially no effects were seen from any of the treatments, is the unexpected mortalities in the control at week 19. This should not be sufficient to invalidate the study, and we believe that repeating such a study on these grounds would be unethical. Consequently the NOEL of 2250 ppm diet (201 mg/kg/day) should still be used in the risk assessment. For pilot reproduction and definitive reproduction studies, adult Northern Bobwhite are housed in battery breeding pens manufactured by GQF Manufacturing Company (Model No. 206 or 0330). Cages of this type have been successfully used to house Northern Bobwhite for more than 40 years. Each pen has	Addressed. The study cannot be considered as reliable due to the high mortality in the control group (>10%)

Birds and mammals (B.9.1 and B.9.3)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			floor space that measures approximately 25 x 51 cm (1275 cm^2 or 638 cm^2 per bird). Floors are sloping so that ceiling height will range from approximately 20 to 26 cm. These measurements exceed those recommended in the *Guide for the Care and Use of Laboratory Animals*, the governing animal welfare regulations in the United States, where the study was performed. The area provided also meets or exceeds recommendations of other husbandry resources. A table is attached that lists a compilation of recommended housing sizes for bobwhite from various sources. The OECD Guideline 206 (1984) value of 0.250 m^2 per pair was apparently based upon the value in the 1978 issue of *Guide* (see above) listed as 0.25 ft^2, with the unit inadvertently miscopied. While it would intuitively seem that "bigger" would be better, that is not the case when housing birds designed to be as close to wild type as possible, a requirement of both the USEPA and OECD guidelines. For bobwhite, where the typical escape response is to flush, a bigger cage can result in more injuries, rather than fewer. In the housing currently used the birds have sufficient room to stretch, and make	

Birds and mammals (B.9.1 and B.9.3)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			normal comfort movements, but not so much room as to encourage any attempt at flight. Cage size also impacts the ability to catch the birds for necessary handling without causing undue stress. A cage sized so that the bird can be caught gently and efficiently limits the amount of chase and handling time. Additionally, since both control and treated birds are housed identically, any minor differences in environmental conditions observed will be uniform across all groups, and would not impact the interpretations of the study RMS: All ecotoxicological studies for the present application for approval renewal of glyphosate were evaluated according to current OECD guidelines, see chapter B.9.2.1.6. The guideline states that the mortality in the controls should not exceed 10 % at the end of the test. This criterion increases the reliability of the result and is should be understood as a internal quality control, in order to conclude that the experiment is working as intended and that the results of the experiment are due to the effect of the variable being tested.	

Birds and mammals (B.9.1 and B.9.3)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			We hesitate to follow the argumentation of the GTF. In our opinion the mortalities show, that the animals in the experiment were stressed towards other variables and the test design cannot be regarded with much confidence. In our opinion the test guideline recommendations concerning loading are not met (a min. floor area of 0,25 m2 is recommended) and therefore probably unfavourable conditions lead to head and other lesions caused by hysteria attack of the animals. Hysteria attack is not seen as normal behaviour even under housing situation. We do not believe that the OECD Guideline 206 (1984) value of 0.250 m^2 per pair was inadvertently miscopied since 30 years, as hypothesized by GTF. Finally we emphasize that the dose spacing was deficient in low dose range (no testing with low doses at 50, 200ppm) to supersede exiting databases (Beavers and Fink, 1978).	

Birds and mammals (B.9.1 and B.9.3)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
5(2)	Vol. 3, Annex B.9.1.3, Subchronic toxicity and reproduction, Study KIIA 8.1.4/02, page 12	GTF: The significant difference between the control and the highest treatment group should not be considered as an adverse effect. The NOEC for mallard ducks should be set at 2250 ppm. *For further explanation please refer to Column 3 of the original commenting table.*	Co-RMS: Column 3 of the original commenting table should be pasted into the actual reporting table to simplify further discussion. RMS: A significant reduction in mean body weight in the highest treatment group of 2250 ppm in 14-day old survivors was observed, and therefore the NOEC was determined to be 1000 mg glyphosate acid/kg feed, corresponding to 116 mg/kg/bw/d. We cannot exclude that the parameter like body weight may affect the vitality especially under conditions of food limitation. This parameter is part of the 'avian reproduction test' and is not considered to be irrelevant for the evaluation of the long-term effects of chemicals on reproduction.	Addressed The point was considered addressed because a lower endpoint was available for risk assessment. Note:: EFSA agrees that a reduction on body weight greater than 10% should be considered as biological relevant at population level for the long term risk assessment. However, in this case the body weight reduction seems not following a dose response relationship. Therefore, the NOEC for mallard ducks could be set at 2250 ppm. However, hatchling effect at this concentration has to be taken into account. RMS to consider in a revised RAR.
5(3)	Vol. 3. Annex B.9, KIIA 8.1.4/03, long-term avian endpoint.	SE: We agree with the RMS conclusion that egg weight in this case is not likely to be relevant for the long-term risk assessment since at the same treatment level there are no effects on number of surviving hatchlings or	Co- RMS: agrees. RMS: Noted.	Addressed.

Birds and mammals (B.9.1 and B.9.3)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		body weight of hatchlings. Especially since egg weight is not listed as a recommended endpoint in OECD 206.		
5(4)	Vol. 3, Annex B.9.1.6, Summary of effects on birds, Table 9.1-10, page 21	GTF: As indicated above, the endpoint from the quail long-term study by Frey (1999) should be added with NOEC = 2250 ppm. The mallard long-term study by Frey et al. (1999) endpoint should be NOEC = 2250 ppm. Detailed comments from the study director can be made available upon request. *For further explanation please refer to Column 3 of the original commenting table.*	Co-RMS: agrees. RMS: RMS proposes different endpoints. Detailed explanations are available in the volume B 9.1 and in the statements above. The quail long-term study by Frey (1999) was evaluated according to current OECD guidelines and was considered to be invalid. For further details please refer to Study KIIA 8.1.4/01 and comment 5 (1). The mallard long-term study by Frey et al. (1999) showed significant reduction in mean body in the treatment group of 2250 ppm and therefore the NOEC was set to 1000 ppm, corresponding to 116 mg/kg/bw/d. For further details please refer to Study KIIA 8.1.4/02 and comment 5 (2).	See 5(2)
5(5)	Vol. 3, Annex B.9.1.7, Risk assessment, page 21	GTF: According to the EFSA guidance document, the chronic endpoints of two reproduction studies in the same species can be taken as one study. As there were no	RMS: As stated in comment 5 (4), 5 (1, 2) the endpoint by Frey (1999) is not considered to be valid. The relevant endpoint of the study by Beavers and Fink, 1978 displays the lowest	Addressed. See also 5(1), NOTE: according to the EFSA

Birds and mammals (B.9.1 and B.9.3)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		ecologically relevant effects in both studies in the quail, and both studies in the mallard, the lowest ecologically relevant endpoint is 201 mg/kg bw/d based on the highest concentration tested in the quail. *For further explanation please refer to Column 3 of the original commenting table.*	ecologically relevant endpoint, a NOEAL =1000 mg glyphosate technical/kg feed, corresponding to 96.3 mg/kg/bw/d. According to EFSA guidance document consideration must also be given to factors that may increase risk. Due to the unique application of glyphosate in various crops and at different seasons during the year in the agricultural landscape the proportion of the population that is exposed is probably remarkable. Therefore RMS does not agree with GTF:	Guidance Document two studies on the same species can be merged but only under certain circumstances as for example when the studies were conducted according to a similar protocol or guideline; when the same test conditions were applied or whether the test substances are chemically equivalent. This was not the case for the two available studies on quail. Moreover, as reported in 5(1) one of the studies was not valid due to the high control mortality. The lowest endpoint is relevant for risk assessment
5(6)	Vol. 3, Annex B.9.1.7.7, Indirect Effects via trophic interactions, page 31	GTF: We agree as to the importance of this topic and that in Europe the issues of farmland biodiversity and ecosystem services have to be addressed across all member states via Common Agricultural Policy (CAP) and local agro-environmental schemes. We agree that various indirect effects can be attributed to agricultural	RMS:The RMS agrees to the GTF that biodiversity-supporting measures can successfully be integrated into high output farming systems. Furthermore, the RMS agrees that such measures conducted in the context of the CAP and the National Action Plans (NAP) of the member states can reduce the risk of indirect effects of glyphosate and other	Addressed Biodiversity-supporting measures to cover indirect effects of herbicides should be considered in the context of the CAP and the National Action Plans (NAP)

Birds and mammals (B.9.1 and B.9.3)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		production in Europe, and the relevant literature shows that there are a variety of causes. However, an Annex I renewal procedure of one active ingredient is not the relevant arena for this discussion. A more extended comment on indirect effects of glyphosate can be made available upon request. *For further explanation please refer to Column 3 of the original commenting table.*	herbicides on non-target species. Nevertheless, the RMS considers indirect effects as legally relevant for the risk assessment and management of PPP under Regulation 1107/2009. When deriving suitable risk management measures, existing CAP and NAP measures should be taken into account. As already stated in Vol. 3, B.9.1.7.7, the RMS is aware that the loss of diversity e.g. in farmland bird species is a multi-causal problem and agrees that the wider agricultural context has to be considered. Nevertheless, there is strong evidence that the use of pesticides is one of the main factors regarding the loss of biodiversity so that a risk assessment and management of such indirect effects of PPPs is one of the necessary measures to ensure a suitable protection of biodiversity. It is true that the existing studies demonstrating indirect effects of herbicide use are not focused on glyphosate. However, it is self-evident that those scientific findings apply to glyphosate as well as the effects trace back to the intended elimination of competing vegetation. Considering the extent of glyphosate use in the EU, a “not-in-my-backyard”	

Birds and mammals (B.9.1 and B.9.3)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			argumentation would therefore not meet the requirements. The GTF argues that a mechanical removal of plant material would cause the same effect to the food web as an herbicide. The RMS would like to point to the fact that mechanical measures are much less eradicative and therefore maintain a certain level of arable wild plants. In fact, the positive effect of low-pesticide-input farming on farmland bird species is well described.	
5(7)	Vol. 3, Annex B.9.1.7.7, Indirect Effects via trophic interactions, page 31	GTF: The RMS highlights the importance of glyphosate regarding indirect effects and concludes that "*glyphosate must therefore be considered the most significant herbicide regarding indirect effects*". We regard this conclusion as highly speculative. As indicated above it is necessary to address the issues of food production and ecosystem services on a broader scale. A more extended comment on relevance of indirect effects of glyphosate can be made available upon request. *For further explanation please refer*	RMS: The RMS disagrees that its conclusions on the relative contribution of glyphosate to the existing indirect effects of herbicides on farmland bird populations is speculative as it is backed up by scientific data and – taking into account the extent of glyphosate use and its general function – after all self-evident. Regarding the GTF statement that it is disproportionate to bring up the risk of indirect effects in the glyphosate RAR, we refer to our comments to no. 52. However, we agree that indirect effects	See 5(6)

Birds and mammals (B.9.1 and B.9.3)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		to Column 3 of the original commenting table.	are also relevant for other substances which should be considered in future assessment reports where applicable.	
5(8)	Vol. 3, Annex B.9.1.7.7, Indirect Effects via trophic interactions, page 35	GTF: The RMS cites a recent report Jahn et al. 2013. We would appreciate this being made available to us and the public.	RMS: The reference project report can be downloaded here: http://www.umweltbundesamt.de/publikationen/protection-of-biodiversity-of-free-living-birds (ISSN 1862-4804)	Addressed.
5(9)	Vol. 3 B.9.7.1	NL: in the acute screening step for birds, the SUV for large herbivorous bird is 50.3 instead of the given 30.5. However, the trigger will still be > 10.	GTF: It is not clear where the 50.3 value was retrieved from by the MS NL. The SV for large herbivorous birds is listed as 30.5 in Table 6, page 28 of EFSA/2009/1438. Annex I, Table I.1, page 127 also lists this value, as well as Appendix A, scenario 64 under 90th percentile SV. Co-RMS: agrees with GTF. RMS: agrees with GTF.	Addressed The value of 30.5 is correct.
5(10)	Vol. 3 B.9.7.1	NL: in the long-term screening step for birds the SUV for large herbivorous birds should be 26.7 instead of 16.2. This results in a lower TER of 2.2 and 6.3 respectively.	GTF: It is not clear where the 26.7 value was retrieved from by the MS NL. Table 10, p. 34 of EFSA/2009/1438 indicates 16.2 as a shortcut value for large herbivorous bird. Annex I, Table I.1., p.127, also lists 16.2 as mean value for	Addressed The value of 16.2 is correct.

Birds and mammals (B.9.1 and B.9.3)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			large herbivorous bird. This value is also found in appendix A, scenario No 64 under the mean SV. Co-RMS: agrees with GTF. RMS: agrees with GTF.	
5(11)	List of Endpoints, Effects on terrestrial vertebrates, Birds	GTF: Long-term endpoints should be 201 mg/kg b.w./d and 300 mg/kg bw/d, based on studies presented *For further explanation please refer to Column 3 of the original commenting table.*	RMS: WE do not agree with the proposed endpoints by GTF for various reasons: Please refer to comment 5 (1), 5 (2), 5 (4) and 5 (5).	Addressed See 5(1) and 5(2)
5(12)	Vol. 3 Table B.9.1-12/13	NL: For the spot treatments the actual application rate was assumed to be 50% of the reported rate. However, the NL does not agree with this approach and is of the opinion that the dose that is applied to the spot treatments should be clearly stated. Otherwise the full dose should be taken into account. In addition we would like to refer to the discussion about this topic in Praper 111 on amitrole.	GTF: There is a difference between application rate per treated area and application rate per cropped area. For application in orchards we recommend that only the strip along the tree line will be treated to create a weed free area (approx. 33% of the cropped area). Consequently the alleys (inter-rows) are left as untreated permanent grassy strips with no exposure to glyphosate. Such areas are going to be much more attractive to herbivorous mammals, as they provide cover, and the untreated alleys will present both more vegetation and more palatable vegetation than	Open point:. For the representative uses with spot applications, it is clearly stated in the GAP table that the actual application rate per hectare would be 33% to 50% of total application rate per treatment. This should be also reflected in the LoEP in the ecotoxicology section. Therefore RMS is requested to add a footnote in the LoEP for exposure estimations which took into account the 50% of the total application rate.

Birds and mammals (B.9.1 and B.9.3)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			the weed-free strips. Co-RMS: Expert consultation is needed to discuss this topic in PRAPeR meeting. RMS: We propose to amend the Colum "application rate" of all tables including the "application rate per treated surface area" as well as adding the "application rate per cropped area" (taking into account only 50 % of the "application rate per treated area" to results in lower RUD values finally). We understood that the product is not applied on the whole field area, but full application rate is only applied in strips leaving a minimum of 50 % of the area untreated providing cover and vegetation. In total the area will therefore only exposed to a max. 50 % of the application rate and the application rate in risk assessment was reduced accordingly. We agree that foraging birds and mammals may not only feed in the untreated area. We agree that harmonisation and further guidance is needed.	Note: EFSA agrees that harmonisation and further guidance is needed on this issue. See also 5(13), 5(74)
5(13)	Vol. 3 B.9	NL: General comment: For the spot treatments the actual application rate was	GTF: See above comment 5 (12)	See 5(12)

Birds and mammals (B.9.1 and B.9.3)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		assumed to be 50% of the reported rate. However, the NL does not agree with this approach and is of the opinion that the dose that is applied to the spot treatments should be clearly stated. Otherwise the full dose should be taken into account. In addition we would like to refer to the discussion about this topic in Praper 111 on amitrole.	Co-RMS: Expert consultation is needed to discuss this topic in PRAPeR meeting. RMS: See above comment 5 (12)	
5(14)	Vol. 3, B.9.1.7.3 higher tier: refined risk assessment to birds Page 29	EFSA: it would be preferable to include in this section the details on the residue data set for validating the approach i.e. the residue decline and the calculation of the refined ftwa.	GTF: Agreed. Co-RMS: agrees. RMS: Agreed.	Open point:. RMS to include the details on the residue data set used to refine the risk assessment to birds in an updated RAR or addendum.
5(15)	Vol.3 B.9.1.7.3	NL: Besides the twa also the MAF is refined. Please mention this.	GTF: Agreed. In addition, the MAF of 1.4 used in the screening and Tier 1 step is not correct because it is derived from an interval of 14 days, which is not according to the GAP. The GAP recommends an interval of 21 days, which results in a MAF of 1.23. RMS: Agreed.	Open point:. RMS to correct MAF refinement in an updated RAR or addendum. The TERs in LoEP should be amended accordingly. Moreover, the LoEP should also report the refined MAF.

Birds and mammals (B.9.1 and B.9.3)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
5(16)	Vol.3 B.9	NL: The methodology used to calculate the TWA is from SANCO/4145/2000, however, risk assessment is done according to EFSA (2009), the TWA should be calculated according to this GD.	GTF: TWA in EFSA/2009/1438 is calculated as [1-e^(-k*i)]/(k*i). In SANCO/4145/2000, TWA is calculated as f_{twa}=[1-e^(-k*t)]/(k*t). The difference between the two approaches is the denomination of the time interval. In EFSA it is i and in SANCO it is t. Else both methods are the same. These analysis and data are included as Appendix I and II of our submission (AIR AIII Doc M Tier II Section 6). RMS: The details on the residue data set for validating the approach i.e. the residue decline and the calculation of the refined ftwa will be included using the denomination of the time interval according to EFSA (2009).	Addressed RMS to consider in a revised RAR
5(17)	Vol. 3, B.9.1.4, Toxicity of the formulation	FR: Two dietary studies conducted with MON 52276 were included in the initial DAR both giving a LC50 > 5620 mg/kg diet (AVS94-116 and 115) corresponding to 1574 mg/kg bw/d in Colinus and 1629 mg/kg bw/d in the mallard. Please clarify the reasons why these studies are not reported. Please clarify whether the endpoints are expressed in product or active substance.	GTF: The two dietary studies were evaluated in the initial Annex I Inclusion process between 1995 and 2002. Since this is a renewal process, the studies should not need to be re-evaluated. The OECD guideline 205 was finalized in 1984. These studies were performed according to this guideline and no deviations were recorded during both studies. In addition, the EFSA guidance (EFSA/2009/1438) does not foresee the use of dietary studies in the risk assessment,	Addressed RMS to list dietary studies in a revised RAR or addendum.

Birds and mammals (B.9.1 and B.9.3)				
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			unless for a weight of evidence. The endpoints are expressed in ppm product, not ppm a.i. Co-RMS: The studies should be mentioned, but not re-evaluated. RMS: The EFSA guidance (EFSA/2009/1438) does not foresee the use of dietary studies in the risk assessment. The studies will be listed, but not re-evaluated.	
5(18)	Vol.3, B.9.1.7.2, Tier 1 acute risk assessment, Cereals pre harvest / crop maturity	FR: Scenario 35 is assessed but scenarios 21 and 34 were not considered although they are worst-case (EFSA 2009, appendix A). The justification to reconsider the shortcut value of scenario 35 is agreed. It would be advisable to consider all the relevant scenarios for a total herbicide use in order to harmonise the assessment.	GTF: The GAP indicates that cereal applications are made for pre-harvest uses and desiccation, which is why the Late season- seed heads scenario is the most relevant one. Scenario 21 is the worst case but an application rate 2.16 kg/ha, SCV of 22.4 and ftwa value of 0.35 results in a DDD value of 16.9 and a TER of 5.7, thus passing the risk assessment Co-RMS: upon request all the relevant scenarios for a total herbicide use may be added to RAR. RMS: It was assumed that in the pre-harvest application seeds grains will presumably be part of the diet of a generic focal species. A mixed diet composed of cereals and insects is likely relevant for the generic focal species"	Open point: RMS to include for the first tier risk assessment to birds all the scenarios relevant for the representative uses (according to EFSA2009) in a revised RAR or addendum. RMS to also amend the LoEP accordingly. See also 5(19), 5(20), 5(21)

Birds and mammals (B.9.1 and B.9.3)				
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			passerine" as well. The relevant scenarios will be considered in risk assessment.	
5(19)	Vol.3, B.9.1.7.2, Tier 1 acute risk assessment, Oilseed pre harvest / crop maturity	FR: Scenario 122 is assessed but scenarios 120, 134 and 138 were not considered although they are not worst-case (EFSA 2009, appendix A). It would be advisable to consider all the relevant scenarios for a total herbicide use in order to harmonise the assessment.	GTF: Scenario 122 (BBCH 80-99, late with seeds) is most relevant to the GAP, and results in the highest default shortcut values (mean SV= 11.4, 90th centile SV = 24.7). With an application rate 2.16 kg/ha, SCV of 11.4 and ftwa value of 0.53 results in a DDD value of 13.1 and a TER of 7.4, thus passing the risk assessment. The scenarios 120, 134, and 138 result in a less risk. These scenarios can be submitted upon request. The concept of risk envelope allows not to provide less conservative risk assessments when the most conservative scenario indicates safe use. Co-RMS: upon request all the relevant scenarios for a total herbicide use may be added to RAR. RMS: The highest default shortcut values in the Scenario 122 (BBCH 80-99, late with seeds) covers the risk for other scenarios with lower SV. Upon request all the relevant scenarios may be added to RAR.	See 5(18)
5(20)	Vol.3, B.9.1.7.2, Tier 1 acute risk	FR: Scenario 146 is assessed but scenario 142 was not considered (EFSA 2009,	GTF: Both scenario 142 and 146 are relevant to the GAP, but 146 presents the worst case and	See 5(18)

Birds and mammals (B.9.1 and B.9.3)				
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	assessment, Orchard _ orchard	appendix A). It would be advisable to consider all the relevant scenarios for a total herbicide use in order to harmonise the assessment.	passes the risk assessment. The concept of risk envelope allows not providing less conservative risk assessments when the most conservative scenario indicates safe use. Co-RMS: upon request all the relevant scenarios for a total herbicide use may be added to RAR. RMS: The worse case represents the most conservative scenario with the highest shortcut value and covers the risk for all other scenarios with lower SV. Upon request all the relevant scenarios may be added to RAR.	
5(21)	Vol.3, B.9.1.7.2, Tier 1 acute risk assessment, Orchard _ vineyard	FR: Scenario 217 is assessed (EFSA 2009, appendix A). The option "not crop directed all season" is not available. Therefore, for zonal registration, scenarios 219 (granivorous) and 231 (omnivorous) have been considered with adaptations to take into account an application to the ground for vineyard herbicide uses: For granivorous and omnivorous birds, no interception has been considered. Moreover for omnivorous bird, the RUD of "non-grass weeds" was substituted by the RUD of "grass + cereals".	GTF: Scenario 217 is used as a worst case scenario. With an application rate 2.88 kg/ha, SCV of 11.5 and ftwa value of 0.53 results in a DDD value of 17.5 and a TER of 5.5, thus passing the risk assessment. The scenarios 219 and 231 result in a less risk. The concept of risk envelope allows not providing less conservative risk assessments when the most conservative scenario indicates safe use. Nevertheless these calculations can be submitted upon request Co-RMS: upon request all the relevant scenarios for a total herbicide use may be added to RAR.	See 5(18)

Birds and mammals (B.9.1 and B.9.3)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		<table><tr><td>219</td><td>Small granivorous “finch”, Small seeds 100% weed seeds **without interception**</td></tr><tr><td>231</td><td>Small omnivorous bird “lark” **25% grass**, 25% weed seeds **without interception**, 50% ground arthropods with interception</td></tr></table> A feedback on this proposal will be appreciated. It would be advisable to consider all the relevant scenarios for a total herbicide use in order to harmonise the assessment.	RMS: Relevant scenarios will be added considering representative species “*Lullula arborea*”. We agree with FR that application is not crop related and therefore no interception should be considered.	
5(22)	Vol.3, B.9.3, LD50 for mammals	FR: The lowest limit LD50 of 2000 mg/kg bw/d was used in the risk assessment however there is evidence that it would be likely over 5000 mg/kg bw/d.	GTF: Agreed, see also Toxicology comment 2(7) RMS: We strongly propose to base risk assessment on the lowest limit LD_{50} of >2000 mg/kg bw/d in order to take into account several aspects. In all acute test performed including the higher test rat of 5000 mg/kg /bw strong clinical signs were observed including ataxia, convulsions, muscle tremors, red nasal discharge, clear oral discharge, urinary staining of the abdomen, diarrhoea, piloerection, lethargy, and fecal staining of the abdomen, decreased spontaneous motor activity and sedation and crouching position.	Addressed. The TERs calculated with ‘lowest greater than’ toxicity endpoint’ were also reported as ‘greater than value’. See also 5(35)

Birds and mammals (B.9.1 and B.9.3)				
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			A few acute tests were performed and the majority resulted in a LD_{50} >2000 mg/kg bw, see Summary of acute glyphosate acid oral toxicity for mammals table 9.3.1. As for animal welfare reason, the assessment of product toxicity will be rather based on the toxicity of the active substance. A potential increase of co-formulants might also occur.	
5(23)	List of Endpoints, Effects on terrestrial vertebrates, Mammals	GTF: The acute oral endpoint in the rat should be at the very least >5000 mg/kg bw, not >2000 mg/kg bw. This point was already commented in the mammalian toxicity Section 4. *For further explanation please refer to Column 3 of the original commenting table.*	Co-RMS: Column 3 of the original commenting table should be pasted into the actual reporting table to simplify further discussion. RMS: Please refer to comment 5 (22).	See 5(22)
5(24)	Vol.3, B.9.3, overall NOAEL for mammals	FR: The overall NOAEL of 50 mg/kg bw/d represents a significant change compared to the previous NOAEL. However, the reasons for this new proposal are well developed.	GTF: The NOAEL of 50 mg/kg bw/d is acceptable according to EFSA GD (2009:1438) for screening step risk assessment. However, in a refined tier 1 risk assessment a more relevant endpoint should be considered. The endpoint of 50 mg/kg bw/d was derived from maternal toxicity in a gavage study. These studies are not feeding studies, but are designed to achieve high levels of internal concentration, with daily	Experts' consultation Mss to discuss and agree the chronic endpoint to be used for risk assessment to mammals. See also 5(25), 5(27), 5(29), 5(36), 5(37), 5(38), 5(40), 5(41).

Birds and mammals (B.9.1 and B.9.3)				
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			gavage doses. Thus the study does not simulate the dietary exposure of animals feeding on treated food items in the wild. In animal feeding studies, animals have consumed much higher doses via the natural route of diet, with no effects observed at rates up to 1000 mg/kg bw/d ([redacted] study). The ecologically relevant reproductive endpoint for the refined Tier 1 assessment should therefore be 1000 mg/kg bw/d, and not 50 mg/kg bw/d. See GTF comments below [5(25)]. In addition, please consider GTF comments in the Toxicology section on the maternal NOAEL (GTF Comments 2(32, 33, 34)), which is NOT relevant for ecological risk assessment, and 2 (41) for developmental effects (NOAEL = 175 mg/kg bw/d), which is relevant for screening step risk (EFSA, 2009:1438), and should be replaced with 1000 mg/kg bw/d for higher tier mammal repro risk assessment. RMS: Please refer also to comment in the toxicological section 2 (42). RMS considers a decreased body weight gain at 200 mg/kg bw/day and above as well as	

Birds and mammals (B.9.1 and B.9.3)				
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			post-implantation losses to be directly linked to population size. Moreover lower foetal weight and a delay in ossification are considered to be adverse and therefore RMS proposes the NOAEL for developmental effects at 50 mg/kg bw/d. According to EFSA guidance document consideration must also be given to factors that may increase risk: Due to the unique application of glyphosate in various crops and at different seasons during the year in the agricultural landscape the proportion of the population that is exposed is probably remarkable. Any changes in physiology are considered to have the potential to increase susceptibility and fitness of the animals.	

Birds and mammals (B.9.1 and B.9.3)				
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5(25)	Vol. 3, Annex B.9.3.2, Summary of terrestrial vertebrate toxicity data, Table B.9.3-3, page 165	GTF: The review of reproduction toxicity did not consider ecological relevance in its assessment of the 2-generation studies. For the study by [redacted] the body-weight differences observed in the F1 males at 10000 ppm, are not ecologically relevant because less than 5% in magnitude and the difference cannot be observed at the end of the study (weeks 9 and 10). Therefore the NOEAEL should be 10000ppm, i.e. 985 mg a.s./kg b.w./d. *For further explanation please refer to Column 3 of the original commenting table.*	Co-RMS: Column 3 of the original commenting table should be pasted into the actual reporting table to simplify further discussion. RMS: Please refer to comment above 5 (24) and to comment 2 (42) in the toxicological section.	See 5(24)
5(26)	Vol. 3, Annex B.9.3.3, Risk assessment, Table B.9.3-5, page 158	GTF: Since voles are not required as focal species in all EU-member states, a more detailed risk assessment with additional generic focal species would be helpful for a possible risk envelope approach	RMS: Agreed. The relevant scenarios will be added.	Open point: RMS to include for the first tier risk assessment to mammals all the scenarios relevant for the representative uses (according to EFSA 2009) in a revised RAR or addendum. RMS to also amend the LoEP accordingly.
5(27)	Vol. 3, Annex B.9.3.3, Risk assessment,	GTF: If using the correct reproductive endpoint (ecologically relevant NOEAEL =	Co-RMS: Column 3 of the original commenting table should be pasted into the actual reporting	See 5(24)

Birds and mammals (B.9.1 and B.9.3)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
	Table B.9.3-6, page 158	985 mg/kg bw/d) the lowest TER value in the screening assay would be 13.22 (All crops, all seeded or transplanted crops) pre planting of crop, at 2x2160 g/ha). *For further explanation please refer to Column 3 of the original commenting table.*	table to simplify further discussion. *Column 3 of the original commenting table:* GTF: In principle, the use of the teratogenicity endpoint in assessing the long-term endpoint for the risk assessment is in accordance with EFSA/2009/1438. However, according to the guidance, it is recommended to use the NOAEL rather than the NOEL. Considering that no reproductive effects could be observed in higher concentrations, over longer periods of exposure, and through more relevant routes of exposure such as in the 2-generation rat study, the endpoint to be used in the reproductive mammal risk assessment at Tier 1 should be based on the 2-generation rat study. When considering ecologically relevant endpoints, it should be noted that no ecologically relevant adverse effect could be observed up to 985 mg/kg bw/d, which is the highest concentration tested. This no ecological adverse effect level (NOEAEL) should be used in the Tier 1 reproductive mammal risk assessment. An endpoint is proposed based on a recent multigeneration rat reproduction study ([redacted] 2000***)*** which was provided in the post Annex I dossier. The	

Birds and mammals (B.9.1 and B.9.3)				
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			toxicological NOAEL level was 3000 ppm (299 - 323 mg/kg bw/d; male-female), but for this ecotoxicological risk assessment the highest rate in the study 10000 ppm (985 - 1054 mg/kg bw/d; male-female), is used as the NOEAEL based on ecologically significant effects. Continuous feeding at this rate had no effect on the propagation of two generations in the rat. The fertility and reproductive performance of each generation of parental animals and the clinical condition and survival of their offspring were not adversely affected. The only effect of treatment observed was a statistically relevant, but not biologically relevant reduction in the bodyweight of the F1A pups in the 10000 ppm glyphosate acid group with a subsequent reduction in bodyweight of the selected F1 parent males for the duration of the pre-mating period. This is not considered to be ecologically relevant. In the study by [redacted] (1992), the effects observed at the highest treatment dose were not ecologically relevant, as they did not affect the reproduction or general fitness of the animals. In addition, the increase in food and water consumption was not of biological	

Birds and mammals (B.9.1 and B.9.3)				
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			relevance in its size. The observation of salivary gland and parotid are not of relevance when considering population-relevant endpoints as it is the case in the ecological risk assessment. For more detail, the endpoints which need to be carefully considered and weighted for ecological risk assessment for mammals are listed in EFSA/2009/1438 on page 41/139 under Step 9 of Module 4.4. Further comments on teratogenicity of glyphosate in rabbits under Vol. 3 B.6.6.11, in rats under Vol. 3 B.6.6.10, and reproductive toxicity under Vol. 3 B.6.6.1. Note that endpoints deemed as relevant for the individual human risk assessment are not automatically relevant for the population wild mammal risk assessment. RMS: As already stated above 5(24, 25) and comment 2 (42) in the toxicological section, the NOAEL is considered to be 50 mg/kg bw/d due to significantly increased post-implantation loss at 200 mg/kg bw/d. Foetal deaths are considering to be ecologically relevant. .	

Birds and mammals (B.9.1 and B.9.3)				
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5(28)	Vol. 3, Annex B.9.3.3, Risk assessment – mammal acute endpoint, page 167	GTF: The acute endpoint for mammals should be >5000 mg/kg bw, not >2000 mg/kg bw. No mortalities were observed in all studies considered valid. The only study with mortalities at this dose is [redacted] (1979) but it is considered supplementary.	Co-RMS agrees with LD50 > 2000 mg a.s./kg bw. RMS: Please refer to comment above 5 (22) and to comment 2 (6) in the toxicological section.	See 5(22)
5(29)	Vol. 3, Annex B.9.3.3, Risk assessment – mammal reproductive endpoint, page 167	GTF: The ecologically relevant endpoint for the reproductive mammal risk assessment should be 985 mg a.s./kg bw/d, based on 2-generation NOEAEL in the rat (Moxon, 2000), not 50 mg/kg bw/d based on developmental study in rabbit. *For further explanation please refer to Column 3 of the original commenting table.*	Co-RMS: Column 3 of the original commenting table should be pasted into the actual reporting table to simplify further discussion. Co-RMS agrees with NOAEL = 50 mg a.s./kg bw/d RMS: Please refer to comment above 5(24, 25) and comment 2 (42), the NOAEL is considered to be 50 mg/kg bw/d due to significantly increased post-implantation loss at 200 mg/kg bw/d. Foetal deaths are considering to be ecologically relevant.	See 5(24)
5(30)	Vol. 3, Annex B.9.3.3, Risk assessment, Table B.9.3-5, page 169	GTF: Using the correct acute endpoint for mammals, i.e. >5000 mg/kg bw/d, the TER for the vole in scenario "all crops, preplanting, 2x2160g/ha" would result in 16, above trigger value 10, including conservative assumption of DT_{50} in foliage = 10 d.	Co-RMS agrees with using the value of LD_{50} > 2000 mg a.s./kg bw. RMS: Please refer to comment above 5 (22) and to comment 2 (6) in the toxicological section.	See 5(22)

Birds and mammals (B.9.1 and B.9.3)				
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		For further explanation please refer to Column 3 of the original commenting table.		
5(31)	Vol. 3, Annex B.9.3.3.2, page 171	GTF: Since voles are not required as focal species in all EU-member states, a more detailed risk assessment with additional generic focal species would be helpful for a possible risk envelope approach	RMS: Relevant scenarios will be added to RAR.	See 5(26)
5(32)	Vol. 3, Annex B.9.3.3.4, (chronic orchards) page 173	GTF: Further refinement for small herbivores: The initial risk assessment for small mammals is based on the worst-case assumptions that herbivores consume 100% treated food in their diet over a 3-week period with no food sourced from adjacent hedges, untreated grassy alleys, grassy field margins or adjacent fields, and no avoidance of dead vegetation. Glyphosate treated weeds are rapidly desiccated and will become unpalatable, and hence are unlikely to be consumed in large quantities. *For further explanation please refer to Column 3 of the original commenting table.*	Co-RMS: Column 3 of the original commenting table should be pasted into the actual reporting table to simplify further discussion. RMS: For the intended us in orchards the actual application rate per ha in orchard or vineyard was set to only 50% of the reported rate in order to take into account that glyphosate is not applied to the grassy alleys between the tree lines. Therefore, the availability of non contaminated vegetation for herbivorous was considered in the risk assessment by exposure refinement. Nevertheless we believe that for glyphosate products different desiccation times must be assumed depending on the adjuvant ingredients in the product. The prediction of the onset of any chronic effect is not possible. Also	Addressed

Birds and mammals (B.9.1 and B.9.3)				
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			desiccation times of longer than 5-10 days are possible. Further refinement should not be considered.	
5(33)	Vol.3, B.9.3.3, All crops	FR: It is questioned why the grassland scenarios were not considered as for birds (tier 1 scenarios 72, 73, 74 and 75). It would be advisable to consider all the relevant scenarios for a total herbicide use in order to harmonise the assessment.	GTF: Grassland uses are not listed in the GAP table for this application. The scenarios for the screening step for mammals are taken from Table 8 in the EFSA guidance document which does not list grassland. RMS: Agreed. Table 8 in the EFSA guidance document lists grassland with the indicator species small herbivorous mammal.	See 5(26)
5(34)	Vol.3, B.9.3.3.2, Tier 1 risk assessment	FR: The risk assessment is conducted for the small herbivorous mammal (vole). The other mammals that might be considered as generic focal species are not assessed as far as there is a need to refine for the vole. It would be advisable to consider all the relevant scenarios for a total herbicide use in order to harmonise the assessment. Options for refinement depend on the generic focal species.	RMS: Agreed. Relevant scenarios will be added.	See 5(26)

Birds and mammals (B.9.1 and B.9.3)				
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5(35)	Vol. 3 B.9.3.3.2	NL: Even with an assumed application rate of 50% the vole is still at risk in the orchard scenario (TER<10). However, this is not mentioned and all acute risk is deemed acceptable. Please explain.	GTF: The TER is greater than 10 for 3 usage patterns (2.88 kg/ha x1, 2.16 kg/ha x 2 and 1.44 kg/ha x3), and so these uses can be recommended. Only the usage scenario of 0.72+0.72+2.88 gives a TER below 10. The second paragraph on page 172 points towards this limited scenario, and mentions "the results of the worst-case assessment indicate a low risk for small herbivorous mammals due to uptake of contaminated food" RMS: We consider that the calculation of TER is in that case too conservative and the DDD is overestimated. Because the third application differs from the other and the total DDD is calculated as a sum of two first applications and then the third, the MAF of 1.08 should be replaced by 0.09. 2x720 g a.s./ha + 2880 g a.s./ha DDD = (0.72/2)x136.4 x 0.09 + (2.88/2) x 136.4 = 4.4 + 196.4 =200.8 The resulting TER is > 10.	Open point: Assuming 50% of 3applications x 2.88 kg a.s./ha with an interval of 28 days (total annual rate of 8.64 kg a.s./ha) for the representative use in ochards, the first tier TER would be >9.3. With the application pattern indicated in the GAP table (total annual rate of 4.32 kg a.s./ha) the TER would be likely above the trigger. However, RMS should clarify this issue in the LoEP (in a footnote).

Birds and mammals (B.9.1 and B.9.3)				
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5(36)	Vol. 3, B.9.3.3.4 refined risk assessment to mammals Page 29	EFSA: the RMS, in accordance to EFSA 2009, has correctly used the for the tier 1 risk assessment the lowest endpoint from mammalian toxicity (i.e. the rabbit developmental NOAEL of 50 mg a.s./kg bw per day). It is noted that this endpoint was then used also for the refined risk assessment, and for some representative uses the TERs resulted still below the trigger. Could the RMS please provide an explanation on why the re-examination of the relevance of the toxicity endpoint was not considered?	GTF: Agreed. The guidance is very explicit regarding relevance of assessment endpoints at higher tier As indicate above this endpoint is from a gavage study. In feeding studies that are much more typical of exposure in the wild the NOELs are much higher. RMS: As considered, the re-examination of the relevance of the toxicity endpoint was performed. RMS concluded that the NOAEL of 50 mg a.s./kg bw per d should be used for risk assessment for the following reasons: Consideration should also be given to factors that may increase risk. Due to the unique application volume of glyphosate in various crops and at different seasons during the year in the agricultural landscape the proportion of the population that is exposed is deemed to remarkable. Please refer also to comment 5 (6). The other mammals that will be considered as generic focal species are not assessed as far, but will be included in the risk assessment. For those generic focal species it is strongly proposed to consider the rabbit developmental NOAEL of 50 mg a.s./kg bw per d. See also comment in the toxicological section	See 5(24)

Birds and mammals (B.9.1 and B.9.3)				
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			2 (42). Please refer also to comment 5 (24).	
5(37)	Vol. 3, Annex B.9.3.3.4, Refined risk assessment, page 173	GTF: If not done already at the screening step (as recommended above), at this stage of the risk assessment additional refinement should be made by using a rodent endpoint, i.e. endpoint from 2-generation rat study ([redacted] 2000) of NOEAEL=985 mg/kg bw/d instead of developmental endpoint NOEL=50 mg/kg based on the rabbit. *For further explanation please refer to Column 3 of the original commenting table.*	RMS: Please refer to comment above 5 (36).	See 5(24)
5(38)	List of Endpoints, Effects on terrestrial vertebrates, Mammals	GTF: Long-term endpoint for the ecological risk assessment should be at least 985 mg/kg bw, based on no ecologically adverse effect observed up to highest concentration tested in 2-generation rat study ([redacted]. 2000). *For further explanation please refer to Column 3 of the original commenting table.*	Co-RMS: Column 3 of the original commenting table should be pasted into the actual reporting table to simplify further discussion. RMS: Please refer to comment above 5(24) and comment 2 (42) in the toxicological section, the NOAEL is considered to be 50 mg/kg bw/d due to significantly increased post-implantation loss at 200 mg/kg bw/d. Foetal deaths are considering to be ecologically relevant.	See 5(24)
5(39)	Vol. 1, Level 1, 2.9.1 Summary of effects on birds and other terrestrial vertebrates,	GTF: The proposed endpoint should be LD_{50} > 5000 mg/kg bw, not >2000 mg/kg bw. *For further explanation please refer*	Co-RMS agrees with using the value of LD_{50} > 2000 mg a.s./kg bw. RMS: Please refer to comment 5 (22)	See 5(22)

Birds and mammals (B.9.1 and B.9.3)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
	page 117	*to Column 3 of the original commenting table.*		
5(40)	Vol. 1, Level 1, 2.9.1 Summary of effects on birds and other terrestrial vertebrates, page 117	GTF: According to EFSA guidance (1438/2009), at the screening level, the lowest endpoint from the 2-generation studies in mammals and the developmental toxicity studies should be considered. The relevance of the selected endpoint should be considered for ecological risk assessment at the Tier1 level. We also note that the EFSA guidelines state that where there are several studies with overlapping NOAELs and LOAELs the chosen endpoint should be HIGHEST NOAEL that does not exceed the lowest LOAEL. *For further explanation please refer to Column 3 of the original commenting table.*	Co-RMS: Column 3 of the original commenting table should be pasted into the actual reporting table to simplify further discussion. RMS: Please refer to comment above 5(24,25) and comment 2 (42), the NOAEL is considered to be 50 mg/kg bw/d due to significantly increased post-implantation loss at 200 mg/kg bw/d. Foetal deaths are considering to be ecologically relevant.	See 5(24)
5(41)	Vol. 1, Level 1, 2.9.1 Summary of effects on birds and other terrestrial vertebrates, page 117	GTF: See comment on Vol. 1, Level 1, 2.6.7.2.2 Rabbit developmental toxicity and teratogenicity, regarding [redacted] (1996, ASB2012-11499), page 75. The GTF believes the developmental NOAEL in [redacted] is 400 mg/kg/day, with no evidence to test substance related dose-	Co-RMS: Column 3 of the original commenting table should be pasted into the actual reporting table to simplify further discussion. RMS: Please refer to comment 2 (34) in the toxicological section, there it is stated that: “the multitude of developmental toxicity studies in	See 5(24)

Birds and mammals (B.9.1 and B.9.3)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		response, citing the published expert review Kimmel et al., 2013, Evaluation of developmental toxicity studies of glyphosate with attention to cardiovascular development, *Crit Rev Toxicol*, 2013; 43(2): 79–95. *For further explanation please refer to Column 3 of the original commenting table.*	rabbits revealed a heterogeneous picture regarding the tolerance towards Glyphosate expressed in differing NOAELs and LOAELs. The overall NOAEL is proposed to be 50 mg/kg bw/d instead of 75 mg/kg bw/d, because the latter was too close to a dose causing maternal lethality in another study in rabbits and therefore considered to be supportive."	
5(42)	Vol. 1, Level 1, 2.9.1 Summary of effects on birds and other terrestrial vertebrates, page 118	GTF: Indirect effects via food chain interference. See comments on Vol. 3, B.9.1.7.7.	RMS: Please refer to comment 5 (6).	See 5(6)

Aquatic organisms (B. 9.2)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
5(43)	List of Endpoints, toxicity data for	GTF: Daphnia, reproduction, glyphosate acid: Change of endpoint (RMS: 12.5 mg/L; notifier:	Co-RMS: noted RMS: In the study Magor, Shillabeer, 1999	Open point: All the valid endpoints should be

Aquatic organisms (B. 9.2)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
	aquatic species Vol. 3, B.9.2.1.5 Page 82	30 mg/L). Endpoint of Wüthrich, 1990 (250795) was not used, endpoint of Magor, Shillabeer, 1999 (BL6535/B) was used.	(BL6535/B) the total number of offspring per parent was significantly lower when compared to control at the nominal concentration of 25 mg/L. Therefore the NOEC was set to 12.5 mg/L.	included in the LoEP. RMS please adds the chronic endpoint for *Daphnia magna* Wüthrich, 1990 (250795).
5(44)	Vol. 3, B.9.2, glyphosate acid, chronic toxicity endpoint for fish Vol. 1, 2.9.2	FR: As indicated the validity of the ELS study with Danio rerio (7 d instead of 30 days) is questionable. In addition D. rerio is the least sensitive species in acute toxicity studies. Therefore, the chronic endpoint for fish should be reconsidered although it is not the most critical to derive a RAC. Please indicate by a note in the summary tables the NOEC which are found at the highest test concentration.	GTF: The [redacted] (2000) study on Danio rerio is a short term toxicity test on embryo and sac-fry stages (OECD 212) terminated prior to complete yolk sac absorption. This study type is typically performed as a screening test prior to fish early life stage studies. As the study is valid and addresses a relevant fish developmental life stage, it is appropriate to be included in the list of endpoints. Subsequent to this study, a full fish early life stage test has been conducted using the most acutely sensitive fish species (rainbow trout) with the achieved endpoint (9.63 mg a.s./L) being appropriately used in the fish long-term risk assessment. Co-RMS: The endpoint 5.6 mg a.s/L reflects sensitivity of fish sac-fry stages, and endpoint from fish early life stage study conducted on rainbow trout (9.63 mg a.s./L) is higher. Using endpoint from the [redacted] (2000) study (5.6 mg a.s/L) provides a sufficient margin of safety and	See 5(45)

<table>
<tr><th colspan="5">Aquatic organisms (B. 9.2)</th></tr>
<tr><td>No.</td><td>Column 1
Reference to DAR (vol., point, page)</td><td>Column 2
Comments from Member States or applicant</td><td>Column 3
Evaluation by (RMS) rapporteur and
- if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant</td><td>Column 4
Data requirement or Open point (if data point not addressed or fulfilled)</td></tr>
<tr><td></td><td></td><td></td><td>cover possible uncertainties.

RMS: The endpoint was considered the lowest chronic endpoint and was therefore considered to be appropriate to be included in the list of endpoints. The full fish early life stage test using rainbow trout achieves the endpoint 9.63 mg a.s./L and can additionally being included in the list of endpoints. Please refer also to comment 5(45).</td><td></td></tr>
<tr><td>5(45)</td><td>Vol. 3, Annex B.9.
KIIA 8.2.3/01,
Early life stage test.</td><td>SE: Although not statistically significant, we would hesitate to set the NOEC to 5.6 mg a.s./L since at this treatment level and the level below the NOEC, a mortality of 16.7% and 10% respectively was observed. Considering these effects would result in a NOEC of 1.0 mg/L. This may need to be discussed further.
<table><tr><th></th><th colspan="8">Glyphosate acid (mg a.s./L)</th></tr><tr><th></th><th>0 (Control)</th><th>0.32</th><th>0.56</th><th>1.0</th><th>3.2</th><th>5.6</th><th>10</th><th>32</th></tr><tr><td>Introduced</td><td>30</td><td>30</td><td>30</td><td>30</td><td>30</td><td>30</td><td>30</td><td>30</td></tr><tr><td>Survided (168 h)</td><td>30</td><td>30</td><td>30</td><td>30</td><td>27</td><td>25</td><td>22</td><td>13</td></tr><tr><td>Mortality (168 h) (%)</td><td>0</td><td>0</td><td>0</td><td>0</td><td>10</td><td>16.7</td><td>26.7*</td><td>56.7*</td></tr></table>*statistically significant different from control</td><td>GTF: The NOEC for [redacted] (2000) D. rerio sac-fry study endpoint is 3.2 mg as./L and not 5.6 as stated in the SE response. The 5.6 mg a.s/L value is the LOEC. It is the 3.2 value that has been used in the risk assessment. The analysis of these data is based on an independent mathematical analysis of the evidence produced in the tests done under GLP. This statistical analysis is there to check whether the observed effects in this scientific study are due to chance or not, and with what probability. If an effect is observed which is statistically significant, the chances are that the observed effect is “real” with usually 95% certainty. Abandoning this scientific rigour will</td><td>Open point:
The mortality effect in the study with Danio rerio (7 d) clearly followed a dose response relationship. EFSA agrees with SE that the NOEC from this study should be 1.0 mg/L.
RMS please amends the chronic TERs for fish based on this endpoint. The amendment has to be reported both in a revised RA/Addendum and in the LoEP.
The outcome of the risk assessment would be unchanged. Furthermore, it has to be noted that the dose-</td></tr>
</table>

Aquatic organisms (B. 9.2)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			lead to scientific chaos and misrepresentation. Co-RMS: Value from study K II 8.2.3/01 was used in the risk assessment. Co-RMS agree that some rules are necessary for evaluation of the studies and only statistically significant effect is real effect. In some cases biologically significant effect 20% should be considered. The value 16.7% is not statistically significant and under 20% trigger. The NOEC 5.6 mg a.s/L is relevant for risk assessment. Please see comment 5(44) RMS: The NOEC and LOEC were determined to be 3.2 mg a.s./L and 5.6 mg a.s./L, respectively by the notifier. Recalculation by RMS was performed and Fishers Exact Binominal Test with Bonferroni Correction was applied. In the study this correction of alpha is missing. Using the corrected alpha results in no significance for 5.6 mg/L. Therefore, NOEC of 3.2 mg a.s./L should not be assumed.	response relationship on mortality was not observed in the other two long-term available studies with rainbow trout and fathead minnow.

Aquatic organisms (B. 9.2)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			Fisher`s Exact Binomial Test with Bonferroni Correction Tab. 7: Fisher's Exact Binomial Test with Bonferroni Correction: Pair-wise comparisons between treatment and control on the multiple significance level (alpha is 0,05; two-sided). Pair-wise comparisons are performed sequentially using the adjusted Alpha' (= alpha/(k-1); k: number of comparisons (after Holm 1979)); Ho (no effect)is accepted, if the probability p > Alpha'. Treatm.[mg/L] Introduced Survived Dead% Fry Mortality p alpha'sig n. Control 30 30 0 0,0 0,320 30 30 0 0,0 1,000 0,050 - 0,560 30 30 0 0,0 1,000 0,025 - 1,000 30 30 0 0,0 1,000 0,017 - 3,200 30 27 3 10,0 0,237 0,013 - 5,600 30 25 5 16,7 0,052 0,010 - 10,000 30 22 8 26,7 0,005 0,008 + 32,000 30 13 17 56,7 <0.001 0,007 + +: significant; -: non-significant A NOEC of 5,600 mg/L is suggested by the program. However, we agree that discussion on effects on mortality can be conducted, even though not statistically significant, we agree that 16.7% mortality is on the limit of acceptability.	
5(46)	Vol. 3, B.9.2, glyphosate acid, Skeletonema costatum (Hugnes, 1987), study 96-00455	FR: It is agreed to consider this study as not valid as proposed.	Co-RMS: noted RMS: Noted	Addressed.
5(47)	Vol. 3, B.9.2,	FR: For classification purposes, it would be nice	Co-RMS: agree	Open point:

Aquatic organisms (B. 9.2)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
	NOEC for algae and aquatic plants Vol. 1, 2.10	to get an overview of the relevant NOEC values in the summary tables for algae and aquatic plants. Please check if reference to 790/2009 (1st ATP) is the correct one (may be replaced by 286/2011 (2nd ATP) for the current classification rules).	RMS: Agreed. NOEC values will be added and reference will be corrected.	RMS to add NOEC values for algae and aquatic plants and correct reference in an updated RAR or addendum.
5(48)	Vol. 3, B.9.2, Risk assessment Vol. 1, 2.9.2 & 3.2	FR: The risk assessment as proposed in the DAR is agreed. **However, attention should be given at the MS level when evaluating the risk for aquatic organisms when the preparation is more toxic than predicted (increase of toxicity may be higher than a factor 100 on green algae).** Under point 3.2, there is no indication with regard to aquatic organisms based on the RAR with the representative preparation MON 52276. The possibility that some preparations are more toxic than predicted is not reflected.	GTF: The EU regulation is explicit on how to handle ecotoxicological data, listing minimum data requirements for formulations and what needs to be done when formulated products are more toxic than the active substance. The notifier does not recommend any special mention for the case of glyphosate. Co-RMS: noted RMS. Noted. We will insert reference to the special chapter to coformulants Vol. 3, B.9. Sections B.9.9.2.1 and B.9.11.	Addressed RMS to consider in a revised RAR
5(49)	Vol. 3, B.9.2.3 literature Review Page 138	EFSA: a toxicity endpoint of 0.22 mg a.s./l for *Miriophyllum aquaticum* is reported from the literature. This value appears to be 10 fold lower than the lowest endpoint used for risk assessment for macrophytes. Could the RMS	GTF: The study by Turgut and Fomin (2002) was submitted by the applicant and evaluated as to its usability for risk assessment. The test item is not sufficiently characterized in the study. In addition, the endpoint of 0.22 mg/L is based on	Open point: RMS to add information in an updated RAR or addendum on the study by Turgut and Fomin (2002) with *Miriophyllum aquaticum*.

Aquatic organisms (B. 9.2)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		pleas clarify why this value was not used?	chlorophyll a content, which is not a valid endpoint for aquatic plant risk assessment. The valid endpoint for risk assessment is the 50% effect on the growth rate of plants / algae, which was not measured in this report. Tested concentrations were not specified in the M&M section. Number of specimens per replicate not reported. Source of test specimens not reported. No analytical confirmation of the test concentrations reported. These shortcomings should be considered as major and the study therefore inappropriate for risk assessment. Co-RMS: agree. The study Turgut and Fomin (2002) does not met criteria for using in the risk assessment. RMS: The Study by Turgut and Fomin (2002) was evaluated and the endpoint was mentioned in the literature review to its usability for risk assessment. Nevertheless, the study was rated finally as supporting information. We agree with the notifier that the test item is not sufficiently characterized in the study and that the endpoint of 0.22 mg/L, which is based on chlorophyll a content, is not a standards endpoint for RA. We agree that shortcomings of	

Aquatic organisms (B. 9.2)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			the study should be reported more in detail. Information for the study in the literature review will be revised.	

Bees and non-target arthropods (B. 9.4 and B.9.5)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
5(50)	Vol. 3, B.9.5 data and risk assessment for non-target arthropods Vol. 1, 2.9.3.2	FR: It would be useful to have the dose rates as kg ae/ha in Tables B.9.5-1 and 2. The correction of the drift rate for application on mature crop is understood but not sufficiently justified to get further harmonisation of the risk assessment at national/zonal levels. The risk assessment is agreed. However, it is considered more appropriate to replace the term " low" by "acceptable according to ESCORT II" (Vol. 3, B.9.5, page 222). It is proposed to consider the drift scenario "ground crop" x 2 for application in mature crops (i.e. 2.77% x 2 = 5.54%) to consider crop height. Surrogate values for "vegetables, ornamentals > 50cm" = "grapes, late stage" = 8.02%". The drift scenario depends also on typical application techniques and not only on crop height, which is not explained in the drift tables.	GTF: the correction for drift rate on mature crop is not acceptable. EU guidance for Non-target arthropod risk assessment (SANCO/10329/2002 rev 2 final) is stating as drift rates for field crops is 2.77 %, without specifying the advancement of the crop. The drift values in the terrestrial guidance document have been subjected to an agreement of the member states. In the interest of consistent and harmonized evaluation of active substances, the EU agreed drift rates should be used at EU level. Co-RMS: agreed, dose rates will be expressed as kg as/ha in Tables B.9.5-1 and 2 and the term "low" will be replaced by "acceptable" according to ESCORT II. RMS: Herbicides have the potential to affect non-target plants exposed to spray drift. In the case of non selective herbicides non-target plants should be protected in order to sufficiently protect biodiversity, food web support and habitat for re-colonisation. In order to minimize effects to non-target species application procedures and nozzle equipment can significantly reduce spray drift. Nevertheless, the possibilities for drift	Experts' consultation Mss to discuss the correction of drift rates as proposed by the RMS for the risk assessment to non-target arthropods and to non-target plants. **Note**: It is acknowledged there is a need to revise the current spray drift rates (see also EFSA PPR opinion on non-target terrestrial plants, EFSA Journal 2014;12(7):3800). However, as recommended by the PPR panel (EFSA Journal 2014;12(7):3800) the use of the current assessment based on FOCUS (2001) should still be followed until the new drift curves will be available. See also 5(55), 5(63), 5(61), 5(66), 5(67),

Bees and non-target arthropods (B. 9.4 and B.9.5)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			reductions can also be achieved by other risk mitigation measures like buffer zones, e.g. in cases where nozzle equipment is not available. The level of drift is mediated by different factors like the wind speed, the crop species and the height or the development of the crop. The spray driftability is increased the higher the equipment is distant from the ground level and the higher the canopy level. In general, this issue is reflected by higher drift deposition values. This is the case for crop canopy >50cm (in vegetables, ornamentals and small fruits: drift deposition of 8.02% at 3 m is considered for one application) or special crop heights in vineyards, orchard and hops. Using the basic drift deposition values for field crops would therefore underestimate risk to non target plants, when application in cereals is performed in BBCH 89 before harvest. Therefore, we proposed to mirror the height of the crop and the potential higher drift deposition in order to reduce risk to non-target plants in the off-crop habitat. New harmonised values at the EU level are under discussion. In order to respect a	

Bees and non-target arthropods (B. 9.4 and B.9.5)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			precautionary principle in the risk assessment for non-target plants the Ganzelmeier tables have been extended to take into account high crops like e.g. sunflowers by using a modified deposition factor for field crops (2.77% *2). Upon publication of harmonised drift data, it is proposed new values in the revised RAR.	
5(51)	Vol. 3, Annex B.9.5.6, Risk assessment, Table B.9.5-7, page 221	GTF: We consider that the use of a MAF value of 1.7 on foliage and 1.9 on soil is over conservative with respect to glyphosate, when the application interval indicated in the GAP is a minimum of 21 days. *For further explanation please refer to Column 3 of the original commenting table.*	Co-RMS: noted. Column 3 of the original commenting table should be pasted into the actual reporting table to simplify further discussion. *Column 3 of the original commenting table:* GTF: We calculate that a 10 half-life and interval of 21 days (a ratio of 1:2) would give a MAF of 1.23 for 2 sprays and 1.29 for 3 sprays (1.3 in ESCORT2). This is conservative given the average DT50 of 2.8 days on foliage referred to in B.9.1.7.3, which we calculate to give a MAF of 1.006. RMS: Even the Application of conservative MAF values resulted in HQ values far below the acceptability criterion and no risk is indicated. We agree to recalculate the MAF value	Open point:. RMS to recalculate the MAF value used for risk assessment to non target arthropods by taking into account the application interval in the GAP. The amendment should be considered for in a revised RAR.

Bees and non-target arthropods (B. 9.4 and B.9.5)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			with a default DT 50 of 10-day and interval of 21 days (a ratio of 1:2). ESCORT2 proposes a MAF of 1.3 for 2 and 3 spray applications.	
5(52)	Vol. 3, Annex B.9.5.6, Risk assessment, Table B.9.5-8, page 222	GTF: We consider that the use of a MAF value of 1.7 on foliage and 1.9 on soil is over conservative with respect to glyphosate, when the application interval indicated in the GAP is a minimum of 21 days. *For further explanation please refer to Column 3 of the original commenting table.*	Co-RMS: Column 3 of the original commenting table should be pasted into the actual reporting table to simplify further discussion. *Column 3 of the original commenting table:* GTF: We calculate that a 10 half-life and interval of 21 days (a ratio of 1:2) would give a MAF of 1.23 for 2 sprays and 1.29 for 3 sprays (1.3 in ESCORT2). This is conservative given the average DT50 of 2.8 days on foliage referred to in B.9.1.7.3, which we calculate to give a MAF of 1.006. RMS: Please refer to comment 5 (51).	See 5(51)
5(53)	Vol. 3, Annex B.9.5.6, Risk assessment, Table B.9.5-9, page 223	GTF: We consider that the use of a MAF value of 1.7 on foliage is over conservative with respect to glyphosate, when the application interval indicated in the GAP is a minimum of 21 days. *For further explanation please refer to Column 3 of the original commenting table.*	Co-RMS: Column 3 of the original commenting table should be pasted into the actual reporting table to simplify further discussion. *Column 3 of the original commenting table:* GTF: We calculate that a 10 half-life and interval of 21 days (a ratio of 1:2) would give a MAF of 1.23 for 2 sprays and 1.29 for 3 sprays	See 5(51)

Bees and non-target arthropods (B. 9.4 and B.9.5)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			(1.3 in ESCORT2). This is conservative given the average DT50 of 2.8 days on foliage referred to in B.9.1.7.3, which we calculate to give a MAF of 1.006. RMS: Please refer to comment 5 (51).	
5(54)	Vol. 3, Annex B.9.5, Effects on other arthropod species (Annex IIA 8.3.2; Annex IIIA 10.5), Table B.9.5-9, page 210	GTF: The RMS argues that a vegetation distribution factor of only 5 (rather than 10) should be considered. This is not in agreement with risk assessment procedures as laid out in the relevant guidance document ESCORT 2 The vegetation distribution factor of 10 as proposed by the GTF is to be maintained in the off-field PER and HQ calculation.	Co-RMS: noted. RMS: The relevant GD (SANCO/10329/2002) states that the vegetation distribution factor (vdf) of 10 "is considered unreliable, therefore more appropriate data should be used as soon as they become available". The RMS proposed a vdf of five as a more reliable based mainly on the 'Retention Area Index' (RAI) characterizing the total retention area of sprayed plant protection products in a canopy per base area. As a 'realistic worst case scenario, meadow canopies < 20 cm height were chosen (Koch and Weisser, 2004; German Federal Environment Agency UBA, 2006). The derived vdf of 5 agrees well with field data by Koch et al. (2003), who compared measured residues of plant protection products	Addressed. **Note:** although the approach proposed by the RMS was also discussed previously in a experts meeting (General Report of PRAPeR Expert Meeting 03, September 2006), it was not yet agreed by MSs.

Bees and non-target arthropods (B. 9.4 and B.9.5)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			on two dimensional surfaces with the measured residues on meadows next to a treated area (factor of 4.4 to 6.5 between median spray residues on leaves when a standard nozzle was used for spray application). German Federal Environment Agency (UBA), 2006. Exposure calculation for arthropods in field border structures - selection of an appropriate 'vegetation distribution factor'. Presented at PRAPeR 1_3, Parma. Koch H and Weisser P, 2004. Die Gesamtoberflaeche in Saumstrukturen als potentielle Retentionsflaeche fuer Driftpartikel, Retention Area Index (RAI). Nachrichtenblatt des Deutschen Pflanzenschutzdienstes, 56, 65-69. Koch H, Weisser P and Landfried M, 2003. Effect of drift potential on drift exposure in terrestrial habitats. Nachrichtenblatt des Deutschen Pflanzenschutzdienstes, 55, 181-188.	
5(55)	Vol. 3, Annex B.9.5, Effects on other arthropod species (Annex IIA 8.3.2;	GTF: The RMS argues that for use on desiccation of mature crops a higher drift rate (2 x 2.77% = 5.54%) should be considered. This is not in agreement with risk assessment	Co-RMS: agreed RMS: Please refer to comment 5 (50).	See 5(50)

Bees and non-target arthropods (B. 9.4 and B.9.5)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
	Annex IIIA 10.5), Table B.9.5-9, page 210	procedures as laid out in the relevant guidance document ESCORT 2, where for field crops 2.77% drift are considered for one application and 2.38% for two applications. The calculation of the off-field PER and HQ should be based on adopted drift rates.		
5(56)	Vol. 3, Annex B.9.5.6, Risk assessment, page 220	GTF: We consider that the use of a MAF value of 1.7 is over conservative with respect to glyphosate, when the application interval indicated in the GAP is a minimum of 21 days. We calculate that a 10-day half-life and interval of 21 days (a ratio of 1:2) would give a MAF of 1.23 for 2 sprays and 1.29 for 3 sprays (1.3 in ESCORT2). This is conservative given the average DT50 of 2.8 days on foliage referred to in B.9.1.7.3, which we calculate to give a MAF of 1.006.	Co-RMS: agreed. RMS: Please refer to comment 5 (51).	See 5(51)

Earthworms and other soil non-target organisms (macro and micro) (B. 9.6, B.9.7 and B.9.8)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point: (if data point not addressed or fulfilled)
5(57)	Vol. 3, B.9.6 data and risk assessment for earthworms Vol. 1, 2.9.4	FR: Please clarify which endpoint for glyphosate acid (technical or pure) should be reported and used in the risk assessment (vol. 3, B.9, pages 226 and 244). No other comment.	GTF: The risk assessment table B.9.6-12 correctly uses the endpoint from the Friedrich (2009) study, i.e. 473 mg a.e./kg dry soil. The table B.9.6-2 could be improved if instead of a.s. (active substance), the acronym a.e. (acid equivalent) was used. Co-RMS: noted RMS: Noted.	Addressed.
5(58)	Vol. 3, Annex B 9.8.1, Laboratory testing, page 253	GTF: KIIA 8.10.1/01: N-transformation study was considered invalid and need for generation of further data was identified. A new GLP study has been generated and can be made available upon request. The following data was given in the first review of glyphosate: no adverse effects at 28.8 mg glyphosate acid/kg dry soil	RMS: We welcome the new GLP study by GTF and kindly ask to submit the study in order to perform a revised quantitative risk assessment.	Data requirement GTF to submit new GLP study on microorganisms (N-transformation).

Other non-target organisms (flora and fauna), sewage treatment (B.9.9 and B.9.10)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
5(59)	Vol. 3, Annex B.9.9.1.1, Seedling emergence, Study KIIA 8.12/01, page 268	GTF: We accept that this 1996 seedling emergence study preceded the current OECD guidelines, but still see this 28 day study is a valid test to show that glyphosate is very much less active pre-emergence than post-emergence. *For further explanation please refer to Column 3 of the original commenting table.*	Co-RMS: Column 3 of the original commenting table should be pasted into the actual reporting table to simplify further discussion. *Column 3 of the original commenting table.* GTF: The reasons for rejecting this study include "no data on visible phytotoxic effects and mean survival of emerged seedlings". This data is presented in Tables 8, 11, 12 and 13, of the original report. These results confirm that there are no treatment related effects from pre-emergence treatments of glyphosate... The temperature variation was a function of natural sunshine in a glasshouse experiment, so outside the control of the study team. RMS:Noted: Based on the mode of action it cannot be excluded on seedling emergence and root growth is possible. Therefore we recommend addressing the risk on the level of product authorization of glyphosate containing products.	See5(66)
5(60)	Vol. 3, Annex B.9.9.1.4, Summary of results on non-target plants,	GTF: The limitations of the seedling emergence study are discussed above, but we believe that this study clearly shows that glyphosate has very little activity as a	Co-RMS: Column 3 of the original commenting table should be pasted into the actual reporting table to simplify further discussion.	See5(66)

Other non-target organisms (flora and fauna), sewage treatment (B.9.9 and B.9.10)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
	page 281	pre-emergence herbicide, and therefore the risk assessment should focus on the post-emergence data. *For further explanation please refer to Column 3 of the original commenting table.*	RMS: Please refer to comment above 5(59).	
5(61)	Vol. 3, Annex B.9.9.1.4, Summary of results on non-target plants, page 281	GTF: The RMS argues that for use on desiccation of mature crops a higher drift rate (2 x 2.77% = 5.54%) should be considered. This is not in agreement with risk assessment procedures as laid out in the relevant guidance document, where for field crops 2.77% drift are considered for one application and 2.38% for two applications. The TER calculation should be based on adopted drift rates.	Co-RMS: agreed. RMS: Please refer to comment 5 (50).	See 5 (50)
5(62)	Vol. 3, Annex B.9.9.1.5, Risk assessment for non-target plants, page 282	GTF: We consider that the use of a MAF value of 1.7 is over conservative with respect to glyphosate on foliage, when the application interval indicated in the GAP is a minimum of 21 days. For further explanation please refer to Column 3 of the original commenting table.	Co-RMS: Column 3 of the original commenting table should be pasted into the actual reporting table to simplify further discussion. *Column 3 of the original commenting table.* GTF: We calculate that a 10 half-life and interval of 21 days would give a MAF of 1.23 for 2 sprays	Experts' consultation MSs experts to discuss the MAF value to be use for risk assessment to terrestrial non-target plants

Other non-target organisms (flora and fauna), sewage treatment (B.9.9 and B.9.10)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			and 1.29 for 3 sprays (or 1.3 as given in the ESCORT2 tables for a 14 day interval). This is conservative given the average DT_{50} of 2.8 days on foliage referred to in B.9.1.7.3, which we calculate to give a MAF of 1.006. As indicated above glyphosate has little activity on plants from natural soils. RMS: Since at the moment no harmonised guidance on multiple exposure exists RMS addressed the risk due to multiple exposure events by the multiple application factor, MAF. RMS proposes to take into account a MAF of 1.7 for the following reason: Plants, in contrast to e.g. arthropods, are sessile and will be affected by each spray drift event. In conclusion plant will be affected at each single application event. The development of approaches to address the impact from multiple exposure events via appropriate extrapolation factors is need.	

Other non-target organisms (flora and fauna), sewage treatment (B.9.9 and B.9.10)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
5(63)	Vol. 3, Annex B.9.9.1.5, Risk assessment for non-target plants, page 282	GTF: An endpoint of ER50 = 146 g a.s./ha was used for risk assessment: Notifier submitted a probabilistic endpoint of HC5 = 206.35 g a.s./ha. New data is available upon request for the representative formulation MON 52776 for a revised risk assessment below	Co-RMS: a revised risk assessment is welcome. RMS: We welcome the new GLP OECD 227 study by GTF and kindly ask to submit the study with the representative formulation MON 52776 in order to perform a revised quantitative risk assessment.	Data requirement GTF is given the possibility to submit new GLP study on terrestrial non-target plants. GTF to provide also a new quantitative risk assessment to terrestrial non-target plants. See also 5(50), 5(64), 5(65), 5(66), 5(67) Open point: The RMS to consider new data, when available, in an Addendum
5(64)	Vol. 3, Annex B.9.9.1.5, NTP probabilistic risk assessment, page 282	GTF: The GTF submitted a probabilistic risk assessment in line with the Guidance Document on Terrestrial Ecotoxicology (SANCO/10329/2002 rev 2 final) page 32. This analysis uses the data from 15 species to calculate the exposure level that is	Co-RMS: Column 3 of the original commenting table should be pasted into the actual reporting table to simplify further discussion. RMS: Please refer to comment 5(63).	See 5(63)

Other non-target organisms (flora and fauna), sewage treatment (B.9.9 and B.9.10)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		protective of 95% of species. The owner of the representative formulation has finalized a study on MON 52276 which can be made available upon request. *For further explanation please refer to Column 3 of the original commenting table.*		
5(65)	Vol. 3, B.9.9.1.5, NTP risk assessment, page 282	GFT: A new GLP OECD 227 study performed by the owner of representative formulation MON 52276 is available for submission upon request. The risk assessment for non-target plants has been updated using the new dataset. This can be made available upon request.	Co-RMS: a new GLP study is welcome. RMS: Please refer to comment 5(63).	See 5(63)
5(66)	Vol. 3, B.9.1.5 risk assessment for non-target plants Page 282	EFSA: the available data do not allow concluding the risk assessment for terrestrial non-target plants for the active substance. The potential effect on seedling emergence could not be addressed because no valid studies are available. Furthermore the endpoint for the most sensitivity species could be underestimated due to the shorter duration of the study and an overall decrease of toxicity endpoints in studies with longer duration. Finally, no data are	Co-RMS: noted. RMS: We welcome the new GLP OECD 227 study by GTF and kindly ask to submit the study with the representative formulation MON 52776 in order to perform a revised quantitative risk assessment.	See 5(62). See also 5(50)

Other non-target organisms (flora and fauna), sewage treatment (B.9.9 and B.9.10)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		available to EFSA to change the trigger value. Therefore, EFSA thinks that more data would be necessary to conclude a quantitative risk assessment.		
5(67)	Vol 3, B.9.9 data and risk assessment for terrestrial plants Vol. 1, 2.9.6 & 3.1.4.9 & 3.2	FR: The correction of the drift rate for application on mature crop is understood but not sufficiently justified to get further harmonisation of the risk assessment at national/zonal levels. It is agreed that study MSL-13320 by Chetram & Lucash, 1994 is not considered sufficient to address the risk of a preparation to non-target plants. The data requirement for MON 52276 is agreed as a reference. Although the proposed increased trigger value (15 instead of 5 page 282 of vol. 3) is debatable, it is agreed that the "Final risk assessment should then be performed on the level of product authorisation with reliable data –sets providing the ER50 values of the plant protection product to non-target plants" (B.9.9, page 282). Therefore, it is suggested to clarify under vol.1, point 3.2 "the risk to non-	Co-RMS: please see 5(55). RMS: We welcome the new data generation by GTF and kindly ask to submit the study with the representative formulation MON 52776 in order to perform a revised quantitative risk assessment. Please refer to comment 5 (50) for information considering drift scenario.	See 5(63). See also 5(50)

Other non-target organisms (flora and fauna), sewage treatment (B.9.9 and B.9.10)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		target plants **with appropriate Annex III data**". It is proposed to consider the drift scenario "ground crop" x 2 for application in mature crops (i.e. 2.77% x 2 = 5.54%) to consider crop height. Surrogate values for "vegetables, ornamentals > 50cm" = "grapes, late stage" = 8.02%". The drift scenario depends also on typical application techniques and not only on crop height, which is not explained in the drift tables.		
5(68)	List of Endpoints, Effects on non-target plants Vol. 3, B.9.9.1.5 page 270	GTF: An endpoint of ER50 = 146 g a.s./ha was used in the original risk assessment, and the notifier submitted an endpoint of HC5 = 206.35 g a.s./ha for a probabilistic risk assessment. New data is submitted for the representative formulation MON 52776, with for a revised risk assessment below.	Co-RMS: please see 5(63). RMS: Please refer to comment 5(63).	5(63)

Other comments				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
5(69)	Vol. 3, B.9. Sections B.9.9.2.1 and B.9.11.	SE: We welcome the literature reviews on the toxicity of glyphosate and POEA surfactants to amphibians and aquatic organisms.	GTF: Polyethoxylated Alkylamine is not a component of the representative formulation MON 52276. Therefore the section on POEA is not considered relevant for the annex I renewal process. See relevant guidance on the annex I renewal for AIR2 (EU Regulation No 1141/2010). RMS: Thanks. Please refer also to comment 5 (70).	Addressed.
5(70)	Vol. 3, B.9.11.1, Literature Review, page 294	GTF: The inclusion of extensive review of a surfactant system which is contained in a plant protection product which is not the representative formulation and therefore not up for review in the Annex I Renewal process is questionable and should be revised by the RMS. The representative formulation (MON52276) that is the basis of this submission does not contain POEA, and consequently is not likely to pose unacceptable risk to aquatic organisms.	RMS: The RMS considers the particularity of glyphosate based formulation with POEA as significant. Therefore, this topic is addressed in the renewal process of the active substance. MS that will evaluate plant protection products based on glyphosate should have access to relevant information.	Addressed.
5(71)	Vol. 3, B.9.12, References relied on, page 300	GTF: The study Annex point is not written out, i.e. needs the final number per annex point. Given that there are many studies for several annex points, adding the final number should help readability.	RMS: Agreed.	Addressed RMS to consider in an updated RAR or addendum.

Other comments				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
5(72)	Vol. 3, B.9.12, References relied on, page 300	GTF: Legend of owner acronyms is incorrect, i.e. ALS = Arysta Lifesciences SAS, MON = Monsanto, SYN = Syngenta. MOT is not correct. Please refer to the Glyphosate Task Force member companies for the correct denomination of the company owning the study.	RMS: Thanks. Acronyms will be corrected.	Addressed RMS to consider in an updated RAR or addendum.
5(73)	Vol. 3, Annex B.9, Evaluation of peer-reviewed literature regarding ecotoxicity of glyphosate, page 1	GTF: The notifier acknowledges the thorough review performed by the RMS of the available literature, while disagreeing with several of the specific evaluations made of individual articles. For further explanation please refer to Column 3 of the original commenting table.	RMS: Noted.	Open point: RMS to clarify why issues related to the systematic review (SR) were not addressed during the SR protocol development performed by the notifier.
5(74)	Vol. 3 B.9	NL: Regarding the spot treatment: Praper 111 regarding the type of application: The experts noted that there is a lack of clarity regarding how the application rate should be expressed in the GAP table for products which will be applied only to small areas e.g. band application in vineyards; the experts strongly suggested that this is harmonised	GTF: in the context of this submission the GAP for spot treatments indicates the application rate per treated area. This is driven by the amount of water in the spray tank, the pressure and the speed at which the applicator is driving. But for the risk assessment, the relevant application rate is the application rate per cropped area, which determines the focal species' habitat, and exposure pattern in the field. Therefore a conversion of the treated area-based application	See 5(12)

Other comments				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		(i.e. is the full dose the equivalent dose in the treated area or does it really relate to the amount per hectare). Moreover, further guidance is needed regarding how to express the application rate (to the treated area) for the purposes of the ecotoxicological risk assessments. It suggested that MS experts discuss this issue in their MS and ensure that the GAP table is clear at the completeness check stage (noting this issue is not just related to ecotox, but also relevant for other specialisms).	rate to a worst-case cropped area-based application rate is a realistic approach. Indeed it would be an improvement if this conversion value was harmonized across all member states. For applications in orchards we recommend that only the strip along the tree line will be treated to create a weed free area (approx. 33% of the cropped area). Consequently the alleys (inter-rows) are left as untreated permanent grassy strips with no exposure to glyphosate. Such areas are going to be much more attractive to herbivorous mammals, as they provide cover, and the untreated alleys will present both more vegetation and more palatable vegetation than the weed-free strips. RMS: We propose to amend the Column "application rate" of all tables including the "application rate per treated surface area" as well as adding the "application rate per cropped area" (taking into account only 50 % of the "application rate per treated area" to results in lower RUD values finally) . We understood that the product is not applied on the whole field area, but full application rate is only applied in strips leaving a	

Other comments				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			minimum of 50 % of the area untreated providing cover and vegetation. In total the area will therefore only exposed to a max. 50 % of the application rate and the application rate in risk assessment was reduced accordingly. We agree that foraging birds and mammals may not only feed in the untreated area. We agree that harmonisation and further guidance is needed.	
5(75)	Vol. B.9	DK: Could you please include and evaluate the reference Marjo Helander, Irma Saloniemi and Kari Saikkonen 2012. Glyphosate in northern ecosystems. Trends in Plant Science, October 2012, Vol. 17, No. 10.	GTF: the literature review by Helander et al. (2012) focuses on glyphosate uses and risk assessment in Nordic countries but is not within the scope of the literature review for AIR2 of glyphosate, since no new data was generated and reported in this article, and which could potentially challenge the risk assessment of glyphosate. RMS: Agreed with DK, reference and evaluation will be included.	Data requirement It is acknowledged that the paper of Marjo Helander, Irma Saloniemi and Kari Saikkonen 2012 was not captured by the systematic literature search because performed for the period 2001-2011. However, the Applicant is given the possibility to provide a summary and full evaluation of the relevance of this paper. Open point: RMS should consider the Applicant's evaluation of the paper Marjo Helander, Irma Saloniemi and Kari Saikkonen 2012 in an addendum.

Other comments				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
				RMS should also clarify whether the systematic literature search report included the references of the papers considered not relevant and the reason for exclusion..
5(76)	Vol. 3, B.9, reference to detailed summaries in the initial DAR and addenda	FR: Detailed summaries in the initial DAR and addenda were not found. However, it is clear that the initial endpoints were all clarified. The details are available in the RAR when necessary (i.e. in support of the chronic endpoints for birds, when the validity of a study is discussed).	GTF: Agreed. RMS: Agreed: Studies which are relevant for risk assessment were described in the available RAR and details of older studies can be found in the initial DAR.	Addressed.
5(77)	Vol.3, B.9.12 References relied on	FR: Some data protection claims may not be considered as justified.	GTF: Data protection is claimed for proprietary reports submitted as new information for the renewal of Annex I listing of Glyphosate. RMS: Noted.	Addressed.

Other comments				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
5(78)	Vol. 4_Monsanto	FR: The compositions of the preparations MON other than MON 52276 and used as test item have not been reported.	RMS: Besides the representative formulations of MON 52276, a few more MON formulations were used: MON78623: was used within an acute oral toxicity with *Northern Bobwhite* and in aquatic studies with *Pseudokirchneriella subcapitata*, *Oncorhynchus mykiss* and *Daphnia magna*. It contains Glyphosate K-salt 48%. MON77973 was used to assess effects towards *Myriophyllum aquaticum* and contains 85.2% glyphosate. MON0139 was used to assess sublethal toxicity to the earthworm *Eisenia fetida* and contains 63.81% w/w Glyphosate IPA salt.	Addressed.
5(79)	Acute and chronic toxicity of glyphosate to aquatic organisms.			Data requirement: Submission of supplemental studies on acute and chronic toxicity of glyphosate to aquatic organisms cited by FAO specifications and evaluations (2000/2001) for glyphosate. Rationale: For aquatic toxicity additional end points are cited, which were not submitted with the

Other comments				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
				supplementary dossier. The data requirement has already been identified in the RAR.

1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(1)	Vol. 4, RAR, AGRIA, C.1.1.2 Method of manufacture, manufacturer, p. 1-2	EFSA: there are some inconsistencies in the description of the manufacturing process, the flow diagram and the starting materials. In the flow diagram [redacted] is a starting material, however looking to the list of starting reagents, it seems that this is also manufactured from them.	AGR: The flow diagram is correct. [redacted] is produced on site and therefore does not appear in the list of starting materials. The production step for [redacted] is not included in the flow diagram. RMS: In addition to the comment of the applicant, it should be noted that the starting materials for [redacted] are listed in Table C.1.1-1.	Addressed.
1(2)	Vol.4 Table C.1.2-1 Agria	FR: Based on the batch analysis, the minimum purity should be increased. Moreover, as impurity [redacted] is a relevant impurity, a specification should be set even if this impurity is not found in the batches.	AGR: The original specification was agreed with the Hungarian authorities following consultation with the BBA and complies with the minimum EU specification. The applicant has no problem if the minimum purity value is increased. [redacted] values from the five batch analysis are effectively [redacted] therefore it was not included in the specification agreed with the regulatory assault above. The applicant agrees that a value should be included that is	See open point 1(1) Vol.4 general information

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			acceptable at European level but unfortunately the applicant does not know what this value is therefore the evaluators suggestion for a value is awaited. RMS: Agree with FR: Based on the data submitted until now, it cannot be evaluated, whether the material used in toxicological studies is representative for the proposed specification or the reference specification. However, the minimum purity is in compliance with Reg. (EU) No. 540/2011 and is therefore acceptable. When the outcome of the peer review is that [redacted] is a relevant impurity, the applicant has to meet the maximum limit which will then be set in the Regulation (EU) No. 540/2011. Nevertheless, the [redacted] could be taken as maximum limit and could be included in a revised RAR.	

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(3)	Vol.4 C.1.2.4 Agria	FR: If the reference specifications from the initial DAR are not covered by tox and eco tox evaluations, it cannot be concluded that this origin is equivalent to the reference specifications. A new evaluation should be performed to set new reference specifications covered by the tox and eco tox evaluation.	AIA: This is currently being addressed by the task force. As the applicant has no access to the studies listed in the dossier this question can only be addressed by the task force. RMS: Noted. Based on the data submitted until now, relevance of impurities cannot be evaluated. Based on the data submitted until now, it cannot be evaluated, whether the material used in toxicological studies is representative for the proposed specification or the reference specification. For the renewal procedure Tier2 ecotoxicological assessment of equivalence was performed on the presumption that the reference specification of the initial DAR is still valid. Should new data become available, a new evaluation would be carried out.	See open point 1(1) Vol.4 general information

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(4)	Vol. 4, C.1.2.4 Comparison of the analytical profile of batches - Toxicological evaluation of specification (2013):	RMS: *The applicant provided no information/data, which would allow to judge whether the impurities are relevant. The notifier provided no evaluation, whether the material used in tox studies is representative for the proposed specification. Based on the available studies submitted, a conclusion on the equivalence of the Agria source cannot be made.* AGR: Additional data/information will be submitted which allow judging whether the impurities are of toxicological relevance or not with regard to the impurities of the reference source. Furthermore, the applicant will provide data/information demonstrating that the material used in toxicological studies is representative for the proposed specification.	AGR: This is currently being addressed by the task force. As the applicant has no access to the studies listed in the dossier this question can only be addressed by the task force as already stated. RMS: In case of the submission of additional data, these could be included in a revised RAR, provided that this is allowed from a procedural point of view. -	Data requirement: Applicant AGRIA to submit data/information concerning the assessment of toxicological relevance of the impurities and data/information demonstrating that the material used in toxicological studies is representative for the proposed specification.

1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(1)	Vol.4 C.1.1.1 Agrichem	FR: FR's point of view is that only the plant location used for the step II of process should be considered. [redacted] should be considered as a starting material.	AGI: No comment. RMS: It is agreed that step II of the process should be considered. However, there seems to be no need to change the description of the manufacturing process.	Addressed.
1(2)	Vol. 4, RAR, AGRICHEM, C.1.3 Methods of analysis, NNG, Table C.1.3-2, p. 11	EFSA: are the concentration units of the linearity range correct? In the 5-batch data [redacted] is [redacted], how was this quantified if the method has an [redacted] of [redacted]?	AGI: According to the method validation report ([redacted]), the LOQ for [redacted]. Recovery at the LOQ (i.[redacted]) was determined and acceptable. RMS: Correct, an LOQ of [redacted] was stated in the study of [redacted]). The value could be amended in a revised RAR.	Addressed.

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(3)	Vol. 4, C.1.2.4 Comparison of the analytical profile of batches - Toxicological evaluation of specification (2013):	RMS: *The applicant provided no information/data, which would allow to judge whether the impurities are relevant.* *The notifier provided no evaluation, whether the material used in tox studies is representative for the proposed specification.* *Based on the available studies submitted, a conclusion on the equivalence of the Agrichem source cannot be made.* AGI: Additional data/information will be submitted which allow judging whether the impurities are of toxicological relevance or not with regard to the impurities of the reference source. Furthermore, the applicant will provide data/information demonstrating that the material used in toxicological studies is representative for the proposed specification.	RMS: In case the applicant provides additional data, these could be included in a revised RAR, provided that this is allowed from a procedural point of view. Based on the data submitted until now, relevance of impurities cannot be evaluated. Based on the data submitted until now, it cannot be evaluated, whether the material used in toxicological studies is representative for the proposed specification or the reference specification.	Data requirement: Applicant Agrichem to submit data/information concerning the assessment of toxicological relevance of the impurities and data/information demonstrating that the material used in toxicological studies is representative for the proposed specification.

1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(1)	Vol. 4, RAR, AGRO, C.1.1.2 Method of manufacture, step 2, p. 2	EFSA: small inconsistency in the description of step 2, the addition of a reactant to obtain the respective product is missing	AGT: Typing mistake: the missing reactant has to be added in the description text but is present in the equations describing the process at the bottom of page 2. RMS: Agreed, the missing reactant could be added in a revised RAR.	Addressed.
1(2)	Vol.4 C.1.2.4 Agro Trade	FR: If the reference specifications from the initial DAR are not covered by tox and eco tox evaluations, it cannot be concluded that this origin is equivalent to the reference specifications. A new evaluation should be performed to set new reference specifications covered by the tox and eco tox evaluation.	AGT: Additional data/information will be submitted which allow judging whether the impurities are of toxicological relevance or not with regard to the impurities of the reference source. RMS: In case the applicant provides additional data, these could be included in a revised RAR, provided that this is allowed from a procedural point of view. Based on the data submitted until now, relevance of impurities cannot be evaluated. Based on the data submitted until now, it cannot be evaluated, whether the material used in toxicological studies is representative for the proposed specification or the reference specification.	See open point 1(1) in RT of Vol.4 general information

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			For the renewal procedure Tier2 ecotoxicological assessment of equivalence was performed on the presumption that the reference specification of the initial DAR is still valid. Should new data become available, a new evaluation would be carried out.	
1(3)	Vol. 4, C.1.2.4 Comparison of the analytical profile of batches - Toxicological evaluation of specification (2013):	RMS: *The applicant provided no information/data, which would allow to judge whether the impurities are relevant.* *The applicant provided no evaluation, whether the material used in tox studies is representative for the proposed specification.* *Based on the available studies submitted, a conclusion on the equivalence of the Agro source cannot be made.* AGT: Additional data/information will be submitted which allow judging whether the impurities are of toxicological relevance or not with regard to the impurities of the reference source. Furthermore, the applicant will provide data/information demonstrating that the material used in toxicological studies is representative for the proposed	AGT: Furthermore, the applicant will provide data/information demonstrating that the material used in toxicological studies is representative for the proposed specification. RMS: In case the applicant provides additional data, these could be included in a revised RAR, provided that this is allowed from a procedural point of view. Based on the data submitted until now, relevance of impurities cannot be evaluated. Based on the data submitted until now, it cannot be evaluated, whether the material used in toxicological studies is representative for the proposed specification or the reference specification.	Data requirement: Applicant Agrotrade to submit data/information concerning the assessment of toxicological relevance of the impurities and data/information demonstrating that the material used in toxicological studies is representative for the proposed specification.

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		specification.		
1(4)	Vol. 4 C.1.3.1 Agro trade	FR: The identity of impurities [redacted] should be confirmed.	AGT: in documents listed KIIA 4.2.3 (Vohra Yusuf, 2009 (5 batches analysis reports), the identity of the impurities was confirmed. RMS: The identity of the impurities [redacted] was confirmed by [redacted] and the comparison of the [redacted] of sample and reference standards. The identity of [redacted] is confirmed by [redacted] after derivatisation with [redacted]. [redacted] is determined by [redacted] after derivatisation with [redacted] which is in compliance with the FAO method for the determination of [redacted] in glyphosate technical. The identity was confirmed by [redacted]. This information could be also stated in a revised RAR.	Addressed.

1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(1)	Vol. 4, RAR, ALB, C.1.1. Manufacturer, p. 1	EFSA: small typo in the name of the product: imini should be imino	ALB: Noted RMS: The typo could be corrected in a revised RAR.	Addressed.
1(2)	Vol. 4, RAR, ALB, C.1.3. Analytical methods, NNG, p. 13	EFSA: the LOQ of the method is 0.3 ppm, however in the 5-batch there are values <0.3 and <0.12 ppm. Is this later value the limit of detection?	ALB: In the report: Glyphosate TC: Method Validation for the Analysis of Manufacturing Process Related Impurities Study: SSL 08807 on page 37 figure 9 shows the linearity plot for [redacted]. The lowest concentration measured was [redacted] and thus this value (approximated to [redacted] m) is assumed to be the limit of detection for this impurity. In those batches where no [redacted] was detected by the method used the concentrations are stated as [redacted] m. RMS: No further comment.	Addressed.
1(3)	Vol. 4 C.1.2.2 Albaugh	FR: There is a typo. Impurity [redacted] is [redacted] not [redacted]	ALB: Noted RMS: The typo could be corrected in a revised RAR.	Addressed.

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(4)	Vol.4 C.1.2.4 Albaugh	FR: If the reference specifications from the initial DAR are not covered by tox and ecotox batches, it cannot be concluded that this origin is equivalent to the reference origin. New evaluation should be performed to set new reference specifications based on toxicological and ecotoxicological studies.	ALB: Additional data can be submitted on request. RMS: In case the applicant provides additional data, these could be included in a revised RAR, provided that this is allowed from a procedural point of view. Based on the data submitted until now, it cannot be evaluated, whether the material used in toxicological studies is representative for the proposed specification or the reference specification.	See open point in comment 1(1) of the RT for Vol.4 general information.

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(5)	Vol. 4, C.1.2.4 Comparison of the analytical profile of batches	RMS: *The applicant provided no information/data, which would allow to judge whether the impurities are relevant.* *The applicant provided no evaluation, whether the material used in toxicological studies is representative for the proposed specification.* *Based on the available studies, a conclusion on the equivalence of the Albaugh source cannot be made.* ALB: Additional data/information will be submitted which allow judging whether the impurities are of toxicological relevance or not with regard to the impurities of the reference source. Furthermore, the applicant could provide data/information demonstrating that the material used in toxicological studies is representative for the proposed specification.	RMS: In case the applicant provides additional data, these could be included in a revised RAR, provided that this is allowed from a procedural point of view. Based on the data submitted until now, relevance of impurities cannot be evaluated. Based on the data submitted until now, it cannot be evaluated, whether the material used in toxicological studies is representative for the proposed specification or the reference specification.	Data requirement: Applicant Albaugh to submit data/information concerning the assessment of toxicological relevance of the impurities and data/information demonstrating that the material used in toxicological studies is representative for the proposed specification.

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(6)	Vol. 4 C.1.3-1 Albaugh	FR: The identity of [redacted] should be confirmed.	ALB: The specificity of the method was demonstrated in report: Glyphosate Wet Cake - Analytical Profile of five Batches Study: SSL 09607 As a fully validated FAO method [redacted]) was used for the analysis it is considered that further validation is not required. The method is fully described in the annex to the above report. RMS: [redacted] is determined by the FAO method for the determination of [redacted] in glyphosate technical. The method uses [redacted] after [redacted]. The identity was confirmed by [redacted] and comparison of the [redacted] of the sample and reference derivatives. This information could be also stated in a revised RAR.	Addressed.

1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(1)	Vol. 4, RAR, ARY, C.1.1.2 Method of manufacture, p. 2	EFSA: there are some inconsistencies in the description of the manufacturing processes: it is stated that both processes use the same synthesis pathway, however in one of them a starting material containing [redacted] was probably left out by mistake	AAP: [redacted] is a starting material for the first step of manufacturing process of both sources. So [redacted] is missing in table C.1.1-2 by mistake. RMS: [redacted] could be added in the table in a revised RAR.	Addressed.
1(2)	Vol.4 Table C.1.2-1 Arysta	FR: Based on the five batches analysis, the minimum purity should be increased and specifications for impurities [redacted] and [redacted] should be removed as these impurities have never been detected at content higher than [redacted] and they are not relevant.	RMS: The minimum purity is in compliance with Reg. (EU) No. 540/2011 and is therefore acceptable. The important issue seems to be that the specification is covered by the current reference specification to ensure that there are no unacceptable effects comparing to the evaluated reference source. Concerning the impurities it is clearly stated in the conclusion that [redacted] and [redacted] ([redacted] source) were removed from the specification because the proposed maximum contents were below [redacted] The values in Table C.1.2-1 are related to the proposal of the applicant	See open point 1(1) in RT for Vol.4 general information. To increase the minimum purity and would mean to have individual specifications for all technical materials.

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			(see table header).	
1(3)	Vol.4 Table C.1.2-2 Arysta life Science	FR: Based on the five batches analysis, the specification for impurity [redacted] should be removed as this impurity has never been detected at content higher than [redacted] and it is not relevant.	RMS: see 1(2)	See comment 1(2)
1(4)	Vol.4 C.1.2.4 Arysta life Science	FR: If the reference specifications from the initial DAR are not covered by tox and eco tox evaluations, it cannot be concluded that this origin is equivalent to the reference specifications. A new evaluation should be performed to set new reference specifications covered by the tox and eco tox evaluation.	RMS: Agreement with FR: based on the data submitted until now, it cannot be evaluated, whether the material used in toxicological studies is representative for the proposed specification or the reference specification. For the renewal procedure Tier2 ecotoxicological assessment of equivalence was performed on the presumption that the reference specification of the initial DAR is still valid. Should new data become available, a new evaluation would be carried out.	See open point 1(1) in RT for Vol.4 general information.
1(5)	Vol. 4, RAR, ARY, C.1.2.4 Specifcations, Conclusion, p. 10	EFSA: it is unclear why [redacted] was removed from the specification? Does it mean that both sources have their own specification? Clarification is needed, whether the proposer's intention is to have two	RMS: The applicant submitted individual specifications for each source. [redacted] was only removed from the specification of the Shanghai source.	Addressed. See also open point 1(1) in RT for Vol.4 general information.

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		different specifications. EFSA agrees that the specifications were proposed based on mean+3SD values, however they seem to be quite tight taking into account that the batch data reflect a manufacturing period of less than one week	Concerning the maximum limits of the impurities there was no reason to reject the proposal of the applicant.	
1(6)	C.1.2.4 Comparison of the analytical profile of batches - Toxicological evaluation of specification (2013):	RMS: *The applicant provided no information/data, which would allow to judge whether the impurities are relevant. The applicant provided no evaluation, whether the material used in tox studies is representative for the proposed specification. It is noted, that most/all impurities are specified in higher levels than they were present in material used in tox studies.* *Impurity [redacted] was reported as [redacted] in the tox batch but was foreseen to be specified. Additionally, the min purity in the specification is slightly below the amount in some of the materials used in tox studies ([redacted]* *Additionally, the mentioned batches were used only in a limited set of studies.* *Impurities [redacted] and [redacted] are specified in*	RMS: In case the applicant provides additional data, these could be included in a revised RAR, provided that this is allowed from a procedural point of view. Based on the data submitted until now, relevance of impurities cannot be evaluated. Based on the data submitted until now, it cannot be evaluated, whether the material used in toxicological studies is representative for the proposed specification or the reference specification.	Data requirement: Applicant Arysta to submit data/information concerning the assessment of toxicological relevance of the impurities and data/information demonstrating that the material used in toxicological studies is representative for the proposed specification.

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		significantly higher amounts than listed in the reference specification. *The notifier has submitted a statement. However, RMS indicates that "the mentioned data/information has not been submitted for the present EU procedure. Hence RMS's tox risk assessor cannot confirm that there is no significant increase in toxicity due to the presence of the impurities".* *In summary, it cannot be evaluated, whether the material used in toxicological studies is representative for the proposed specification.* *Based on the available studies submitted, a conclusion on the equivalence of the Arysta sources cannot be made.* AAP: Regarding the impurities [redacted] and [redacted] additional data could be submitted. Furthermore, sufficient information/data could be submitted for the present EU procedure which allow judging whether the impurities are toxicologically relevant or not with regard to the impurities of the reference source.		

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(7)	C.1.2.4 Comparison of the analytical profile of batches – Ecotoxicological evaluation of specification (2013):	RMS: *For the impurity [redacted] further ecotox assessment is required as the evaluation according to SANCO/10597/2003 rev 10.1. The impurity [redacted] is present in the specification from the manufacturer "[redacted]" and the manufacturer "[redacted]" at max [redacted] and max [redacted] g/kg respectively. The equivalence of this source to the reference source cannot be substantiated with sufficient certainty; additional information addressing the ecotox representativeness of the specification is required.* *Based on the available studies submitted, a conclusion on the equivalence of the Arysta sources cannot be made.* AAP: Additional data will be provided	RMS: Additional information addressing the ecotoxicological representativeness is appreciated.	See data requirement 1(6)
1(8)	Vol. 4, RAR, ARY, C.1.3 Analytical methods, p. 13-16 and Table C.1.5-1, p.22	EFSA: it is not clear what is the LOQ for the determination of [redacted] and [redacted]	AAP: LOQ for the determination of [redacted] was [redacted] and [redacted] in [redacted] (2004) and [redacted] (2006), respectively. For [redacted] LOQ was [redacted] and [redacted] in [redacted] (2004) and [redacted] (2006), respectively. RMS: The values stated by the applicant for	Addressed.

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			the LOQ of [redacted] and [redacted] are interchanged. In the study of [redacted] (2006) the LOQ for [redacted] is [redacted] (p. 26) and for [redacted] (p. 21).	
1(9)	Vol. 4 C.1.3.1 Arysta life Science	FR: Two methods are available for the determination of impurities ([redacted] and [redacted] specify the method used for the determination of content in table C.1.2-1 and C.1.2-2	AAP: The analytical method reported in [redacted] (2004) corresponds to the table C.1.2-1 while [redacted] (2006) describes the method used for the 5-batch analysis that result in table C.1.2-2. RMS: Table C.1.2-1: The methods reported in [redacted] (2004) were used for the determination of [redacted] and [redacted] was determined by [redacted] This method is validated in the 5-batch analysis study [redacted] (2009). Table C.1.2-2: The methods reported in [redacted] (2006) were used for the determination of [redacted] and [redacted] in the batches.	Addressed.
1(10)	Vol. 4 C.1.3.1 table C.1.2-2 Arysta life Science	FR: As the LOQ for the determination of [redacted] is [redacted] it is perferable indicate [redacted]	RMS: Comment noted.	Addressed.

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(11)	Vol. 4 C.1.3.1 table C.1.2-2 Arysta life Science	FR: The LOQ of formaldehyde should be expressed in g/kg in order to compare the LOQ with the content of formaldehyde found in tables C.1.2-1 and table C.1.2-2.	RMS: The LOQ of [redacted] is stated as [redacted] below table C.1.3-9. In the tables C.1.2-1 and table C.1.2-2 the mass fraction of [redacted] is given in ppm which is equal to mg/kg. However, it could be pointed out in a revised Volume 4 that some contents of [redacted] in table C.1.2-2 are below the LOQ.	Addressed.
1(12)	Vol. 4 C.1.3.1 Arysta life Science	FR: The identity of each impurity should be confirmed.	RMS: The identity of [redacted] was confirmed by [redacted] and the [redacted] of sample and reference standards. The identity of [redacted] and [redacted] was only determined by [redacted] of the sample with reference standard. Additional information in order to confirm the identity of the impurities could be required by the applicant. [redacted] is determined by [redacted]t which is in compliance with the [redacted] for the determination of [redacted] in glyphosate technical. The confirmation	Addressed.

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			of the identity by [redacted] is considered as acceptable. This information could be also stated in a revised RAR.	
1(13)	C.1.3-1 Analytical methods. Validation data for the determination of the impurity 6	RMS: *In case of impurity 6 the determination of the precision cannot be regarded as acceptable as matrix effects and sample preparation are not taken into account.* AAP: In Guidance document SANCO 3030/99 rev. 4 it is stated under 3.1.2 (iii) that the accuracy of the method for **significant and/or relevant impurities** should be reported as mean recovery ± relative standard deviation in the technical material. Arysta provided two analytical method validations ([redacted] 2004 and 2006): In the validation report from 2004 [redacted] was found to be below the [redacted] mg/kg. Therefore, [redacted] is not a significant impurity and the validation using a calibration solution should be acceptable. Nevertheless, in the second validation the precision was measured with five	RMS: Agreed, the validation data in table C.1.3-1 for impurity [redacted] are not relevant for the evaluation.	Addressed.

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		preparations of glyphosate in concentration ranges of [redacted]. Therefore the matrix effects were taken into account.		
1(14)	C.1.3-3 Analytical methods. Validation data for the determination of the impurity 2	RMS: *With respect to validation data for the determination of the impurity [redacted] the method should be described in detail by the applicant. The use of the reaction solution is not mentioned within the sample preparation.* AAP: Additional data will be submitted.	RMS: No further comment. However, in case the applicant provides additional data, these could be included in a revised RAR, provided that this is allowed from a procedural point of view.	Data requirement: Applicant Arysta to provide additional validation data for the determination of the impurity [redacted]
1(15)	C.1.3-9 Analytical methods. Validation data for the determination of the impurity 21	RMS: *With respect to validation data for the determination of the impurity [redacted] the fortification levels for the determination of the accuracy should be given by the applicant with respect to glyphosate technical in %.* AAP: Additional data will be submitted.	RMS: No further comment. However, in case the applicant provides additional data, these could be included in a revised RAR, provided that this is allowed from a procedural point of view.	Data requirement: Applicant Arysta to provide the fortification levels for the determination of the accuracy data for the determination of the impurity [redacted]

1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(1)	Vol. 4 C.1.1.1 Barclay chemicals	FR: The third source of active substance (manufacturer [redacted] should be clarified, it should be indicated if Barclay has access to all origins from [redacted] or only one, and in this case clarify which.	BCL: Barclay has been in contact with [redacted] and [redacted] have agreed to contact DKC directly with the required information. This is due to the confidential nature of the information.DKC should expect this information shortly. RMS: No further comment.	Addressed.
1(2)	Vol. 4 C.1.1.2 2.Barclay chemical Manufacturing Barclay chemicals	FR: Data concerning the purity of starting materials should be reported in the table C.1.1-2.	BCL: Data is not available to address this point. RMS: No further comment.	Data gap: The purity of starting materials should be reported. Relevant for Applicant Barclay chemicals See also comment 1(3)
1(3)	Vol. 4, RAR, BAR, C.1.1.2 Method of manufacture, p. 6	EFSA: no information about the purity and commercial availability of the starting materials used	BCL: Data is not available to address this point. RMS: No further comment.	See data gap in comment 1(2)
1(4)	Vol. 4, RAR, BAR, C.1.2.3 Five batch data, p. 12-13	EFSA: are these batch data representative to the production? No manufacturing dates are mentioned.	BCL: Manufacturing dates for both sources are available and have been included in an updated Doc J included separately to this document. The manufacturing processes have not	Data requirement: Applicant Barclay to submit the manufacturing dates for both sources to be included in a revised RAR

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			changed since the 5-batch analyses and therefore the batches tested are representative of the manufacturing processes. RMS: In case the applicant provides additional data, these could be included in a revised RAR, provided that this is allowed from a procedural point of view.	
1(5)	Vol. 4, RAR, BAR, C.1.2.3 Five batch data, Table C.1.2-2, p.13	EFSA: based on batch data, considering the a.s. content and the content of impurities, a higher minimum a.s. content might be specified.	BCL: For both sources the minimum a.s. content has been calculated by the standard method using the formula; Mean of individual 5 batch results – 3x Std deviation of the individual 5 batch results. In the case of the Barclay source, 4 out of the 5 batch results are quite similar and one is much lower. This has the effect of creating a large standard deviation and therefore the minimum a.s. content as calculated by the formula above gives a much lower value than the mean. If necessary, Barclay could raise the minimum a.s. content to 975 or 980g/Kg. However going above 980g/Kg would not result in a robust specification	See open point 1(1) in the RT for the Vol.4 general information.

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No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			based on the 5 batch results. RMS: The minimum purity is in compliance with Reg. (EU) No. 540/2011 and is therefore acceptable. The important issue seems to be that the specification is covered by the current reference specification to ensure that there are no unacceptable effects comparing to the evaluated reference source.	
1(6)	Vol.4 C.1.2.4 Barclay chemicals	FR: If the reference specifications from the initial DAR are not covered by tox and eco tox evaluations, it cannot be concluded that this origin is equivalent to the reference specifications. A new evaluation should be performed to set new reference specifications covered by the tox and eco tox evaluation.	BCL: Barclay understands that this issue does not relate specifically to Barclay's sources of Glyphosate. Rather it is an issue that is being addressed by DKC and an independent third party whereby QSARs and REACH data are being used to determine the toxicological relevance of impurities. RMS: Agreement with FR: based on the data submitted until now, it cannot be evaluated, whether the material used in toxicological studies is representative for the proposed specification or the reference specification. For the renewal procedure Tier2	See open point 1(1) in the RT for the Vol.4 general information.

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			ecotoxicological assessment of equivalence was performed on the presumption that the reference specification of the initial DAR is still valid. Should new data become available, a new evaluation would be carried out.	
1(7)	Vol. 4, RAR, BAR, C.1.2.4 Specifcations, p. 14	EFSA: Clarification is needed, whether the proposer's intention is to have two different specifications or just one covering all sources?	BCL: Since Barclay does not know the specification of the Monsanto source it is not possible to have a single specification covering all sources. RMS: Due to the fact that the applicant has submitted separate specification for the sources and that are is no obligation to cover the sources by one specification, the RMS does not see the need for any further action.	Addressed. See also open point 1(1) in the RT for the Vol.4 general information.
1(8)	Vol 4 C.1.2.4 Comparison of the analytical profile of batches (5-batch analysis)	RMS: *The maximum content of the impurity* ■ *should be clarified. The maximum content is amended to be in compliance with the analytical data. However, an updated Document J should be submitted by the applicant.* BCL: Additional data will be submitted.	BCL: This has been corrected in the updated Doc J included separately to this document. RMS: The corrected data could be included in a revised RAR.	Open point: RMS to correc the data for the maximum content of the impurity 20 in a revised Vol.4.

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		The N-nitroso Glyphosate content has been amended to 0.0004g/kg (0.4mg/kg).		
1(9)	Vol 4 C.1.2.4 Comparison of the analytical profile of batches - Toxicological evaluation of specification (2013):	RMS: *The applicant provided no information/data, which would allow to judge whether the impurities are relevant* *The applicant provided no evaluation, whether the material used in tox studies is representative for the proposed specification.* *Based on the submitted data, a conclusion on the equivalence of the Barclay sources cannot be made.* BCL: Additional data/information will be submitted which allow judging whether the impurities are of toxicological relevance or not with regard to the impurities of the reference source. Furthermore, the applicant could provide data/information demonstrating that the material used in toxicological studies is representative for the proposed specification.	BCL: As per 1(6) Barclay understands that this issue does not relate specifically to Barclay's sources of Glyphosate. Rather it is an issue that is being addressed by DKC and an independent third party whereby QSARs and REACH data are being used to determine the toxicological relevance of impurities. RMS: In case the applicant provides additional data, these could be included in a revised RAR, provided that this is allowed from a procedural point of view. Based on the data submitted until now, relevance of impurities cannot be evaluated. Based on the data submitted until now, it cannot be evaluated, whether the material used in toxicological studies is representative for the proposed specification or the reference specification.	Data requirement: Applicant Barclay to submit data/information concerning the assessment of toxicological relevance of the impurities and data/information demonstrating that the material used in toxicological studies is representative for the proposed specification
1(10)	Vol. 4, RAR, BAR, C.1.3 Analytical methods,	EFSA: small typo in the description of the mobile phase	BCL: This is an issue for the RMS RMS: The typo could be corrected in a	Open point: RMS to correct the typo concerning the

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No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
	C.1.3.1, p. 15		revised RAR.	mobile phase in a corrignedum.
1(11)	Vol. 4, RAR, BAR, C.1.3 Analytical methods, NNG, p. 16	EFSA: small typo in the description of the mobile phase: 'certyl…'	BCL: This is an issue for the RMS RMS: The typo could be corrected in a revised RAR	Open point: RMS to correct the typo concerning the mobile phase in a corrignedum.
1(12)	Vol. 4 C.1.3.1 [redacted] source Barclay chemicals	FR: The identity of impurity [redacted] and [redacted] should be confirmed.	BCL: In report DNA0775 (2009) the identity of [redacted] and [redacted] have been confirmed by [redacted], whereby the spectrum of the impurity has been compared with that of a certified reference standard. We therefore believe that the identities of the impurities have been confirmed. Ref SANCO 3030/99 rev. 4 *"Confirmatory techniques are required to support identification of the a.s. and significant and/or relevant impurities, when the primary method of determination is not GC-MS or another highly specific method such as HPLC-UV DAD. Confirmation should normally involve using a spectroscopic method. Chromatographic confirmatory methods should be*	Addressed.

Identity (B.1, Annex C)				
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			used, where practical, such as GC-MS, LC-MS and HPLC-DAD." RMS: No further comment.	
1(13)	Vol. 4 C.1.3.1 Barclay source Barclay chemicals	FR: In the table C.1.2-2, content of [redacted] is below [redacted]).	BCL: This has been corrected in the updated Doc J included separately to this document. RMS: The values could be corrected in a revised RAR.	Open point: RMS to correct the content of NNG in the table C.1.2-2 in an updated Vol.4
1(14)	Vol. 4 C.1.3.1 Barclay source Barclay chemicals	FR: For better clarity, the LOQ of [redacted] should be indicate in g/kg in order to compare the LOQ with the content of [redacted] found in tables analytical profile of batches.	BCL: The study used the [redacted] content in Glyphosate samples. This method is validated and has been shown to be linear over the range 0.3-14ppm and has a limit of detection of 1ppm or 0.001g/Kg RMS: No LOQ is given in the [redacted]	Addressed.
1(15)	Vol. 4 C.1.3.1 Barclay source Barclay chemicals	FR: The identity of each impurity should be confirmed.	BCL: As the method employs derivatisation it is not practical to use HPLC-DAD, GC-MS or LC-MS or peak collection followed by spectroscopic examination to confirm analyte identification as detailed in Sanco/3030/99rev.4 as none	Addressed.

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			of these methods are suitable to detect a fluorescent derivative. In an attempt to perform this analysis to Sanco/3030/99rev.4 guidelines Life Scientific carried out a literature search to find a suitable method, however, none were found. It was decided that the only solution was to carry out the specificity testing by confirming [redacted]. RMS: The identity of the impurities was only determined by [redacted] of sample and reference standard. The comment of the applicant is unfortunately unclear. A confirmation of the identity by comparison of characteristic sample and reference spectra seems to be possible. This could be conducted with or without derivatisation.	

Identity (B.1, Annex C)				
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1(16)	Vol 4, C.1.3.7 - Validation data for the determination of the impurity [redacted]	RMS: *The applicability of the method must be demonstrated. Appropriate chromatograms have to be submitted by the applicant. The applicant stated that representative chromatograms are available if required.* BCL: Additional data will be submitted.	BCL: Chromatograms are available if requested. RMS: The chromatograms could be taken up in a revised RAR provided that this is possible from a procedural point of view.	Data requirement: Applicant Barclay to submit representative chromatograms for the determination of the impurity [redacted] to be evaluated in a revised Vol.4

1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(1)	C1 rar_22_volume4_general_information	NL: In the table on page 5, for the Brokden source no impurities at all are indicated. In volume 4 for Brokden (rar_22_volume4_Brokden_2013_12_18 impurities are indicated, also at significant level but somehow not on the specification. NL agrees with the RMS that technical equivalence can not be evaluated this way. However at table 5 it should be indicated that the Brokden specification is preliminary since it is not supported by the batches. Should Brokden then be included as one of the notifiers, when the specification is not supported by the batches?	BRO: Specifications supported by the 5 batches and accepted by the CRD UK authorities for the equivalence are as follow: Substance | Specification proposed by applicant [g/kg] [redacted]	Open point: RMS to include the provided specification for Brokden in an updated Vol.4

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			RMS: It is stated in the conclusion that the applicant has only submitted the minimum purity of the technical active substance and that a complete specification is required. The specification that is now provided could be taken up in a revised RAR in case that this is possible from a procedural point of view.	
1(2)	Vol. 4, RAR, BRO, C.1.1.2 Method of manufacture, p. 1	EFSA: no information about the purity and commercial availability of the starting materials used	BRO: All starting materials indicated are common components and they can be easily bought in the market. Companies where these materials can be bought/ registration in Echa [redacted] Registered in Echa: [redacted] Registered in Echa: [redacted]	Open point: RMS to include the information about the starting materials for Brokden in an updated Vol.4

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			[redacted] Registered in Echa: [redacted] Registered in Echa: [redacted] Registered in Echa: [redacted]	

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			[redacted] Registered in Echa: [redacted] Registered in Echa: [redacted] RMS: It is noted that the starting materials are commercial available. The question on the purity of the starting materials which are used by the manufacturer is still open.	

Identity (B.1, Annex C)				
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1(3)	Vol 4 C.1.1.2	RMS: *The applicant has to clarify whether or not the starting materials are commercially available.* BRO: All starting materials indicated are common components and they can be easily bought in the market.	BRO: Please refer to comment addressed in No. 1(2) in column 3 RMS: see comment 1(2)	Addressed: See comment 1(2)
1(4)	Vol 4 C.1.2.3	RMS: *No information on the date of production of the batches has been stated*. BRO: Please see production date of the five batches samples in column 3. Batch number / Production date 071600 / Aug. 25, 2007 072020 / Sep. 3, 2007 072380 / Sep. 9, 2007 072682 / Sep. 14, 2007 073112 / Sep. 21, 2007	BRO: Please refer to comment addressed in No. 1(4) in column 2 RMS: The production dates could be taken up in a revised RAR in case that this is possible from a procedural point of view.	Open point: RMS to include the information about the date of production of the batches for Brokden in an updated Vol.4

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(5)	Vol 4 C.1.2.4 Comparison of the analytical profile of batches	RMS: *The applicant has only given the minimum purity of the technical active substance. Maximum contents of the significant impurity* [redacted] *are required.* BRO: - Maximum contents of the significant/ relevant impurities above mentioned were provided to RMS/EFSA. - The data provided were the same as the data provided for the application of equivalence of Brokden glyphosate source in CRD UK. In these specifications the maximum contents of the significant/relevant impurities were declared.	BRO: Please refer to comment addressed in No. 1(1) in column 3 RMS: see comment 1(1)	See open point in comment 1(1)
1(6)	Vol. 4, RAR, BRO, C.1.2.4 Specifcations, p.7	EFSA: the date of the manufactured batches and the specification are missing	BRO: Please refer to comment addressed in No. 1(1) in column 3 (specification) and 1(4) in column 2 (date of the manufactured batches) RMS: see comment 1(1) and 1(4)	Addressed. See comments 1(1) and 1(4)
1(7)	Vol 4 C.1.2.4 Comparison of the analytical profile of	RMS: *The applicant provided no information/data, which would allow to judge whether the impurities are relevant.*	BRO: Please refer to comment addressed in No. 1(7) in column 2	Data requirement: Applicant Brokden to submit

Identity (B.1, Annex C)				
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	batches - Toxicological evaluation of specification (2013):	*The applicant provided no evaluation, whether the material used in tox studies is representative for the proposed specification. Based on the data submitted, a conclusion on the equivalence of the Brokden source cannot be made.* BRO: Additional data/information will be submitted which allow judging whether the impurities are of toxicological relevance or not with regard to the impurities of the reference source. Furthermore, the applicant will provide data/information demonstrating that the material used in toxicological studies is representative for the proposed specification.	RMS: In case the applicant provides additional data, these could be included in a revised RAR, provided that this is allowed from a procedural point of view. Based on the data submitted until now, relevance of impurities cannot be evaluated. Based on the data submitted until now, it cannot be evaluated, whether the material used in toxicological studies is representative for the proposed specification or the reference specification.	data/information concerning the assessment of toxicological relevance of the impurities and data/information demonstrating that the material used in toxicological studies is representative for the proposed specification.
1(8)	Vol 4 C.1.2.4 Comparison of the analytical profile of batches - Toxicological evaluation of specification (2013)	RMS: *Based on the data submitted, a conclusion on the equivalence of the Brokden source cannot be made.* BRO: Data for relevant impurities were provided.	BRO: Please refer to comment addressed in No. 1(8) in column 2 RMS: see 1(8). RMS's toxicology expert is not aware of any toxicological data on relevant impurities which were submitted by the notifier.	See data requirement in comment 1(7)
1(9)	Vol. 4, RAR, BRO, C.1.3 Analytical methods,	EFSA: the LOQ of the [redacted] is of [redacted] while the 5-batch table contains values of <1 ppm	BRO: The LOQ of the [redacted] (see batch analysis report nr A7190 pg 22).	Open point: RMS to update the LOQ of the [redacted]

Identity (B.1, Annex C)				
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	NNG, p. 9		The 5-batch table contains values are between LOD ([redacted]) and LOQ ([redacted]. The value indicated in the specifications is [redacted] corresponding to LOQ. RMS: The LOQ could be changed in a revised RAR.	method in an updated Vol.4 for Brokden
1(10)	Vol. 4, RAR, BRO, C.1.3 Analytical methods, [redacted] p. 10	EFSA: the LOQ of the [redacted] while the 5-batch table contains values [redacted]	BRO: The LOQ if the [redacted] (see batch analysis report A7190 pg 22). The 5-batch table contains values are between LOD ([redacted]) and LOQ [redacted]). RMS: In a revised RAR the LOQ could be changed from [redacted]. Then, the values in table C.1.2-1 could be also changed [redacted] for [redacted]	Open point: RMS to update the LOQ of the [redacted] and values in table C.1.2-1 in an updated Vol.4 for Brokden.

1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(1)	Vol. 4, RAR, BRS, C.1.2.3 Five batch data, Table C.1.2-1, p.6	EFSA: based on batch data, considering the a.s. content, a higher minimum a.s. content might be specified.	BSJ: Additional data can be submitted on request RMS: Additional data could be taken into account in case that this is possible from a procedural point of view.	See open point 1(1) in the RT for Vol.4 general information To increase the minimum purity specification would mean to have individual specifications for all technical materials. It should be noted that the proposal is to set one reference specification, independent from the synthesis pathway.

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(2)	Vol. 4, RAR, BRS, C.1.2.3 Five batch data, Table C.1.2-1, p.6 and C.1.3 Analytical methods, p. 9-12	EFSA: clarification is needed whether the 5-batch data can be relied on considering the conclusion of the RMS that the methods used for the quantification of the significant impurities are not acceptably validated.	BSJ: Additional data/information could be submitted regarding the validation of the analytical methods (see below 1(7)-1(10)). RMS: Additional data could be taken into account in case that this is possible from a procedural point of view.	Data requirement: Applicant Bross to submit additional data/information regarding the validation of the analytical methods used for the quantification of the significant impurities. See also comments 1(7), 1(8), 1(9), 1(10)
1(3)	Vol.4 Table C.1.2-1 Bros Spolka	FR: Based on the 5-batch analysis, minimum purity should be increased and specification for all impurities should be decreased.	BSJ: Additional data can be submitted on request RMS: The minimum purity is in compliance with Reg. (EU) No. 540/2011 and is therefore acceptable. The important issue seems to be that the specification is covered by the current reference specification to ensure that there are no unacceptable effects comparing to the evaluated reference source. See also comment 1(1).	See open point 1(1) in RT for Vol.4 general information To increase the minimum purity and decrease the impurities specification would mean to have individual specifications for all technical materials. It should be noted that the proposal is to set one reference specification, independent from the synthesis pathway.
1(4)	Vol 4, C.1.2.4 Comparison of	RMS: *The proposed levels for impurity* ■ *and impurity* ■ *are higher than the batch*	RMS: Additional data could be taken into account in case that this is possible from	Data requirement: Applicant Bross to submit an updated

Identity (B.1, Annex C)				
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	the analytical profile of batches	*data indicate are necessary. A justification is needed by the applicant why the proposed maximum contents for those impurities are necessary.* BSJ: Additional information will be submitted. The specification provided to RMS was not in line with Manual on development and use of FAO and WHO specifications for pesticides and proposed levels for impurity [redacted] and impurity [redacted] were miscalculated. BSJ, if requested can submit corrected manufacturing specification, which is mainly based on the 5-batch mean values of the content for each impurity plus / minus 3 standard deviations	a procedural point of view.	technical specification.
1(5)	Vol 4, C.1.2.4 Comparison of the analytical profile of batches - Toxicological evaluation of specification (2013):	RMS: *The applicant provided no information/data, which would allow to judge whether the impurities are relevant. The applicant provided no evaluation, whether the material used in tox studies is representative for the proposed specification. The impurities [redacted] are specified in significantly higher amounts than listed in the reference*	RMS: In case the applicant provides additional data, these could be included in a revised RAR, provided that this is allowed from a procedural point of view. Based on the data submitted until now, relevance of impurities cannot be evaluated. Based on the data submitted until now, it cannot be evaluated, whether the material used in toxicological studies	Data requirement: Applicant Bros to submit data/information concerning the assessment of toxicological relevance of the impurities and data/information demonstrating that the material used in toxicological studies is representative for the proposed specification

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		specification. For the impurity [redacted] *further tox assessment is required according to the criteria given in SANCO/10597/2003. Statements have been reported by the notifier; however, the RMS indicates that "the mentioned data/information has not been submitted for the present EU procedure. Hence it cannot confirm that there is no significant increase in toxicity due to the presence of the impurities." The applicant provided no evaluation, whether the material used in toxicological studies is representative for the proposed specification.* *Based on the available studies which were submitted for the renewal of glyphosate, a conclusion on the equivalence of the Bros source cannot be made.* BSJ: Additional data/information could be submitted which allow judging whether the impurities are of toxicological relevance or not with regard to the impurities of the reference source. Furthermore, GTF will provide data/information demonstrating that the material used in toxicological studies is	is representative for the proposed specification or the reference specification.	

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		representative for the proposed specification. In July 2013 BSJ informed RMS that additional data (including a Position Paper on impurities, based on available, supporting evidence and literature data) could be submitted, when requested by RMS. BSJ proposed the date of submission, but there was no formal request from RMS to provide this data. To our knowledge it is not possible to submit any additional information for EU procedure without a formal request from relevant authority. When requested by EFSA, above mentioned data could be submitted, including reports from GLP acute toxicity studies of BSJ glyphosate. The glyphosate batch used in these studies was covered by BSJ glyphosate specification.		
1(6)	Vol 4, C.1.2.4 Comparison of the analytical profile of batches - Ecotoxicology	RMS: *For the impurity [redacted] further ecotox assessment is required as the evaluation according to SANCO/10597/2003-rev10.1, since representativeness of this source cannot substantiated with sufficient certainty; additional information*	RMS:For the impurity [redacted] additional information and Results of study on Algae addressing the representativeness of the specification should be requested.	Data requirement: Applicant Bros to submit for the impurity [redacted] additional information and results of study on algae

Identity (B.1, Annex C)				
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		addressing the ecotox representativeness of the specification is required. *Based on the available studies, a conclusion on the equivalence of the Bros source cannot be made.* BSJ: Additional data/information could be submitted. In July 2013 BSJ informed RMS that additional data (including a Position Paper on impurities, based on available, supporting evidence and literature data) could be submitted, when requested by RMS. BSJ proposed the date of submission, but there was no formal request from RMS to provide this data. To our knowledge it is not possible to submit any additional information for EU procedure without a formal request from relevant authority. Results of study on Algae for Impurity ■ or BSJ glyphosate with determined content of Impurity 15could be submitted, when requested by EFSA.		addressing the representativeness of the specification .
1(7)	Vol 4,	RMS: *The analytical method for the*	RMS: Additional data could be taken into	See data requirement in comment 1(2)

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	C.1.3-1 Analytical methods. Methods of analysis for the determination of impurities [redacted]	*determination of impurity* [redacted] *and impurity* [redacted] *is not acceptably validated as the test for accuracy was conducted with standard solutions which cannot be regarded as a representative sample.* *Matrix effects are not taken into account by the analysis of standard solutions*. BSJ: Additional data/information could be submitted. In July 2013 the following comment was provided to RMS by BSJ: "The accuracy was tested by measuring the recovery and RSD% of Impurity sample, which was prepared by [redacted] with SANCO/3030/99 rev.4 Appendix 2 of the SANCO 3030 states that "However a well characterised sample must be used. An example of this would be a reference standard."	account in case that this is possible from a procedural point of view.	

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		- The main reason is that a sample matrix without the presence of the analyte was not avaliable. - Specificity for each Impurity indicated the Impurity peak was not attributable to more than one component in the Glyphosate manufactured by BSJ, so the sample matrix has no interference with the Impurities, the background of solvent blank and the sample matrix have the same effect. - According to published literature data addition of isotope standard caused ionization suppression of glyphosate, with matrix effect of 7,4%, therefore was not included in further analyses. -One can argue whether [redacted] would further bring more data concerning matrix effect, but we believe that our current method is sufficiently reliable and reproductible, while the achieved process efficiency is high with efficiency of sample preparation shows acceptable RSD% (according to Horwitz equation), with negligible analyte ionization variability."		

Identity (B.1, Annex C)				
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		RMS did not reference this comment directly in RAR. Thus BSJ cannot judge if this justification is considered acceptable or not. If EFSA requests, new validation could be performed with accuracy data measured with the technical material.		
1(8)	Vol 4, C.1.3-2 Analytical methods. Methods of analysis for the determination of impurity [redacted]	RMS: *The analytical method for the determination of impurity [redacted] is not acceptably validated as the test for accuracy was conducted with standard solutions which cannot be regarded as a representative sample.* *Matrix effects are not taken into account by the analysis of standard solutions.* BSJ: Additional data/information could be submitted. See above.	RMS: Additional data could be taken into account in case that this is possible from a procedural point of view.	See data requirement in comment 1(2)
1(9)	Vol 4, C.1.3-3 Analytical methods. Validation data for the determination of the impurity [redacted]	RMS: *The analytical method for the determination of impurity [redacted] is not acceptably validated as the test for accuracy was conducted with standard solutions which cannot be regarded as a representative sample.* *Matrix effects are not taken into account*	RMS: Additional data could be taken into account in case that this is possible from a procedural point of view.	See data requirement in comment 1(2)

Identity (B.1, Annex C)				
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		*by the analysis of standard solution*s. BSJ: Additional data/information could be submitted. See above.		
1(10)	Vol 4, C.1.3-4 Analytical methods. Validation data for the determination of the impurity [redacted]	RMS: *The analytical method for the determination of impurity* [redacted] *is not acceptably validated as the test for accuracy was conducted with standard solutions which cannot be regarded as a representative sample.* *Matrix effects are not taken into account by the analysis of standard solutions.* BSJ: Additional data/information could be submitted. See above.	RMS: Additional data could be taken into account in case that this is possible from a procedural point of view.	See data requirement in comment 1(2)

1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(1)	Vol. 4, RAR, CHE, C.1.1.2 Method of manufacture, manufacturer 1, p. 2	EFSA: a description of the manufacturing process for the [redacted] would be useful to understand which route is followed in the manufacturing process 1. Our understanding is that basically is following the '[redacted] route'	CHE: It can be confirmed that manufacturing process 1 (Vol. 4, RAR, Cheminova, C.1.1.2, p. 2-3) follows the '[redacted] route". RMS: No further comment.	Addressed.
1(2)	Vol. 4, RAR, CHE, C.1.2.4 Specifications, manufacturer 1, p. 16	EFSA: is Cheninova proposing different specifications for each manufacturing site or just a common one covering all saurces?	CHE: The manufacturing sites included in Vol. 4 are all approved in [redacted] Member State each. In the approval process Member States have requested one specification per manufacturing site. Cheminova therefore proposes one specification per manufacturing site. RMS: No further comment.	Addressed. However, see comment 1(1) in the RT for Vol.4 general information.
1(3)	Vol.4 Table C.1.2-1 Cheminova	FR: Based on the 5-batch analysis, the specification for impurity [redacted] should be decreased.	CHE: The proposed upper limit for Impurity [redacted] is supported with quality control data. This is mentioned as a note below Table C.1.2-1. RMS: No further comment.	Addressed.

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1(4)	Vol.4 Table C.1.2-3 Cheminova	FR: The date of manufacture of batches from the three analyses should be indicated.	CHE: If considered necessary, information on manufacturing dates can be provided. RMS: Additional data could be taken up in a revised RAR in case that this is possible from a procedural point of view.	Data requirement: Applicant Cheminova to submit the missing manufacturing dates of the batches.
1(5)	Vol.4 Table C.1.2.4 Cheminova	FR: If the reference specifications from the initial DAR are not covered by tox and eco tox evaluations, it cannot be concluded that this origin is equivalent to the reference specifications. A new evaluation should be performed to set new reference specifications covered by the tox and eco tox evaluation.	RMS: Agreement with FR: based on the data submitted until now, it cannot be evaluated, whether the material used in toxicological studies is representative for the proposed specification or the reference specification. For the renewal procedure Tier2 ecotoxicological assessment of equivalence was performed on the presumption that the reference specification of the initial DAR is still valid. Should new data become available, a new evaluation would be carried out.	See open point 1(1) in the RT for Vol.4 general information
1(6)	Vol 4, C.1.2.4 Comparison of the analytical profile of batches - Toxicological evaluation of	RMS: *The applicant provided no information/data, which would allow to judge whether the impurities are relevant. The applicant provided no evaluation, whether the material used in tox studies is representative for the proposed*	RMS: In case the applicant provides additional data, these could be included in a revised RAR, provided that this is allowed from a procedural point of view. Based on the data submitted until now, relevance of impurities cannot be	Data requirement: Applicant Cheminova to submit data/information concerning the assessment of toxicological relevance of the impurities and data/information

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No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
	specification (2013):	*specification. It is noted, that several impurities are specified in higher levels than they were present in material used in tox studies.* *Impurity* [redacted] *was not reported in the tox batches but is foreseen to be specified. Also, the min purity in the specification is slightly below the amount in materials used in tox studies* [redacted]*). Additionally, the mentioned batches were used only in a limited set of studies.* *In summary, it cannot be evaluated, whether the material used in tox studies is representative for the proposed specification.* *Based on the available data submitted, a conclusion on the equivalence of the* Cheminova sources cannot be made. CHE: Additional data/information could be submitted which allow judging whether the impurities are of toxicological relevance or not with regard to the impurities of the reference source. Furthermore, the applicant could provide data/information demonstrating that the	evaluated. Based on the data submitted until now, it cannot be evaluated, whether the material used in toxicological studies is representative for the proposed specification or the reference specification.	demonstrating that the material used in toxicological studies is representative for the proposed specification

Identity (B.1, Annex C)				
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		material used in toxicological studies is representative for the proposed specification. For the first Annex I listing of glyphosate, Cheminova was one of the notifying companies and Cheminova's technical glyphosate was considered as fully equivalent to the established reference profile. The specifications supporting Cheminova's technical glyphosate for Annex I Renewal are considered to fall within the specification supported at the first Annex I listing and are supported by an updated confidential dossier (Doc J) included with the current submission.		

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1(7)	Vol. 4 C.1.3.1 Table C.1.2-3 Cheminova	FR: The LOQ of [redacted] is 1g/kg. However, in the table C.1.2-3 (batch 0903-0605), the content of [redacted] is 0.83 (< LOQ). Please RMS clarifies.	CHE: It is considered that the LOQ is the lowest fortification level used in the recovery tests in the validation of the method. The recovery was done at three fortification levels: approx. 0.07%, 1.64% and 3.33%. The LOQ is considered to be 733 ppm (ca. 0.07%). If the comment from FR originates from the fortification levels mentioned in Sec. 1.3, Table C.1.3-2 of Vol. 4 it is believed (not confirmed) that the values given in the table have been rounded to one digit in the preparation of the RAR. One digit is also presented for the two other fortification levels. The non-rounded value for the lowest fortification level is therefore the above 0.07 %, which is lower than the value of 0.83 g/kg (0.083%) measured in batch 09030605. RMS: It can be confirmed that the lowest fortification level was 0.07 % which was rounded to 0.1 % in Table C.1.3-2. Since the applicant defines the lowest fortification level as LOQ the values in Table C.1.2-3 are beyond the LOQ.	Addressed.

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Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(1)	Vol. 4, RAR, DOW, C.1.2.2 Impurities, p. 10, Table C.1.2-1 p.13	EFSA: small typo in the code of impurity 19	RMS: The typo will be corrected in a revised RAR.	Open point: RMS to correct the code of impurity 19 in an updated Vol.4
1(2)	Vol. 4, RAR, DOW, C.1.2. Five batches, Table C.1.2-4, p. 16	EFSA: are these data representative to the production, if manufactured in such a short period of time?	DOW: Additional data can be submitted on request RMS: Additional data could be taken up in a revised RAR in case that this is possible from a procedural point of view.	Addressed.
1(3)	Vol. 4, RAR, DOW, C.1.2.4 Specifications, p. 17	EFSA: clarification is needed whether the notifier intends to have separate specification for all the different manufacturing sites	DOW: Additional data can be submitted on request RMS: The applicant submitted separate specifications for the different manufacturing sites. The intention of the applicant was clear for the RMS. However, there is only one source remaining as the sources [redacted] and [redacted] will not be longer supported (see comments 1(5) and (6)).	Addressed. See also comments 1(5) and (6)
1(4)	Vol. 4, C.1.2.4 Comparison of	RMS: *With respect to the determination of the impurity 20 in the technical material, it*	RMS: Additional data could be taken up in a revised RAR in case that this is possible	Data requirement: Applicant Dow to submit the new

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
	the analytical profile of batches	*should be noted that the usage of analytical method* [redacted] *was stated for both glyphosate sources. However, this method differs from method* [redacted] *which was submitted for monitoring purposes concerning the used HPLC column, eluent and detection wavelength.* *Only the specificity and the linearity of the method were demonstrated.* DOW: Further data will be provided. DAS will provide a new study.	from a procedural point of view.	study in relation to the comment concerning impurity 20.
1(5)	Vol. 4, C.1.2.4 Comparison of the analytical profile of batches - Toxicological evaluation of specification (2013):	RMS: *The applicant provided no information/data, which would allow to judge whether the impurities are relevant. Impurities 4, 10, 13 and 14 are specified in* [redacted] *amounts than listed in ref specification. The applicant informed that equivalency is being confirmed from DAS and response will be available by July 31, 2013.* *But the mentioned data/inform has not been submitted for the present EU procedure. Hence, it cannot be evaluated/ confirmed that there is no significant increase in toxicity due to the presence of the impurities.The applicant provided no*	DOW: As the 2 sources [redacted] and [redacted] will not be longer supported the impurities 10, 13 and 14 are not relevant anymore. Additional data for impurity 4 can be submitted on request. A general statement for reference specification will be provided from MON as lead of the GTF. RMS: The sources [redacted] and [redacted] will be removed in a revised RAR.	Data requirement: Applicant Dow to submit data/information concerning the assessment of toxicological relevance of the impurities and data/information demonstrating that the material used in toxicological studies is representative for the proposed specification. Open point: RMS to update the Vol.4 for Dow with the information from the col. 3 of the confidential RT.

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		evaluation, whether the material used in tox studies is representative for the proposed specification. DOW: Additional data/information will be submitted which allow judging whether the impurities are of toxicological relevance or not with regard to the impurities of the reference source. Furthermore, the applicant will provide data/information demonstrating that the material used in toxicological studies is representative for the proposed specification.		
1(6)	Vol. 4, C.1.2.4 Comparison of the analytical profile of batches - Ecotoxicology	RMS: *For the impurity 10 and 13* [redacted] *further ecotox assessment is required as the evaluation according to SANCO/10597/2003 rev 10.1.* *The impurity 10 was present in the specifications at* [redacted] *and impurity 13 at* [redacted]*, respectively.* *The equivalence of both sources to the reference source cannot be substantiated with sufficient certainty; additional information addressing the ecotox representativeness of the specifications is required.*	DOW: As the 2 sources [redacted] and [redacted] will not be longer supported the impurities 10 and 13 are not relevant anymore. RMS: The sources [redacted] and [redacted] will be removed in a revised RAR. Open point until submission of official document, confirming that sources are not longer supported.	Data requirement: Applicant Dow to submit an official document, confirming that the respective sources are not longer supported. See also open point in comment 1(5)

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No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		Based on the available studies which were submitted for the renewal of glyphosate, a conclusion on the equivalence of the DOW sources cannot be made. DOW: Further data will be provided		
1(7)	Vol.4 Tables C.1.2-2 and C.1.2-3 Dow Agro Sciences	FR: Based on the 5-batch analysis and QC data, the certified values proposed for impurities 14 and 1 should be decreased.	DOW: Additional data can be submitted on request RMS: The comment of the applicant is unclear since it was stated in 1(5) and (6) that the corresponding source in Tables C.1.2-2 and C.1.2-3 ([redacted]) will not be longer supported.	Addressed. See open point in comment 1(5)
1(8)	Vol. 4 C.1.3.1 table C.1.2-1, C.1.2-2, C.1.2-3, C.1.2-4 Dow agro Sciences	FR: When the content of impurities in the analytical profile of batches is below the LOQ, please RMS indicates <LOQ for better clarity.	RMS: This could be done in a revised RAR.	Addressed.
1(9)	Vol. 4 C.1.3.1 (Nelson (2008) Dow agro Sciences	FR: The identity of each impurity should be confirmed.	RMS: The identity of the impurities was confirmed in the batch analysis studies by retention time match and comparison of mass spectra of samples and reference standards obtained by GC-MS after derivatisation. This information could be also stated in a	Addressed.

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			revised RAR.	
1(10)	Vol. 4 C.1.3.1 Dow agro Sciences	FR: As the content of [redacted] (table C.1.2-2 and table C.1.2-4), an analytical method for the determination of [redacted] in the technical active substance should be provided.	DOW: Validation data for [redacted] are provided in the method report [redacted] RMS: The method is described in C.1.3.1. However, a method for [redacted] seems to be not required anymore because the corresponding sources [redacted] and [redacted] will not be longer supported by the applicant (see 1(6)).	Addressed. See also open point in comment 1(5)
1(11)	Vol. 4, C.1.3.2 Analytical methods. Validation data for the determination of the impurity 20	RMS: *The repeatability of the method was not determined although spiking of technical glyphosate with impurity 1 was possible. Therefore, the method as a whole cannot be regarded as acceptable. The applicant stated that data on the repeatability could be provided by December 2013.* DOW: Further data will be provided.	RMS: Additional data could be taken up in a revised RAR in case that this is possible from a procedural point of view.	See data requirementin comment 1(4)
1(12)	C2.2. rar_25_volume4_dow_2013-12-18	NL: Impurity [redacted] is available in higher amounts than in the reference specification, for sources of DOW. Please indicate this in the conclusion on page 17.	DOW: As the 2 sources [redacted] and [redacted] will not be longer supported the impurity 10 is not relevant anymore. RMS: No further comment.	Addressed See open point in comment 1(5)

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No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(1)	Vol. 4 Table C.1.2-1 Excel Crop	FR agrees that a clarification is needed by the applicant concerning the fact that the account of the three batches is lower than 980g/kg. Additionally, based on the 5-batch analysis, the minimum purity should be increased or QC data should be provided to justify this value.	XLE: The new GLP 5 batch study being undertaken by XLE, will address this point satisfactorily. RMS: The new study could be taken into account in case that this is possible from a procedural point of view. The minimum purity is in compliance with Reg. (EU) No. 540/2011 and is therefore acceptable. The important issue seems to be that the specification is covered by the current reference specification to ensure that there are no unacceptable effects comparing to the evaluated reference source.	Data requirement: Applicant Excel to submit the new GLP 5 batch data.
1(2)	Vol. 4, Table C.1.2-1: Analytical profile of batches and specification	RMS: *Clarification by the applicant is needed concerning the fact that the account of three batches is lower than 980 g/kg.* XLE: Additional data will be submitted. New GLP 5-Batch study has been initiated by Excel Crop Care (Europe) NV, the final	XLE: The new GLP 5 batch study being undertaken by XLE, should address this point. RMS: The new study could be taken up in a revised RAR in case that this is possible from a procedural point of view.	See data requirement in comment 1(1)

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		report is expected to be in hand by July/August 2014 and will be submitted.		
1(3)	Vol. 4, RAR, EXC, C.1.1.2 Method of manufacture, p. 2	EFSA: small typo in the formula of glyphosate in the reaction scheme	XLE: Noted will be corrected in future submission. RMS: In case of a revision of the RAR, the typo will be corrected.	Addressed.
1(4)	Vol. 4, RAR, EXC, C.1.2.3 five-batch data, p. 6	EFSA agrees with the RMS on the need for clarification on not meeting the minimum account of 980 g/kg for three of the batches out of five	XLE: The new GLP 5 batch study being undertaken by XLE, should address this point. RMS: The new study could be taken up in a revised RAR in case that this is possible from a procedural point of view.	See data requirement in comment 1(1)
1(5)	Vol.4 C.1.2.4 Excel Crop	FR: If the reference specifications from the initial DAR are not covered by tox and ecotox batches, it cannot be concluded that this origin is equivalent to the reference origin. New evaluation should be performed to set new reference specifications based on toxicological and ecotoxicological studies.	RMS: Agreement with FR: based on the data submitted until now, it cannot be evaluated, whether the material used in toxicological studies is representative for the proposed specification or the reference specification. For the renewal procedure Tier2 ecotoxicological assessment of equivalence was performed on the presumption that the reference specification of the initial DAR is still valid. Should new data become	See open point 1(1) in the RT of Vol.4 genaral information

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			available, a new evaluation would be carried out.	
1(6)	Vol. 4 , C.1.2.4 Comparison of the analytical profile of batches - Toxicological evaluation of specification (2013):	RMS: *The applicant provided no information/data, which would allow to judge whether the impurities are relevant. The applicant provided no evaluation, whether the material used in tox studies is representative for the proposed specification.* [redacted] *were not reported in the tox batch but are foreseen to be specified. The min purity in the specification is slightly below the amount in material used in tox studies* [redacted] *Additionally, the mentioned batches were used only in a limited set of studies.* *The notifier provided no evaluation, whether the material used in tox studies is representative for the proposed specification. In summary, it cannot be evaluated, whether the material used in tox studies is representative for the proposed specification.* *Based on the available studies which were submitted for the renewal of glyphosate, a conclusion on the equivalence of the Excel*	XLE: Fresh acute mammalian toxicity studies using counter sample from one of the batches from the new 5-Batch study is being undertaken by XLE (Excel Crop Care (Europe) NV), these reports will be submitted together with the new 5-Batch study. RMS: In case the applicant provides additional data, these could be included in a revised RAR, provided that this is allowed from a procedural point of view. Based on the data submitted until now, relevance of impurities cannot be evaluated. Based on the data submitted until now, it cannot be evaluated, whether the material used in toxicological studies is representative for the proposed specification or the reference specification.	Data requirement: Applicant Excel to submit data/information concerning the assessment of toxicological relevance of the impurities and data/information demonstrating that the material used in toxicological studies is representative for the proposed specification.

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No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		source cannot be made. XLE: Additional data/information will be submitted which allow judging whether the impurities are of toxicological relevance or not with regard to the impurities of the reference source. Furthermore, the applicant will provide data/information demonstrating that the material used in toxicological studies is representative for the proposed specification. Fresh acute mammalian toxicity studies using counter sample from one of the batches from the new 5-Batch study is being undertaken by Excel Crop Care (Europe) NV, these reports will be submitted together with the new 5-Batch study.		
1(7)	Vol. 4, RAR, EXC, C.1.3.1 Analytical methods, p. 11	EFSA agrees with the RMS on the need for additional validation data concerning the method for [redacted]	RMS: No comment.	Data requirement: Applicant Excel to submit additional validation data concerning the method for [redacted]
1(8)	Vol. 4 C.1.3.1	FR: The identity of [redacted] should be confirmed.	XLE: The identification data of [redacted] was submitted earlier, however, along with the new 5 batch study report this data	Addressed

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
	Determination of Bis PMA Excel Crop		would be made available again. RMS: In the method by Sydney [redacted], which was not accepted due to the high recovery values, the identity of [redacted] was confirmed by retention time match and the comparison of mass spectra of sample and reference standard obtained by GC-MS. This information could be also stated in a revised RAR.	See also comment 1(1)
1(9)	Vol. 4 C.1.3.1 Determination of NNG Excel Crop	FR agrees with the conclusion of RMS concerning the LOQ.	XLE: Along with the new 5 batch study report this data would be made available. RMS: The new study could be taken up in a revised RAR in case that this is possible from a procedural point of view.	See data requirement 1(7)
1(10)	Vol. 4, C.1.3-2 Validation data for the determination of the impurity 5 in technical glyphosate	RMS: *The RSD of the repeatability of 5.8 % at a content of 0.41 % slightly exceeds the corresponding modified Horwitz RSD value of 3.1 %. Nevertheless, the method can be regarded as fit for purpose for the*	XLE: Along with the new 5 batch study report this data would be made available. RMS: see comment 1(9)	See data requirement in comment 1(1)

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No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		determination of the impurity [redacted] in the technical material. XLE: Additional data will be submitted.		
1(11)	Vol. 4, C.1.3-3 Validation data for the determination of the impurity [redacted] in technical glyphosate	RMS: *As the LOQ exceeds the proposed max content of [redacted] in the tech material, the applicant has to demonstrate that this value can be monitored with the method.* *The applicant stated that a report could be provided to extend the LOQ investigation and to confirm that the lower level could be accurately quantified.* XLE: Additional data will be submitted.	XLE: Along with the new 5 batch study report this data would be made available. RMS: see comment 1(9)	See data requirement 1(7) See also comment 1(1)
1(12)	Vol. 4, C.1.3.2 Validation data for the determination of the impurity 2 and 5 in technical glyphosate	RMS: *This method did not meet the requirements of Guidance Document SANCO9303/99 rev. 4 and so cannot be considered acceptable for the determination of impurity 2 and impurity 5 in the technical material.* XLE: [redacted] is not part of the specification of the technical material provided by Excl. Therefore no an analytical method for monitoring is not	XLE: [redacted] is not part of the specification of the technical material provided by Excl. Therefore no an analytical method for monitoring is not required. Same as noted in column 2. RMS: This seems to be a misunderstanding. Under C.1.3.2., methods are listed which which do not meet the requirements. Nevertheless, the method in the study of	Addressed.

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		required. For [redacted] an analytical method is provided and accepted by the RMS (see C.3 of the RAR).	Comb (2005, NUF/083) was accepted by the RMS for the determination of impurity 5 and for impurity 2 no method is required because it is not in the specification.	

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No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(1)	Vol. 4 Feinchemie Schwebda C.1.1.1	FR: Please RMS clarify the part: "in October 2012, the ..... declared that the licence for manufacturing glyphosate has been transferred to .....". If the manufacturer is the one reported at the end of this part, the first reported should be removed for better clarity.	FCS: In the equivalence report issued by Germany on 08 July 2011 the original manufacturer is still mentioned. In order to avoid misunderstandings we suggest to keep a remark explaining that, although a legal transfer of the manufacturing license occurred in October 2012, neither the manufacturing process nor the manufacturing plant was changed RMS: Agreement with the applicant.	Addressed.
1(2)	Vol. 4 C.1.2.2 Feinchemie Schwebda	FR: The identity of [redacted]) should be reported.	FCS: The identity of impurity [redacted]) is reported in Vol. 4, RAR, C.1.2.2, p. 5. RMS: [redacted] was removed from section C.1.2.2 since it was not detected in the batch analysis and it is not part of the specification.	Open point: RMS to include the identity of [redacted] in a revised Vol.4. See also comment 1(3)
1(3)	Vol. 4, RAR, FEI, C.1.2.2 Impurities, p. 4	EFSA: [redacted] is missing from C.1.2.2, while mentioned in 5-batch data	FCS: as above. The identity of [redacted]) is reported in Vol. 4, RAR, C.1.2.2, p. 5 RMS: See comment 1(2).	See open point in comment 1(2)

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1(4)	Vol 4 Table C.1.2-1 Feinchemie Schwebda	FR: Based on the batch analysis, minimum purity should be increased or QC data should be provided to justify the proposed value.	FCS: QC data can be submitted upon request of the RMS or EFSA RMS: The minimum purity is in compliance with Reg. (EU) No. 540/2011 and is therefore acceptable. The important issue seems to be that the specification is covered by the current reference specification to ensure that there are no unacceptable effects comparing to the evaluated reference source.	See open point 1(1) in the RT for Vol.4 general information To increase the minimum purity specification would mean to have individual specifications for all technical materials. It should be noted that the proposal is to set one reference specification, independent from the synthesis pathway.
1(5)	Vol. 4, C.1.2.4 Comparison of the analytical profile of batches - Toxicological evaluation of specification (2013):	RMS: *The applicant provided no information/data, which would allow to judge whether the impurities are relevant. The applicant provided no evaluation, whether the material used in tox studies is representative for the proposed specification. It is noted, that some impurities are specified in higher levels than they were present in material used in tox studies.* *Impurity 21 was not reported in the tox batches but is foreseen to be specified. The min purity in the specification is slightly below the amount in material used in tox*	FCS: Additional data/information will be submitted on [redacted] as part of a joint submission of the Task Force. Impurities 20 (N-Nitroso-glyphosate IDA) and 21 (Formaldehyde) are relevant impurities acc. to the FAO specification with defined maximum contents. Whilst impurity 21 was found at a level close to [redacted] of the defined limit, impurity 20 could not be detected in any of the 5 batches analysed.	Data requirement: Applicant Feinchemie to submit data/information concerning the assessment of toxicological relevance of the impurities and data/information demonstrating that the material used in toxicological studies is representative for the proposed specification.

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		studies ([redacted]). Additionally, the mentioned batches were used only in a limited set of studies. In summary, it cannot be evaluated, whether the material used in tox studies is representative for the proposed specification. *Based on the available studies, a conclusion on the equivalence of the Feinchemie source cannot be made.* FCS: Additional data/information will be submitted which allow judging whether the impurities are of toxicological relevance or not with regard to the impurities of the reference source. Concerning the representativity of the material used in the tox studies we refer to the argumentation presented in more detail in point Vol 4, C.1.5. What impurity 21 is concerned we would like to point out that the specified content is based on the FAO specification for glyphosate and that the actual content in the technical material is [redacted] of the specified value.	[redacted]) could not be detected in any of the 5 batches and should not be part of the specification. Therefore, information on the relevance of this impurity is not required RMS: In case the applicant provides additional data, these could be included in a revised RAR, provided that this is allowed from a procedural point of view. Based on the data submitted until now, relevance of impurities cannot be evaluated. Based on the data submitted until now, it cannot be evaluated, whether the material used in toxicological studies is representative for the proposed specification or the reference specification.	

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No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(6)	Vol. 4 C.1.3 Determination of formaldehyde Feinchemie Schwebda	FR: The identity of the impurity should be confirmed.	FCS: The identity was confirmed in the 5 batch analysis by analytical determination using an acceptably validated analytical method with a LOQ of [redacted] (HPLC using UV detector at 365 nm on a C18 column) RMS: Formaldehyde was determined by [redacted] reference standard. Possible derivatives can also be formed [redacted] but these can be excluded due to the synthesis path of glyphosate where only formaldehyde is used.. Therefore, the method is considered specific for the determination of formaldehyde and is appropriate to confirm the identity of formaldehyde.	Addressed.
1(7)	Vol. 4, C.1.3-1 Analytical methods. Validation data for the determination of the impurities 2 and 3	RMS: *With respect to validation data for the determination of the impurities 2 and 3, the applicant should explain the different RSD values of the repeatability of the fortified and not fortified samples.* FCS: The determination of the RSD of the	RMS: The comment by the applicant will be taken into account in a revised RAR.	Addressed.

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		method was done on an unspiked study sample in an analytical sequence run on June 28th 2009, when the response of the detector was optimum and signal / noise ratio of the chromatograms was very high. The accuracy of the method was determined in a sequence run on August 1st. At this time, the detector's response was much less sensitive, as can be seen on sample chromatograms given in appendix G3, page 173 and following pages. The higher background noise resulted in a less precise integration of the signals, resulting in turn in a higher variability of the results. However the accuracy calculated with these analyses was found acceptable. Moreover, on study sample run in the same sequence gave results very close to the results of the batches run in the previous sequence, which is a confirmation of the validity of the august 1st analytical sequence. (Comment supplied by Christian Wasser, the Scientific director of Anadiag, where the study was performed. He also added the following:		

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		"I need to add that these analyses are very delicate, since large amounts of glyphosate are injected in the system, which may contribute to alter the column and MS source".)		
1(8)	Vol. 4, C.1.5 Other confidential information	RMS: *It seems that the batches 1993 and 1998 cannot be correlated with batches used in toxicological studies*. FCS: As well as the batches characterized in 1993 and 1998 the technical material used in the toxicological studies was manufactured by [redacted] Since in addition the same route of synthesis was kept over the period of toxicity testing it can be assumed that the impurity profile of the batches used in the toxicological studies is within the range of these specifications, incl. for impurities nos. 3, 9, 11 and 20, which were only determined in the 1998 analysis but which can be assumed to have been present also in the 1993 and earlier batches. As a conclusion, the impurity profile of the batches used in the toxicological studies can be assumed to be properly	RMS: Noted. It appears that the composition of batches 60, 46 and "01/06/97" are not available. Apparently, the notifier refers to analytical results determined in other batches originating from the same plant. Production dates of the tox batches are given by the notifier under 1(9).	

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		described by the impurity profiles of the batches analysed in 1993 and 1998 presented in table C.1.5-1.		
1(9)	Vol. 4, RAR, FEI, C.1.5 Other confidential information, tox batches, p. 13	EFSA: it is not clear what is the relationship between the tox batches named 1993 and 1998 and batches used in tox studies named 60, 46 and 01/06/97	FCS: the relationship between these batches is their identical manufacturing process and production site [redacted]. For this reason - although they have not been used in the 5 batch analysis performed in 1993 and 1998 - the impurities in batches 60 (manufactured August 1990), 46 (manufactured January 1992) and 01/06/97 (=manufacturing date) can be assumed to be similar to those of the batches analysed in 1993 and 1998 presented in table C.1.5-1 and which were considered to present no toxicological or environmental concern in the Review report on glyphosate*. Except from determination of purity no further analyses are available on batches 60, 46 and 01/06/97. *Review report on glyphosate, p. 5: For the active substance notified by Feinchemie Schwebda GmbH none of the manufacturing impurities were considered, on the basis of the information available,	Addressed: The tox batches named 1993 and 1998 and batches used in tox studies named 60, 46 and 01/06/97 are different batches produced under identical manufacturing process and production site. The composition of batches 60, 46 and “01/06/97” are not available.

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			to be of toxicological or environmental concern. RMS: Agreement with EFSA. It appears that the composition of batches 60, 46 and "01/06/97" are not available. Apparently, the notifier refers to analytical results determined in other batches originating from the same plant.	

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Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(1)	Vol. 4, RAR, HEL, C.1.2.1 Minimum purity, p. 13	EFSA: clarification is needed whether the notifier intends to have 7 different specifications or just one covering all sources? EFSA thinks that it is rather difficult to handle a situation of one notifier having many specifications for the same a.s. Probably maximum two different specifications covering the two main processes would be more appropriate.	HEL: Each source has to be assessed for equivalence separately. Therefore an individual specification is needed for each source which is directly linked to the 5-batch analysis. The specified min content of a.s. must be the mean of the 5 batch analysis – 3 SD, and the max. content of impurities the mean + 3 SD. If a "combined" specification is developed, there is too much risk to have equivalence denied for all sources where the data justify non-equivalence only for one of the sources. RMS: There is no reason to reject individual specifications of different sources as long as each specification is equivalent to the reference source.	Addressed See also open point 1(1) in the RT for Vol.4 general information It should be noted that the proposal is to set one reference specification, independent from the synthesis pathway.
1(2)	Vol.4 Table C.1.2.3 Helm	FR: Based on the 5-batch analysis, the specification for [redacted] should be decreased or QC data should be provided.	HEL: o.K. RMS: In case that the comment of the applicant means to decrease the maximum limit of the impurity, this is supported by the RMS. QC data could be	Data requirement: Applicant Helm to provide new specification for [redacted]

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			taken into account in case that this is possible from a procedural point of view. However, it should be noted that the proposed maximum limit is in compliance with the current reference specification and therefore considered acceptable.	See also open point 1(1) in the RT for Vol.4 general information
1(3)	Vol.4 Table C.1.2.4 Helm	FR: Based on the 5-batch analysis, the specification for [redacted] should be decreased or QC data should be provided.	HEL: o.K. RMS: see comment 1(2)	Data requirement: Applicant Helm to provide new specification for [redacted] See also open point 1(1) in the RT for Vol.4 general information
1(4)	Vol.4 Table C.1.2.7 Helm	FR: Based on the 5-batch analysis, the specification for [redacted] should be decreased or QC data should be provided.	HEL: o.K. RMS: Agreement with the comment by FR.	Data requirement: Applicant Helm to provide new specification for [redacted] See also open point 1(1) in the RT for Vol.4 general information
1(5)	Vol. 4, C.1.2.4 Comparison of the analytical profile of batches - Toxicological evaluation of specification (2013):	RMS: *The applicant provided no information/data, which would allow to judge whether the impurities are relevant. The applicant provided no evaluation, whether the material used in tox studies is representative for the proposed*	RMS: In case the applicant provides additional data, these could be included in a revised RAR, provided that this is allowed from a procedural point of view. Based on the data submitted until now, relevance of impurities cannot be	Data requirement: Applicant Helm to submit data/information concerning the assessment of toxicological relevance

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		specification. It is noted, that several impurities are specified in higher levels than they were present in material used in tox studies. Impurity 5 was not reported in the tox batches but is foreseen to be specified. Additionally, the min purity in the specification is [redacted] *the amount in material used in tox studies* [redacted] *Additionally, the mentioned batches were used only in a limited set of acute tox studies which are less relevant to assess the specification.* *Based on the available studies submitted, a conclusion on the equivalence of the Helm sources cannot be made.* HEL: Additional data/information will be submitted which allow judging whether the impurities are of toxicological relevance or not with regard to the impurities of the reference source. Furthermore, the applicant will provide data/information demonstrating that the material used in toxicological studies is representative for the proposed specification.	evaluated. Based on the data submitted until now, it cannot be evaluated, whether the material used in toxicological studies is representative for the proposed specification or the reference specification. -	of the impurities and data/information demonstrating that the material used in toxicological studies is representative for the proposed specification.

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1(6)	Vol. ,4 C.1.2.4 Comparison of the analytical profile of batches - Toxicological evaluation of specification (2013):	RMS: [redacted] *are specified in significantly higher amounts than listed in the reference specification. Regarding these impurities, the applicant did not submit any comment/information/data.* HEL: Additional data will be submitted.	RMS: see 1(5)	See data requirement in comment 1(5)
1(7)	Vol. 4, C.1.2.4 Comparison of the analytical profile of batches - Toxicological evaluation of specification (2013):	RMS: *The* [redacted] *depending on the source. According to SANCO/10597/2003 – rev. 10.1, depending on the amount of a new / increased impurity, different data/information need to be provided. An Ames test with technical material has been submitted. This single study might be sufficient to assess the amount the* [redacted] *the source 5* [redacted] *). But this study is not sufficient to assess the amount in the sources 2, 4 and 6 because there this impurity is specified in amounts* [redacted] *Nevertheless, considering, that the technical material was tested, it was not addressed whether the highest dose was high enough to adequately investigate the mutagenic potential of the impurity being present at low levels.*	RMS: see 1(5)	See data requirement in comment 1(5)

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		Based on the available studies submitted, a conclusion on the equivalence of the Helm sources cannot be made. HEL: Additional data will be submitted.		
1(8)	Vol. 4, C.1.2.4 Comparison of the analytical profile of batches - Toxicological evaluation of specification (2013):	RMS: *Currently, the no data/information has been submitted for the present EU procedure regarding* [redacted]*. Hence RMS's toxicological risk assessor cannot confirm that there is no significant increase in toxicity due to the presence of the impurities.* *Based on the available studies submitted, a conclusion on the equivalence of the Helm sources cannot be made.* HEL: Additional data will be submitted.	RMS: see 1(5)	See data requirement in comment 1(5)
1(9)	Vol. 4, C.1.2.4 Comparison of the analytical profile of batches – Ecotoxicology:	RMS: *For the* [redacted] *source 4 further ecotox assessment is required as the evaluation according to SANCO/10597/2003 rev 10.1. The equivalence of this source to the reference source cannot be substantiated with sufficient certainty; additional information addressing the ecotox representativeness of the specification is required.*	RMS: Additional data for the [redacted] is appreciated.	Data requirement: Applicant Helm to submit study on alage according to OECD 201 for [redacted]

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		Based on the available studies submitted, a conclusion on the equivalence of the Helm sources cannot be made. HEL: Additional data will be submitted. Please provide study on alage according to OECD 201 for [redacted] TEA)		
1(10)	Vol. 4, RAR, HEL, C.1.3 Analytical methods, NNG, p. 30	EFSA: small typo in the description of the mobile phase: 'certyl…'	HEL: o.K. RMS: The typo could be corrected in a revised RAR.	Addressed.
1(11)	Vol. 4, C.1.3-11 Analytical methods. Validation data for the determination of the impurity 21 (source 3)	RMS: *In case of the determination of the accuracy only the concentration in the spiked solutions has been given. The applicant should state the fortification levels in relation to the technical material (in %).* HEL: Additional data will be submitted. This should be clarified (maybe the laboratory can provide a statement).	RMS: Additional data could be taken up in a revised RAR in case that this is possible from a procedural point of view.	Data requirement: Applicant Helm to submit additional validation data for the determination of the impurity 21 (source 3)

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1(12)	Vol. 4, C.1.3-12 Analytical methods. Validation data for the determination of the [redacted] (source 4)	RMS: *There seems to be an interference of [redacted] with the glyphosate peak in the chromatogram. The applicant should demonstrate that the specificity of the method is ensured.* HEL: Additional data will be submitted. This should be clarified (maybe the laboratory can provide a statement).	RMS: Additional data could be taken up in a revised RAR in case that this is possible from a procedural point of view.	Data requirement: Applicant Helm to submit additional validation data for the determination of the impurity 1 (source 4) See also comment 1(14)
1(13)	Vol.4 Table C.1.3-9 Helm source 3	FR: Without recovery data, the analytical method cannot be considered as validated, consequently contents [redacted] found in the 5-batch cannot be considered a new batch analysis is required for this plant location using fully validated analytical methods.	HEL: Additional data will be submitted. RMS: Additional data could be taken up in a revised RAR in case that this is possible from a procedural point of view..	Data requirement: Applicant Helm to submit additional validation data for the method for determination of impurities 1, 3, 5 and 9 found in the 5-batch.
1(14)	Vol. 4, RAR, HEL, C.1.3 Analytical methods, Table C.1.3-12, p. 38	EFSA agrees with RMS on the need for additonal validation data for the determination of [redacted]	HEL: Additional data will be submitted. RMS: Additional data could be taken up in a revised RAR in case that this is possible from a procedural point of view.	See data requirement in comment 1(12)
1(15)	Vol. 4, C.1.3-23 Analytical methods. Validation data for the determination of the impurity 21 (source	RMS: *The LOQ was only determined as the lowest concentration of the calibration standard [redacted] In order to take matrix effects into account the applicant should determine the LOQ in relation to*	RMS: Additional data could be taken up in a revised RAR in case that this is possible from a procedural point of view.	Data requirement: Applicant Helm to submit additional validation data for the method for determination of impurity 21.

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	5)	*the technical material. The lowest levels used for the determination of the accuracy and repeatability exceed the proposed maximum content of 0.8 g/kg formaldehyde in the technical material.* HEL: Additional data will be submitted. This should be clarified.		
1(16)	Vol. 4, C.1.3 Determination of impurity 23 (source 5)	RMS: *The content of water was determined by loss on drying which is not specific to water.* HEL: Additional data will be submitted. This should be clarified.	RMS: Additional data could be taken up in a revised RAR in case that this is possible from a procedural point of view.	Data requirement: Applicant Helm to submit additional validation data for the method for determination of impurity 23.
1(17)	Vol. 4, C.1.3-27 Analytical methods. Validation data for the determination of the impurity 20 (source 6)	RMS: *The applicant should explain why standard addition was not used for the determination of the repeatability.* *The fortification levels for the determination of the accuracy have not been stated explicitly, the levels should be clarified.* HEL: Additional data will be submitted. This should be clarified (maybe the	RMS: Additional data could be taken up in a revised RAR in case that this is possible from a procedural point of view.	Data requirement: Applicant Helm to submit additional validation data for the method for determination of impurity 20.

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		laboratory can provide a statement).		
1(18)	Vol. 4, C.1.3-28 Analytical methods. Validation data for the determination of the impurity 21 (source 6)	RMS: *With respect to linearity and accuracy and repeatability the method for the determination of impurity 21 in the tech material can be considered acceptably validated. However, the applicant should explain why standard addition was not used for the determination of the repeatability.* HEL: Additional data will be submitted. This should be clarified (maybe the laboratory can provide a statement).	RMS: Additional data could be taken up in a revised RAR in case that this is possible from a procedural point of view.	See data requirement in comment 1(15)
1(19)	Vol. 4, C.1.3 Determination of impurity 23 (source 5)	RMS: *The content of water was determined by loss on drying which is not specific to water.* HEL: Additional data will be submitted. This should be clarified:	RMS: Additional data could be taken up in a revised RAR in case that this is possible from a procedural point of view.	See data requirement in comment 1(15)
1(20)	Vol. 4, RAR, HEL, C.1.5 Tox batches, Table C.1.5-1, p. 54	EFSA:was the NNG content of batch '20090506' [redacted]?	HEL: Additional data will be submitted. RMS: Additional data could be taken up in a revised RAR in case that this is possible from a procedural point of view. The content of NNG in the provided	Data requirement: Applicant Helm to submit additional data about the NNG content of of batch '20090506'

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			document was [redacted]	

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1(1)	Monsanto source, Vol 4 C.1.1.1: Manufacture of the active substance	UK: The UK has considered batch data for these sources and it is apparent that the sources are manufactured as slurries/wet cakes. This is not made that clear in the manufacturing details provided. Furthermore, the batch data have been generated on the wet cake but the results from this analysis and a specification for the material that is actually manufactured has not been given. Only the batch data for the dry material and its specification are given. It is important to have a specification of the material that is actually manufactured and hence all subsequent batches must comply with. It would appear that there is no specification for what is actually manufactured. The specification provided would appear to be for a dried material that is never actually produced. It is important to know how the batch analysis data have been generated, and how the specification has been established and if MS agree with this approach. This will have an impact on other actives and	MOD: Glyphosate acid is indeed manufactured as a "wetcake". Whilst this is an apparently dry, powdered material it does contain a significant amount of water given its hygroscopic properties. The glyphosate assay in the wetcake is best established after drying, since this gives a more precise result and is therefore preferable to using the wetcake as such. Since the water content of the wetcake is also measured, the concentration of glyphosate in the wetcake is easily calculated. The impurities are assayed using wetcake to prevent losing any volatile materials during drying (please see original submission in Confidential Doc. J). However, the only way to compare impurity levels between batches and fix upper spec limits, is by converting these wet-base values to a dry weight basis (using the water content, as presented in the RAR). This has been the convention for many years in setting the FAO	Open point: RMS to add the information from the col.3 of the RT (concerning the manufacture as wet cake) in the updated Vol.4 for Monsanto

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		also has an impact on the assessment of the tox/ecotox batches and whether they support the TGAI as manufactured. For TK (which would be applicable to a wet cake/slurry) it would be appropriate to have a specification of the material manufactured and then determine a dry weight specification by calculation for the minimum purity in the implementing regulation and for performing technical equivalence. However, for transparency the data should all be outlined clearly giving MS the opportunity to see what was analyzed, the results for this analysis, the conversion of the batch data to a dry weight basis, and how the specification has been derived. Given that it would appear the RAR has not been transparent on how the TGAI is manufactured, what has been analysed and how the specification has been derived then MS have not been given the opportunity to comment on this and hence an agreed approach established. The RAR should be updated to reflect these issues and MS should have the opportunity to discuss them.	specification & the EU reference specification for glyphosate. In order to fix the upper spec limits for impurities in wetcake we would need to fix a minimum specification for water content; for which we have no purpose since our only concern is to have a limit for the maximum water content. The lower the water content gets the closer the upper spec limits for the impurities would approach those developed on a dry weight basis. Whilst the wetcake is analysed as manufactured, a dry weight specification in conjunction with the water content is the most practical solution. RMS: 1. If required, a statement could be added in C.1.1.2 that technical glyphosate is produced as wet cake. 2. In C.1.2.3 it is clearly stated that the impurities were analysed in the wet cake and the content of glyphosate was determined after drying. A justification was given that glyphosate is not regarded	

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			as volatile under the conditions of drying. The "loss on drying" is given for each batch and the term for the calculation of the dry weight content is also stated. The results of the batch analysis were reported on dry weight basis as the proposed specification and the reference specification as well are also based on the dry material. 3. The wording in 1.11 of regulation 544/2011 is “Representative samples of the active substance must be analysed for content of pure active substance …”. The aim is getting knowledge on the composition of the technical material. In case of a wet cake this can be also achieved by the separation of the volatile compounds and the following analysis of both, the volatiles and the “dried” material. Here, the pure glyphosate was determined in the dried material and the impurities in the wet cake. One can assume that the loss of glyphosate during the drying process was negligible. This means that the active substance as manufactured is well characterised. In case of a monitoring of the wetcake,	

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			the water content must be always determined anyway in order to check the compliance with the minimum purity of regulation 540/2011 which is based on the dry material.	
1(2)	Vol. 4, RAR, MON, C.1.2.2 Impurities, p. 4	EFSA: is [redacted] not a possible impurity?	MOD: Please note that this impurity was not notified by Monsanto and has no relevance to Monsanto's overall impurity specification for technical glyphosate. The formation of [redacted] cannot be excluded, but with the Monsanto process it is expected to occur only at concentrations well below the Limit of Quantification. In order to form [redacted] must compete for the nitrite source with glyphosate, which is in a large excess of approximately 100-fold relative to the [redacted] RMS: No further comment.	Addressed.
1(3)	Monsanto source, Vol 4 C.1.2.3: Analytical profile of batches	UK: The batches have been manufactured in a short interval of time and no assessment as to whether the batches are representative of the manufacturing process has been made. It is also noted that in some cases the time	MOD: Monsanto accepts that taking samples from 5 consecutive days raises legitimate questions regarding representativeness of the batches if one site is considered in isolation. However, sampling was randomised across the five locations and	Open point: RMS to add the information from the col.3 of the RT (concerning the representativeness of the batches) in the updated Vol.4 for Monsanto

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		period from manufacture to analysis appears to be significant. In particular for the [redacted] plant the batches were manufactured from the end of Dec 2007 to the beginning of Jan 2008 with the batch analysis study being completed in 2010. Depending on how the technical material is manufactured then taking batches in a short period of time/consecutive days may not be representative. If the time period from manufacture to analysis is significant then it raises concerns on the stability of the TGAI in terms of the actives and impurities. While there is clearly no formal data requirement to address the stability of the TGAI, the batches must be representative of the material that will be used in the PPP. If it has degraded then it is clearly not representative.	the manufacturing process and quality controls in place ensure the representativeness of the batches. On a randomly chosen date, usually commencing on a Monday, sampling of the 5-batch test kicks off. The plant starts taking samples with a 24 hour delay for 5 consecutive days. This does not mean 5 consecutive batches as 40 to 50 batches are produced in 24hours. Two hundred to 250 reactor batches are produced over the five days that the samples are taken. The analyses of samples taken from this randomly determined period of production is used to check against the existing specification. The entire yearly production has to meet the specification at all times. This is monitored via QC on a constant basis. Therefore 5-batch samples taken at any time will be representative of the production. In practise it does not matter that samples are taken on consecutive days since the entire production must meet the specification at all points of the production run.	

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			The storage stability of glyphosate and the relevant impurities has been evaluated in separate studies on glyphosate wetcake. Sample stability of over 18 months was demonstrated with respect to NNG in glyphosate wet cake. Sample stability of over 13 months was demonstrated with respect to formaldehyde in glyphosate wet cake. In the case of technical glyphosate, data can be provided on glyphosate wet-cake indicating a minimum shelf life of 5 years. These data represent various manufacturing lots of MON 77973 (glyphosate wetcake) spanning 5 years and can be used to show storage stability for the active. Initial and assays after 5 years revealed a change in assay over time of less than 1.0% in all cases. The results of the analysis show that, with 95% confidence, there is not a statistically significant difference between the glyphosate assay data sets at the time of manufacture in 2005 and when analysed 5 years later in 2010. RMS: The information given by the applicant	

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			could be included in a revised RAR provided that this is possible from a procedural point of view. Concerning the stability of the samples from the [redacted] it should be noted that the experimental work was done from 01.08.2008 to 11.11.2008 while the batches were produced from 11.12.2007 to 04.01.2008. The report MSL0022744, however, was finalised on 21.05.2010. Furthermore, the applicant declared in this report that the stability of the test substance was demonstrated by the analysis of the active substance in one lot at the start and end of the experimental part of the study.	
1(4)	Monsanto source, Vol 4 Tables C.1.2-1 – C.1.2.5	UK: There appears to be very little resemblance between the batch data provided and the specification for each source. The levels of the impurities are in most cases significantly below the level stated in the specification. The specification should be based on the batch analysis data. It is noted for some of the other applicant's the specifications for their sources are more in line with the	MOD: The Monsanto Manufacturing Specification is developed based on 5-batch analyses from all of the manufacturing sites. Individual Manufacturing Specifications for each site are not developed. Sampling over 5 consecutive days at each of the 5 sites is considered to give an acceptable overview of the variability of the glyphosate manufacturing process. The	See data requirement in comment 1(9) However, see open point 1(1) in the RT fro Vol.4 general information

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		batch data. Consistency is required.	compiled 5-batch results are used to compare the glyphosate production process against the Monsanto Manufacturing specification, however the 5-batch results for each site are also required to meet, or be equivalent to, this specification. The impurity limits in the proposed Monsanto Manufacturing specification are based on the results of the 5-batch analyses across the five sites. However, these limits are not calculated solely from the mean values and their standard deviations since QC and process capability data are also taken into consideration. Monsanto can provide Quality Control data if required. RMS: The applicant intended to use a common specification that covers the composition of the technical material from all manufacturing sites. Based on the results of the batch analyses the maximum limits of three impurities were increased which is, except for the impurity [redacted] justified for the RMS. A maximum limit of [redacted] would be	

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			more appropriate instead of 12 g/kg. Under the assumption that the current reference specification is of no toxicological concern a Tier I equivalence assessment was conducted. The result was that the technical material is equivalent to the current reference specification and could be therefore accepted. Nevertheless, additional QC data could be taken up in a revised RAR in case that this is possible from a procedural point of view.	
1(5)	Vol.4 Tables C.1.2-1, C.1.2-2, C.1.2-3, C.1.2-4 and C.1.2-5 Monsanto	FR: Specifications for impurities are not in accordance with the batch analyses, they should be revised or QC data should be provided.	MOD: See response above 1(4) RMS: See comment 1(4).	See comment 1(4)
1(6)	Monsanto source, Vol 4 Table C.1.2-5	UK: The level of [redacted] It is therefore unclear why the specification has been set at 8 g/kg and in the reference specification at 7 g/kg. The batch data show that the level in the specification is exceeded and hence cannot	MOD: Only for [redacted] the mean + 3SD were s above the FAO equivalence threshold. A revised specification limit for IDA of 8 g/kg was set by the RMS limit (please refer to Volume 4 for Monsanto Europe SA) based on the overall results across	See data requirement in comment 1(9)

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		be complied with.	the five manufacturing sites whilst taking into account the toxicology properties of IDA presented in the dossier (AII-DOC J). The individual IDA results from [redacted] were all found to be below this revised specification limit of [redacted] (= limit + 50% as per SANCO/10597/2003-rev9 page 6). Two [redacted] were found to be above this revised specification limit of [redacted]. The mean of the 5 results was below [redacted] but within the equivalence limit of 12 g/kg (= limit + 50% as per SANCO/10597/2003-rev9 page 6). RMS: The fact that the maximum content of IDA is exceeded in two batches was unfortunately overlooked by the RMS. This applies also for [redacted] in one batch of the [redacted] source. The applicant should state how to deal with batches	

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			that do not meet the specification. The argumentation of the applicant to apply the criteria of SANCO/10597/2003 is not acceptable. Only technical material which meets the agreed specification may be used for the formulation of the product.	
1(7)	Vol. 4, RAR, MON, C.1.2.3 Proposed specification, p. 10	EFSA: small typo in the reference to the proposed specification (C.1.1.2.4)	RMS: The typo will be corrected in a revised RAR.	Addressed.
1(8)	Vol. 4, RAR, MON, C.1.2.3 Batch data, specification, p. 11-21	EFSA: the five batch data from the different sources do not support neither the proposed nor the reference specification in the case of a considerable number of impurities.	MOD: See response above 1(4) RMS: See comments 1(4), 1(6) and 1(9).	See data requirement 1(9)
1(9)	Vol. 4, RAR, MON, C.1.2.3 Batch data, specification, p. 11-21	EFSA: based on the batch data of all sites it is not clear why impurities 6, 7, 8, 10 and 28 should be specified? All the measured values, even with mean values+3xSD added are [redacted].	MOD: Whilst it was indeed the case that these impurities were found at concentrations[redacted] in the 5-batch analyses, upper specification limits have been retained as Quality Control data indicates that they can be detectable. RMS: The additional QC data will be taken up in a revised RAR provided that this is possible from a procedural point of view.	Data requirement: Applicant Monsanto to provide an updated technical specification based on batch data or QC data supporting the proposed limits for impurities.

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1(10)	Vol. 4, RAR, MON, C.1.2.3 Batch data, specification, Conclusion, p. 21	EFSA: inconsistency concerning [redacted]: based on batch data RMS doesn't see the need to specify imp.12 (EFSA agrees), however agrees to specify for example [redacted] with similar measured values	MOD: See response above 1(9) RMS: See comment 1(9).	See data requirement in comment 1(9)
1(11)	Vol. 4, RAR, MON, C.1.2.3 Batch data, specification, Conclusion, p. 21	EFSA disagrees with the conclusion of the RMS that "It is demonstrated that the composition of the representative batches complies with the proposed specification of the technical active substance"	MOD: See response above 1(4) RMS: See comments 1(4), 1(6) and 1(9).	See data requirement in comment 1(9)
1(12)	Monsanto source, Vol 4 C.1.2.4: Comparison of analytical profile of batches	UK: Given that the specification is not equivalent to the reference specification then a tier II assessment should be conducted. Some of the batch data for IDA show the level specified is exceeded. While the batch data for [redacted] show that this impurity is [redacted] and hence does not need to be specified the applicant has specified it at [redacted]. It is unclear why the RMS has not accepted the level of [redacted] given the very generous limits allowed for the other impurities compared to the batch data. The conclusions reached on the impurities	MOD: See responses above 1(4), 1(6) and 1(9). RMS: 1. The comment that a tier II assessment should be conducted when the specification is not equivalent to the reference specification is unfortunately unclear. 2. Concerning the exceeded maximum limits of IDA see comment 1(6). 3. Concerning the maximum limit of [redacted] see comment 1(9). 4. According to SANCO/10597/2003 rev. 10.1 an additional toxicological evaluation would generally not be	See data requirement in comment 1(9) However, see open point 1(1) in the RT fro Vol.4 general information

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		are for the tox assessment to make and not as part of the tier I assessment.	required for compounds for which the toxicity is known to be low.	
1(13)	Vol. 4 C.1.2.4 Monsanto	FR: Proposed specification is not covered by Tox profile. Consequently, FR disagrees with the proposed specifications.	MOD: Since there is a large body of toxicology studies and data for glyphosate, including data which was generated using test items which were possibly of lower purity compared to more recent glyphosate production we consider that the glyphosate test items used to generate toxicology data are fully representative. In addition Monsanto refers to the analysis carried out by DKC which matches the test items used in toxicology studies to Reference specifications for glyphosate. See also EFSA comments No. 2(92) and MOD comments No.1(16) below. RMS: Agreement with FR: based on the data submitted until now, it cannot be evaluated, whether the material used in toxicological studies is representative for the proposed specification or the reference specification.	See data requirement in comment 1(9) However, see also open point 1(1) in the RT fro Vol.4 general information

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No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(14)	Vol. 4, C.1.2.4 Comparison of the analytical profile of batches	RMS: *Glyphosate was determined in the batches by the analytical method PC-ME-0765. The validation data are acceptable. It should be noted that the method PC-ME-0765 needs to be submitted in the EU process; so far it was submitted only in the context of national authorisations.* MOD: PC-ME-0765 can be submitted upon request.	RMS: The study could be taken up ion a revised RAR in case that this is possible from a procedural point of view.	Data requirement: Applicant Monsanto to submit the analytical method PC-ME-0765
1(15)		RMS: *The applicant provided no information/data, which would allow to judge whether the impurities are relevant.* MOD: Although some information was available and has been submitted in AII DOC J, additional data/information can be submitted upon request which will allow judging whether the impurities are of toxicological relevance or not with regard to the impurities of the reference source. **Relevant impurities** Two impurities of substances of well known toxicity, namely formaldehyde and an N-nitroso substance, N-nitroso glyphosate (NNG). Existing thresholds were used by the FAO evaluator to define	RMS: Noted. Based on the data submitted until now, relevance of impurities cannot be evaluated. Formaldehyde and nitrosamines are toxicologically relevant impurities as evaluated in Vol. 4 (general information). [redacted] was evaluated in Vol. 4 (general information). The report Wratten et al (2013) is not available to RMS's toxicology expert.	Data requirement: Applicant Monsanto to submit the report Wratten et al (2013)

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		their maximum concentration, and the same evaluator reviewed the data for Annex I inclusion in 2002. o The FAO evaluation report notes that "for formaldehyde the limit was set to 1.3 g/kg on a glyphosate acid basis, according to the rules of the FAO as published in the Manual. This limit corresponds closely to the limit in the US OSHA regulations and was set on an 'as is' basis not on an 'acid basis'." o The limit for NNG was derived from a US EPA limit: "the Agency has determined that technical glyphosate contains N-nitroso glyphosate (NNG) as a contaminant of 0.1 ppm or less. The Agency has determined that oncogenicity testing of N-nitroso contaminants will be required only in those cases in which the level of nitroso compounds exceeds 1.0 ppm (see 'Pesticide Contaminated with N-nitroso Compounds, proposed policy 45 FR 42854 (June 25, 1980))". The EU now takes a similar view, as in the Guidance Document on Equivalence SANCO/10597/2003-rev.10.1 "If		

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		analytical results indicate that total nitrosamine levels exceed 1 mg/kg in the technical material, the following toxicological requirements must be addressed". Thus the maximum concentrations of these substances are set at levels which are not considered to be toxic. Although the FAO Specification refers to them as 'relevant' impurities, according to the FAO Guidance Document they are not relevant unless they exceed the limits. Data can be submitted upon request. **Impurities considered to be non-relevant** [redacted] Based on the conclusions in the RAR, AMPA should be considered non-relevant from a tox-ecotox perspective. [redacted] Data were submitted in Doc J for these impurities because our increased specification levels (mean +3 SD) were beyond the FAO specification/ equivalence threshold. Based on this information the RMS concluded "According to the criteria given in Tier I		

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		of Guidance Document SANCO/10597/ 2003 rev 10.1 the proposed specification is regarded as equivalent to the reference source." In addition, the RMS stated that "The maximum content of glycine is regarded as acceptable as glycine is a biosynthesised amino acid which acts as a precursor for proteins and is an approved food additive according to Directive 95/2/EC." [redacted] these impurities were new compared to the reference specification. A further toxicological and ecotoxicological assessment is not deemed to be required (as suggested by the RMS in C.1.2.4 Conclusions of the RAR) due to the nature of these compounds. These and the other inorganic substances are well-known chemicals that are commonly encountered in many foods and environmental samples. [redacted] This impurity was determined in the batches but was not specified in the reference specification. However, based on the submitted batch data the RMS considered there is no need to specify a		

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		limit for the impurity (same reference as above). **Other impurities**: The report by Wratten et al (2013) assesses the occurrence and toxicology of all the impurities in the MON specification (relevant impurities, non-relevant including inorganic, glyphosate related at high prominence and glyphosate related at low levels). This report has already been submitted (in an earlier version) in AII Doc J but an updated version is available upon request. It should be referenced as a justification of the non-relevance of these impurities.		
1(16)	Vol. 4, C.1.2.4 Comparison of the analytical profile of batches - Toxicological evaluation of specification (2013):	RMS: *The applicant provided no evaluation, whether the material used in tox studies is representative for the proposed specification. It is noted, that several impurities are specified in higher levels than they were present in material used in tox studies. The min purity in the specification is* [redacted] *the amount in material used in tox studies (*[redacted]*. Additionally, the mentioned batches were used only in a limited set of studies. In summary, it cannot be evaluated,*	RMS: In case the applicant provides additional data, these could be included in a revised RAR, provided that this is allowed from a procedural point of view. Based on the data submitted until now, it cannot be evaluated, whether the material used in toxicological studies is representative for the proposed specification or the reference specification.	Data requirement: Applicant Monsanto to provide data/information demonstrating that the material used in toxicological studies is representative for the proposed specification.

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		whether the material used in toxicological studies is representative for the proposed specification. *Based on the available studies submitted, a conclusion on the equivalence of the Monsanto sources cannot be made.* MOD: Upon request, the applicant can provide data/information demonstrating that the material used in toxicological studies is representative for the proposed specification. The specification is minimum 95% glyphosate on a dry basis. Therefore, the concentration in manufactured technical glyphosate and the test substances will be greater than 95%.		
1(17)	Monsanto source, Vol 4 C.1.3: Analytical methods	UK: Given the batch analysis data (as determined without correction to a dry weight) has not been presented then it is difficult to assess if the validation data support the TGAI. It is not clear if the validation data relate to the material actually analysed and the results obtained or if the validation data have been correct to reflect the dry weight analysis	MOD: See response above 1(1) RMS: The validation of the methods and the determination of the impurities in the batches were conducted with the wet cake. However, the applicant should clarify whether or not the LOQ and the fortification level for the determination of the accuracy are related to the wet	See open point in comment 1(1)

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		The RAR should be updated to include the batch analysis results obtained without the correction to a dry weight. It should be made clear what the validation data cover.	cake. However, the relevance of the possible variation in the validation data is not seen.	
1(18)	Monsanto source, Vol 4 C.1.3: Analytical methods	UK: As stated above a full assessment of the validation data cannot be made at this time. However, the following points are noted: For [redacted] The levels in some batches were below this and hence are not supported. It is not stated what concentration the repeatability has been generated at. Methods of analysis for the technical material are pre-registration methods that must support the results in the study and as accuracy and repeatability are concentration dependent then the data must cover the levels determined in the batches. Usually the specification is based on the batch data and hence validation data for the TGAI can usually be considered to support the batch data and specification. However, in this case the specification bears very little resemblance to the batch analysis results and hence the validation	MOD: In a second accuracy study [redacted] at fortification levels of [redacted] were evaluated – this study appears to have been missed by the evaluator in this case. The confusion exists since [redacted] are different abbreviations for the same compound [redacted] Full details of all experimental parameters, concentrations etc. are provided in the submitted reports. RMS: 1. The maximum limit of [redacted] is [redacted]. The used fortification levels are considered as acceptable for the determination of the accuracy for the monitoring of the impurity [redacted] in the technical material. However, the comment of the applicant could be taken up in a revised RAR.	Open point: RMS to include the information from the col.3 of the RT concerning anlytical methods of section C.1.3 in an updated Vol.4

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		data do not fully support the underlying batch data.	2. Comment noted. Could be taken into account in further RAR/DAR provided that there is a common understanding that this information should be included. 3. Disagreed. The analytical methods submitted under the Annex point 4.2.3 are monitoring methods.	
1(19)	Vol. 4 C.1.3.1 Monsanto	FR: The identity of each impurity should be confirmed.	MOD: Reports detailing confirmatory methods are available for all impurities. RMS: The additional data will be taken up in a revised RAR provided that this is possible from a procedural point of view.	Data requirement: Applicant Monsanto to submit information detailing with confirmatory methods available for all impurities
1(20)	Vol. 4, C.1.3-1 Analytical methods. Validation data for the determination of the impurity 1	RMS: *The applicant stated that a revised evaluation of the precision of method* [redacted] *with respect to the impurity 1 has been conducted and could be submitted. The precision has been considerably improved compared to the previous precision.* MOD: Additional data can be submitted upon request.	RMS: The additional data will be taken up in a revised RAR provided that this is possible from a procedural point of view.	Data requirement: Applicant Monsanto to submit revised evaluation of the precision of method [redacted] with respect to the impurity 1
1(21)	Vol. 4, C.1.4-1 Identity, content and function of	RMS: *It should be noted that the MSDS of the formulants are not in compliance with the requirements according to REACH.*	RMS: The additional data will be taken up in a revised RAR provided that this is possible from a procedural point of view.	Data requirement: Applicant Monsanto to submit MSDSs which are in line with the requirements

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	formulants	*However, the applicant stated that MSDSs which are in line with the requirements for REACH for* [redacted] *be submitted.* MOD: Additional data can be submitted upon request		for REACH for the [redacted]
1(22)	Vol. 4, RAR, MON, C.1.5 Other confidential information, Table C.1.5-1, p. 33	EFSA: are the values for *N*-nitroso glyphosate also expressed as %?	MOD: Values for N-nitroso glyphosate are expressed as mg/kg or ppm. RMS: The given value and units are reported as given in the study. The comment from the applicant is unfortunately unclear.	Data requirement: Applicant Monsanto to clarify the units the values for *N*-nitroso glyphosate are expressed in Table C.1.5.

1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(1)	Vol.4 C.1.1.1 Nufarm	FR: The address of the manufacturer should be added.	NUF: The address of the manufacturer is: [redacted] RMS: The address could be added in a revised RAR.	Addressed.
1(2)	Vol.4 Table C.1.2-1 Nufarm	FR: If the reference specifications from the initial DAR are not covered by tox and eco tox evaluations, it cannot be concluded that this origin is equivalent to the reference specifications. A new evaluation should be performed to set new reference specifications covered by the tox and eco tox evaluation.	NUF: availability of supportive information or studies is available on this source RMS: In case the applicant provides additional data, these could be included in a revised RAR, provided that this is allowed from a procedural point of view. Based on the data submitted until now, it cannot be evaluated, whether the material used in toxicological studies is representative for the proposed specification or the reference specification. For the renewal procedure Tier2 ecotoxicological assessment of equivalence was performed on the presumption that the reference	See open point 1(1) in RT for Vol.4 general information It should be noted that the proposal is to set one reference specification, independent from the synthesis pathway.

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			specification of the initial DAR is still valid. Should new data become available, a new evaluation would be carried out.	
1(3)	Vol. 4, C.1.2.4 Comparison of the analytical profile of batches - Toxicological evaluation of specification (2013):	RMS: *The applicant provided no information/data, which would allow to judge whether the impurities are relevant. It is noted, that some impurities are specified in higher levels than they were present in material used in toxicological studies.* [redacted] *was not reported in the tox batches but is foreseen to be specified. Impurity 20 was reported as "< 0.0001 %" in the tox batches but is foreseen to be specified. Additionally, in case "Mastra" and "BIOK" can be correlated with tox batches used in specific tox studies, the mentioned batches were used only in a limited set of studies.In summary, it cannot be evaluated, whether the material used in toxicological studies is representative for the proposed specification.* *Based on the available studies submitted, a conclusion on the equivalence of the Nufarm source cannot be made.*	NUF: (additional comment) The specification given under C.1.2.4 is related to the [redacted] source that contained [redacted]) at a max level of [redacted]. In the Mastra source (tox studies related) this impurity 1 (unfortunately given as N-methylaminomethyl phosphonic acid that is wrong) is present and specified at maximum [redacted] (5 batch report is available upon request). So, in tables C.1.5-1 and C.1.5-2 we should read instead of "[redacted]. Impurity 20 (NNG) is foreseen to be specified as it is considered as a tox-relevant impurity despite the fatc the level is very low. RMS: In case the applicant provides additional data, these could be included in a revised RAR, provided that this is allowed from a procedural point of view.	Data requirement: Applicant Nufarm to submit additional data/information concerning the assessment of toxicological relevance of the impurities and data/information demonstrating that the material used in toxicological studies is representative for the proposed specification

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		NUF: Additional data/information will be submitted which allow judging whether the impurities are of toxicological relevance or not with regard to the impurities of the reference source. Furthermore, the applicant will provide data/information demonstrating that the material used in toxicological studies is representative for the proposed specification.	Based on the data submitted until now, relevance of impurities cannot be evaluated. Based on the data submitted until now, it cannot be evaluated, whether the material used in toxicological studies is representative for the proposed specification or the reference specification. The content of the impurities in table C.1.5-1 and C.1.5-2 corresponds to the submitted data. However, the new information that [redacted] in the Mastra batch should read [redacted] could be taken up in a revised RAR.	
1(4)	Vol. 4, RAR, NUF, C.1.5 Tox batches, Table C.1.5-1 and Table C.1.5-2, p. 14	EFSA: clarification is needed on the identity of tox batch identified as 'Mastra' as the two tables contain different values for the a.s content and identical values for the impurities	NUF: Besides the fact that the purity in the tox batch was correctly given (see comment [1(6)]). As the 2 batches used for tox and ecotox were not fully analysed for impurity levels the specified max levels of each impurity were given instead of. RMS: Concerning the EFSA comment see 1(6). Concerning the comment of the notifier, it appears that the composition of tox	See open point in comment 1(6)

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			batches is not available. Apparently, the notifier gave numbers from the specification instead. The notifier gave further information under 1(5).	
1(5)	Vol. 4, C.1. 5.1 Tox profile	RMS: *It seems difficult to correlate the batches "Mastra" and "BIOK" with the batch numbers given in the study reports. It is noted that "Mastra" is correlated once with batch H05H016A and another time with batch H95D161A. In summary, the meaning of "Mastra" and "BIOK" seems unclear.* NUF: Mastra and BIOK were suppliers of glyphosate technical to Nufarm in the past. A number of tox studies were carried out with the Mastra technical material characterized by a typical batch identification starting with H+ 2 digits for the year + mixture of letter and numbers; whilst BIOK had their own identification of batches starting with the year + 5 digits. The meaning of Mastra and BIOK can be explained as follows: Mastra: the full name of the Malaysian	NUF: No further comments RMS: Noted. It appears that the composition of tox batches is not available.	Addressed: The impurity content of the tox batches is not known.

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		manufacturer is: [redacted] BIOK: [redacted]		
1(6)	Vol. 4, C.1. 5.1 Tox profile	RMS: *the purity of the technical grade for Mastra source is given as 94.7%.* NUF: the value is not correct. All studies were run with Batch H05H016A containing 95.7%. or batch H95D161A containing 95.3%.	NUF: No further comments RMS: The purity of the Mastra batches H05H016A and H95D161A will be corrected in a revised RAR. Furthermore, it will be pointed out that the composition of the tox and ecotox batches is not available.	Open point: RMS to correct the purity of the Mastra batches H05H016A and H95D161A in a revised Vol.4
1(7)	Vol. 4, C.1. 5. Page 15	RMS: *Information, which batch has been used in the respective studies* NUF: a number of major tox studies have not been listed in the table. Following studies run with batch H05H016A (95.7%) are missing:	NUF: The tox studies provided by Nufarm should be added to the dossier. RMS: The studies Wood (2009a) and Wood (2009b) are included in Vol. 3, B.6.5 (page 460 or 502, respectively)	Addressed.

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		IIA, 5.5.2/08: Glyphosate Technical: Dietary Combined Chronic Toxicity/ Carcinogenicity in the Rat, 2009a, Wood, E, *et al*. IIA, 5.5.3/02: Glyphosate technical: Dietary Carcinogenicity Study in the Mouse, 2009b, Wood, E. et al.	The table in chapter C.1.5 was provided by the notifier.	

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Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(1)	Vol.4 Table C.1.2-1 Rotam	FR: No specification should be set lower than 1 g/kg for not relevant impurities.	DKC agreed RMS: Comment noted.	Addressed. See comment 1(2)

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(2)	Vol.4 C.1.2.3.1 Rotam	FR: If the reference specifications from the initial DAR are not covered by tox and eco tox evaluations, it cannot be concluded that this origin is equivalent to the reference specifications. A new evaluation should be performed to set new reference specifications covered by the tox and eco tox evaluation.	GTF: A general statement for reference specification will be provided from MON as lead of the GTF RMS: In case the applicant provides additional data, these could be included in a revised RAR, provided that this is allowed from a procedural point of view. Based on the data submitted until now, it cannot be evaluated, whether the material used in toxicological studies is representative for the proposed specification or the reference specification. For the renewal procedure Tier2 ecotoxicological assessment of equivalence was performed on the presumption that the reference specification of the initial DAR is still valid. Should new data become available, a new evaluation would be carried out.	See open point 1(1) in RT for Vol.4 general information

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(3)	Vol. 4, C.1.2.4 Comparison of the analytical profile of batches - Toxicological evaluation of specification (2013):	RMS: *The applicant provided no information/data, which would allow to judge whether the impurities are relevant. The applicant provided no evaluation, whether the material used in toxicological studies is representative for the proposed specification. Hence, it cannot be evaluated, whether the material used in tox studies is representative for the proposed specification.* *Based on the available studies submitted, a conclusion on the equivalence of the Rotam source cannot be made.* RTA: Additional data/information will be submitted which allow judging whether the impurities are of toxicological relevance or not with regard to the impurities of the reference source. Furthermore, the applicant will provide data/information demonstrating that the material used in toxicological studies is representative for the proposed specification.	RMS: In case the applicant provides additional data, these could be included in a revised RAR, provided that this is allowed from a procedural point of view. Based on the data submitted until now, relevance of impurities cannot be evaluated. Based on the data submitted until now, it cannot be evaluated, whether the material used in toxicological studies is representative for the proposed specification or the reference specification.	Data requirement: Applicant Rotam to submit data/information concerning the assessment of toxicological relevance of the impurities and data/information demonstrating that the material used in toxicological studies is representative for the proposed specification

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(4)	Vol. 4 C.1.3.1 Rotam	FR: The identity of impurities [redacted] should be confirmed.	RMS: The identity of the [redacted] has been confirmed based on eluation pattern and retention time (compare the certified reference material) and by mass. Impurity 21 by eluation pattern and retention time. The other two inorganic compounds by ion chromatography based on eluation pattern and retention time. This seems to be acceptable for the RMS as the synthesis of glyphosate and its related impurities are well known over the last decades.	Addressed.
1(5)	Vol. 4, RAR, ROT, C.1.3 Analytical methods, AMPA, p. 11	EFSA: the method is stated to be LC-MS/MS, however a detector wavelength is given	DKC: [redacted] is determined with LC-MS/MS. The allegation of a wavelength is not correct. RMS please correct this RMS: Could be corrected in a revised RAR in case that this is possible from a procedural point of view.	Addressed.

1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(1)	Vol. 4, RAR, SAB, C.1.2.3 Five batch data, Table C.1.2-1, p.7	EFSA: based on batch data, considering the a.s. content, a higher minimum a.s. content might be specified.	RMS: The minimum purity is in compliance with Reg. (EU) No. 540/2011 and is therefore acceptable. The important issue seems to be that the specification is covered by the current reference specification to ensure that there are no unacceptable effects comparing to the evaluated reference source. However, in case the applicant provides additional data, these could be included in a revised RAR, provided that this is allowed from a procedural point of view.	See open point 1(1) in RT for Vol.4 general information To increase the minimum purity specification would mean to have individual specifications for all technical materials. It should be noted that the proposal is to set one reference specification, independent from the synthesis pathway.
1(2)	Vol. 4, RAR, SAB, C.1.2.3 Five batch data, Table C.1.2-1, p.7	EFSA: usually the significant impurities below 1g/kg should not be specified	DKC agreed RMS: Comment noted.	Data requirement: Applicant Sbaro to provide an updated technical specification removing the non significant impurities. See also comment 1(1)
1(3)	Vol. 4 Table C.1.2-1	FR: Based on the 5-batch analysis, the minimum purity should be increased or	RMS: see comment 1(1).	See data requirement in comment 1(2)

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
	Sabero	QC data should be provided. It should be clarified if some of the impurities are considered as relevant, in the other case, no specification should be proposed below 1 g/kg.		
1(4)	Vol.4 C.1.2.4 Sabero	FR: If the reference specifications from the initial DAR are not covered by tox and eco tox evaluations, it cannot be concluded that this origin is equivalent to the reference specifications. A new evaluation should be performed to set new reference specifications covered by the tox and eco tox evaluation.	GTF: A general statement for reference specification will be provided from MON as lead of the GTF RMS: In case the applicant provides additional data, these could be included in a revised RAR, provided that this is allowed from a procedural point of view. Based on the data submitted until now, it cannot be evaluated, whether the material used in toxicological studies is representative for the proposed specification or the reference specification. For the renewal procedure Tier2 ecotoxicological assessment of equivalence was performed on the presumption that the reference specification of the initial DAR is still valid. Should new data become available, a new evaluation would be carried out.	See open point 1(1) in RT for Vol.4 general information

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(5)	Vol. 4, C.1.2.4 Comparison of the analytical profile of batches - Toxicological evaluation of specification (2013):	RMS: *The applicant provided no information/data, which would allow to judge whether the impurities are relevant. The applicant provided no evaluation, whether the material used in tox studies is representative for the proposed specification.* *Based on the available studies submitted, a conclusion on the equivalence of the Sabero source cannot be made.* SAO: Additional data/information will be submitted which allow judging whether the impurities are of toxicological relevance or not with regard to the impurities of the reference source. Furthermore, the applicant will provide data/information demonstrating that the material used in toxicological studies is representative for the proposed specification.	RMS: In case the applicant provides additional data, these could be included in a revised RAR, provided that this is allowed from a procedural point of view. Based on the data submitted until now, relevance of impurities cannot be evaluated. Based on the data submitted until now, it cannot be evaluated, whether the material used in toxicological studies is representative for the proposed specification or the reference specification.	Data requirement: Applicant Sabero to submit data/information concerning the assessment of toxicological relevance of the impurities and data/information demonstrating that the material used in toxicological studies is representative for the proposed specification.
1(6)	Vol. 4 C.1.3.1 Sabero	FR: The identity of each impurity should be confirmed.	RMS: The identity of the impurities has been confirmed by comparison with certified reference material. This seems to be acceptable for the RMS as the synthesis of glyphosate and its	Addressed.

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			related impurities are well known over the last decades.	
1(7)	Vol. 4, C.1.3-1 Comparison of the analytical profile of batches - Validation data for the determination of impurities 1 and 9:	RMS: *Regarding the validation data for the determination of impurities 1 and 9, the peaks of those impurities in the chromatograms show a considerable interference with other compounds. The applicant stated that a new study can be submitted by December 2013 in order to demonstrate that the specificity of the method is ensured.* SAO: New information will be submitted	RMS: In case the applicant provides additional data, these could be included in a revised RAR, provided that this is allowed from a procedural point of view.	Data requirement: Applicant Sabero to submit validation data for the determination of impurities 1 and 9.
1(8)	Vol. 4, C.1.3-2 Comparison of the analytical profile of batches - Validation data for the determination of impurity 2:	RMS: *Regarding the validation data for the determination of impurity 2, the RSD of the repeatability exceeds* [redacted] *The applicant stated that a new study can be submitted by December 2013 in order to demonstrate that the precision of the method is acceptable.* SAO: New information will be submitted	RMS: In case the applicant provides additional data, these could be included in a revised RAR, provided that this is allowed from a procedural point of view.	Data requirement: Applicant Sabero to submit validation data for the determination of impurity 2.

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(9)	Vol. 4, C.1.3-6 Comparison of the analytical profile of batches - Validation data for the determination of impurity 21:	*RMS: Regarding the validation data for the determination of impurity 21, the RSD of the repeatability slightly exceeds* [redacted] *The applicant stated that a new study can be submitted by December 2013 in order to demonstrate that the precision of the method is acceptable.* SAO: New information will be submitted	RMS: In case the applicant provides additional data, these could be included in a revised RAR, provided that this is allowed from a procedural point of view.	Data requirement: Applicant Sabero to submit validation data for the determination of impurity 21.
1(10)	Vol. 4, C.1.3 Determination of impurity 23:	*RMS: The content of water was determined by loss on drying which is not specific to water.* *The applicant stated that a more specific method, such as a Karl Fischer titration can be submitted by December 2013.* SAO: New information will be submitted	RMS: In case the applicant provides additional data, these could be included in a revised RAR, provided that this is allowed from a procedural point of view.	Data requirement: Applicant Sabero to submit more specific data for the determination of impurity 23.
1(11)	Vol. 4, RAR, SAB, C.1.3 Analytical methods, NMG, IDA, Conclusion, p. 10	EFSA: it is not clear how the method for NMG and IDA can be acceptably validated and in the same time having considerable interference with other compounds, with recoveries around 100%?	SAO: Additional data can be submitted on request RMS: It is already mentioned in the RAR that additional data to confirm the specificity of the method could be provided by the applicant (see also comment above). However, In case the applicant provides	Data requirement: Applicant Sabero to submit additional data for the determination of impurities NMG and IDA.

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			additional data, these could be included in a revised RAR, provided that this is allowed from a procedural point of view	

1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(1)	Vol.4 C.1.1.1 SAPEC	FR: it should be noted that the first plant location has been evaluated according to the article 38 and equivalence report available on CIRCA.	RMS: Comment noted. However, the mentioned report has not been conducted according to the criteria of Art. 38 of 1107/2009 as it was done by UK before 1107/2009 was applicable.	Addressed.
1(2)	Vol.4 Table C.1.2.3-1 SAPEC	FR: Based on the 5-batch analysis, minimum purity should be increased and specification for [redacted] should be decreased or QC data should be provided	SAP: QC data for batches produced between July 2008 to December 2010 [redacted]) were submitted for the equivalence assessment by CRD UK and support the specification of minimum 975g/kg for glyphosate. Regarding the maximum content for [redacted] the proposed maximum limit was calculated using the formula average + 3 × standard deviation, and the value obtained was rounded up to the nearest integer. RMS: The minimum purity is in compliance with Reg. (EU) No. 540/2011 and is therefore acceptable. The important issue seems to be that the specification is covered by the current reference specification to ensure that there are no unacceptable effects comparing to	See open point 1(1) in RT for Vol.4 general information To increase the minimum purity and decrease the impurities specification would mean to have individual specifications for all technical materials. It should be noted that the proposal is to set one reference specification, independent from the synthesis pathway.

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			the evaluated reference source. However, in case the applicant provides additional data, these could be included in a revised RAR, provided that this is allowed from a procedural point of view.	
1(3)	Vol.4 Table C.1.2.3-2 SAPEC	FR: Based on the 5-bath analysis, specification for [redacted] should be decreased or QC data should be provided	SAP: given the 5-ba results for [redacted] in Flag source, where standard deviation was small, which would lead to a tight specification, a maximum content to the second nearest integer was then proposed for IDA. RMS: The important issue seems to be that the specification is covered by the reference specification to ensure that there are no unacceptable effects comparing to the evaluated reference source.	See open point in comment 1(2)
1(4)	Vol. 4, RAR, SAP, C.1.2.3 Five batch data, p.9	EFSA: small typo in the enumeration of the compounds analysed for in the QC, the first [redacted]	SAP: see our comment below to 1(5). RMS: Could be corrected in a revised RAR.	See open point in comment 1(5)

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(5)	Vol. 4, C.1.2.3, Analytical profile of batches	SAP: Where it is stated "*The batches were analysed for (…)* [redacted] *(…)*", should be written "*The batches were analysed for (…)* [redacted] *(…)*".	RMS: Could be corrected in a revised RAR.	Open point: RMs to correct the typo in a revised Vol.4 See also 1(4)
1(6)	Vol. 4, RAR, SAP, C.1.2.4 Specifications, p. 12	EFSA: clarification is needed whether the notifier intends to have separate specification for the different manufacturing sites or just covering all?	SAP: We intend to have separate specification for each manufacturing site. RMS: No further comment. However, in case the applicant provides additional data, these could be included in a revised RAR, provided that this is allowed from a procedural point of view.	Addressed. However, see also comment 1(2)

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(7)	Vol. 4 C.1.3.1 Sapec	FR: The identity of each impurity should be confirmed.	SAP: Identity of each impurity was confirmed by fortifying samples of technical material with the corresponding analytical standard. All known glyphosate impurities were determined using several different and specific analytical methods. All significant and the 2 relevant impurities were identified and quantified in both glyphosate sources. RMS: See comment above. However, in case the applicant provides additional data, these could be included in a revised RAR, provided that this is allowed from a procedural point of view.	Addressed.
1(8)	Vol. 4, C.1.3.1, Methods of analysis for the determination of impurities	SAP: In table C.1.3-3, column "*Recovery*", please replace the values of ***104.3%*** and ***122.9%*** for ***122.9%*** and ***104.3%***, respectively.	RMS: Could be corrected in a revised RAR.	Open point: RMS to correct the typos in Vol. 4, C.1.3.1 in an updated Vol.4

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(9)	Vol. 4, C.1.2.4 Comparison of the analytical profile of batches - Toxicological evaluation of specification (2013):	RMS: *The applicant provided no information/data, which would allow to judge whether the impurities are relevant. The applicant provided no evaluation, whether the material used in toxicological studies is representative for the proposed specification.* *Based on the available studies submitted, a conclusion on the equivalence of the Sapec source cannot be made.* SAP: Additional data/information will be submitted which allow judging whether the impurities are of toxicological relevance or not with regard to the impurities of the reference source. Furthermore, the applicant will provide data/information demonstrating that the material used in toxicological studies is representative for the proposed specification.	RMS: In case the applicant provides additional data, these could be included in a revised RAR, provided that this is allowed from a procedural point of view. Based on the data submitted until now, relevance of impurities cannot be evaluated. Based on the data submitted until now, it cannot be evaluated, whether the material used in toxicological studies is representative for the proposed specification or the reference specification.	Data requirement: Applicant SAPEC to submit data/information concerning the assessment of toxicological relevance of the impurities and data/information demonstrating that the material used in toxicological studies is representative for the proposed specification.

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Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(1)	Vol. 4 C.1.1.2 Table C.1.1-1 Société Financière de Pontarlier	FR: Information concerning the CAS Number of each starting material should be reported.	SFP: SFP indicates the following CAS are available: RMS: No further comment.	Addressed.
1(2)	Vol. 4, C.1.2.4 Comparison of the analytical profile of batches	RMS: *According to the criteria given in Tier I of Guidance Document SANCO/10597/ 2003 rev 10.1 the proposed specification cannot be regarded as equivalent to the reference source as the specified value for impurity 3 is outside of the acceptable tolerance.* *A Tier II assessment is necessary.* SFP: Additional data will be submitted.	SFP: SFP can refer to all data necessary to confirm non-relevance of this impurity (letter of access available). Acute oral, dermal and inhalation study showed a toxicity similar to the ai: oral tox is higher than 2000 mg/kg bw (vs 5000 proposed for active), acute dermal >5000 (same proposed for ai), acute inhal > 6.1mg as/L (vs 5.18 for ai). The compound of concern was demonstrated to be non-irritant for skin, but	Data requirement: Applicant SFP to submit data/information demonstrating that the material used in toxicological studies is representative for the proposed specification

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		However, SFP wants also to underline that comments performed during RAR seem to have not been taken into account by the RMS. We showed that there are a lot of publically available data on the compound of concern (ECHA and EPA data basis in particular), showing its non-relevance. These data are very old (all before 1990) but conducted under GLP procedure and considered reliable by both EPA and ECHA during registration process of the concerned compound.	severely for eyes. It is not a sensitizer. The same is to be considered for the ai. All these data were accepted by EPA and ECHA when registring the compound. They deal with old studies but all performed under GLP conditions ensuring their reliability. Further on, Ames test performed recently with our TGAI showed the test to be non-mutagen. QSAR of the impurity also confirmed the absence of such concern as well as carcinogenicity, chromosome damage and genotoxicity, based on structures alerts. These both reports (136011 and ERA-0101-A respectively) are available and will be submitted if requested. Hence, sufficient data are available to confirm the non-relevance of this impurity, by this way, the equivalence of SFP's source to the reference one. RMS: noted. It is noted that the comments submitted by the notifier were taken into account and were included in Vol. 4 (C.1.2.4). In case the applicant provides additional data, these could be included in a revised RAR, provided that this is allowed from a	

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			procedural point of view. Based on the data submitted until now, relevance of impurities cannot be evaluated. Based on the data submitted until now, it cannot be evaluated, whether the material used in toxicological studies is representative for the proposed specification or the reference specification.	
1(3)	Vol. 4, C.1.2.4 Comparison of the analytical profile of batches - Toxicological evaluation of specification (2013):	RMS: *The applicant provided no information/data, which would allow to judge whether the impurities are relevant.* [redacted] *is specified in significantly higher amounts than listed in the reference specification. Regarding this issue, the applicant has submitted a statement but RMS also indicates that "currently, the mentioned data/information has not been submitted for the present EU procedure. Hence RMS cannot confirm that there is no significant increase in toxicity due to the presence of the impurity." The applicant provided no evaluation, whether the material used in tox studies is representative for the proposed specification.*	SFP: SFP has access to data showing the non-relevance of the [redacted] As given above, the acute oral, dermal, inhalation toxicity is similar to the ai. The compound is not irritant to skin nor a sensitizer but irritant to eyes as for the active. RMS: See 1(2).	See dat requirement in comment 1(2)

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		Based on the available studies submitted, a conclusion on the equivalence of the SFP source cannot be made SFP: Additional data/information will be submitted which allow judging whether the impurities are of toxicological relevance or not with regard to the impurities of the reference source. SFP will also demonstrate that data submitted for registration of this compound ([redacted] under EPA and ECHA processes, showing the non-relevance of this impurity, can not be considered as being still under protection. Otherwise, agreement for the access to these data will be discussed and found with their owners.		
1(4)	Vol. 4, C.1.2.4 Comparison of the analytical profile of batches - Ecotoxicology	RMS: *Based on the available studies, which were submitted for the renewal of glyphosate, a conclusion on the equivalence of the SFP source cannot be made.* SFP: SFP did not perform any ecotox study with its technical ingredient, so there is no need and no possibility to	SFP: In addition to previous comment, it is reported in the same annex point that "For the [redacted] further ecotoxicological assessment is not required as the evaluation according to SANCO/10597/2003 rev 10.1 showed that the increase in toxicity is not seriously (<2) higher than the known effect values in comparison to the reference	Addressed.

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		demonstrate such a reliability.	specification." Comparison of ecotox profile of SFP's source with the reference or profile of tested batched in ecotox studies with specifications proposed by SFP should not be an issue. RMS: No further ecotoxicological assessment is required as the evaluation according to SANCO/10597/2003-rev10.1 showed that the increase in toxicity is not seriously (<2) higher than the known effect values in comparison to the reference specification.	
1(5)	Vol. 4 C.1.3.1 Determination of formaldehyde and NNG Société Financière de Pontarlier	FR: The identity of impurities [redacted] NNG and formaldehyde should be confirmed.	SFP: Report from Huazhen Wen (IIA 4.2.1.2=4.2.3.2, Nutriechem laboratory, May 2009) showed in figures 8 to 10, then in figures 11 to 13, DAD spectrum of impurity in the sample, the same spectrum with the sample spiked with standard of the impurity, and the same spectrum with a standard of the impurity alone. Similarity of all spectra and superposition of these spectra should be sufficient to confirm identity of the analytes ([redacted] and formladehyde). In addition, in regards to formaldehyde, its assay is based on an internationally recognized method (FAO method), allowing a less complete validation	See data requirement in comment 1(6).

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			to be conducted. For [redacted] on the other hand, confirmation of identity was ensured by fortification of a sample with standard and further analysis by 31P NMR. However, if this was considered as not sufficient, fully validated methods for determination of [redacted] in TGAI (report 14-919044-006), for the detemination of formaldehyde in SFP's formulation (report 13-919068-004) and for determination of nitrosamines in formulation (report 13-919068-003) are available and can be provided if requested. All these methods will cover data requirements. RMS: See comment above. However, in case the applicant provides additional data, these could be included in a revised RAR, provided that this is allowed from a procedural point of view.	

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1(6)	Vol. 4, RAR, SFP, C.1.3 Analytical methods, Table C.1.3-2, p. 11	EFSA agrees with RMS on the need for additonal validation data for the determination of [redacted]	SFP: See previous comment. In addition, a fully validated method (report 14-919044-006) is available and report can be provided on request. RMS: Comment noted. In case the applicant provides additional data, these could be included in a revised RAR, provided that this is allowed from a procedural point of view.	Data requirement: Applicant SFP to submit report 14-919044-006
1(7)	Vol. 4, C.1.3-2 Analytical methods. Validation data for the determination of the [redacted]	RMS: *With respect to validation data for the determination of the [redacted] Clarification is needed concerning the fortification levels used for the determination of the accuracy and repeatability. It seems that pure standard solutions have been used for the measurements. However, the accuracy and repeatability should be determined with spiked technical material. The fortification levels should be stated in % related to the tech material.* SFP: In appendix 2 of SANCO 3030/99 rev. 4 it is stated that "accuracy may be measured in different ways(…). Assessment may be made by analysing a sample of known concentration and	SFP: If requested a fully validated method (report 14-919044-006) is available and can be provided for the determination of [redacted] in TGAI. RMS: The response of the applicant is unfortunately unclear. The description in the quoted appendix 2 is rather a general description of the principles than a definite description. The important part is given in 3.1.2 (iii) Accuracy, where it is clearly stated that "… *Recoveries should be determined at levels appropriate of the material specification*."	See data requirement in comment 1(6).

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		comparing the measured value to the true value. However a well characterized sample must be used. An example of this would be a reference standard." Usual validation for impurities request two fortifications. In this validation, 6 levels were tested with two determinations each time. RSD was estimated on all levels ensuring a worst case as a simple repeatability on one level. Therefore, the validation should be considered as acceptable. Anyway, if necessary, further validation data will be provided.		

1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis

Identity (B.1, Annex C)				
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1(1)	Vol. 4 C.1.1.1 Manufacturing process Sinon	FR: More details concerning each step of the manufacturing process should be reported.	SNN: Additional data can be submitted on request RMS: The comment from FR is unfortunately unclear. The given information is in compliance with the current requirements. However, in case the applicant provides additional data, these could be included in a revised RAR, provided that this is allowed from a procedural point of view.	Addressed.
1(2)	Vol. 4 C.1.1.1 Table C.1.2.3-1 Manufacturing process Sinon	FR: As the profil of batch has more than 10 years, a new profil of batches should be provided.	SNN: Additional data can be submitted on request RMS: The comment from FR is unfortunately unclear. The data requirement FR refers to is not applicable for AIR II substance. However, in case the applicant provides additional data, these could be included in a revised RAR, provided that this is allowed from a procedural point of view.	Addressed.

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1(3)	Vol.4 Table C.1.2.3-1 Sinon	FR: The specifications are not in accordance with the batch analysis, they should be modified to be in accordance with the thumb rule or QC data should be provided. This DRAR is performed for a total re evaluation of the active substance.	SNN: Additional data can be submitted on request RMS: The important issue seems to be that the specification is covered by the reference specification to ensure that there are no unacceptable effects comparing to the evaluated reference source. However, in case the applicant provides additional data, these could be included in a revised RAR, provided that this is allowed from a procedural point of view.	Data requirement: Applicant Sinon to provide an updated technical specification based on batch data or QC data to support the specification
1(4)	Vol. 4, RAR, SIN, C.1.2.3 Five batch data, p.6	EFSA: manufacturing dates are missing	SNN: Additional data can be submitted on request RMS: Comment noted. Already mentioned in the RAR.	Data requirement: Applicant Sinon to provide manufacturing dates of the batches

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1(5)	Vol. 4, RAR, SIN, C.1.2.3 Five batch data, p.6	EFSA: it is not clear what is the additional study supporting the specification of the three impurities whose specifications are not supported by the five-batch data?	SNN: Additional data can be submitted on request RMS: From EFSA's point of view it can be interpret like this. However, the important issue seems to be that the specification is covered by the reference specification to ensure that there are no unacceptable effects comparing to the evaluated reference source. However, in case the applicant provides additional data, these could be included in a revised RAR, provided that this is allowed from a procedural point of view.	See data requirement in comment 1(3)
1(6)	Vol. 4, C.1.2.4 Comparison of the analytical profile of batches - Toxicological evaluation of specification (2013):	RMS: *The applicant provided no information/data, which would allow to judge whether the impurities are relevant. The applicant provided no evaluation, whether the material used in tox studies is representative for the proposed specification.* *Based on the available studies submitted, a conclusion on the equivalence of the Sinon source cannot be made.* SNN: Additional data/information will be submitted which allow judging whether	RMS: In case the applicant provides additional data, these could be included in a revised RAR, provided that this is allowed from a procedural point of view. Based on the data submitted until now, relevance of impurities cannot be evaluated. Based on the data submitted until now, it cannot be evaluated, whether the material used in toxicological studies is representative for the proposed specification or the reference specification.	Data requirement: Applicant Sinon to submit data/information concerning the assessment of toxicological relevance of the impurities and data/information demonstrating that the material used in toxicological studies is representative for the proposed specification.

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		the impurities are of toxicological relevance or not with regard to the impurities of the reference source. Furthermore, the applicant will provide data/information demonstrating that the material used in toxicological studies is representative for the proposed specification.		
1(7)	Vol. 4, C.1.3-1 Analytical methods. Validation data for the determination of the [redacted]	RMS: *Clarification is needed concerning the fortification levels for the determination of the accuracy. The applicant stated that the standard addition level (%) was done at 37%, 47% and 54%. However, these values seem to be not reliable and the sample preparation, i.e. weighing and dilution of the technical material, is not described. The fortification levels have to be stated in % related to the technical material. The RSD of the precision exceeds the Horwitz value which is 2.7% for a concentration of 1%. According to SANCO/3030/99 an explanation is required by the applicant.* SNN: Additional data/information will be submitted.	RMS: In case the applicant provides additional data, these could be included in a revised RAR, provided that this is allowed from a procedural point of view.	Data requirement: Applicant Sinon to provide additional validation data for the determination of the [redacted]

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1(8)	Vol. 4, RAR, SIN, C.1.3.1 Analytical methods, p. 9-12	EFSA agrees with the RMS on the need for additional clarifications concerning the methods for the determination of the impurities of the technical material	SNN: Additional data/information will be submitted. RMS: In case the applicant provides additional data, these could be included in a revised RAR, provided that this is allowed from a procedural point of view.	Data requirement: Applicant Sinon to provide additional validation data for the determination of the impurities of the technical material
1(9)	Vol. 4, C.1.3-2 Analytical methods. Validation data for the determination of the [redacted]	RMS: *With respect to validation data for the determination of the [redacted], the fortification levels are not appropriate to the specified values of [redacted] respectively. Furthermore, the determination of the repeatability by repeated injection of a standard solution is not acceptable. A minimum of five replicate determinations in the tech material must be made.* SNN: Additional data/information will be submitted.	RMS: In case the applicant provides additional data, these could be included in a revised RAR, provided that this is allowed from a procedural point of view.	See data requirement in commen t1(8)
1(10)	Vol. 4, C.1.3-3 Analytical methods. Validation data for the determination of the [redacted]	RMS: *With respect to validation data for the determination of the [redacted] clarification is needed concerning the fortification levels for the determination of the accuracy. The applicant stated that the standard addition level (%) was done at 32%, 41% and 49%. However, these*	RMS: In case the applicant provides additional data, these could be included in a revised RAR, provided that this is allowed from a procedural point of view.	See data requirement in commen t1(8)

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		values seem to be not reliable and the sample preparation, i.e. weighing and dilution of the tech material, is not described. The fortification levels have to be stated in % related to the technical material. The RSD of the precision exceeds the Horwitz value which is 3.7% for a concentration of 0.12%. According to SANCO/3030/99 an explanation is required by the applicant. SNN: Additional data/information will be submitted.		
1(11)	Vol. 4, C.1.3-4 Analytical methods. Validation data for the determination of the impurity 20	RMS: *The fortification levels are not appropriate to the specified value of 1 ppm. Furthermore, the determination of the repeatability by repeated injection of a standard solution is not acceptable. A min of 5 replicate determinations in the tech material must be made.* SNN: Additional data/information will be submitted.	RMS: In case the applicant provides additional data, these could be included in a revised RAR, provided that this is allowed from a procedural point of view.	See data requirement in commen t1(8)

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1(12)	Vol. 4, C.1.3-5 Analytical methods. Validation data for the determination of the impurity 20	RMS: *Clarification is needed concerning the fortification levels for the determination of the accuracy. The applicant stated that the standard addition level (%) was done at 52 %, 57 % and 69 %. However, these values seem to be not reliable and the sample preparation, i.e. weighing and dilution of the technical material, is not described. The fortification levels have to be stated in % related to the tech material.* SNN: Additional data/information will be submitted.	RMS: In case the applicant provides additional data, these could be included in a revised RAR, provided that this is allowed from a procedural point of view.	See data requirement in commen t1(8)

1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis

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1(1)	Vol. 4 C.1.1.1 Syngenta	FR: The second source of active substance [redacted]) should be clarified, it should be indicated if Syngenta has access to all origins from [redacted] or only one, and in this case clarify which.	SYD: The manufacturing source address is stated in the Document J section IIA 1.2.1. RMS: The manufacturing site in question is clearly stated in C.1.1.1.	Addressed.
1(2)	Vol. 4, C.1.1, Toxicological evaluation of specification	Applicant: Syngenta acknowledges the RMS comment "For the renewal procedure (2013), none of the applicants provided sufficient information/data, which would allow to judge whether the impurities are relevant. It is noted that Syngenta submitted a case on relevance of impurities; this case is evaluated in the respective Vol. 4." Dr Knoell will address this on behalf of the Task Force.	SYD: No further comment required RMS: Noted (this comment relates to "Volume 4 general information")	Addressed.
1(3)	Vol. 4, C.1.1, Toxicological evaluation of specification	Applicant: Syngenta acknowledges the RMS comment "For the renewal procedure (2013), none of the applicants provided a sufficient evaluation, whether the material used in toxicological studies is representative for the respectively proposed specifications or the reference	SYD: No further comment required RMS: Noted (this comment relates to "Volume 4 general information")	Addressed.

Identity (B.1, Annex C)				
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		specification derived during the previous EU evaluation. Hence, it cannot be evaluated, whether the material used in toxicological studies is representative for the proposed specification or the reference specification derived during the previous EU evaluation“ Dr Knoell will address this on behalf of the Task Force.		
1(4)	Vol. 4, C.1.1, Toxicological evaluation of specification	Applicant: Syngenta acknowledges the RMS comment “No data or information was submitted that would allow setting maximum limits for relevant impurities. In summary, based on the currently available data and information, safe maximum levels for relevant impurities [nitrosamines and formaldehyde] cannot be derived. Dr Knoell will address this on behalf of the Task Force.	SYD: No further comment required RMS: Noted (this comment relates to “Volume 4 general information”)	Addressed.
1(5)	Vol. 4 C.1.1.2 Syngenta	FR: Please MS clarify how two different processes are used in the same location. It should be indicated if production is performed simultaneously using both processes or not.	SYD: Glyphosate technical material is manufactured using [redacted]. The two processes are operated on different plant facilities at this manufacturing site and therefore may	Addressed.

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			be operated simultaneously however the plant operations are separate. RMS: The French comment is unfortunately unclear. The important issue is that the technical material that is used for the ppp is in compliance with the set specification. Whether in this case the technical material is produced in one vessel or in two vessels at the site is irrelevant as long as the specification is met.	
1(6)	Vol. 4, RAR, SYN, C.1.1.2 Method of manufacture, [redacted] p.3	EFSA: the description of the manufacturing process is not always clear. Is step 4 an additional 'purification' step, as from the glyphosate obtained in step 3, after this step glyphosate is resulting? Also the naming used is slightly confusing: in step 4 xxx [redacted] is used, however the reaction scheme shows an ammonium salt.	SYD: Steps 3 and 4 are purification steps. [redacted] Syngenta can confirm that the name is incorrect; it should be [redacted] RMS: See applicant's comment above. The corrections could be included in a revised RAR.	Addressed.
1(7)	Vol. 4, RAR, SYN, C.1.1.2 Method of manufacture, [redacted]	EFSA: is [redacted] not a possible impurity?	SYD: Theoretically, [redacted] A is a potential impurity of the [redacted] manufacturing route, however its	Addressed.

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	impurities, p. 9		formation would depend on the presence of suitable nitrosating agents during the synthesis. A survey of the synthentic steps demonstrates that nitrosating agents are not present and therefore the formation of this species remains theoretical only. The absence of suitable nitrosating agents is further corroborated by the fact that there is no detection of *N*-nitrosoglyphosate in the representative batches. RMS: See applicant's comment above.	
1(8)	Vol. 4, RAR, SYN, C.1.2.4 Comparison of analytical batches, Conclusion, p. 16	EFSA only partly agrees with the statement that 'It is demonstrated that the compositions of the representative batches comply with the proposed specifications of the technical active substances.' as the purity of the a.s. for example could be higher based on the batch and QC data, or the proposed specifications [redacted] are not supported by batch data, but possibly by the QC data.	SYD: Syngenta acknowledges the comments of EFSA. In respect of the a.i. minimum purity looking at the two routes of manufacture separately: [redacted] route: Whilst the average minus three standard deviation value is 975g/kg, from an examination of the QC data it is clear that purity values approaching 960g/kg are observed. Given the proposed minimum purity value is only 1% lower than this "QC minimum" it would be sensible to maintain the 950g/kg minimum purity value to avoid excessive product failure, disposal or-re-work.	Addressed.

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			[redacted] route: The average minus three standard deviation value is 955g/kg; no QC data is available for this route. Given the noted average minus three standard deviations value the 950g/kg minimum purity is justified. With respect to the noted impurities it can be clarified that these are indeed supported by QC data which is presented in the DAR Volume 4 p13. RMS: Comment noted. The important issue seems to be that the specification is covered by the reference specification to ensure that there are no unacceptable effects comparing to the evaluated reference source.	
1(9)	Vol. 4, C1.2.4, Comparison of the analytical profile of batches	Applicant: Syngenta acknowledges the RMS comment that in respect of the proposed specification clause [redacted] that is has been removed from the proposed specification by the RMS. However, it should be noted that the specification is therefore not consistent with the FAO specification which requires insolubles	SYD: No further comment required RMS: No further comment.	Addressed.

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		to be listed.		
1(10)	Vol. 4, C1.2.4, Comparison of the analytical profile of batches – [redacted] route	Applicant: Syngenta acknowledges the RMS comment that in respect of the proposed specification for the [redacted] route technical material that a Tier II assessment is necessary in respect of the [redacted]. Syngenta will provide, on request, a Tier II toxicological assessment according to guidance document SANCO 10597 in respect of the [redacted], to demonstrate equivalence to the reference source and that there is no significant increase in toxicity as a result of the proposed specification limits, for the noted impurities.	SYD: No further comment required RMS: In case the applicant provides additional data, these could be included in a revised RAR, provided that this is allowed from a procedural point of view. Based on the data submitted until now, it cannot be evaluated, whether the material used in toxicological studies is representative for the proposed specification or the reference specification.	See open point in comment 1(1) in the RT for Vol.4 general information

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(11)	Vol. 4, C1.2.4, Comparison of the analytical profile of batches – toxicological equivalence	Applicant: Syngenta acknowledges the RMS comment "the information provided by the applicant is not sufficient to establish relevance/non-relevance of impurities". Syngenta has tried to address this by the use of QSAR analysis and specific toxicological data where that is available but it recognises that there is no specific guidance relating to how to address relevance/non-relevance of impurities. Please can the RMS comment – how should this be assessed? Dr Knoell will address this on behalf of the Task Force.	SYD: No further comment required RMS: In case the applicant provides additional data, these could be included in a revised RAR, provided that this is allowed from a procedural point of view. Based on the data submitted until now, relevance of impurities cannot be evaluated.	Data requirement: Applicant Syngenta to submit the assessment of the relevance/non-relevance of impurities on behalf of the Task Force.
1(12)	Vol. 4, C1.2.4, Comparison of the analytical profile of batches – toxicological equivalence	Applicant: Syngenta acknowledges the RMS comment "Impurities formaldehyde (impurity 21) and *N*-nitrosoglyphosate (impurity 20) were reported as "not analysed" in the tox. Batches but are foreseen to be specified" However, this is because the analysis of most of the toxicological batches was conducted before the analysis of relevant impurities was a formal	SYD: No further comment required RMS: Notifier confirmed that the content of formaldehyde (impurity 21) and N-nitrosoglyphosate (impurity 20) were not analysed.	Addressed.

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		requirement. However, it is clear that these known toxicologically relevant impurities are specified in the FAO specification which must be respected and that the impurities are controlled below the agreed (FAO) specification limits as demonstrated by the batch analysis.		
1(13)	Vol. 4, C1.2.4, Comparison of the analytical profile of batches – toxicological equivalence	Applicant: Syngenta acknowledges the RMS comment [redacted] were reported as "not analysed" in the tox. batch Bx20100609 from the [redacted] route but are foreseen to be specified" For [redacted] this was mistakenly reported as "NA" when it is clear from the analytical report it should be "ND" - which is not detected. [redacted] was however detected in batch Bx 20070911 also used in toxicity testing. Whilst [redacted] were not	SYD: No further comment required RMS: The information submitted by the notifier on the composition of the tox batches was included in chapter C.1.5. The information that [redacted] was not detected in batch Bx20100609 (instead of "not analysed") could be taken up in a revised RAR.	Open point: RMS to update the Vol. 4 with the information presented in col. 3 of the RT concerning [redacted]

Identity (B.1, Annex C)				
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		analysed in this particular batch, other batches used for toxicological studies did contain these two impurities which were analysed and reported		
1(14)	Vol. 4, C1.2.4, Comparison of the analytical profile of batches – toxicological equivalence	Applicant: Syngenta acknowledges the RMS comment "[redacted] are intended to be specified with 10g/kg but were reported to be present in the tox batch P24 with only [redacted] respectively. Additionally the results of an Ames test are available. For the evaluation of an impurity above/equal to 10 g/kg, the results of the in vitro genotoxicity testing battery are needed" Syngenta is currently considering the implications of this request related to the impurities [redacted] and is reviewing different options to address the reviewer's concern. Syngenta commits to providing further information on this point.	SYD: For [redacted]), after extensive discussions with the supplier it has been agreed to reduce the proposed specification limit for [redacted]. Syngenta therefore respectfully submits that the existing toxicological database, including negative Ames study on the noted isolated impurity, supports the limit for the specified impurity. For [redacted] Syngenta is still currently considering the implications of this request. Syngenta commits to providing further information on this point. RMS: The proposed maximum limit of 9 g/kg for the impurity [redacted] could be taken up in a revised RAR. In case the applicant provides additional data, these could be also included in a revised RAR, provided that this is allowed from a procedural point of view.	Data requirement: Applicant Syngenta to provide further information concerning [redacted] Open point: RMS to update Vol.4 with the information frrom col. 3 of the RT concerning impurity [redacted]

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			Based on the data submitted until now, it cannot be evaluated, whether the material used in toxicological studies is representative for the proposed specification or the reference specification.	

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(15)	Vol. 4, C1.2.4, Comparison of the analytical profile of batches – toxicological equivalence	Applicant: Syngenta acknowledges the RMS comment "[redacted] but was reported to be present in the tox batch Bx20070911 with only [redacted] Additionally the results of an Ames test are available. For the evaluation of an impurity [redacted] the results of the in vitro genotoxicity testing battery are needed. Tox batch Bx20070911 was mainly used for acute toxicity studies and one Ames test" [redacted] was present in batch Bx20070911 [redacted] which tested negative in an Ames study and an *in vivo* mouse micronucleus assay. In addition, a bacterial reverse mutation assay has been conducted on [redacted] in six bacterial strains (Reynolds and Riach, 1988). The results of these studies demonstrate that [redacted] has no bacterial mutagenic activity or clastogenicity activity *in vivo*. Syngenta commits to providing the additional genotoxicity data to support glyphosine at the level in the proposed specification.	SYD: Syngenta commits to providing further information on this point. RMS: In case the applicant provides additional data, these could be also included in a revised RAR, provided that this is allowed from a procedural point of view. Based on the data submitted until now, it cannot be evaluated, whether the material used in toxicological studies is representative for the proposed specification or the reference specification.	Data requirement: Applicant Syngenta to provide additional genotoxicity data to support glyphosine at the level in the proposed specification.

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(16)	Vol. 4, C1.2.4, Comparison of the analytical profile of batches – toxicological equivalence	Applicant: Syngenta acknowledges the RMS comment "[redacted] Tox batch Bx20070911 was mainly used for acute toxicity studies and an Ames test. The intended amount would be within the acceptable increase for non-relevant impurities according Tier I of SANCO/10597/2003 – rev. 10.1" Syngenta commits to providing further data to demonstrate that [redacted] is indeed not relevant and therefore the proposed specification limit of 5g/kg will be supported by the existing toxicological study database according to a Tier I assessment using SANCO/10597/2003 – rev. 10.1. Dr Knoell will address this on behalf of the Task Force.	SYD: No further comment required RMS: In case the applicant provides additional data, these could be also included in a revised RAR, provided that this is allowed from a procedural point of view. Based on the data submitted until now, relevance of [redacted] cannot be evaluated. Based on the data submitted until now, it cannot be evaluated, whether the material used in toxicological studies is representative for the proposed specification or the reference specification.	See data requirement in comment 1(11)

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(17)	Vol. 4, C1.2.4, Comparison of the analytical profile of batches – toxicological equivalence	Applicant: Syngenta acknowledges the RMS comment "[redacted] was mainly used for acute toxicity studies and one Ames test. The intended amount would be within the acceptable increase for non-relevant impurities according Tier I of SANCO/10597/2003 – rev. 10.1." Syngenta commits to providing further data to demonstrate that glycine is indeed not relevant and therefore the proposed specification [redacted] will be supported by the existing toxicological study database according to a Tier I assessment using SANCO/10597/2003 – rev. 10.1. Dr Knoell will address this on behalf of the Task Force.	SYD: No further comment required RMS: In case the applicant provides additional data, these could be included in a revised RAR, provided that this is allowed from a procedural point of view. Based on the data submitted until now, it cannot be evaluated, whether the material used in toxicological studies is representative for the proposed specification or the reference specification.	See data requirement in comment 1(11)

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(18)	Vol. 4, C1.2.4, Comparison of the analytical profile of batches – toxicological equivalence	Applicant: Syngenta acknowledges the RMS comment [redacted] was mainly used for acute toxicity studies and one Ames test. The intended amount would be within the acceptable increase for non-relevant impurities according Tier I of SANCO/10597/2003 – rev. 10.1." Syngenta commits to providing further data to demonstrate that glycine is indeed not relevant and therefore the proposed specification [redacted] will be supported by the existing toxicological study database according to a Tier I assessment using SANCO/10597/2003 – rev. 10.1. Dr Knoell will address this on behalf of the Task Force.	SYD: No further comment required RMS: see 1(17)	See data requirement in comment 1(11)

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(19)	Vol. 4, C1.2.4, Comparison of the analytical profile of batches – toxicological equivalence	Applicant: Syngenta acknowledges the RMS comment [redacted] Tox batch Bx20070911 was mainly used for acute toxicity studies and one Ames test. The intended amount would be outside the acceptable increase for non-relevant impurities according Tier I of SANCO/10597/2003 – rev. 10.1.“ After extensive discussions with the supplier it has been agreed to reduce the proposed specification limit for [redacted]. Syngenta therefore respectfully submits that the existing toxicological database supports this limit for triethylamine.	SYD: No further comment required RMS: The proposed maximum limit of 4 g/kg for the impurity [redacted] could be taken up in a revised RAR. Based on the data submitted until now, it cannot be evaluated, whether the material used in toxicological studies is representative for the proposed specification or the reference specification.	Open point: RMS to update the specification for [redacted] according to col. 3 of the RT in an udated Vol.4
1(20)	Vol. 4, C1.2.4, Comparison of the analytical profile of batches – ecotoxicological equivalence	Applicant: Syngenta acknowledges the RMS comment [redacted] respectively, which were used in several toxicological studies. Eco-toxicological studies were	SYD: Syngenta is currently considering the implications of this request and will provide further information related to [redacted] to address this concern on request. RMS: Additional information addressing the	Data requirement: Applicant Syngenta to submit further information related to [redacted] addressing the ecotoxicological representativeness of the specification.

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		performed with the batches P24 and P30, which do not contain this impurity. Thus, the equivalence of this source [redacted]) to the reference source cannot be substantiated with sufficient certainty; additional information addressing the ecotoxicological representativeness of the specification is required. If this information is not available an appropriate bridging study is required according to guideline OECD 201 (due to animal welfare reasons and the specific mode of action of glyphosate other studies are not required) to prove the eco-toxicological representativeness" Syngenta is currently considering the implications of this request and will provide further information related to [redacted] to address this concern on request.	ecotoxicological representativeness is appreciated.	
1(21)	Vol.4 Table C.1.2-1 Syngenta	FR: Based on the 5-batches and QC data, the minimum purity should be increased. As different specifications were proposed for each process, the minimum purity should not necessary be similar for both	SYD: Syngenta acknowledges the comments of France, looking at the two routes of manufacture separately: [redacted]route: Whilst the average minus	Addressed Howver see also open point in comment 1(1) of the RT for Vol.4

Identity (B.1, Annex C)				
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		processes.	three standard deviation value is 975g/kg, from an examination of the QC data it is clear that purity values approaching 960g/kg are observed. Given the proposed minimum purity value is only 1% lower than this "QC minimum" it would be sensible to maintain the 950g/kg minimum purity value to avoid excessive product failure, disposal or-re-work. [redacted] route: The average minus three standard deviation value is 955g/kg; no QC data is available for this route. Given the noted average minus three standard deviations value the 950g/kg minimum purity is justified. RMS: The minimum purity is in compliance with Reg. (EU) No. 540/2011 and is therefore acceptable. The important issue seems to be that the specification is covered by the current reference specification to ensure that there are no unacceptable effects comparing to the evaluated reference source.	general information.
1(22)	Vol. 4 Table C1.2-1	FR: Information on the date of production of the batches should be reported.	SYD: date of production of the representative batches is available in the individual batch	Addressed.

<table>
<tr><th colspan="5">Identity (B.1, Annex C)</th></tr>
<tr><td>No.</td><td>Column 1
Reference to DAR (vol., point, page)</td><td>Column 2
Comments from Member States or applicant</td><td>Column 3
Evaluation by (RMS) rapporteur and
- if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant</td><td>Column 4
Data requirement or Open point (if data point not addressed or fulfilled)</td></tr>
<tr><td></td><td>Syngenta</td><td></td><td>reports and is reproduced here for ease:

[redacted] route:
<table><tr><td>Batch number</td><td>Production date</td></tr><tr><td>JSA1010004-1</td><td>17.10.2010</td></tr><tr><td>JSA1010002-6</td><td>12.10.2010</td></tr><tr><td>JSA1010003-5</td><td>15.10.2010</td></tr><tr><td>JSA1010004-6</td><td>20.10.2010</td></tr><tr><td>JSA1010005-4</td><td>23.10.2010</td></tr></table>[redacted] route:
<table><tr><td>Batch number</td><td>Production date</td></tr><tr><td>Bx 2007 0910</td><td>10.9.2007</td></tr><tr><td>Bx 2007 0911</td><td>10.9.2007</td></tr><tr><td>Bx 2007 0916</td><td>14.9.2007</td></tr><tr><td>Bx 2007 0917</td><td>15.9.2007</td></tr><tr><td>Bx 2007 0918</td><td>17.9.2007</td></tr></table>
RMS: The productions dates are included in the study but were not copied by the RMS. The date could be included in a revised RAR. See applicant's comment above.</td><td></td></tr>
<tr><td>1(23)</td><td>Vol.4
Table C.1.2-2
Syngenta</td><td>FR: Based on the 5 batches, specifications for impurities 21 and [redacted] should be removed and specifications for impurities 2 and 2 should be decreased or QC data should be provided</td><td>SYD: Impurity 21 (formaldehyde): this impurity was detected in the [redacted] route technical material but not in the [redacted] route technical material. However formaldehyde is used as a starting material in this route and therefore potentially may</td><td>Addressed.

See also open point in comment 1(1) of the RT for Vol.4 general information.</td></tr>
</table>

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			be carried over into the final technical material. Formaldehyde is listed as a relevant impurity in the FAO specification for glyphosate and therefore Syngenta believes that the specifications it proposes for Annex I inclusion should be consistent with the FAO specification. [redacted] [redacted] Syngenta acknowledges the EFSA comment and in addition the RMS comment that in respect of the proposed specification clause '[redacted] that is has been removed from the proposed specification by the RMS. However, it should be noted that the specification is therefore not consistent with the FAO specification which requires insolubles to be listed. Syngenta therefore seeks clarification as to whether this should be listed in the proposed specification. [redacted] the proposed specification limit is justified by QC data (see DAR Volume 4 p13.) RMS: The important issue seems to be that	

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			the specification is covered by the reference specification to ensure that there are no unacceptable effects comparing to the evaluated reference source. The comment above from the applicant could be taken up in a revised RAR.	
1(24)	Vol. 4 C.1.2.4 Syngenta	FR: According to the applicant, the [redacted] no longer formed at significant levels (<1g/kg). So the profile of batches (table C.1.2-2) is not in accordance with the manufacturing process. A new five batches analysis should be provided.	SYD: As proposed (see page 17, DAR Volume 4). Syngenta can provide a further five batch analysis to substantiate the claim for removal of [redacted] RMS: No further comment. However, in case the applicant provides additional data, these could be included in a revised RAR, provided that this is allowed from a procedural point of view.	Data requirement: Applicant Syngenta to submit further five batch analysis to substantiate the claim for removal of [redacted]
1(25)	Vol. 4 C.1.3.1 Determination of NNG and formaldehyde Syngenta	FR: Validation data for the determination of NNG and formaldehyde in the glyphosate technical should be reported.	SYD: both NNG and formaldehyde are analysed using FAO ring-tested methods and therefore are considered acceptably validated. In addition, Syngenta has conducted further validation of these methods and can provide the reports on request. RMS: The French comment is unfortunately unclear. As clearly stated the applicant has	Addressed.

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			used the FAO methods provided by FAO with the specification. In the RAR it is also clearly stated that "*The applicability of the FAO method has been demonstrated. The method is acceptably validated and allows the determination of … in the technical material.*" This is acceptable for the RMS and it is also in compliance with the conducted review assessment of the MS so far.	
1(26)	Vol. 4, C1.3-1, Validation data for the determination of impurities in technical glyphosate	RMS: *The analytical methods are acceptably validated and allow the determination of the impurities in the technical material. However, clarification on the concentration levels in mg/mL used for the linearity test of the* [redacted] *is still needed.* Applicant: Data can be provided on request	SYD: No further comment required RMS: In case the applicant provides additional data, these could be included in a revised RAR, provided that this is allowed from a procedural point of view.	Data requirement: Applicant Syngenta to submit clarification on the concentration levels in mg/mL used for the linearity test of the impurities [redacted]

1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(1)	Vol. 4, C.1.2.4 Comparison of the analytical profile of batches - Toxicological evaluation of specification (2013):	*RMS: The applicant provided no information/data, which would allow to judge whether the impurities are relevant. The applicant provided no evaluation, whether the material used in tox studies is representative for the proposed specification. Hence, it cannot be evaluated, whether the material used in tox studies is representative for the proposed specification.* *Based on the available studies submitted, a conclusion on the equivalence of the UPL source cannot be made* UPL: Additional data/information will be submitted which allow judging whether the impurities are of toxicological relevance or not with regard to the impurities of the reference source. Furthermore, the applicant will provide data/information demonstrating that the material used in toxicological studies is representative for the proposed specification.	RMS: In case the applicant provides additional data, these could be included in a revised RAR, provided that this is allowed from a procedural point of view. Based on the data submitted until now, relevance of impurities cannot be evaluated. Based on the data submitted until now, it cannot be evaluated, whether the material used in toxicological studies is representative for the proposed specification or the reference specification.	Data requirement: Applicant United Phosphorous to submit data/information concerning the assessment of toxicological relevance of the impurities and data/information demonstrating that the material used in toxicological studies is representative for the proposed specification

Identity (B.1, Annex C)

No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(2)	Vol.4 Table C.1.2-1 United phosphorus	FR: Based on the 5-batch analysis, minimum purity should be increased and specification for [redacted] should be decreased or QC data should be provided to justify these values.	UPL: the following technical specification can be proposed on the basis of the 5-batch analysis results: Active Glyphosate: Min. 97.0 % [redacted] N-Nitrosoglyphosate (ppm): Max. 0.7 ppm [redacted] Formaldehyde (g/kg): Max. 0.3 % [redacted]: [redacted] included A new technical specification sheet can be prepared accordingly. RMS: The minimum purity is in compliance with Reg. (EU) No. 540/2011 and is therefore acceptable. The important issue seems to be that the specification is covered by the current reference specification to ensure that there are no unacceptable	Open point: RMS to include the new proposed specification for United Phosphorous in an updated Vol.4 See also open point 1(1) in RT for Vol.4 general information

Identity (B.1, Annex C)				
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			effects comparing to the evaluated reference source. However, in case the need to amend the specification is seen by the majority of the RMS, the specification could be amended according to the proposal by the applicant (see above), provided that this is possible from a procedural point of view.	
1(3)	Vol. 4 C.1.3.1 United Phosphorus	FR: The identity of each impurity should be confirmed.	UPL: The identity of the impurities has been confirmed by reference to an analytical reference standard only. No further identification work was done, but this could be done as part of a possible new study, if required. RMS: See comment above. However, in case the applicant provides additional data, these could be included in a revised RAR, provided that this is allowed from a procedural point of view.	Data requirement: Applicant United Phosphorous to provide additional information on the determination of identity of each impurity.

Identity (B.1, Annex C)				
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1(4)	Vol. 4, RAR, UPL, C.1.3.1 Analytical methods, p. 12	EFSA agrees with the RMS on the need for additional validation data for the method for the determination of NNG	UPL: The analytical method for NNG will be re-validated in an additional study. It is noted that only linearity needs to be assessed as the LOQ (0,7 ppm) was outside the linearity range (0,05 – 0,5 ppm). RMS: Comment noted.	Data requirement: Applicant United Phosphorous to provide additional validation data for the method for the determination of NNG See also comment 1(5)
1(5)	Vol. 4, C.1.3-4 Analytical methods. Validation data for the determination of the impurity 20	RMS: *With respect to validation data for the determination of the impurity 20, the method for the determination of the impurity 20 in the tech material is considered not acceptably validated as the fortification level for the accuracy test is not appropriate to the specified value of 0.7 ppm.* UPL: In appendix 2 of SANCO 3030/99 rev. 4 it is stated that "accuracy may be measured in different ways(…). Assessment may be made by analysing a sample of known concentration and comparing the measured value to the true value. However a well characterized sample must be used. An example of this would be a reference standard." The validation of the method was done	UPL: See comment in column 2 RMS: The response of the applicant is unfortunately unclear. The description in the quoted appendix 2 is rather a general description of the principles than a definite description. The important part is given in 3.1.2 (iii) Accuracy, where it is clearly stated that "… *Recoveries should be determined at levels appropriate of the material specification*."	See data rquirement in comment 1(4)

Identity (B.1, Annex C)				
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		with preparations of glyphosate technical material and the reference material of impurity 20. The concentration of impurity 20 was well known during the validation. Therefore, the method should be acceptable.		

1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(1)	Vol. 4, RAR, WYN, C.1.2.3 Five batch data, Table C.1.2-1, p.7	EFSA: based on batch data, considering the a.s. content, a higher minimum a.s. content might be specified.	WYC: Additional data can be submitted on request RMS: The minimum purity is in compliance with Reg. (EU) No. 540/2011 and is therefore acceptable. The important issue seems to be that the specification is covered by the current reference specification to ensure that there are no unacceptable effects comparing to the evaluated reference source. However, in case the applicant provides additional data, these could be included in a revised RAR, provided that this is allowed from a procedural point of view.	See open point 1(1) in RT for Vol.4 general information To increase the minimum purity specification would mean to have individual specifications for all technical materials. It should be noted that the proposal is to set one reference specification, independent from the synthesis pathway.

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No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(2)	Vol. 4, RAR, WYN, C.1.2.3 Five batch data, Table C.1.2-1, p.7	EFSA: considering the batch dates, are they representative to the production?	WYC: Additional data can be submitted on request RMS: Yes, otherwise a remark and/or a requirement would have been set. However, in case the applicant provides additional data, these could be included in a revised RAR, provided that this is allowed from a procedural point of view.	Addressed.
1(3)	Vol.4 Table C.1.2-1 Wynca	FR: Based on the 5 batches analyzed, the minimum purity should be increased, specification for formaldehyde should be decreased and specification for [redacted] should be removed as its maximum content is [redacted] Please RMS confirms that no evaluation can be performed for the variants.	WYC: Additional data can be submitted on request RMS: The minimum purity is in compliance with Reg. (EU) No. 540/2011 and is therefore acceptable. The important issue seems to be that the specification is covered by the current reference specification to ensure that there are no unacceptable effects comparing to the evaluated reference source. However, in case the applicant provides additional data, these could be included in a revised RAR, provided that this is allowed from a procedural point of view.	See open point 1(1) in RT for Vol.4 general information To increase the minimum purity and decrease the impurities specification would mean to have individual specifications for all technical materials. It should be noted that the proposal is to set one reference specification, independent from the synthesis pathway.

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			Concerning the second part of the French comment, unfortunately the comment is unclear. In Volume 4 the information with respect to the salts, it is clearly stated that these are regarded as "additional data".	
1(4)	Vol. 4, C.1.2.4 Comparison of the analytical profile of batches - Toxicological evaluation of specification (2013):	RMS: *The applicant provided no information/data, which would allow to judge whether the impurities are relevant. The applicant provided no evaluation, whether the material used in toxicological studies is representative for the proposed specification* *Based on the available studies which were submitted for the renewal of glyphosate, a conclusion on the equivalence of the Wynca source cannot be made.* WYC: Additional data/information will be submitted which allow judging whether the impurities are of toxicological relevance or not with regard to the impurities of the reference source. Furthermore, the applicant will provide data/information demonstrating that the material used in toxicological studies is	GTF: A general statement for reference specification will be provided from MON as lead of the GTF RMS: In case the applicant provides additional data, these could be included in a revised RAR, provided that this is allowed from a procedural point of view. Based on the data submitted until now, relevance of impurities cannot be evaluated. Based on the data submitted until now, it cannot be evaluated, whether the material used in toxicological studies is representative for the proposed specification or the reference specification.	Data requirement: Applicant Wynca to submit data/information concerning the assessment of toxicological relevance of the impurities and data/information demonstrating that the material used in toxicological studies is representative for the proposed specification

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		representative for the proposed specification.		
1(5)	Vol. 4, C.1.3-4 Methods of analysis for the determination of impurities- Validation data for the determination of the [redacted]9	RMS: *The method is not acceptably validated, but can be used to confirm the results for the determination of the* [redacted]. WYC: Other acceptable methods have already been provided. As there are other methods provided for the determination of [redacted], no further action is needed	RMS: Comment noted.	Addressed.

Comments on the addendum of September 2015 for glyphosate

1. Exposure data

No.	Subject	Discussion Written Procedure	EFSA's conclusion
1	1.4.1	UK (SB): I agree with RMS that data from supervised trials at maximum application rates results in much more conservative scenarios compared to the monitoring studies considered by IARC.	Noted.
1.2		UK (LMC): no comments.	-
1.3	Glyphosate Addendum 1 to RAR: 1. Exposure data	SE: No essential comments at this time.	-
1.4		BE: No comments.	-
1.5		FR: No comment.	-
1.6		ES: No comment.	-
1.7		EFSA: No comments.	-
1.8	1 Exposure Data 1.3 Measurement and analysis	IE: Thank you for your addendum for glyphosate. IE: Method validation is an essential prerequisite to accurate exposure determination. The omission of the 40 RAR volume 3 studies and dependence on 16 public domain studies demonstrating partial method validation is worrying. Can DE describe the elements of validation missing from the public domain studies?	Addressed: The weaknesses of the validation methods in the public domain are noted. RMS to consider the elements of validation methods missing from the public domain in an amended addendum 1 to the RAR, if available, this action is needed according to SANCO/10190/2013-rev.1.
1.9	1.4.1.1 Occupational exposure	IE: There are significant flaws in the occupational and para-occupational studies cited in the IARC report for example Centre de Toxicologie du Québec, 1988, does not describe either the product used or the rate of application; Jauhiainen et al., 1991, only found 2 air values above 1.25 µg/m^3 and was limited to 5 operators; Johnson et al., 2005, shows air concentrations 1000 times more than the air samplers calibrated range "mg rather than µg ranges". In the Curwin et al., 2007 study, product applied (1	Addressed: Exposure estimates have already been agreed during the peer review. The new information does not invalidate the previously agreed assessment. The weaknesses of the referred occupational and para-occupational

No.	Subject	Discussion Written Procedure	EFSA's conclusion
		of 7 various pesticides was used), application rate and application rate were omitted. Also in the Acquavella et al., 2004 study product and application rate not clearly stated. It would appear that none of the cited occupational exposure studies comply with OECD guidance. Can DE comment on this? In addition it is suggested that even accepting the outcomes of the aforementioned deficient studies exposure values were not in excess of those predicted by the German exposure model used in the RAR. Can DE comment on the exposure predicted by the new EFSA OpEx model?	studies are noted.

2. Studies of cancer in humans

No.	Subject	Discussion Written Procedure	EFSA's conclusion
2.1	Introduction	UK (SB): I agree with the limitations of the epi studies highlighted in the second paragraph.	See expert's consultation in 2.7.
2.2	Introduction	UK (ID): It would be useful if the document included a brief introduction to epidemiology clarifying that it is not just the headline OR/RR that is important but also the 95% CI range.	Addressed: RMS to consider adding a brief introduction to epidemiology clarifying the importance of the 95% CI range in an amended addendum 1 to the RAR, this action is needed according to SANCO/10190/2013-rev.1.
2.3	Cohort studies	UK (SB): It is evident that the cohort studies show no increased risk of any tumour type. It would be helpful to add that where the risk estimate is >1 but the lower C.I. is below 1, the increased association is not statistically	Experts consultation: MSs experts to discuss the evidence of association of glyphosate to

No.	Subject	Discussion Written Procedure	EFSA's conclusion
		significant.	carcinogenicity in cohort studies, in particular multiple myeloma, in an experts meeting. See also comments 2.9, 2.10
2.4	Case-control studies on NHL	UK (SB): I agree with the conclusions of the RMS that due to a number of limitations (low power, glyphosate or glyphosate formulation), very few studies show marginally increased ORs. In addition, in many studies, these ORs were not statistically significant.	Experts consultation: MSs experts to review the evidence of association of glyphosate to non-Hodgkin lymphoma (NHL), in an experts meeting. See also 2.6, 2.11, 2.13, 2.14, 2.19
2.5	Table 2.3-1	UK (ID): In the conclusion for Carreon et al, 2005 it is unclear why the risk is reduced. As the CI range extends around 1.0 we consider the conclusion should be no increased risk, as is given for studies with similar CI ranges.	Experts consultation: MSs experts to discuss the evidence of association of glyphosate to carcinogenicity in other cancer sites (gliomas) in an experts meeting.
2.6	Meta-analysis	UK (SB): A meta-risk ratio of 1.3 (CI 1.03-1.65) for NHL on the basis of 6 studies appears rather weak. It is impossible to exclude that it is due to chance.	See experts consultation in 2.4
2.7	Co-formulants	UK (SB): I agree with the RMS that IARC has not taken into account the role that co-formulants play in the toxicity of glyphosate and the PPPs containing them.	Experts consultation: MSs experts to discuss the evidence of association of glyphosate to carcinogenicity in meta-analysis studies and the overall evidence from epidemiological studies in an experts meeting.

No.	Subject	Discussion Written Procedure	EFSA's conclusion
			See also 2.1, 2.8, 2.12, 2.15, 2.16, 2.17, 2.18, 2.19, 2.20, 2.21, 2.22, 5.1
2.8	Conclusion on human data	UK (SB): I agree with IARC and the RMS that the only possible conclusion is "limited evidence of carcinogenicity in humans" as causality has not been established and the findings could be due to chance, bias or confounding. Given the very weak, inconsistent (across studies) and in most cases non-statistically significant associations reported, it would have been useful for IARC to have performed an analysis of causality according to the Bradford-Hill criteria.	See experts consultation in 2.7
2.9	Addendum 2.1., Cohort studies – De Roos 2005a	UK (LMC): Agree that there is limited power for the analysis of myeloma although there is a suggestion of a trend, increasing risk with increasing exposure.	See experts consultation in 2.3
2.10	Addendum 2.1., Cohort studies – Sorahan 2015	UK (LMC): The re-analysis still seems to show suggestion of a trend of increased risk of multiple myeloma with increasing exposure, regardless of dataset used. There is very little power with so few cases of multiple myeloma, particularly when split into categories of exposure.	See experts consultation in 2.3
2.11	Addendum 2.4., meta-analysis	UK (LMC): Case-control studies, while potentially affected by recall, have the benefit of being focussed on specific causes of death and comparing the exposures experienced by the cases to that of the controls. The inclusion of the Hardell study in the meta-analysis will have inflated the resulting RR as this study found the highest RR of all included in the meta-analysis, but also had the widest confidence interval, as there were only 8 cases and controls who had glyphosate exposure.	See experts consultation in 2.4
2.12	Addendum 2.5.2., Conclusions on the classification of the evidence	UK (LMC): Overall there is limited evidence of carcinogenicity of glyphosate in humans – where there is a suggestion of an association the cohort studies have limited power to conclude a statistically significant relationship/trend.	See experts consultation in 2.7

No.	Subject	Discussion Written Procedure	EFSA's conclusion
	relevant to carcinogenicity	There is mixed evidence from the case-control studies.	
2.13	Table 2.2-2, De Roos et al., 2003, p18	BE: It is not very transparent why the study authors considered the result from hierarchical regression model (providing more conservative estimates than logistic regression, according to IARC) as significant, with an OR 1.6, 95% CI 0.9-2.8. Moreover, it is stated that the description of the study design, analysis and results do not allow assessing methodological quality.	See experts consultation in 2.4
2.14	Table 2.2-2, De Roos et al., 2005, p19	BE: It is unclear why the much bigger study of the prospective AHS cohort was not given a higher weight in the overall assessment of the possible association between glyphosate use and NHL.	See experts consultation in 2.4
2.15	2.5.2 Conclusions on the classification… (p26)	BE: As regards the choice in categories, some doubts remain, and this should be discussed. It seems that classification as "Inadequate evidence of carcinogenicity…" is also defendable. It is agreed that 4 epidemiological studies on 16 are of acceptable quality/power, but overall, the results are far from consistent. On the other hand, stating that there is "limited evidence of carcinogenicity…for which a causal interpretation is considered credible…" is not entirely supported by the facts as well. RMS is right in clarifying that it is a matter of expressing the remaining uncertainty, and it seems that the choice was merely driven by the precautionary principle.	See experts consultation in 2.7
2.16	2.5.2 Conclusions on the classification… (p27)	BE: concurs with RMS that there could be a problem with the formulation. Since epidemiological data are by definition collected on people who have been in contact with the product and not with the pure a.s. itself, BE re-iterates its request to adopt an EU position in banning suspicious coformulants with glyphosate.	See experts consultation in 2.7
2.17	Glyphosate Addendum 1 to RAR: 2. Studies of cancer in	SE: We note that the RMS "adopts a more cautious view since no consistent positive association was observed, and the most powerful study showed no effect. The IARC interpretation is more precautionary. It was also noted that	See experts consultation in 2.7

No.	Subject	Discussion Written Procedure	EFSA's conclusion
	humans	in the epidemiological studies a differentiation between the effects of glyphosate and the co-formulants is not possible." It should be noted that the IARC and the CLP criteria for sufficient and limited evidence of cancer in humans are virtually identical, and still the RMS and IARC assessments differ. We believe that the IARC conclusion is admittedly precautionary but still feasible. Furthermore, we agree to the RMS conclusion that a differentiation between the effects of glyphosate and the co-formulants is not possible adding further uncertainty to the assessment of glyphosate. We would also like to underline that the final harmonised classification of substances as regards carcinogenicity and other endpoints is decided by the Commission after a RAC Opinion that would include an assessment of the evidence of cancer in humans.	
2.18	2.Studies of cancer in humans	FR: FR agrees that it is difficult to use the results of epidemiological studies in order to demonstrate or not a carcinogenicity potential for glyphosate. In addition, based on the available human data, FR agrees that it is not possible to make a difference between the effects of the active substance and the coformulants.	See experts consultation in 2.7
2.19	2. Studies of cancer in humans	ES: We agree with the RMS in highlighting the limitations of the epidemiological studies: multiple exposure, low power, very few studies show marginally increased ORs (not always statistically significant), quality criteria not always detailed, literature search and delection of literature done for IARC not described in detail, internal validity not assess due to limitations in the reporting of the study. No measures from biomarkers from the blood are used (Exposure measured through interviews or questionnaires), the number of cases involved and no knowledge of glyphosate or the type of glyphosate formulate used.	See experts consultation in 2.4 and 2.7

No.	Subject	Discussion Written Procedure	EFSA's conclusion
		It is noteworthy that the most powerful study, the AHS (Agricultural Health Study), the prospective cohort-study, which in epidemiological terms is best suited to study the relationship showed no association with cancer incidence. This study should be given a higher weight in the overall assessment of the possible association between glyphosate use and NHL (non-Hodgkin lymphoma). We agree with the RMS that in the epidemiological studies a differentiation between the effects of glyphosate and the co-formulants is not possible. Therefore, it is difficult to use the results of epidemiological studies to demonstrate a carcinogenicity potential of glyphosate, given the very weak, inconsistent (across studies) and in most cases non- statistically significant associations reported.	
2.20	Addendum 2.5.2, Conclusions on the classification of the evidence relevant to carcinogenicity from studies in humans into the IARC categories, p. 26-27	EFSA: There seems to be a consensus regarding the conclusion on epidemiological studies in classifying glyphosate in the 3rd IARC category 'limited evidence of carcinogenicity'. It is agreed that carcinogenic effects cannot be ruled out, however as most studies (including the most powerful one (the AHS prospective cohort-study) do not show a positive association of carcinogenicity with glyphosate, the relative weighting of the different studies could be further discussed.	See experts consultation in 2.7
2.21	2., Cancer in humans	IE: In cohort studies no biomarkers from the blood are used. Exposure was measured through interviews or questionnaires. We agree with DE that there is a big recall problem to judge the amount of exposure to chemicals or what substance or product was used over time. We also agree that there may be a recall biases since individuals with cancer are more likely to think about possible reasons for their cancer than healthy individuals.	See expert consultation in 2.7
2.22	2.2 Case–control studies on	IE: The 4 medium to high validity epidemiological studies McDuffie et al.	See experts consultation in 2.7

No.	Subject	Discussion Written Procedure	EFSA's conclusion
	non-Hodgkin lymphoma, multiple myeloma, and leukaemia	2001, Eriksson et al. 2008, De Roos et al. 2005, Orsi et al. 2009, seem to suffer from the problems of multiple exposures and of the possible effect of Frequently used co-formulants. Are epidemiological studies on products not always hampered by these effects? The fact that glyphosate is routinely formulated with POE-tallowamine creates difficulties as this substance is more irritant and toxic than glyphosate itself. Can DE comment on the carcinogenicity of this substance?	

3. Cancer in experimental animals

No.	Subject	Discussion Written Procedure	EFSA's conclusion
3.1	[redacted] 1983	UK (SB): The different results obtained between the original pathologist and the PWG raise a concern about the reliability of this study in CD-1 mice.	Experts consultation: MSs to discuss the carcinogenic profile in mice (renal tumours, haemangiosarcoma, malignant lymphomas) and relevance of different statistical analysis proposed in an experts meeting. See also 3.2, 3.3, 3.4, 3.10, 3.11, 3.12, 3.15, 3.16, 3.21, 3.22, 3.24
3.2	[redacted] 1993	UK (SB): It is also a concern that the same strain of mice (CD-1 mice) gives a completely different cancer profile response (renal tumours in the study above and haemangiosarcoma in this study). The reliability of the study is therefore questioned.	See experts consultation 3.1
3.3	[redacted] 2001	UK (SB): The increase in malignant lymphoma in Swiss albino mice stands against a very high background level in controls and historical controls. In	See experts consultation 3.1

No.	Subject	Discussion Written Procedure	EFSA's conclusion
		addition, it has not been reproduced in any other strain of mice (or in rats) questioning its relevance to human cancer hazard.	
3.4	Table 3-4 and elsewhere	UK (ID): We would question the suitability of relying on a trend test where the incidence in controls is zero and the only group responding, with no pairwise significance, is the top dose group. The trend test gives an extreme response e.g. compare the p values for Sugimoto and Kumar – intuitively the Kumar data could be seen as more significant due to the result at a mid-dose.	See experts consultation 3.1
3.5	[redacted] 1990	UK (SB): Regardless of statistics, the biological plausibility of the reported tumours in SD rats in this study points towards chance. The pancreas adenoma in males was increased only at the lowest dose and did not progress to carcinoma. The liver adenoma in males was increased at the top dose against a very high background in controls and did not progress to carcinoma. The thyroid C-cell adenoma in females showed a very flat response and did not progress to carcinoma.	Experts consultation: MSs experts to discuss the carcinogenic profile observed in rats in an experts meeting. See also 3.13, 2.23, 3.24
3.6	Overall conclusions	UK (SB): With so many studies (6 in the mouse and 10 in the rat), consistency and reproducibility are very important factors to take into account in making a decision. The overall WoE indicates that there is no unequivocal evidence of carcinogenicity in animals. Therefore, I agree with the conclusions of the RMS and I disagree with the conclusions of IARC.	Experts consultation: MSs experts to discuss the overall weight of evidence and need for classification according to CLP regarding the carcinogenic profile of glyphosate in an experts meeting. See also 3.9, 3.12, 3.14, 3.15, 3.17, 3.18, 3.19, 3.20, 3.23, 3.24, 5.2, 5.3, 5.4
3.7		UK (ID): The document does not mention the extensive discussions at the PRAPeR meeting where the conclusion of the experts based mainly on the animal data was no classification for cancer. We feel this would be a useful	Addressed: RMS to consider adding details on the discussion held on the carcinogenic

No.	Subject	Discussion Written Procedure	EFSA's conclusion
		addition.	potential of glyphosate in the pesticides peer review meeting PPR 125 in an amended addendum 1 to the RAR.
3.8	Animal studies in rats: minor remark	BE: Table 3.1, p33: [redacted] 1981 study: results 3rd column combined adenoma or carcinoma incidence, correct typos (4,4,4,2%)	Addressed: RMS to correct typos in Table 3.1, 3rd column of [redacted] 1981, p. 33, in an amended addendum 1 to the RAR, this action is needed according to SANCO/10190/2013-rev.1.
3.9	Animal studies in mice and rats: general observation	BE: it is obvious that the overall evaluation by RMS and IARC cannot be the same, since a number of studies in the EU-dossier were not available for the IARC workgroup. An overall assessment is in this case justified to put into perspective the observed (non-statistically significant) elevated tumour incidences at the top-doses.	See experts consultation in 3.6
3.10	Table 3-1 (p29), mouse studies: renal tumours ([redacted] 1983)	BE: it is observed that only in one mouse study, both renal tubule adenoma and carcinoma appear at a higher incidence at the top-dose. The increase is not statistically significant (n.s.s.), and is only flagged positive by IARC because of the borderline significant trend test. Although it is observed that there are marginal increases of adenoma but not carcinoma at the top-doses of two other studies ([redacted] 1997 and [redacted] 2001), it seems debatable, in the absence of renal findings in the other mouse studies, if the renal findings are sufficient to classify for carcinogenicity.	See experts consultation in 3.1
3.11	Table 3-1 (p29), mouse studies: haemangiosarcoma ([redacted] 1993)	BE: increased incidence at top-dose (1000 mkd) considered spurious, in the absence of the same finding in the other mouse studies (except 2 cases in the Sugimoto study at the top-dose). If really compound-related, it is unlikely that the same tumour would not have been detected at higher incidence in the studies in CD-1 mice with top-doses >4000 mkd.	See experts consultation in 3.1

No.	Subject	Discussion Written Procedure	EFSA's conclusion
3.12	Table 3.6-3.9 (p38-39), mouse studies: malignant lymphoma ; conclusion p44	BE: Except for the [redacted] 2001 study, the slightly elevated incidences of lymphoma in ♂at the top-doses are either within HCD, or display poor dose-response. For the study on Swiss Albino (2001), the rationale on the basis of known high spontaneous background levels in this strain by the RMS is supported. Although the top-dose lymphoma findings in 3/5 mouse studies (where trend-tests or pair-wise comparisons were significant) are the most consistent among the observed malignancies in the mouse, the overall weight of evidence would indicate that it is equivocal for classification.	See experts consultation in 3.1 and 3.6
3.13	Table 3-2 (p31), rat studies: pancreas, liver, C-cell tumours ([redacted], 1990)	BE: Pancreas: there is definitely no proper dose-response (5,18,10,15% in ♂; 8,2,7,0% in ♀), and no carcinoma. In two other rat studies, the combined incidences also show no dose-response, or are absent. Overall, pancreatic lesions do not trigger any classification. Liver: only trend in increased adenoma (11,9,8,19%), with a poor dose response, and no carcinoma. C-cell adenoma: slight trend: 3,3,10,10%, but without progression to carcinoma.	See experts consultation in 3.5
3.14	Conclusions p44	BE: In this DAR, RMS has well elucidated the possible causes of a different classification outcome between the EU and IARC. It was unfortunate that IARC did not take into account 3 guideline studies in both mice and rats, since this could have put the overall conclusions in another perspective. Next, relying on significant trends to declare a finding eligible for classification is a policy decision not supported by the EU. Further, CLP-criteria such as spontaneous incidence and excessive toxicity confounders are key elements in the discussion by the RMS, and supported. One important point, perhaps under stressed, is the consistency of outcome, which is poor among the various studies. Finally, IARC's decision is also influenced by its opinion on glyphosate being genotoxic, inducing oxidative stress and –to a lesser extend- receptor-mediated effects, influencing cell proliferation/death, or affect the immune system. Since the first two key mechanisms are considered unproven, at	See experts consultation in 3.6

No.	Subject	Discussion Written Procedure	EFSA's conclusion
		least for the a.s., these may not increase the level of concern as regards the carcinogenic outcome of glyphosate.	
3.15	Glyphosate Addendum 1 to RAR: 3. Studies of cancer in experimental animals	SE: We note that IARC and the RMS have diverging assessments regarding kidney tumours in male CD-1 and Swiss mice, haemangiosarcoma in male CD-1 mice, liver cell adenoma in male SD rats and thyroid C-cell adenoma in female SD rats and malignant lymphoma in CD-1 mice. In these studies statistical analysis with the Cochran-Armitage trend test yielded a significant result, whereas the analysis by pair-wise comparisons indicated no statistically significant differences. It is generally believed that trend tests are more sensitive than e.g. pair-wise comparison methods and from a precautionary assessment point of view trend tests would be preferable. In our view the evidence for carcinogenicity in experimental animals is at least limited as compared to the IARC and CLP criteria. We don´t believe that reference to historical control data can abrogate the positive results from the trend tests. Possibly, the high doses and resulting toxicity may have influenced the tumour outcome in the high dose groups in some of the rodent studies. It should be noted that the IARC and the CLP criteria for sufficient and limited evidence of cancer in experimental animals are virtually identical, and still the RMS and IARC assessments differ. We agree that the diverging assessments are mainly due to differences in the choice of statistical assessment methods. As above we like to underline that the final harmonised classification of substances as regards carcinogenicity and other endpoints is decided by the Commission after a RAC Opinion that would include an assessment of the evidence of cancer in experimental animals.	See experts consultation in 3.6

No.	Subject	Discussion Written Procedure	EFSA's conclusion
3.16	Addendum 1 to RAR., Cancer in experimental animals, table 3-1	NO: Due to the application of different statistical approaches selected for the evaluation, IARC and RMS came to diverging conclusions. Why does the RMS consider the statistical evaluation provided with the study reports as more appropriate than the trend test used by IARC? According to the OECD guidance document on the conduct and design of chronic toxicity and carcinogenicity studies, significance in either kind of test is sufficient to reject the hypothesis that chance accounts for the result.	See experts consultation in 3.1
3.17	Addendum 1 to RAR., Cancer in experimental animals, point iii) differences in decision criteria, page 42	NO: It is stated on page 42 in the addendum that "Since no consistent significant increase in any of the tumour types was originally reported in the available studies, the apparent effects were not considered sufficient for classification in the RAR." However, we are of the opinion that effects do not necessarily have to appear in a consistent dose-dependent manner, in order to be considered as a treatment-related effect.	See experts consultation in 3.6
3.18	Addendum 1 to RAR., Cancer in experimental animals, point iii) differences in decision criteria, additional criteria CLP, page 43	NO: As stated in the addendum, the RMS has also taken into account additional criteria when evaluating the carcinogenic effects. To what extent should these additional criteria and the listed factors which may be taken into consideration, determine the conclusion with respect to a potential carcinogenic effect. In our opinion, too much weight is given to the factors "progression of lesions to malignancy" as well as "whether responses are in single or both sexes". This will for instance implicate that studies, in which a treatment-dependent increase in adenomas in male rats is demonstrated, will not be taken into consideration when evaluating the carcinogenic potential.	See experts consultation in 3.6
3.19	3. Cancer in experimental animals	FR: FR agrees with RMS that a weight of evidence approach, based on all available carcinogenicity studies, has to be adopted. Based on the RMS analysis, the active substance glyphosate does not satisfy the CLP criteria for carcinogenicity classification.	See experts consultation in 3.6

No.	Subject	Discussion Written Procedure	EFSA's conclusion
3.20	Cancer in experimental animals	ES: We agree with the RMS that the large volume of animal data for glyphosate should be evaluated using a weight approach. It should be avoided to base any conclusion only on the statistical significance of an increased tumour incidence identified in a single study, without consideration of biological significance of the finding. In most cases tumours incidence were not statistically significant, no dose dependent and within the range of historical controls. Confounding effect of excessive toxicity cannot be excluded and be the cause of the increased incidence of tumours at the highest dose in life time studies. Consistency and reproducibility are very important factors to take into account in making a decision. Thus, based on the data from six carcinogenicity studies in mice and ten chronic toxicity and carcinogenicity in rats, the weight of evidence suggest that no hazard classification for carcinogenicity is warranted for glyphosate according to the CLP criteria.	See experts consultation in 3.6
3.21	Addendum 3, Cancer in experimental animals, summary and conclusion, pp. 28-44	EFSA: The statistical analysis methods should be discussed considering that, according to the OECD 451 guideline for carcinogenicity studies, "the statistical method most appropriate for the analysis of results, given the experimental design and objectives, should be established before commencing the study".	See experts consultation in 3.1
3.22	Addendum 3, Cancer in experimental animals, summary and conclusion, pp. 29-31 Addendum 5.3, animals carcinogenicity data, pp. 89-91 and Table 5.3-1	EFSA: In mice positive trends reported in the IARC assessment: renal tubular adenoma and carcinoma [redacted], 1983), haemangiosarcomas ([redacted] 1993) and malignant lymphomas ([redacted] 2001 -already discussed during the expert's meeting 125 in February 2015) are limited to high dose levels ≥ 1000 mg/kg bw per day; the background incidence and biological relevance of the findings should be discussed further.	See experts consultation in 3.1
3.23	Addendum 3, Cancer in experimental animals, summary and conclusion,	EFSA: In rats, positive trends in adenomas are noted in one out of nine valid studies ([redacted] 1990). While there is no clear dose-response relationship in the incidence of pancreatic islet-cell adenomas, liver cell and	See experts consultation in 3.5 and 3.6

No.	Subject	Discussion Written Procedure	EFSA's conclusion
	pp. 32-34	thyroid C-cell adenomas appear at high dose levels around the limit dose of 1000 mg/kg bw per day. These findings should be discussed in line with the CLP criteria.	
3.24	3., Cancer in experimental animals	IE. It appears that 14 acceptable animal carcinogenicity studies (5 mouse and 9 rat) were available for evaluation. IARC have considered 2 of the 5 mouse studies and 6 of the 9 rat studies. Using trend analysis IARC has concluded that there is a positive trend to carcinoma in the mouse and adenoma in the rat. In the rat IARC agree with the DE evaluation of the other 5 studies indicating no concern regarding carcinogenicity. In the rat IARCs failure to evaluate the 3 other studies is not helpful. Compiling the rat data (as evaluated by IARC) we note 5 negative studies and 1 that shows a trend for c Cell adenomas of the thyroid (it is noted in the IARC monograph that there was no apparent progression to carcinoma). We do not consider the aforementioned data sufficient for classification as carcinogenic under CLP criteria. Furthermore, inclusion of the 3 other rat studies not evaluated by IARC adds further weight to this conclusion. In the mouse IARC have noted a positive trend for renal tubule adenoma and carcinoma in 1 study ([redacted], 1983) and a positive trend for haemangiosarcoma in another. DE evaluated 3 other mouse studies of those 2 [redacted] 1997 and [redacted] 2001 showed a positive trend for renal tubular adenomas in mice. We note that doses of 4000-5000 mg/kg bw day were administered in 2 of the studies with 1460mg being the top dose in the 3rd. Again, using the IARC data alone it is difficult to justify a classification for carcinogenicity. There is no pattern of tumours in the studies and the doses are excessive. However, the renal tubular adenomas in the other mouse studies may require further investigation. Can DE comment? Generally it would appear that the use of trend analysis rather than other statistical tools has led to different findings in 3 of the 14 studies. These	See experts consultation in 3.1, 3.5 and 3.6

No.	Subject	Discussion Written Procedure	EFSA's conclusion
		statistical differences are pivotal to the disparity of conclusions drawn by IARC and DE. Can DE comment on the differences in the 2 statistical methods used? The omission by IARC of the findings of 6 reliable studies has a significant bearing on the conclusions drawn. Were these studies available to IARC? It is not clear what historical controls IARC referenced. They do not appear to be date or test house specific but from the open literature. Can DE comment on this?	

4. Mechanistic and other relevant data

No.	Subject	Discussion Written Procedure	EFSA's conclusion
4.1	Genotoxicity	UK (SB): The conclusion of IARC on genotoxicity is simply wrong. The in vitro and in vivo WoE shows that glyphosate is not genotoxic. I also agree with the RMS that AMPA is not genotoxic in vivo. There remains an uncertainty about the genotoxicity of glyphosate-based formulation, but further genotoxicity testing of these formulations should be left a MS level at product authorisation.	Experts consultation: MSs experts to discuss the genotoxic potential of glyphosate See also 4.2, 4.6, 4.8, 4.9, 4.10, 4.11, 4.12, 4.13, 4.14, 4.15, 5.4
4.2		UK (ID): We would be cautious about placing too much reliance on results from new assay types in unusual species (e.g. Comet assay in eels), when there is no indication of a concern from standard regulatory studies.	See experts consultation in 4.1
4.3	Receptor-mediated mechanism	UK (SB): Clearly IARC was not aware of the results of the US EPA EDSP which concluded that based on Tier 1 studies and some higher tier studies, it glyphosate is not an ED. In addition, the study by Bailey (2013) confirms	Addressed: It is noted that the draft EFSA conclusion mentions a data gap for submission of

No.	Subject	Discussion Written Procedure	EFSA's conclusion
		that glyphosate is negative in both the male and female pubertal assays.	the studies available to the EPA EDSP to enable an independent assessment. See also 4.7
4.4	Oxidative stress	UK (SB): Although there are some indications in vitro of oxidative stress, the in vivo study in rats (Astiz, 2009b) shows effects that cannot be relied upon as the study was conducted by i.p. administration, By this route of exposure, the normal, physiological detoxification mechanisms of glyphosate are bypassed. On this point, I disagree with IARC and RMS that there is significant evidence that glyphosate causes adverse effects through oxidative stress. Further studies by relevant routes of exposure should be performed.	Experts consultation: MSs experts to discuss the potential mode of action of glyphosate through oxidative stress in an experts meeting. See also 4.16, 5.4
4.5	Inflammation and immunomodulation	UK (SB): I agree that there is very little evidence to conclude that glyphosate causes immunosuppression. I also agree that the endpoint has not been evaluated adequately.	Experts consultation: MSs experts to discuss the immunosuppression potential of glyphosate in an experts meeting. See also 4.17, 5.4
4.6	4.2.1 Genetic and related effects, overall conclusions (p49)	BE: concurs with RMS to conclude that, on a WoE basis, glyphosate should not be considered a genotoxic agent. This conclusion is mainly based upon established guideline studies. It was unfortunate that most of the *in-vivo* micronucleus assays submitted in the EU-dossiers were unavailable to IARC, as the result of these could have put into context the few positive published studies, which became decisive in the IARC conclusion. Inconsistent results were obtained in the published studies on indicator genotoxicity endpoints (DNA strand break, DNA adducts). In the IARC monograph, these tests are listed among the other studies on chromosome aberration, without further interpretation.	See experts consultation in 4.1

No.	Subject	Discussion Written Procedure	EFSA's conclusion
4.7	4.2.2 receptor-mediated mechanism (p68)	BE: acknowledges that some studies with some formulations had positive outcomes in mostly *in-vitro* systems targeting hormone production or activity. However, in most cases glyphosate itself was devoid of endocrine activity. Based on negative EPA EDSP Tier 1 testing, it was concluded that for glyphosate there was no convincing evidence of potential interaction with the oestrogen, androgen or thyroid pathways. RMS' conclusion that glyphosate is devoid of endocrine activity is thus supported.	See 4.3
4.8	Glyphosate Addendum 1 to RAR: 4. Mechanistic and Other Relevant Data	SE: We are concerned by the data on genotoxicity of glyphosate. Some in vitro and in vivo studies seems to suggest clastogenic effects. Possibly, a modern Comet assay in relevant target tissues such as kidney, liver and bone marrow should be undertaken. Presently, the genotoxicity data would contribute to an increased level of concern in the weight of evidence assessment of glyphosate carcinogenicity.	See experts consultation in 4.1
4.9	Addendum 1 to RAR, 4.2.1., Genetic and related effects	NO: A number of non-regulatory studies both *in vitro and in vivo* investigating glyphosates DNA damaging potential have shown positive results. We suggest that a regulatory *in vivo* mammalian alkaline comet assay (for instance, in the rat liver and kidney) should be conducted according to OECD 489.	See experts consultation in 4.1
4.10	Addendum 1 to RAR, 4.2.1 Genetic and related effects, tables 4.2-3, 4.2-4, 4.2-5 and 4.2-7	NO: It would be interesting to know which mouse strains are used in the tests for genotoxicity, since it pointed to a possible strain specific effect in mice (in the conclusion from RMS on section 3 Cancer in experimental animals on page 44).	See experts consultation in 4.1
4.11	4.2.1 Genetic and related effects/glyphosate	FR: FR agrees with the RMS that, by weight of evidence, the active substance glyphosate can be considered as devoid of genotoxic properties and that a classification for mutagenicity is not warranted according to the CLP criteria.	See experts consultation in 4.1

No.	Subject	Discussion Written Procedure	EFSA's conclusion
4.12	4.2.1 Genetic and related effects/glyphosate-based formulations	FR: FR agrees with the RMS that based on the results of published data, no firm conclusions can be drawn on the genotoxic potential of the formulations.	See experts consultation in 4.1
4.13	4.2.1 Genetic and related effects/glyphosate	ES: The *in vitro* and *in vivo* studies show that glyphosate is not genotoxic. A classification for mutagenicity is not warranted according to the CLP criteria.	See experts consultation in 4.1
4.14	4.2.1 Genetic and related effects/glyphosate-based formulations	ES: There remains an uncertainty about the genotoxicity (comet assay) of glyphosate-based formulation.	See experts consultation in 4.1
4.15	Addendum 4.2.1, genotoxicity	EFSA: A critical difference between the IARC monograph and the RAR relates to the genotoxic potential of glyphosate. It should be confirmed by the experts that the few positive results (*in vitro* DNA damage and *in vivo* tests) in the database can be reliably discounted by the (numerous) negative results.	See experts consultation in 4.1
4.16	Addendum 4.2.3.1, oxidative stress, pp. 74-79	EFSA: indications of the occurrence of oxidative stress have been observed in one *in vivo* study in combination with cytotoxic/degenerative effects upon intraperitoneal injections to male rats (Astiz *et al*. 2009b). A parallel could be established with slightly increased tumour incidence in some studies at high dose levels.	See experts consultation in 4.4
4.17	Addendum 4.2.3.2, Inflammation and immunomodulation, p. 79-82	EFSA: as the evidence from the available data on immunosuppression is insufficient to conclude on the immunomodulatory action of glyphosate, it should be discussed whether a concern remains that should be addressed regarding this endpoint.	See experts consultation in 4.5
4.18		IE Not comments	-

5. Summary of data reported

No.	Subject	Discussion Written Procedure	EFSA's conclusion
5.1	Human data	UK (SB): I agree with IARC and the RMS that the only possible conclusion is "limited evidence of carcinogenicity in humans" as causality has not been established and the findings could be due to chance, bias or confounding.	See experts consultation in 2.7
5.2	Animal data	UK (SB): With so many studies (6 in the mouse and 10 in the rat), consistency and reproducibility are very important factors to take into account in making a decision. The overall WoE indicates that there is no unequivocal (sufficient) evidence of carcinogenicity in animals. Therefore, I agree with the conclusions of the RMS and I disagree with the conclusions of IARC.	See experts consultation in 3.6
5.3		UK (ID): Additional discussion could be useful on the fact that there are no reports of renal or pancreatic tumours in the epidemiology versus the animal findings. In addition the lack of consistency within the animal studies, and within the epidemiology, could be brought out further. Table 5.3-1 is excellent in displaying the variability between similar studies.	See experts consultation in 3.6
5.4	Mechanistic data	UK (SB): I agree with RMS that the in vitro and in vivo WoE shows that glyphosate is not genotoxic. Recent evidence shows that glyphosate is not an ED. I disagree with IARC and RMS that there is significant evidence that glyphosate causes adverse effects through oxidative stress. I agree that there is very little evidence to conclude that glyphosate causes immunosuppression. Overall, there is insufficient animal, human and mechanistic data to support the conclusion that glyphosate is carcinogenic.	See experts consultation in 3.6, 4.1, 4.4 and 4.5

No.	Subject	Discussion Written Procedure	EFSA's conclusion
5.5	5.5 further conclusions and recommendations	BE: based upon the many uncertainties regarding key genotoxicity endpoints, some formulations of glyphosate should be further investigated in the frame of the re-registration at zonal level.	Noted: EFSA agrees that this is an important issue to be considered further. However it is not under the remit of the current assessment and should be discussed in the appropriate forum. See also 5.6, 5.7 and 5.8
5.6	Further considerations and recommendations	DK: Given the documentation and assessment provided for glyphosate and products containing glyphosate we support the recommendation to require data on genotoxicity for the products. In general we recommend that given the current situation where data and evaluations of data are lacking for the vast majority of coformulants, and the implementation of article 27 of regulation 1107/2009 is outstanding, the Commission should urgently initiate the work to establish a negative list for co-formulants and develop criteria and guidance for this area.	See 5.5
5.7	5.5 Further conclusions and recommendations	FR: In view of the positive results observed in non-regulatory genotoxicity assays conducted with the representative formulation, the RMS concluded that no firm conclusions can be drawn on the genotoxic potential of the formulations. Moreover the RMS recommends *"further genotoxicity studies (…) for the representative formulation as confirmatory information for the authorisation of plant protection products*". In that case, considering uncertainties about the genotoxicity of the representative formulation, would it be possible to identify a safe use in the context of the renewal of approval of glyphosate?	Noted: It is noted that toxicity alerts have been found regarding the tallowamine co-formulant, however no such alert have been identified for the co-formulants included in the representative formulation under peer review. See also 5.5
5.8	5.5 Further conclusions and recommendations	ES: Based on the results of published data, no firm conclusions can be drawn on the genotoxic potential of the formulations. Further genotoxicity testing of these formulations should be left at MS level at product	See 5.5

No.	Subject	Discussion Written Procedure	EFSA's conclusion
		authorisation as confirmatory information for the authorisation of plant protection products.	
5.9		EFSA: see comments in sections 2, 3, 4	-
5.10		IE Not comments	-

6. Other comments

No.	Subject	Discussion Written Procedure	EFSA's conclusion
6.1	General	UK (SB, ID): We would like to thank the DE RMS for the addendum and the analysis provided. It is well structured, extremely thorough and of outstanding quality.	Noted.
6.2	General	DK: We would like to echo the comment of UK on the excellent quality of the addendum. On the specific evaluations and conclusion we will address this at the expert meeting	Noted.
6.3	General comment	FR: France acknowledges the good quality of the scientific analysis and the huge work provided by Germany on the IARC conclusions.	Noted.
6.4	General comment	ES: Spain thanks the thorough analysis provided by Germany.	Noted.
6.5		BE: No further comments	-
6.6	General	EFSA: The considerable amount of work invested by DE in the production of the addendum (in much reduced timelines) is highly appreciated, thank you.	Noted.
6.7		IE No comments	-

PEER REVIEW REPORT ON **GLYPHOSATE** OCTOBER 2015

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27.02.2015	Pesticides Peer Review expert meeting 125	Mammalian Toxicology
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05.03.2015	Pesticides Peer Review expert meeting 128	Ecotoxicology
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REPORT OF PESTICIDES PEER REVIEW MEETING 126

GLYPHOSATE

Rapporteur Member State: DE

Specific comments on the active substance in the section

4. Environmental Fate and Behaviour

are already listed in the relevant reporting table. Comments submitted for this meeting are listed below.

1. Comments submitted for this meeting:

Date	Supplier	File Name
None.		

2. Documents submitted for meeting:

Date	Supplier	File Name
29.01.2015	DE	Glyphosate_evaluation table_AIR II_section_4_2015-01_29.doc
29.01.2015	DE	Glyphosate_RAR_12_LoEP_CA-CP_rev 2015-01_29.docx
14.07.2014	DE	Glyphosate_reporting table_rev 0__2014-07-14.doc
25.07.2014	DE	Glyphosate reporting table_public consultation.doc
29.01.2015	DE	Glyphosate_RAR_01_Volume1_2015-01_29.docx
10.02.2015	DE	Glyphosate_RAR_10_Volume3CA-CP_B-8_2015-02-10.docx
29.01.2015	DE	Glyphosate_RAR_22_Volume4_all applicants_2015-01-29.doc (Representing all individually submitted files)

3. Documents tabled at the meeting:

Date	Supplier	File Name
None.		

Appendix 1: Discussion table: GLYPHOSATE

Appendix 1: Discussion Table, Glyphosate

4. Environmental Fate and Behaviour

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
Experts' consultation 4.1 Member state experts to discuss the field dataset and kinetic fitting for glyphosate and AMPA and agree the way to interpret AMPA dissipation rates from experiments where no decline of AMPA is observed. See reporting table 4(37)	**Background** **RT 4(37)** Vol 3. B.8.1.2.2 Field studies. Table B.8.1-101 AMPA in Shultz 1992. Dar PP 131-152 **EFSA**: If visual fitting suggest AMPA to be persistent in this field a default DT50 = 1000 may need to be incorporated to the data set, even if the calculated fitted parameters are not statistically reliable to avoid the bias towards more favourable situations. **RMS**: The observed residues of AMPA will be the result of similar formation and degradation of AMPA during the shorter study duration. Above all it was shown in the study of Hill 1992 that AMPA is degrading with half-lives between 284 and 633 d. The study period in Shultz is too short to derive reliable half-lives compared with the study of Hill, in which a similar residue situation at corresponding sample points like in Shultz 1992 was observed. The default values of 1000 d would lead to an overestimation of the persistence of AMPA in the field. This approach is supported by results of laboratory studies, which show clear biological degradation with maximum half-life of 301 d for AMPA. According to experience studies with the metabolite as parent result in significant lower half lives of metabolites compared with half-lives from degradation studies with parent. Therefore the approach of RMS in the RAR should be assessed as conservative. 5 field studies with 10 soils were conducted in Europe. For 8 soils a persistent endpoint for glyphosate could be derived. For 5 soils (Hill, 1992) a pathway fit could be conducted for AMPA (DT_{50} = 282 - 633 d) showing that AMPA is degrading in field (sufficiently large dataset). For 2 soils no pathway fit could be conducted for AMPA because no reliable kinetic model could be obtained for the parent compound. For 1 soil (Buchen soil, Hill, 1992) no acceptable fit could be obtained due to strong data scattering in the decline phase.	The experts agreed with the evaluation and endpoint selection of the RMS.

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
	For 2 soils (Dietgen soil and Menslage soil, Schulz, 1992) no acceptable fit was achieved due to a poor fit of the decline phase which is represented by the last two data points only, this could be due to the continuous replenishment of AMPA from the degradation of glyphosate so that the decline phase of AMPA was not reached during the study period. This is supported by study of Hill 1992 with longer study duration where AMPA has been degraded with half-lives between 284 and 633 d. The results of laboratory studies (max DT_{50} = 301 d) clearly show biological degradation of AMPA in soil. RMS conclusion: To use a default of 1000 d for degradation of AMPA would lead to an overestimation of the persistence in field. Experts agreed with the conclusions of the RMS that with this dataset, taking account of all the available information it would not be appropriate to allocate default DT_{50} of 1000 days to the trial sites where sampling was of a shorter duration and decline was not apparent, due to the studies having been terminated sooner than would have been ideal in relation to following the fate of AMPA. The long sampling intervals between ca. 60 and 200 days in the Schulz experiments also contribute to the inability to derive decline endpoints for AMPA.	
Experts' consultation 4.2 Member state experts to discuss the batch adsorption results where calculated 1/n values were <0.7. Experts to conclude on which of the following options to follow with this data set. Should the lower than 1/n	**Background** In the RAR the RMS proposed to use 1/n default values of 0.9 in cases where no reliable 1/n value could be derived in the study and 1.0 in cases where no investigations of the relationship between soil solution concentration and adsorption behaviour were conducted in the study. Reference is made to: ´Clarification note from EFSA concerning data requirements, study guideline, guidance and consensus of member state fate and behaviour experts on soil adsorption measurements and selection of the slope (1/n value) that describe the Freundlich coefficient´ that is included in FOCUS version control documents. The clarification note and FOCUS documents indicate that the use of 0.9 was envisaged when there are experimental difficulties (for example a labile active substance).	Open point RMS to remove the 4 adsorption results for the soils investigated in the Van Noorloos & Slangen (2001) experiment from the list of agreed endpoints. RMS to remove 3 AMPA default 0.9, 1/n values from Wittig (2002) and replace with the experimentally determined values. Finally recalculate the average KFoc and 1/n values for both glyphosate and AMPA. (adsorption section of the endpoints)

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
values be retained or should the adsorption experiments be considered unreliable and excluded or should a default 1/n of 0.9 be ascribed to soils where 1/n was <0.7? Note the same conclusion does not have to be reached for every soil, it might be dependent on the results in each batch experiment. See reporting table 4(48)	In this case the use of default 0.9 concerns the data of Table B8.2-5 (old study of Van Noorloos & Slangen) for which in three out of four soils the 1/n was < 0.7. These values replaced with 0.9. This does not seem logical. The philosophy in the clarification note is that either the 1/n values as measured should be used (when considered reliable) or the experiments should be left out due to „unrealistic/unexpected" (low) 1/n values. Besides the effect of the 1/n value selection on the modelling results, particularly on PECgw, would probably be marginal as glyphosate and AMPA are strongly adsorbing to soil particles. The RMS has revisited the Van Noorloos & Slangen and Wittig experiments assessing the reliability criteria from the OECD guideline in relation to the product of the Kd with the soil/solution ratio is > 0.3, when measurements are based on concentration decrease in the aqueous phase (indirect method), or > 0.1, when both phases are analysed (direct method). This assessment confirms that in this respect the use of the indirect method of KFoc and 1/n determination was an appropriate study design. No other reason other than possibly degradation during the equilibrium time was identified (relating to glyphosate but not AMPA) to consider these values from this study more unreliable than the other experiments in the dataset. Experts noted that in practice all the adsorption experiments available have measured the adsorption behaviour of a calcium complex of glyphosate / AMPA. This was accepted as glyphosate and AMPA are strongly adsorped and counter ions will be present in soils (though not always calcium). It was also noted that desorped glyphosate was degrading in soil solution within the equilibrium time of batch experiments, though it was noted that the Van Noorloos & Slangen experiment the equilibrium time was longer and more degradation of glyphosate was apparent. On balance the experts considered that the results of the Van Noorloos & Slangen experiments should be excluded from the dataset as the longer batch equilibrium time	Open point: In the PEC groundwater and surface water sections of the list of endpoints RMS to add footnotes indicating what the correct values for use in any future modelling would be.

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
	(compared to other investigations or investigations where soils were sterilised) meant that degradation of glyphosate that occurred during the study resulted in lower confidence in these data. It was noted that desorbed AMPA was not degrading in soil solution within the equilibrium time of batch experiments in the study Wittig. Therefore experts agreed that the Wittig KFoc results were reliable. Experts concluded that the 1/n values associated with these KFoc values should be the agreed endpoints (and not a default of 0.9). The experts agreed that no additional exposure calculations were necessary, due to the limited effect on the mean endpoints that are calculated.	

REPORT OF PESTICIDES PEER REVIEW MEETING 125

GLYPHOSATE

Rapporteur Member State: DE

Specific comments on the active substance in the section

2. Mammalian Toxicology

are already listed in the relevant reporting table. Comments submitted for this meeting are listed below.

1. Comments submitted for this meeting:

Date	Supplier	File Name
None		

2. Documents submitted for meeting:

Date	Supplier	File Name
29.01.2015	DE	Glyphosate_evaluation table_AIR II_section 2_2015-01_29.doc
29.01.2015	DE	Glyphosate_RAR_12_LoEP_CA-CP_rev 2015-01_29.docx
14.07.2014	DE	Glyphosate_reporting table_rev 0__2014-07-14.doc
25.07.2014	DE	Glyphosate reporting table_public consultation.doc
29.01.2015	DE	Glyphosate_RAR_01_Volume1_2015-01_29.docx
29.01.2015	DE	Glyphosate_RAR_08_Volume3CA-CP_B-6_2015-01-29.doc
29.01.2015	DE	Glyphosate_RAR_22_Volume4_all applicants_2015-01-29.doc (Representing all individually submitted files)

3. Documents tabled at the meeting:

Date	Supplier	File Name
None.		

Appendix 1: Discussion table: GLYPHOSATE

Appendix 1: Discussion Table, Glyphosate

2. Mammalian Toxicology

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
Experts' consultation 2.1 The developmental toxicity potential of glyphosate to be discussed in a meeting of experts. See reporting table 2(41) See also 2(27), 2(39)	**BACKGROUND** **RAR:** **Brooker, 1991:** developmental toxicity in rabbits (IIA, 5.6.11/05, pp. 646-653 of the revised RAR – January 2015) Groups of 16 - 20 time-mated female New Zealand White rabbits were administered glyphosate by gavage at dose levels of 0, 50, 150 or 450 mg/kg bw per day from Day 7 to Day 19 of pregnancy. *RMS:* The study is considered acceptable. There was a significant increase in embryonic death and post-implantation loss in treated groups compared to controls, however without a clear dose-relationship. Regarding the post-implantation loss, values for the low and high dose groups are outside the historical control range. The cardiac malformation observed with greatest frequency in this study was the interventricular septal defect. At 450 mg/kg bw per day this effect was outside the historical control range (4.2 % compared to 0.66 % in historical controls). Taken into account the high post-implantation loss at the same dose level, the incidence of additional cardiac malformation may be covered. At mid dose level foetuses with a higher incidence of retro-oesophageal right subclavian artery were reported. However, this effect has to be considered equivocal, because no clear-dose relationship could be established. The NOAEL for maternal toxicity is **50 mg/kg bw per day** based on slightly reduced feed consumption and body weight gain, and soft/liquid faeces at 150 mg/kg bw per day. The developmental NOAEL is **150 mg/kg bw per day** based on the post-implantation loss, late embryonic death and increase in cardiac malformations at 450 mg/kg bw per day. [redacted]**1993**: developmental toxicity in rabbits (IIA, 5.6.11/06, pp. 653-661 of the revised RAR – January 2015) Groups of presumed mated female New Zealand White rabbits were administered by	The majority of the experts (except NO) accepted the evaluation and the conclusion of the RMS. It was acknowledged that glyphosate is not teratogenic taking into account all available studies. The majority of experts agreed on the conclusion drawn by the RMS that glyphosate should not be classified regarding developmental toxicity.

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
	gavage, glyphosate at dose levels of 0, 20, 100 or 500 mg/kg bw per day from Day 6 to Day 18 of pregnancy. *RMS:* The study is considered supplementary due to several weaknesses including a small number of litters for examination (low pregnancy rate at all dose levels, lethality in mid and high dose dams) and reporting deficiencies. The percentage of foetuses with 'dilated heart' was significantly increased at all dose levels. However, the absolute number of affected foetuses and litters is quite small and did not show a marked difference between the treated groups. Furthermore, the diagnosis 'dilated heart' was not defined in this study report and neither criteria used to this diagnosis nor measurements of the heart were provided. The NOAEL for maternal toxicity is still considered **20 mg/kg bw per day**, because it cannot be excluded, that the intercurrent four deaths at 100 mg/kg bw per day were substance-related. The developmental NOAEL **100 mg/kg bw per day**. [redacted] **1989**: Developmental toxicity in rabbits (IIA, 5.6.11/07, pp. 662-666 of the revised RAR – January 2015) Groups of 15 New Zealand White female rabbits received doses of 0, 125, 250 and 500 mg/kg bw per day test substance by gavage from Gestation Day 6-18 after successful mating. *RMS:* The study is considered supplementary due to serious reporting deficiencies (e.g. no individual data, no statistical analysis, no uterine weights, no results of maternal necropsy). The NOAEL for maternal and developmental toxicity is **250 mg/kg bw per day** based on reduced food consumption and body weight gain at 500 mg/kg bw per day in does. Developmental effects were visible as foetolethality and several malformations (external, including abnormal tails, visceral, skeletal) at high dose levels. Total number of foetuses per litter with malformations was higher in the groups receiving the mid and high dose level, but without statistical significance. However, it remains unclear, whether statistical analysis of the data had been performed at all. Ventricular septal defects were noted in 2 out of 78 foetuses in the high dose group (control incidence 0/109). The higher number of further visceral malformations at the top dose level was due to absent kidneys and postcaval lung lobes. Because no individual data are provided it is not identifiable, whether the malformations described were confined to single foetuses or if the foetuses were	

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
	multiple malformed. Comments: - ES: In the developmental toxicity study in rabbits ([redacted] 1991), there was an increase in interventricular septal defects (4.2%), at high dose (450 mg/kg bw per day). At this dose this effect was outside the historical controls range (0.66%) and it occurs without maternal toxicity. Therefore a classification for glyphosate due to developmental toxicity should be considered. - FR: In several developmental studies in rabbit suspected occurrence of heart malformations were observed. Indeed, in the study by [redacted] (1991) cardiac malformation mainly intraventricular septal defect was observed at 450 mg/kg bw per day, highest dose tested. This heart finding was slightly outside of the historical background. Moreover, post implantation losses and late embryonic death were also observed in the high-dose group (450 mg/kg bw per day). In the study by [redacted] (1993), the percentage of foetuses with "dilated heart" was increased in the high dose group despite a low number of foetuses and litters included in the high-dose group. Moreover, in the study by [redacted] (1989), ventricular septal defects as in the study by [redacted] (1991) were also noted in the high dose group. A higher number of further visceral malformations at the top dose level were due to kidneys defects. The relevance of the heart and kidney findings observed in several studies should be discussed. - NO: [redacted] 1991a: the NOAEL for developmental toxicity in this study should be set at 50 mg/kg bw per day based on the increase in the occurrence of the retroesophageal right subclavian artery at 150 mg/kg bw per day. Based on the increase in the occurrence of the cardiovascular malformations and in the post- implantation loss in this study, glyphosate should be considered for a classification as a developmental toxicant. The developmental toxicity study in the rabbit ([redacted] 1991) shows a treatment-related increase in a variety of malformations of the heart and great vessels (interventricular septal defects, retroesophageal right subclavian artery and other malformations) at 450 mg/kg bw per day. An increase, above the historical control data, in the retroesophageal right subclavian	

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
	artery was also seen at 150 mg/kg bw per day. The increase in the occurrence of this malformation did not follow a clear dose-response. However a possible dose-response relationship for this effect may have been masked by the limited number of foetuses at the highest dose level. A treatment-related increase in the post-implantation loss was seen at 450 mg/kg bw per day. This parameter was also statistically significant increased at 50 and 150 mg/kg bw per day, but without a clear dose-response. The developmental toxicity was observed in the presence of maternal toxicity. One death occurred at 450 mg/kg bw per day. However, the maternal toxicity observed in the remaining dams consisted of a slight reduction in the body weight gain associated with a reduction in food consumption. An increase in the occurrence of soft/liquid faeces was also observed, but gross-examination at necropsy did not identify any treatment-related findings. - See also comments in experts' consultation 2.9 below. - See also comments in experts' consultation 2.10 below. **PESTICIDE PEER REVIEW 125** The RMS confirmed that seven rabbit studies are available, four were already submitted for the first Annex I inclusion and additional 3 studies have been submitted under the renewal procedure. These studies were intensively evaluated or re-evaluated in the RAR. Three out of the seven studies were considered supplementary only. The meeting agreed on the German consideration of these studies concerning the validity and reliability as presented in Volume 1 of the RAR. Table 2-6-14 in Volume 1 of the RAR presents a summary of the three "new" studies. An increased incidence of anomalies in foetuses and excessive maternal toxicity as observed in the four old studies were not seen in these three more recent studies. Malformations observed in the old studies are mostly related to severe maternal toxicity. In summary there is no consistency among the studies with regard to maternal NOAELs. The RMS concluded that developmental toxicity is related to the maternal toxicity (mortality). The effects in the study by [redacted] (1991) are summarised in Vol. 3 B.6, table 6-6-42. MSs comments are mainly related to the interventricular septal defect. Four litters were	

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	affected at the high dose levels, one litter at mid dose level, the low dose level and the control. The RMS did not consider this effect relevant for classification, since it was not observed in the 3 "new" independent studies. The majority of the experts (except NO, who confirms the previous comment on Brooker 1991) accepted the evaluation and the conclusion of the RMS and acknowledged that glyphosate is not considered teratogenic (cardiac effects) taking into account all available studies. Possible classification and labelling based on the post implantation loss in the [redacted] 1991 study was discussed. Post implantation loss was observed in [redacted] 1991 and [redacted] 1996 and the evaluation was presented in detail in the RAR. Even in the presence of maternal toxicity the post implantation loss has to be considered as a treatment related effect, which nevertheless will not trigger classification and labelling because of an unclear dose response. The results are presented in Volume 3; B.6, table 6-6-44. The meeting confirmed the assessment and the conclusions of the RMS. The majority of experts agreed on the conclusions drawn by the RMS suggesting that classification regarding developmental toxicity is not appropriate for glyphosate Expert's consultation fulfilled.	
Experts' consultation 2.2 Necessity for deriving an ARfD to be discussed in a meeting of experts. See reporting table	**Background** **RAR:** **Vol. 1, 2.6.13, ARfD**, p. 106 of the revised RAR – January 2015 *RMS:* A low acute oral toxicity of glyphosate was shown in a huge number of studies. In an acute neurotoxicity study, the NOAEL for systemic effects was 1000 mg/kg bw (i.e., the limit dose that might justify a need for an ARfD) and there was no evidence of neurotoxicity. There is no evidence that adverse effects in repeated dose studies, including developmental studies in rats or rabbits, might result from a single oral exposure or would occur within the first days of treatment. Accordingly, no ARfD is needed.	The experts agreed to set an ARfD. The relevant NOAEL is 50 mg/kg bw per day from the [redacted] 1996 study, with an UF of 100 resulting in an **ARfD of 0.5 mg/kg bw**. Open point for section 3: Please consider that an ARfD (0.5

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2(63)	The notifiers have also not suggested an ARfD. The same approach has been taken by the WHO/FAO in its 2004 evaluation (JMPR, 2004, ASB2008-6266). Comments: - FR: Based on the study by [redacted](1991), the developmental NOAEL of 50 mg/kg bw per day due to post implantation losses is considered acceptable. This effect could be considered as a consequence of cardiac malformation observed in foetuses. The observed post implantation losses could be considered as an acute adverse effect occurring within the first days of treatment. As a consequence, an ARfD could be derived based on this effect on the development and the resulting ARfD for glyphosate would be of 0.5 mg/kg bw (with a safety factor of 100). **PESTICIDE PEER REVIEW 125** Acute toxicity of glyphosate is low and in the vast majority of repeated-dose studies, there is no evidence of acute adverse effects. However, the pregnant rabbit proved more vulnerable than the other laboratory animals. The pronounced maternal toxicity in the does, including maternal deaths below 500 mg/kg bw per day in several studies, might trigger a need for setting an ARfD even though these deaths occurred not immediately after commencement of treatment but later in the course of studies. The majority of the experts agreed to set an ARfD based on maternal toxicity and post implantation loss ([redacted] 1991 and [redacted] 1996). However, in the Brooker et al. study, the post implantation losses are only considered relevant at the highest dose 450 mg/kg bw per day (refer to the discussions under 2.1). The relevant NOAEL is 50 mg/kg bw per day from the [redacted] 1996 study, with an UF of 100 resulting in an ARfD of 0.5 mg/kg bw. Expert's consultation fulfilled.	mg/kg bw) has been proposed.
Experts' consultation 2.3 ADI and AOEL of glyphosate to be confirmed in a meeting	**Background** **RAR:** **Vol. 1, 2.6.12, ADI**, pp. 104-106 of the revised RAR – January 2015 *RMS:* Based on the six combined chronic toxicity/carcinogenicity studies that are now considered valid by the RMS (see Table 2.6–17), an "overall NOAEL" in the magnitude of	The experts confirmed the RMS's proposal for the ADI and the AOEL **ADI: 0.5 mg/kg bw per day** based on the NOAEL of 50 mg/kg bw per day from the rabbit developmental

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of experts. See reporting table 2(93)	100 mg/kg bw per day was considered reasonable. It seems most appropriate to derive the ADI from the NOAEL for both maternal and developmental toxicity of 50 mg/kg bw per day as established independently by [redacted] (1991, TOX95523931) and [redacted] (1996, ASB2012-11499). In fact, a lower maternal NOAEL of 20 mg/kg bw per day was found in the study by [redacted] (1993, TOX9551106) but it is in no way mandatory and not usual to use the lowest available value if there is evidence that it results mainly from dose spacing. The proposed figure of 50 mg/kg bw per day is well below the LOAEL of 100 mg/kg bw per day in the study by [redacted] (1993, TOX9551106). In contrast, for the maternal NOAEL of 75 mg/kg bw per day in the study by [redacted] (1980, TOX9552392), the margin to a dose causing maternal death in another experiment (100 mg/kg bw per day according to [redacted] 1993, TOX9551106) might be too small. If 50 mg/kg bw per day is accepted as point of departure, the resulting **ADI for glyphosate is 0.5 mg/kg bw per day.** This reference dose as proposed by the RMS is slightly higher than the previously established value in the EU of 0.3 mg/kg bw per day and by 50 % lower than the ADI that was set by JMPR (2004, ASB2008-6266). However, it must be emphasised that the database that was available for the WHO/FAO evaluation did not contain many of the studies that have been considered for this EU review. Thus, only two of the developmental studies in rabbits ([redacted]., 1991, TOX95523931 and [redacted], 1996, TOX2000-2001) were evaluated by JMPR in 2004. The notifiers, i.e., the GTF, had proposed a markedly higher ADI of 3 mg/kg bw per day, derived from the NOAEL in the long-term rat study by [redacted] (1993, TOX9750499) which had been set at 300 mg/kg bw per day, in contrast to the RMS's evaluation. **Vol. 1, 2.6.14, AOEL**, pp. 107-108 of the revised RAR – January 2015 The selection of studies comprising 90-day studies in rodents and dogs, 1-year dog study, subchronic neurotoxicity, reproduction (one- or two-generation) and developmental studies is summarised in Table 2.6–18. The rabbit appeared the most sensitive species providing the lowest NOAELs and LOAELs with the most serious effects among all species at relatively low dose levels. Based on the same considerations as for the ADI, the AOEL should be derived from the NOAEL of 50	study, 100 UF applied. **AOEL: 0.1 mg/kg bw per day** based on the same NOAEL as the ADI of 50 mg/kg bw per day, 100 UF applied and correcting for the limited oral absorption by 20%**.**

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	mg/kg bw per day for maternal and developmental toxicity in the rabbit [redacted]l., 1991 (TOX95523931); [redacted] 1996, ASB2012-11499), supported by [redacted] (1993, TOX9551106) and [redacted] (1980, TOX9552390). The maternal NOAEL of 75 mg/kg bw per day in the latter study had been used as the basis for AOEL setting during the previous EU evaluation (DAR, 1998, ASB2010-10302). Using the safety factor of 100 and the previous assumption of 30 % oral absorption, a numeric value of 0.2 mg/kg bw per day was calculated. The safety factor of 100 should be maintained but oral absorption is now assumed to be as low as 20 % (see 2.6.1). If 50 mg/kg bw per day is used as the suitable point of departure [because the NOAEL in the study by[redacted] (1980, TOX9552390), was too close to a dose causing maternal deaths in another study in rabbits] **the resulting AOEL is 0.1 mg/kg bw per day.** The GTF had proposed a different systemic AOEL that was by 12 times higher. The suggested numeric value of 1.2 mg/kg bw per day was based on the 90-day rat study by [redacted] (1996, TOX2000-1990) in which the NOAEL was 414 mg/kg bw per day. This NOAEL was agreed with by the RMS but it is higher than the overall NOAELs for both maternal and developmental toxicity in the rat and, in particular, does not take into consideration the developmental studies in rabbits. The latter studies were not used because it was argued that the effects were due to gavage administration of a low pH organic acid causing mucosal irritation in the gut to which the rabbit is particularly sensitive. However, it was not proven that the effects were local by nature and also the low pH is an inherent property of glyphosate that might produce adverse effects. Numerically, the proposed NOAEL was also slightly higher than the (overall) NOAEL for subchronic toxicity in the dog and the NOAELs for parental, offspring and reproductive toxicity as obtained in two-generation studies in rats. Furthermore, the GTF used the previous assumption of 30% oral absorption for correction of the systemic AOEL instead of 20% as it is proposed now by the RMS. Comments: - GTF: The notifiers wish to ensure the statement "Where possible, on the basis of all reliable studies and information, it was tried to establish "overall" NOAELs/LOAELs for a specific toxicological endpoint taking dose spacing into account" is applied	

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	consistently for the NOAEL used for ADI and AOEL calculations". The notifiers believe the NOAEL selected by the Rapporteur for ADI and AOEL calculations, 50 mg/kg bw per day, does not reflect an accurate overall NOAEL/LOAEL for the separate toxicological endpoints of maternal toxicity and offspring effects, as discussed below. An overall NOAEL for maternal toxicity of 75 mg/kg bw per day is reflected in the rabbit maternal data set. **PESTICIDE PEER REVIEW 125** The experts agreed on the relevant NOAEL of 50 mg/kg bw per day (developmental and maternal toxicity, rabbit) for the setting of the AOEL considering an oral absorption rate of 20% resulting in an AOEL of 0.1 mg/kg bw per day. The ADI is based on the same NOAEL of 50 mg/kg bw per day with a UF of 100 resulting in an ADI of 0.5 mg/kg bw. The setting of the ADI is described in the RAR, Volume 1, 2.6.6 The section on residues needs to be informed about the confirmation of the reference values proposed by the RMS. Expert's consultation fulfilled.	
Experts' consultation 2.4 MSs to discuss the genotoxicity of glyphosate. See reporting table public consultation 2(13)	**Background** **RAR:** **Vol. 3, B.6.4, Genotoxicity**, pp. 305-442 of the revised RAR **Vol. 1, 2.6.5 Summary of genotoxicity**, pp. 53-57 of the revised RAR – January 2015 After submission of the first draft of the RAR for public comment additional studies have been included in the revised RAR. A new comprehensive review on genotoxicity studies of glyphosate and glyphosate-based formulations was submitted by Kier and Kirkland (2013, ASB2014-9587). The authors concluded that an overwhelming preponderance of negative results in well-conducted bacterial reversion and *in vivo* mammalian micronucleus and chromosomal aberration assays indicates that glyphosate and its formulations were not genotoxic in these core assays. Negative results for *in vitro* gene mutation and a majority of negative results for chromosomal effect assays in mammalian cells add to the weight of evidence that	The meeting confirmed that the active substance glyphosate is devoid of genotoxic potential.

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	glyphosate was not genotoxic. Mixed results were observed for micronucleus assays of formulations in non-mammalian systems. Reports of positive results for DNA damage endpoints indicate that some formulations tend to elicit DNA damage effects at high (toxic) dose levels but the data suggest that this is due to cytotoxicity rather than to DNA interaction, perhaps associated with the surfactants present in many products. Taking a weight of evidence approach, it may be concluded that there is no *in vivo* genotoxicity and mutagenicity potential of glyphosate or its formulations to be expected under normal exposure scenarios, i.e., below toxic dose levels. Regarding the use of Klimisch criteria, see expert consultation 2.7 below. Comments: - PAN-Europe, PAN UK, Agrar Koordination: The claim in the RAR of a lack of mutagenicity or even that results of studies are consistently and unequivocally negative (Vol. 1) is false. Genotoxic effects on the contrary are already long known and available to the reviewers. Kale, 1995, showed mutations in fruit flies, Vigfussen, 1980, showed sister chromatin exchanges in human lymphocytes, just as Bolognesi in 1997. Peluso in 1998 showed increased DNA adducts in mice. Gasnier, 2009, showed DNA damage, as well as Manas, 2009. Some are captured in the industry review, others not, for unknown reason. All are dismissed in the end. Numerous other studies have confirmed DNA damage in mouse, bovine, fish, caiman, tadpole, fruit fly, sea urchin, onion, and bacterial cells. PAN-Europe further criticise the use of Klimisch criteria to assess the reliability of toxicological studies. **PESTICIDE PEER REVIEW 125** The genotoxicity was evaluated and presented in the RAR Volume 3, B.6.4, pp. 305 – 442. The RMS included an addendum in the RAR, which was already prepared in 2000 and reports studies referred to in the public comments (see above). All data (including those published after 2000 and data on formulations) were taken into consideration and evaluated for quality and relevance. The meeting confirmed that the active substance glyphosate is devoid of genotoxic	

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	potential. Expert's consultation fulfilled.	
Experts' consultation 2.5 MSs to discuss the carcinogenicity of glyphosate. See reporting table public consultation 2(21)	**Background** **RAR:** **Vol. 3, B.6.5, Long term toxicity and carcinogenicity**, pp. 443-548 of the revised RAR **Vol. 1, 2.6.6 Summary of long term toxicity and carcinogenicity**, pp. 58-61 of the revised RAR – January 2015 Long-term toxicity and carcinogenicity of glyphosate were investigated in a large number of studies in rats and mice that were performed over the course of time on behalf of different notifiers. All studies previously evaluated in the EU were subject to rigorous re-evaluation for purposes of the RAR including an assessment of their quality and reliability according to current standards. For the new evaluation, five chronic or combined chronic toxicity/carcinogenicity studies in rats and three long-term studies in mice were additionally provided. There was no evidence of carcinogenicity of glyphosate in any of the rat studies. Chronic toxicity was confined to high dose levels in all the studies but remarkable differences became apparent in what was actually observed. In mice, the previously known studies did not provide evidence of carcinogenicity up to the high dose levels tested. The most recent 80-Week dietary mouse study conducted by [redacted] (2009, ASB2012-11492) can be considered very comprehensive with regard to histopathology. There were no adverse effects up to the highest dose level of 5000 ppm, that was equivalent to 810 or 1081 mg/kg bw per day in males and females, respectively. The carcinogenicity study in Swiss albino mice by [redacted] (2001, ASB2012-11491) revealed an increase in malignant lymphoma incidence (quite common in ageing mice) at the top dose level of around 1460 mg/kg bw per day. Malignant lymphoma accounted for 54.6 % of all tumours that were detected in all animals in the study by [redacted] (2001, ASB2012-11491). Malignant lymphoma incidence was significantly elevated as compared to the actual control groups in both sexes, was above the mean values of the (relatively small)	The experts (except BE expressing an uncertainty on this issue because of the lack of in-house HCD for the Wood study and exceedance of HCD in the [redacted] study) consider highly unlikely the carcinogenic potential of glyphosate. However, the background incidences of malignant lymphomas should be further elucidated for the Swiss albino mouse strain in a revised RAR. The reference values are considered to be protective with regard to the dose level where the malignant lymphomas occur. Open point: RMS to present the information available on the background incidences for the Swiss albino strain in a revised RAR.

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historical control and, for males, outside the historical control range.

Table Error! No text of specified style in document.**-1: Total incidence of malignant lymphoma in long-term studies with glyphosate in different mouse strains**

Study, Strain		**Males**				**Females**			
[redacted] 2009, ASB2012-11492 Crl:CD-1 (ICR) BR	Dose (ppm)	0	500	1500	5000	0	500	1500	5000
	Affected	0/51	1/51	2/51	5/51	11/51	8/51	10/51	11/51
[redacted] 2001, ASB2012-11491 HsdOLA:MF1 (Swiss albino)	Dose (ppm)	0	100	1000	10000	0	100	1000	10000
	Affected	10/50	15/50	16/50	19/50*	18/50	20/50	19/50	25/50*
[redacted] 1997, ASB2012-11493 Crj:CD-1 (ICR)	Dose (ppm)	0	1600	8000	40000	0	1600	8000	40000
	Affected	2/50	2/50	0/50	6/50	6/50	4/50	8/50	7/50
[redacted] 1993, TOX9552382, CD-1 (not further specified)	Dose (mg/kg bw per day)	0	100	300	1000	0	100	300	1000
	Affected **	4/50	2/50	1/50	6/50	14/50	12/50	9/50	13/50

* increase statistically significant, for females based on percentage and not on total number of affected mice
** based on histological examination of lymph nodes with macroscopic changes

Overall, a treatment-related effect in the study by [redacted] (2001, ASB2012-11491) cannot be completely excluded and there is limited evidence of a carcinogenic potential of glyphosate as a high-dose phenomenon in mice of a susceptible strain.

Since the more frequent occurrence of malignant lymphoma was confined to a very high

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	dose level that was administered over a long period, glyphosate is considered unlikely to pose a carcinogenic risk in humans. Classification and labelling for carcinogenicity is not considered appropriate by the RMS because of the following considerations: (1) The presumed effect was statistically significant in only one of five long-term studies in mice in a strain with a rather high background incidence of malignant lymphoma. Evidence coming from one more study is even more equivocal because a certain increase there did not gain statistical significance. In a third study, a (non-significant) increase in top dose incidence was explained and contravened by historical control data. (2) Although the increase in lymphoma incidence in the study by [redacted] (2001, ASB2012-11491) was statistically significant in both sexes, it was still within the (small) historical control range for females. No evidence of a similar effect in female mice was obtained in any other study. (3) No evidence of carcinogenicity was obtained in a total of six valid 2-yr studies in rats (see above) in which sufficiently high dose levels were employed. (4) The dose with a significantly higher lymphoma incidence (1460 mg/kg bw per day) is by more 2900 times higher than the proposed ADI and the margin to the expected consumer exposure is even wider. (5) There is no convincing evidence of carcinogenicity of glyphosate in humans coming from the epidemiological studies. Comments: - PAN-Europe, EGM, PAN UK, UIM, PAN Germany, SA, Agrar Koordination: A major failure in the testing systems used is the lack of exposure in-utero of the test animals. It is well-known that many chronic diseases develop in-utero (not only for cancer) and as such tests lacking in-utero exposure cannot be qualified as a 'state-of-the art' scientific approach. The conclusion that the substance is not carcinogen needs to be justified. We therefore propose EFSA requires the applicant to test again with in-utero exposure, performed with blind testing in an independent laboratory. EU legislation provides for a high level of human health protection based on the precautionary principle and requires special attention for the vulnerable, the unborn and the elderly. The test system disregards the effects on the vulnerable groups in	

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	society. **PESTICIDE PEER REVIEW 125** The RMS presented the assessment on carcinogenicity in Volume 1 pp. 58-61 and Volume 3 B.6.5. The total incidence of malignant lymphoma in long-term studies with glyphosate in different mouse strains was presented in an overview table and discussed during the meeting. Historical control data for lymphoma were provided for 2 studies ([redacted] 2001; [redacted] 1997) but not submitted for the most recent [redacted] 2009 study although requested by EFSA under the clock stop procedure. It was discussed whether historical control data for the [redacted] 2009 study would be needed to conclude on this point. Data available from the literature for the CD1 mouse strain showed a historical control range up to 20 % in males which is well above the ca. 10% incidence at the top dose level in the [redacted] study. For the Swiss albino mice historical control data are available and the results of the study show an exceedance at the high dose (males only). This strain has a high background incidence of malignant lymphomas (as commented by the RMS), but this should be further substantiated in a revised RAR by additional information. The experts considered that this information would be helpful to reliably conclude on the point; however a major concern was not raised. The lymphomas are the second most spontaneous tumour for this strain. The RMS provided the information that IARC will evaluate the carcinogenic potential of glyphosate in the near future. It was discussed whether the conclusion of IARC could be used for the EU evaluation but it was doubted to be available before the draft conclusion. The experts (except BE expressing an uncertainty on this issue because of the lack of in-house HCD for the [redacted] study and exceedance of HCD in the [redacted] study) consider highly unlikely the carcinogenic potential of glyphosate. However, the background incidences of malignant lymphomas should be further elucidated for the Swiss albino mouse strain in a revised RAR. The reference values are considered to be protective with regard to the dose level where the malignant lymphomas occur.	

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	Open point: RMS to present the information available on the background incidences for the Swiss albino strain in a revised RAR. Expert's consultation fulfilled.	
Experts' consultation 2.6 MSs to discuss the possible endocrine disrupting properties of glyphosate. See reporting table public consultation 2(22)	**Background** **RAR:** **Vol. 1, Studies with formulations/Published data,** pp. 81-85 of the revised RAR Glyphosate was included into the U.S. EPA Endocrine Disruptor Screening Program's (EDSP) first list of 67 compounds that were foreseen to Tier 1 Screening. The compounds were selected on their potential for exposure rather than suspected interference with the endocrine system. The EPA will evaluate the full battery of Tier 1 screening assays for glyphosate's potential to interact with the oestrogen, androgen and thyroid endocrine pathways. The first published data for glyphosate revealed no effects on androgenic or oestrogenic pathways in the Hershberger and Uterotrophic assays (Saltmiras *et al.*, 2012, ASB2012-12016). Levine *et al.* (2012, ASB2014-9609) published a short summary of the results. They concluded that, based on the Tier 1 assays that had been performed at different independent laboratories and taking into account the 'higher tier' regulatory safety studies glyphosate might not be considered an endocrine disrupter. Later on, Bailey *et al.* (2013, ASB2013-3464) summarized the first results of the male and female pubertal assays in which glyphosate did not exhibit evidence of endocrine disruption. Published studies on glyphosate formulations are summarised. Comments: - PAN-Europe, EGM, PAN UK, PAN Germany, Agrar Koordination: Next point is the extreme high doses used in notifier's testing. More evidence is available in literature (see Vandenberg et al. 2012 review) that low doses can harm, many times in the developing phase of the organism and many times for endocrine disrupting chemicals. Since Glyphosate has endocrine disrupting properties, EFSA should perform a thorough review on the data in independent literature, and require applicant to do a series of low dose testing on endocrine adverse effects. EFSA should require the applicant to do new testing of the substance including a	The experts agreed with RMS's conclusion that there is no evidence of endocrine mediated effects.

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	range of low doses. **PESTICIDE PEER REVIEW 125** The RMS reported that there is no evidence of endocrine effects in the *in vivo* studies in appropriate animal models with the available protocols submitted for the active substance glyphosate. Evidence of endocrine effects in open literature was claimed in *in vivo* and in *in vitro* studies with glyphosate based formulations and therefore not considered relevant for the present assessment. The experts agreed with RMS's conclusion that there is no evidence of endocrine mediated effects. Expert's consultation fulfilled.	
Experts' consultation 2.7 MSs to discuss the hazard characterisation for glyphosate. See reporting table public consultation 2(33) See also 2(34)	**Background** **RAR:** *RMS:* Appropriate and complete hazard characterisation and risk assessment were performed by the RMS. This becomes evident from the whole RAR. Concerning the comment on the so called "Klimisch-mill", please see our comment to 2(13) from expert consultation 2.4: RMS: The Klimisch score is a method to assess the reliability of toxicological studies, which was published in *Regulatory Toxicology and Pharmacology*. The scoring system is the standard method used in the EU regulatory scheme. ECHA has produced guidance on how to assess the reliability of data (2), which was applied by the BfR. This is based on the validity of the test methods and of the quality of the laboratory practice including documentation of raw data. Following this approach, the legally required standard studies performed according to an applicable guideline (i.e. OECD, EU Test Methods) and good laboratory practice (GLP) will be usually considered to be of higher reliability than most published studies. Even if peer-reviewed, the latter are often flawed by reporting deficiencies. Frequently, non-validated methods and missing background data are employed and endpoints of uncertain relevance addressed.	The experts agreed with RMS conclusion that both hazard characterisation and risk assessment for glyphosate have been appropriately performed, based on the available data.

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	(1) http://en.wikipedia.org/wiki/Klimisch_score (2) http://guidance.echa.europa.eu/docs/guidance_document/information_requirements_r4_en.pdf In contrast to this approach it was proposed by PAN that in principle "…independent literature …should be qualified as more reliable than industry-sponsored studies with an inherent conflict of interest." This approach is not supported by the rapporteur and can't be the basis of the scientific toxicological assessment of glyphosate in the submitted RAR - further explanations see statement 2(5). **Vol. 3, B.6.6.12, Published data (released since 2000), *In vitro* DART/ED publications:** **Paganelli et al. 2010**, see p. 677 of the revised RAR Three *in vitro* assays were conducted, (i) frog embryos exposed to glyphosate formulation; (ii) frog embryos directly injected without injection blank negative controls; and (iii) fertilised chicken embryos exposed directly to a glyphosate formulation through a hole cut in the egg shell. Key issues surrounding this research include irrelevant routes of exposure as well as excessively high and environmentally unrealistic doses. **Klimisch evaluation** Reliability of study: Not reliable Comment: Non-guideline study that is not sufficiently described for assessment. Inadequate positive and negative control experiments. Relevance of study: Not relevant: Irrelevant routes of exposure and inappropriately high doses. Test system not adequate for human risk assessment. Klimisch code: 3 Comments: - PAN-Europe, EGM, PAN UK, UIM, PAN Germany, SA, Agrar Koordination: a big omission in the German RAR is the lack of a hazard characterization of	

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	Glyphosate. In many EFSA opinions it is stated that the first step of risk assessment is the hazard characterization. We observe that Germany just moves on directly to risk characterisation and standard setting, and ignores the evidence on hazards A hazard characterization is important to learn about the mechanism of toxicity of Glyphosate. Without the knowledge of the hazards it will be difficult to select in the next steps of risk assessment what data are useful and not. Germany just puts all evidence in the "Klimisch-mill" with the obvious effect of all independent science disregarded. - We urge EFSA to include a hazard characterisation in the peer-review. This should be done by using all in-vitro studies available, disregarding none, and all mechanistic studies available. The peer-review should focus on what mechanistic evidence is present on teratogenicity, on DNA-damage., etc. The study of Paganelli et al. 2010 presents interesting evidence on the mechanism of action. During early embryonic development, retinoic acid generated in a specific region of the embryo helps determine position along the embryonic anterior/posterior axis by serving as an intercellular signaling molecule that guides development of the posterior portion of the embryo. It acts through Hox genes, which ultimately control anterior/posterior patterning in early developmental stages. The findings of Marc et al. '05 support this, offering a general mechanism of action for teratogenicity. **PESTICIDE PEER REVIEW 125** The available data are robust enough and always carefully considered to conclude on the toxicological profile of glyphosate including hazard characterisation. The study of Paganelli *et al* 2010 was performed with extreme exposure conditions with both glyphosate and glyphosate based formulations. Although the study identified a potentially relevant mechanism of action, this does not automatically mean that it is relevant and that it can be considered for a regulatory process. Furthermore higher tier data are available overruling the results of Paganelli et al 2010. The experts agreed with RMS conclusion that both hazard characterisation and risk assessment for glyphosate have been appropriately performed, based on the available	

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
	data. Expert's consultation fulfilled.	
Experts' consultation 2.8 MSs to discuss the reprotoxicity of glyphosate. See reporting table public consultation 2(35) See also 2(36)	**Background** **RAR:** **Vol. 3, B.6.6.1 Two generation reproductive toxicity in the rat**, p. 548 of revised RAR *RMS:* The reproductive toxicity of glyphosate was tested in a variety of multi-generation studies in rats. For the previous EU evaluation, a total of 8 studies in rats had been submitted of which four were still considered acceptable or, in case of a single one-generation study, at least supplementary upon re-evaluation. The studies by [redacted] (1981, TOX9552385), by [redacted] (1985, TOX9650161) and by [redacted] (both 1988, TOX9551832 and TOX9551965), however, were deleted from current evaluation due to major deficiencies and/or because the dose levels were much too low and therefore one could not expect the occurrence of any toxic effects. Three new studies were provided in the GTF dossier and were submitted either for the first time for this evaluation or had been subject to JMPR evaluation (JMPR, 2004, ASB2008-6266) yet. Comments: - PAN-Europe, EGM, PAN UK, UIM, PAN Germany, SA, Agrar Koordination: many multi-generation tests in the RAR with their very high (and unrealistic) doses, endpoints which are not the state-of-the-art cannot provide for the final answer on reproductive toxicity. The results are not clear anyway with a study that shows effects at low doses but is dismissed in the end by the Rapporteur. And studies showing effects on the offspring also accepted because they are observed at high doses. Combined with the many studies in open literature on malformations of the offspring and developmental effects, a peer-review by EFSA of all evidence is more than necessary. The industry-sponsored OECD tests are known for their insensitivity and this could explain the very remarkable difference seen between the industry-sponsored studies	The experts considered the available studies as sensitive for the definition of the reproductive potential of the active substance glyphosate.

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
	and independent literature. The high doses used are close to the acute poisoning doses and poisoning effects are common in these tests, while more subtle effects could be missed. - We again question the use of extreme high exposure doses such as 15.000 ppm or 1000 mg/kg, more than 1000x the ADI. Animals should be tested at realistic doses and no extrapolation used. The high doses are close to the acute poisoning doses used and poisoning effects are common in these tests, while more subtle effects could be missed. **PESTICIDE PEER REVIEW 125** The reproductive toxicity of the active substance glyphosate has been extensively assessed according to internationally recognised and validated protocols and methodologies. The experts considered the available studies as sensitive for the definition of the reproductive potential of the active substance glyphosate. Expert's consultation fulfilled.	
Experts' consultation 2.9 MSs to discuss the developmental toxicity of glyphosate (see other RT 2(41) See reporting table public consultation 2(37)	**Background** See experts' consultation 2.1 above. RMS response to comment: Teratogenic effects were doubtless not observed in rats, whereas all findings in rabbits were discussed on their possible teratogenic potential in detail. In general please also refer to comment given by the RMS at 2(5), for the evaluation of an active substance all available experimental studies on developmental toxicity are taken into consideration but should not be mixed up with studies or assays which were performed with a product containing beside glyphosate a couple of further known or unknown components (e.g. tallow amine). Furthermore, the Rapporteur has to consider the quality and reliability of each available study. For glyphosate, a weight of evidence approach revealed that the active substance was devoid of a teratogenic potential in mammals	The experts agreed that the case reports mentioned have major methodological drawbacks which do not allow any conclusion on the teratogenicity potential.

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
	Comments: - PAN-Europe, EGM, PAN UK, PAN Germany, Agrar Koordination: We especially encourage EFSA to take a look at teratogenicity. The pre-2001 studies of Monsanto show teratogen effects, a range of independent studies report these effects, these effects are also observed in areas with Roundup monocultures (soy) in epidemiology studies and even in bio industry where piglets fed on soy have these effects. In the first DAR on Glyphosate in 2001, the UK experts commented that -based on the Monsanto studies- a single study might not raise concerns, but that the teratogenic effects that kept being observed in the Monsanto-studies, pointed at a pattern that should not be dismissed in the risk assessment. EFSA should asses if in the two-generation studies the animals are properly exposed during vulnerable windows during development and if a large range and relevant endpoints are considered for teratogenicity and development during later life of the offspring. **PESTICIDE PEER REVIEW 125** The RAR Volume 3, B.6.8.3.3 – published data - has been updated recently. The experts agreed that the case reports mentioned have major methodological drawbacks which do not allow any conclusion on the teratogenicity potential (see above). Expert's consultation fulfilled.	
Experts' consultation 2.10 MSs to discuss the teratogenicity of glyphosate. See reporting table	**Background** See experts' consultation 2.1 above **:** **Suresh (1993),** p. 653 of the revised RAR Table B.6.6-52: Summary of relevant external, visceral and skeletal findings (litter data), p. 660 of the revised RAR. RMS response to comment: Not agreed. Upper cleft palate was observed in control and low dose foetuses only, but not at mid or high dose levels. These findings did not occur in a dose related manner.	The experts agreed to the RMS's assessment.

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
public consultation 2(46)	Comments: - PAN-Europe, EGM, PAN UK, UIM, PAN Germany, SA, Agrar Koordination: also this study shows effects at the lowest dose tested, 20 mg/kg, upper cleft palate, 15% vs. 5% in the control, and dilated heart, 23,1% vs. 0% in the control. There is a clear pattern of malformations of the foetus in all rabbit studies **PESTICIDE PEER REVIEW 125** The RMS concluded that the study by Suresh has its limitations. It was only reliable with regard to maternal effects. According to CLP regulation, foetal effects at dose levels with > 10% maternal mortality should not be taken into account. . In addition, there were no measurements to support the claimed effect of "dilated heart". The RMS explained that there was no dose-response seen with the regard to the cleft palate (present at the low dose level). The experts agreed to the RMS's assessment. Expert's consultation fulfilled.	
Experts' consultation 2.11 MSs to discuss the developmental neurotoxicity of glyphosate. See reporting table public consultation	**Background** **RAR:** **Vol. 3, B.6.7.1 Published data on neurotoxicity**, pp. 714-721 of the revised RAR **Garry (2002)** In evaluating attention-deficit disorder / attention-deficit hyperactive disorder (ADD/ADHD), a positive association with glyphosate use was reported, but cases were reported by parents with no clinical confirmation and the reported incidence rate of approximately 1 % for the study population was well below the general population incidence rate of approximately 7 %. **Barbosa (2001)**	The experts agreed that there is no evidence for a neurotoxic potential of glyphosate.

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
2(59)	A single case of a 54-year-old man accidentally sprayed himself with glyphosate formulation is reported. One month later, he developed a symmetrical parkinsonian syndrome. Two years after the initial exposure to glyphosate, magnetic resonance imaging revealed bilateral hyperintense signal in the globus pallidus and substantia nigra. RMS response to comment: Garry et al. (2002) reported an incidence rate of ADD/ADHD of approximately 1% for the study population which was well below the general population incidence rate of approximately 7%. Furthermore, the cases were reported without clinical confirmation. These limitations and further deficiencies of the study are reported in detail in the RAR. Furthermore, in the RAR it is comprehensively discussed that there is no convincing evidence for a relation between Parkinson`s disease (which was described in a single person in the report of Barbosa et al., 2002) and glyphosate exposure. Concerning the results of animal studies, it is important to emphasize that multiple studies, among them all long-term animal studies have failed to demonstrate any evidence of neurotoxicity of glyphosate. Comments: - PAN Europe, EGM, PAN UK, UIM, PAN Germany, SA, Agrar Koordination: Epidemiology studies have been published pointing at Glyphosate of causing mental disorders of children born to pesticide applicators in the US, Garry, 2002. Even acute poisoning could lead to brain damage, Barbosa, 2001. Animal studies have demonstrated that Glyphosate depletes serotonin and dopamine, Anadon, 2008, and causes a loss of mitochondrial transmembrane potential in rat brain cells, especially in the substantia nigra region of the brain, Astiz, 2009. There is evidence of developmental neurotoxicity of Glyphosate and EFSA should pay good attention to this adverse effect in their peer-review. **PESTICIDE PEER REVIEW 125** From the available data there is no evidence for neurotoxicity and developmental neurotoxicity for the active substance glyphosate, mainly based on both experimental and epidemiological studies.	

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
	Expert's consultation fulfilled.	

REPORT OF PESTICIDES PEER REVIEW MEETING 127

GLYPHOSATE

Rapporteur Member State: DE

Specific comments on the active substance in the section

3. Residues

are already listed in the relevant reporting table. Comments submitted for this meeting are listed below.

1. Comments submitted for this meeting:

Date	Supplier	File Name

2. Documents submitted for meeting:

Date	Supplier	File Name
29.01.2015	DE	Glyphosate_evaluation table_AIR II_section 3_2015-01_29.doc
29.01.2015	DE	Glyphosate_RAR_12_LoEP_CA-CP_rev 2015-01_29.docx
14.07.2014	DE	Glyphosate_reporting table_rev 0__2014-07-14.doc
25.07.2014	DE	Glyphosate reporting table_public consultation.doc
29.01.2015	DE	Glyphosate_RAR_01_Volume1_2015-01_29.docx
29.01.2015	DE	Glyphosate_RAR_09_Volume3CA-CP_B-7_2015-01-29.docx
29.01.2015	DE	Glyphosate_RAR_22_Volume4_all applicants_2015-01-29.doc (Representing all individually submitted files)
26/02/2015	EFSA	Glyphosate trials Barley Oats.xls
26/02/2015	EFSA	Glyphosate trials Wheat Rye.xls
26/02/2015	EFSA	Glyphosate Conversion factors.xls
26/02/2015	EFSA	Glyphosate Animal Intake & Feeding.xls

3. Documents tabled at the meeting:

Date	Supplier	File Name

Appendix 1: Discussion table: GLYPHOSATE

Appendix 1: Discussion Table, Glyphosate

3. Residues

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
Experts' consultation 3.1 A general approach for the selection of the residue trials relevant for the MRL calculations on cereals, should be discussed in an expert meeting. See also comment 3(31), 3(34), 3(36), 3(52), 3(54), 3(55) and 3(82) See reporting table 3(33)	Tox PRAPeR expert Meeting proposed an ARfD: 0.5 mg/kg bw (based on the reprotox study). The ADI value remains unchanged. The proposed RDs for enforcement and risk assessment based on the metabolism studies conducted on conventional and GMO crops and reported in the LoEPs by the RMS are agreed. EFSA referred to the draft OECD GD on crop field trials and to the template on "MRL management" discussed at the PSC (June 2014) and at the SCoPAFF (February 2015). The main criteria for the selection of the trials are listed hereafter: -a single residue value should be selected per location site, -If same experimental conditions in the trials (varieties, doses, location site) (trials considered as replicates), the <u>mean</u> residue value should be selected; -If different experimental conditions characterize the trials (difference on at least 2 parameters) (trials considered as independent), the <u>HR</u> value should be selected. Based on the extrapolation GD (SANCO 7525/VI/95- rev.9 -Table 3), sufficient residue trials are available respectively on barley to be extrapolated to oats and on wheat to be extrapolated to rye (resp. NEU and SEU GAPs). <u>Wheat/rye</u>: the NEU and SEU data sets on wheat are sufficient to be extrapolated to rye. Furthermore 5 trials on rye (NEU GAP) are available. MRL proposal of <u>20</u> mg/kg based on merged NEU/SEU GAP-compliant residue trials. <u>Barley/oats</u>: A complete residue data set was provided respectively on barley and oats for the northern zone. Although only 6 residue trials are available on barley (SEU GAP), 44 trials are available in total on barley and oats (NEU/SEU GAPs). The meeting was of the opinion that 2 additional residue trials on barley (SEU GAP) will not impact significantly the MRL calculation and are therefore not needed. The meeting also agreed with the RMS assessment to consider the mean of the residue values for all the reported residue trials characterized by doses of application that ranged within the	The meeting agreed on the following MRL proposals: 20 mg/kg on wheat/rye, 30 mg/kg on barley/oats.

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
	acceptable 25 % tolerance limit. In that case, a MRL of 30 mg/kg is proposed. The meeting agreed on how the RMS selected the trials and the MRL on barley/oats was derived based on the NEU residue data package.	
Experts' consultation 3.2 The setting of a conversion factor (CF) for risk assessment on cereals (maize excluded) should be discussed in an expert meeting. See reporting table 3(37)	Barley/oats; wheat/rye: CFs ranged between 1.01 and 1.07 (AMPA>LOQ) RMS is of the opinion that considering the analytical uncertainty and the 25 % tolerance applied to the dose of application; the derived CFs for risk assessment may be regarded as insignificant. Furthermore, the impact of setting CFs for risk assessment is negligible in view of the large margin of safety the consumers are exposed to considering the representative uses. The meeting supports the RMS' view and agreed not to derive CF_S for risk assessment considering the representative uses on conventional crops.	The setting of a conversion factor (CF) for risk assessment on small grain cereals is not required.
Experts' consultation 3.3 MSs to discuss the recoveries after storage under frozen conditions. Note: EFSA remains of the opinion that concurrent recoveries (= fresh or procedural recoveries) **have not** to be used to correct the recovery values observed after storage under frozen conditions and therefore, that the columns "corrected %" should be deleted from the different tables in the RAR. Concurrent recoveries should be used only to confirm that the analytical method has been correctly	EFSA is of the opinion that concurrent recoveries should be used only to confirm that the analytical method has been correctly implemented at the different control time points and that, low storage recovery observed at a certain control point, may be explained by a low procedural recovery. The recoveries observed at each storage time point should not be corrected by the procedural recoveries (see current EC GD SANCO 7032/ VI/95 rev.5 and OECD GD 506). In case of a significant residue decline observed at a storage time point, we should refer to the procedural recoveries to state whether the analytical method is correctly implemented and to conclude on whether low storage recoveries may be explained by low procedural recoveries. No harmonised approach could be achieved with regard to the interpretation of the current guideline. For glyphosate, based on the reported data, acceptable storage stability was demonstrated.	Although no harmonised approach could be achieved with regard to the interpretation of the current guideline, the meeting concluded that the uncorrected recoveries and procedural recoveries must always be reported for sake of transparency. For glyphosate, based on the reported data, acceptable storage stability was demonstrated.

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
implemented at the different control time points and that, low storage recovery observed at a certain control point, may be explained by a low procedural recovery. Considering that the rational to support the stability was based on the nominal spiking rates (and not the residue level measured at T0), the RMS conclusion on stability are agreed. See reporting table 3(40)		
Experts' consultation 3.4 MSs to discuss the results of the processing studies in soya bean. AMPA residue levels are expressed as AMPA equivalent. Note: In absence of data on acetyl-glyphosate and acetyl-AMPA, EFSA remains of the opinion that PF and CF should be considered as a "best case" in term of residue transfer in processed commodities.	US processing trials on soya bean were reported in the DRAR for the determination of glyphosate and AMPA residues. Based on these trials, processing factors (PFs) of 1 and 0.1 were derived for glyphosate respectively for meal and crude oil and were considered as acceptable. It is noted that registered US GAPs for comparison with these trials were not reported. There is no information on whether soya bean was a conventional or a GMO crop. Therefore, considering that soya bean is not a representative use and the lack of key information (GAPs, nature of the crop), the meeting decided not to propose conversion factors (CFs) for risk assessment in processed soya bean commodities.	- The derived PFs for glyphosate on soya bean meal (1) and crude oil (0.1) were considered as acceptable. - The meeting was unable to derive CFs for risk assessment since the registered US GAPs for comparison with these trials were not reported and also the nature of the crops was not specified (conventional or GMO crop).

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
See reporting table 3(43)		
Experts' consultation 3.5 MSs to discuss the results of the processing studies in barley. Note: Processing studies conducted at higher application rates (4300 and 8600 g/ha) and with PHI ≥ 7 days should indeed be taken into account to derive PF and CF (and not only studies conducted at application rates in compliance with the cGAP). A sufficient number of processing studies is therefore available to derive PF and CF for barley malt. See reporting table 3(44)	RMS disregarded the submitted processing trials on barley since no validation of the data was reported and significant residue levels of glyphosate were recovered in the control samples (up to 5 mg/kg). The meeting decided not to derive PFs and CFs on barley processed commodities.	PFs and CFs could not be derived from the available processing trials.
Experts' consultation 3.6 Setting of conversion factors for risk assessment in animal matrices, based on the representative uses, should be discussed in an expert meeting. See reporting table 3(80)	RMS decided not to derive CFs for commodities of animal origin since the livestock exposure to glyphosate and AMPA residues based on the representative uses has a very limited applicability to the practical conditions of exposure (livestock exposure to GMO crops not considered in the framework of the peer review). Furthermore, the ratio glyphosate/AMPA found in the animal commodities reflects the ratio used in the feeding study (mixture of glyphosate and AMPA in a 9:1 ratio). It is also highlighted that based on the feeding studies and the calculated dietary burden, AMPA residues are quantifiable only in kidney. Therefore, it can reasonably be assumed that based on the representative uses, there is no need to derive CFs for risk assessment considering the low contribution of kidney to the overall consumer dietary burden.	The setting of CFs for risk assessment in commodities of animal origin is not required considering the representative uses.

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
Experts' consultation 3.7 MSs to discuss this general aspect in an expert meeting. See reporting table 3(83)	During the last SCoPAFF (February 2015), it was agreed that the sum up of the LOQ of each compound included in the RD for enforcement should be considered for MRL setting purposes. The following MRL proposals are for: -swine and poultry fat and liver: 0.1*mg/kg -muscle, eggs and milk: 0.05*mg/kg. To be confirmed (analytical methods).	The sum up of the LOQ of each compound included in the RD for animal commodities should be considered.

REPORT OF PESTICIDES PEER REVIEW MEETING 128

GLYPHOSATE

Rapporteur Member State: DE

Specific comments on the active substance in the section

5. Ecotoxicology

are already listed in the relevant reporting table. Comments submitted for this meeting are listed below.

1. Comments submitted for this meeting:

Date	Supplier	File Name
None		

2. Documents submitted for meeting:

Date	Supplier	File Name
29.01.2015	DE	Glyphosate_evaluation table_AIR II_section_5_2015-01_29.doc
29.01.2015	DE	Glyphosate_RAR_12_LoEP_CA-CP_rev 2015-01_29.docx
14.07.2014	DE	Glyphosate_reporting table_rev 0__2014-07-14.doc
25.07.2014	DE	Glyphosate reporting table_public consultation.doc
29.01.2015	DE	Glyphosate_RAR_01_Volume1_2015-01_29.docx
29.01.2015	DE	Glyphosate_RAR_11_Volume3CA-CP_B-9_2015-01-29.docx
29.01.2015	DE	Glyphosate_RAR_22_Volume4_all applicants_2015-01-29.doc (Representing all individually submitted files)

3. Documents tabled at the meeting:

Date	Supplier	File Name
None.		

Appendix 1: Discussion table: GLYPHOSATE

Appendix 1: Discussion Table, Glyphosate

5. Ecotoxicology

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
Experts' consultation 5.1 MSs to discuss and agree the chronic endpoint to be used for risk assessment to mammals. See also 5(25), 5(27), 5(29), 5(36), 5(37), 5(38), 5(40), 5(41). See reporting table 5(24)	The RMS introduced the substance, explaining the rationale behind the choice of the endpoint for the mammals reproduction risk assessment. All experts agreed that the chronic endpoint for the mammalian risk assessment should be derived from the developmental data on the rabbit, because the rabbit was found to be consistently more sensitive than the rat. Due to the number of available studies, it was argued that the endpoint could be refined considering all the studies together. Indeed, some studies reported endpoints that were between 50 and 200 mg/kg bw/d (LOAEL in the study from where the NOAEL was derived based on implantation loss). It was pointed out that even if the effects at 200 mg/kg bw per day were not statistically significant, the importance of the observed effects at population level cannot be ignored. It was also highlighted that the comparability of the studies should be assessed in order to ensure a comprehensive evaluation of the available studies. The focus should be on ecologically relevant effects. Effects in other studies were often similar, but also some other effects. It was proposed to consider 175 mg/kg bw per day (developmental toxicity NOAEL in [redacted] 1996) as an overall NOAEL, but some concerns were raised due to the small distance to 200 mg/kg bw per day (LOAEL) developmental effects were clearly seen. A proposal for the setting of the NOAEL at 100 mg/kg bw per day was discarded because maternal mortality was recorded at this dose in another study ([redacted] 1993). **Overall conclusion** All experts agreed to keep the NOAEL at 50 mg/kg bw per day , in accordance with the initial proposal from the RMS and also in accordance with the NOAEL discussed and agreed in the the section on mammalian toxicology. However, the experts considered it useful to have all the available data taken into account to acheive this conclusion in the ecotox section of the revised renewal assessment report (RAR), and an open point was identified for the RMS to amend the RAR accordingly.	Open point RMS to amend the assessment report by considering all the available data on mammals (reproductive, maternal, and devolpmental toxicity) used to set overall NOAEL.

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
Experts' consultation 5.2 Mss to discuss the correction of drift rates as proposed by the RMS for the risk assessment to non-target arthropods and to non-target plants. **Note**: It is acknowledged there is a need to revise the current spray drift rates (see also EFSA PPR opinion on non-target terrestrial plants, EFSA Journal 2014;12(7):3800). However, as recommended by the PPR panel (EFSA Journal 2014;12(7):3800) the use of the current assessment based on FOCUS (2001) should still be followed until the new drift curves will be available. See also 5(55), 5(63), 5(61), 5(66), 5(67), See reporting table 5(50)	The proposal from the RMS is derived from a published WUR report (inventory report Van de Zande J.C., M. Wenneker, A. de Bruine. 2011. Inventarisatie kleinfruitteelten en afleiden driftdepositie en maatregelpakketten. PRI report 398.) that harmonises drift values derived from the central EU zone (mainly Germany and The Netherlands). Some experts reported that this report is part of the revision process of the drift rates. Some experts agreed that the default drift values should be updated considering the desiccation scenario, however, for sake of harmonisation, the current assessment should be based on the current agreed FOCUS values. The RMS pointed out that, in the new revision for the drift values, the desiccation scenario will probably not be considered. Some experts proposed to use 8.02% as a surrogate default value (vegetables, ornamentals, small fruits higher than 50 cm) in order to take into account for higher crops. However, this was considered not acceptable due to some differences in the spraying techniques for these crops. The RMS acknowledged that new drift values, which have not yet been agreed, should not be introduced during the peer review of a substance or discussed in experts meetings. However, the specific desiccation use should be taken into account. EFSA raised some concerns about values, which were taken into consideration, but were derived from a report that was not previously evaluated (i.e. not available in the dossier). However, EFSA also proposed that a particular situation like the desiccation scenario might be taken into account to perform some kind of uncertainty analysis highlighting that the exposure for this scenario is likely underestimated. **Overall conclusion** The experts agreed that for the present evaluation the risk assessment should rely on the FOCUS default drift values. However, all experts also agreed that there is the need to revise these values GD considering the specificity of the desiccation scenario (see general report). An open point for the RMS was identified. The assessment should be amended using the FOCUS default drift values, highlighting the uncertainties and the possible underestimation of the exposure.	Open point RMS to amend the risk assessment to non-target arthropods and to non-target plants using the FOCUS default drift values, highlighting the uncertainties and the possible unersetimation of the exposure Additional errors were noted regarding the MAF values for NTA. The RMS should also take into account spray drift values for multiple applications. The amendment should be considered both in a revised DAR and the LoEP.

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
Experts' consultation 5.3 MSs experts to discuss the MAF value to be use for risk assessment to terrestrial non-target plants. See reporting table 5(62)	The RMS explained that for glyphosate it was not considered appropriate to calculate a MAF based degradation of the substance, as the onset of the effect is immediate, and it is not related to the persistence of the substance. The rationale suggested by the RMS is that a fraction of the non-target terrestrial plants (NTTPs), that are only partially affected by the first application, would probably suffer more severe effects (e.g. mortality) after subsequent applications. The RMS however acknowledged that there is no sound data to estimate a MAF able to grasp the sum of the effects of multiple applications (effect-MAF). Some MSs pointed out that the only sound way to estimate the effect of multiple applications is to simulate such application profile in the toxicity tests. In this specific case, no testing was available to account for multiple applications. Indeed, in the NTTP opinion (EFSA PPR Panel (EFSA Panel on Plant Protection Products and their Residues), 2015. Scientific Opinion addressing the state of the science on risk assessment of plant protection products for non-target arthropods. EFSA Journal 2015;13(2):3996, 212 pp), the effect-MAF is considered in relation to the toxicity testing phase. Concerns were raised about the use of different MAFs for NTA and NTTP. However, some experts also pointed out that there is uncertainty in reading across MAF values conceived for NTA to be used for NTTP risk assessment. One major uncertainty is related to the mobility, which is a trait not shared by NTA and NTTP. Some experts proposed to use the default MAF value of 1.7 as a first tier, while a MAF based on the specific foliar degradation time of glyphosate could be used as a refinement at a higher tier level. However, the majority of experts disagreed with that approach, and agreement with the RMS. Some experts highlighted that even if recovery at population level is possible between applications, repeated spraying could favour some more opportunistic taxa that have the potential to colonise faster the ecological space, which was made available by the effect of the previous application. Some experts also added that this process could lead to a reduction in the taxonomic diversity in the field margins in the long-term **Overall conclusion** The experts agreed to use the default MAF values to account for effects on NTTP due to multiple applications of glyphosate.	The experts agreed to use the default MAF values to account for effects on NTTP due to multiple applications of glyphosate.

REPORT OF PESTICIDES PEER REVIEW TELECONFERENCE 117

GLYPHOSATE

Rapporteur Member State: DE

Specific comments on the active substance in the section

2. Mammalian Toxicology

are already listed in the relevant reporting table. Comments submitted for this meeting are listed below.

1. Comments submitted for this meeting:

Date	Supplier	File Name
28.09.2015	ECHA	__Glyphosate comments ECHA subm for TC_2015-09-28.docx

2. Documents submitted for meeting:

Date	Supplier	File Name
31.08.2015	Germany	_Glyphosate_Addendum 1_IARC-Monograph_2015-08-31.pdf
22.09.2015	EFSA	_Glyphosate_commenting table_ addendum Sept 2015.docx
31.03.2015	Germany	Glyphosate_RAR_01_Volume 1_rev 2015-03-31.docx
31.03.2015	Germany	Glyphosate_RAR_08_Volume 3CA-CP_B-6_rev 2015-03-31.docx
27.02.2015	EFSA	Report Pesticides Peer Review 125_01 Glyphosate 2015-02-27.docx
22.09.2015	EFSA	DRAFT Report Pesticides Peer Review TC 117 Glyphosate 2015-09-29.docx

3. Documents tabled at the meeting:

Date	Supplier	File Name
None.		

Appendix 1: Discussion table: GLYPHOSATE

Appendix 1: Discussion Table, Glyphosate

2. Mammalian Toxicology

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
Experts consultation 2.3: MSs experts to discuss the evidence of association of glyphosate to carcinogenicity in cohort studies, in particular multiple myeloma, in an experts meeting. See also comments 2.9, 2.10	**BACKGROUND** **ADDENDUM:** **Table 2.1 1:** Discussion of studies in section 2.1 Cohort studies of the IARC monograph **De Roos, 2005a**: For multiple myeloma the relative risk was 1.1 (0.5-2.4) when adjusted for age, but was 2.6 (0.7-9.4), when adjusted for multiple confounders. The study had limited power for the analysis of multiple myeloma. Missing data limit the interpretation of the findings. Interpretation of multiple myeloma is limited. **Soharan 2015:** confirmed that the excess risk of multiple myeloma was present only in the subset with no missing information. No significantly increased risk of multiple myeloma based on the AHS data. **COMMENTS:** No increased risk of any tumour type is concluded from one expert considering that the increased association is not statistically significant where the risk estimate is >1 but the lower C.I. is below 1. The limited power for the analysis of myeloma was highlighted by another expert; however a trend was suggested of increasing risk of multiple myeloma with increasing exposure, regardless of the dataset used. **PESTICIDES PEER REVIEW TC117** The power of the available studies was considered. It was noted that, although the AHS is the largest one, it could be less powerful than the case-control studies for rare cancers and may not have greater weight. Four more case-control studies are available to the US-EPA not showing significant evidence for multiple myeloma. Two of them are cited in the IARC monograph and the	There is no statistically significant increased incidence of multiple myeloma linked to glyphosate exposure in the studies of cancer in humans.

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
	addendum prepared by DE. The results of the Landgreen study (2009) were briefly discussed. The RMS agreed with the assessment of IARC. There is no significant association of decreased monoclonal gammopathy that could have been linked to an increased incidence of myelomas. Conclusion: The participants agreed with the evaluation of the RMS (DE): There is no statistically significant increased incidence of the multiple myeloma linked to glyphosate exposure.	
Experts consultation 2.4: MSs experts to review the evidence of association of glyphosate to non-Hodgkin lymphoma (NHL), in an experts meeting. See also 2.6, 2.11, 2.13, 2.14, 2.19	**BACKGROUND** **ADDENDUM:** **Table 2.2 2:** Summary of the RMS assessment on the strength of evidence and validity of epidemiological studies mentioned by IARC **De Roos et al. 2003**: reported an association between NHL and glyphosate use. No unequivocal evidence for causation of NHL by glyphosate based on a pooled analysis of three case control studies and reported exposures with 47 pesticides. Logistic regression and hierarchical model provide significant effect (OR, 2.1 with 95% confidence interval (CI) 1.1 to 4.0) and non-significant effect (OR, 1.6 with 95% CI 0.9 to 2.8), respectively, the latter with adjustment for multiple exposures and using prior probability of 0.3 for glyphosate as being carcinogenic. Contrary to common standards, the authors consider the result from the hierarchical model as significant. The description of the study design, analysis and results do not allow assessing methodological quality. The relevance of the study for the current risk question is high. **McDuffie et al. 2001**: mentioned a non-significant positive association between self-reported glyphosate exposure and NHL in a Canadian study. OR_{adj} = 1.20 (0.83/1.74): low effect size, not significant; no unequivocal evidence for causation of NHL by glyphosate. Low/medium relevance case control study. **Eriksson et al. 2008**: reported a case-control study which included 910 cases of NHL and 1016 controls living in Sweden. Glyphosate exposure was reported by 29 cases and 18 controls, and the corresponding OR was 2.02 (1.10-3.71) medium effect size, significant; a multivariate analysis gave no significant results. Medium relevance. **De Roos et al. 2005**: make use of the AHS cohort. OR = 1.1 [0.7, 1.9] for NHL, adjusted for age, demographic and lifestyle factors, and other pesticides. High/medium relevance.	The majority of the experts agreed that there is very limited evidence of association of glyphosate with NHL.

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
	Orsi et al. 2009: did not find an association between NHL and glyphosate handling in a French case control study (OR = 1.0) [0.5, 2.2] for any exposure (12 cases, 24 controls), OR = 1.0 [0.3, 2.7] for professional exposure (5 cases, 24 controls). Medium relevance. **Hardell et al. 2002:** not relevant for the link between glyphosate and NHL as the study reported NHL and HCL diagnosis. **COMMENTS:** Regarding case-control studies on NHL, due to a number of limitations (low power, glyphosate or glyphosate formulation), very few studies show marginally increased ORs. In addition, in many studies, these ORs were not statistically significant. A meta-risk ratio of 1.3 (CI 1.03-1.65) for NHL on the basis of 6 studies appears rather weak. It is impossible to exclude that it is due to chance. Case-control studies, while potentially affected by recall, have the benefit of being focussed on specific causes of death and comparing the exposures experienced by the cases to that of the controls. The inclusion of the Hardell study in the meta-analysis will have inflated the resulting RR as this study found the highest RR of all included in the meta-analysis, but also had the widest confidence interval, as there were only 8 cases and controls who had glyphosate exposure. Regarding De Roos et al 2003, it is not very transparent why the study authors considered the result from hierarchical regression model (providing more conservative estimates than logistic regression, according to IARC) as significant, with an OR 1.6, 95% CI 0.9-2.8. Moreover, it is stated that the description of the study design, analysis and results do not allow assessing methodological quality. Regarding De Roos et al 2005, it is unclear why the much bigger study of the prospective AHS cohort was not given a higher weight in the overall assessment of the possible association between glyphosate use and NHL. A higher weight in the overall assessment of the possible association between glyphosate use and NHL (non-Hodgkin lymphoma) should be given to the most powerful study, the AHS (Agricultural Health Study), the prospective cohort-study, which in epidemiological terms is best suited to study the relationship showed no association with cancer incidence.	

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
	PESTICIDES PEER REVIEW TC117 It was noted that there is a statistically significant association between glyphosate exposure and NHL, but the number of studies is small. Therefore, more studies would be needed to make stronger conclusion of the causality. There was a question on the use of the hierarchical regression model, it was clarified that both models (logistic regression and hierarchical models) analysis were considered by IARC. The link of exposure to NHL cannot be fully supported by the RMS. Some experts expressed also the view that there is inadequate evidence due to the poor consistency and statistical power. Some experts commented on the limited quality of the studies and therefore, placing the causality under discussion. The quality of the studies was not questioned by the majority of the experts, only the consistency of the results. As NHL is not a rare tumour, a greater weight should be given to the cohort study. The Assessment of the RMS was based on association and not on causality. Other experts expressed the view that there is credible evidence, however limited as chance, bias and confounding could not be ruled out. <u>Conclusion:</u> The majority of the experts agreed that there is very limited evidence of association of glyphosate with NHL (Minority views were expressed for the IARC classification "limited evidence" and for "inadequate evidence"; see above.) The overall discussion on classification will take into account all points (human, animal data and mechanistic data).	
Experts consultation 2.5: MSs experts to discuss the evidence of association of	**BACKGROUND** **ADDENDUM:** **Table 2.3-1:** Discussion of studies in section 2.3 'Case-control studies on other cancer sites' and section 2.4 'Meta-analyses' of the IARC monograph **Carreon et al, 2005:** Regarding pesticide exposure and risk of gliomas, there was a	For the Carreon *et al* 2005 study it was agreed, that there is no evidence for an increased risk for gliomas.

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
glyphosate to carcinogenicity in other cancer sites (gliomas) in an experts meeting.	reduced risk for glyphosate (OR 0.7 (0.4 - 1.3). **COMMENTS:** It should be clarified why or whether the risk is reduced. As the CI range extends around 1.0 the conclusion should be no increased risk, as is given for studies with similar CI ranges. **PESTICIDES PEER REVIEW TC117** For the Carreon *et al* 2005 study it was agreed, that there is no evidence for an increased risk for gliomas.	
Experts consultation 2.7: MSs experts to discuss the evidence of association of glyphosate to carcinogenicity in meta-analysis studies and the overall evidence from epidemiological studies in an experts meeting. See also 2.1, 2.8, 2.12, 2.15, 2.16, 2.17, 2.18, 2.19, 2.20, 2.21, 2.22, 5.1	**BACKGROUND** **ADDENDUM:** Possible classification of glyphosate as 'limited evidence of carcinogenicity in humans' based on epidemiological studies. **COMMENTS:** - role of co-formulants in epidemiological studies, there could be a problem with the formulation. Since epidemiological data are by definition collected on people who have been in contact with the product and not with the pure a.s. itself. - causality has not been established and the findings could be due to chance, bias or confounding - inconsistency across studies and in most cases non-statistically significant associations are reported, an analysis of causality according to the Bradford-Hill criteria would have been useful. - where there is a suggestion of an association the cohort studies have limited power to conclude a statistically significant relationship/trend, there is mixed evidence from the case-control studies. - as regards the choice in categories, some doubts remain, and this should be discussed. It seems that classification as "Inadequate evidence of carcinogenicity…" is also defendable. It is agreed that 4 epidemiological studies on 16 are of acceptable quality/power, but	There is very limited evidence for an association between glyphosate based formulations and NHL. Overall inconclusive for a causal or clear associative relationship between glyphosate and cancer in human studies.

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
	overall, the results are far from consistent. On the other hand, stating that there is "limited evidence of carcinogenicity…for which a causal interpretation is considered credible…" is not entirely supported by the facts as well. RMS is right in clarifying that it is a matter of expressing the remaining uncertainty, and it seems that the choice was merely driven by the precautionary principle. - cautious vs. precautionary approach are mentioned - the limitations of the epidemiological studies were highlighted: multiple exposure, low power, very few studies show marginally increased ORs (not always statistically significant), quality criteria not always detailed, literature search and deletion of literature done for IARC not described in detail, internal validity not assess due to limitations in the reporting of the study. No measures from biomarkers from the blood are used (exposure measured through interviews or questionnaires), the number of cases involved and no knowledge of glyphosate or the type of glyphosate formulate used. Therefore, it is difficult to use the results of epidemiological studies to demonstrate a carcinogenicity potential of glyphosate, given the very weak, inconsistent (across studies) and in most cases non-statistically significant associations reported. - as most studies (including the most powerful one (the AHS prospective cohort-study) do not show a positive association of carcinogenicity with glyphosate, the relative weighting of the different studies could be further considered. - there is a big recall problem to judge the amount of exposure to chemicals or what substance or product was used over time and there may be a recall biases since individuals with cancer are more likely to think about possible reasons for their cancer than healthy individuals. **PESTICIDES PEER REVIEW TC117** The assessment the RMS presented in the addendum was supported. See experts consultation 2.4 above: There is very limited evidence for an association between glyphosate-based formulations and NHL. Overall inconclusive for a causal or a clear associative relationship between glyphosate and cancer in human studies.	

<table>
<tr><th>Subject</th><th>Discussion Pesticides Peer Review Meeting</th><th>Conclusions Pesticides Peer Review Meeting</th></tr>
<tr><td></td><td>Some MS highlighted that the terminology is not in line with CHL criteria. One MS considered that the epidemiological data support the IARC classification as limited evidence for cancer in humans and that the CLP criteria for limited evidence for cancer in humans are fulfilled.</td><td></td></tr>
<tr><td>Experts consultation 3.1:
MSs to discuss the carcinogenic profile in mice (renal tumours, haemangiosarcoma, malignant lymphomas) and relevance of different statistical analysis proposed in an experts meeting.

See also 3.2, 3.3, 3.4, 3.10, 3.11, 3.12, 3.15, 3.16, 3.21, 3.22, 3.24</td><td>BACKGROUND
ADDENDUM:
Table 3-1: Animal studies in mice reported by IARC and/or RMS
Table 5.3-1: summary of selected tumour incidences in male CD-1 mice
[redacted] 1983: 2-yr carcinogenicity study in CD-1 mice treated with dietary dose levels of 0, 1000, 5000, 30000 ppm (equal to 157/190; 814/955; 4841/5874 mg/kg bw per day in m/f);
Incidence of renal tubular adenomas and carcinomas in males:
<table>
<tr><th>Dose level (ppm):</th><th>0 (control)</th><th>1000</th><th>5000</th><th>30000</th></tr>
<tr><td>Adenomas</td><td>0/49</td><td>0/49</td><td>1/50 (2%)</td><td>3/50 (6%)</td></tr>
<tr><td>Adenomas (EPA PWG report)</td><td>1/49 (2%)</td><td>0/49</td><td>0/50</td><td>1/50 (2%)</td></tr>
<tr><td>Carcinomas</td><td>0/49</td><td>0/49</td><td>1/50 (2%)</td><td>2/50 (4%)</td></tr>
<tr><td>Combined</td><td>1/49 (2%)</td><td>0/49</td><td>1/50 (2%)</td><td>3/50 (6%)</td></tr>
</table>
[redacted] 1993: 2-yr carcinogenicity study in CD-1 mice treated with dietary dose levels of 0, 100, 300, 1000 mg/kg bw per day
<table>
<tr><th>Dose level (mg/kg bw per d):</th><th>0 (control)</th><th>100</th><th>300</th><th>1000</th></tr>
<tr><td>Haemangiosarcoma (males)</td><td>0/50</td><td>0/50</td><td>0/50</td><td>4/50 (8%)</td></tr>
<tr><td>Histiocytic sarcoma in the lymphoreticular/ haemopoietic tissue (males)</td><td>0/50</td><td>2/50 (4%)</td><td>0/50</td><td>2/50 (4%)</td></tr>
<tr><td>Haemangiosarcoma (females)</td><td>0/50</td><td>2/50 (4%)</td><td>0/50</td><td>1/50 (2%)</td></tr>
<tr><td>Histiocytic sarcoma in the lymphoreticular/ haemopoietic tissue (females)</td><td>0/50</td><td>3/50 (6%)</td><td>3/50 (6%)</td><td>1/50 (2%)</td></tr>
</table></td><td>There is no evidence of carcinogenicity in either rats or mice in experimental studies.
Overall, it was concluded that there is no evidence for carcinogenicity in mice due to lack of statistical significance in pair-wise tests, lack of consistency in multiple animal studies at dose levels at or above the limit dose/MTD, lack of pre-neoplastic lesions, and/or within historical control range.</td></tr>
</table>

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting

[redacted] **2001**: 18-month carcinogenicity study in Swiss albino mice

Table Error! No text of specified style in document.**-2:** Total incidence of malignant lymphoma in long-term studies with glyphosate in different mouse strains – also discussed during the Pesticides Peer Review Meeting 125 (25 – 27 February 2015)

Study, Strain		**Males**				**Females**			
[redacted] 2009, ASB2012-11492 Crl:CD-1 (ICR) BR	Dose (ppm)	0	500	1500	5000	0	500	1500	5000
	Affected	0/51	1/51	2/51	5/51	11/51	8/51	10/51	11/51
[redacted] 2001, ASB2012-11491 HsdOLA:MF1 (Swiss albino)	Dose (ppm)	0	100	1000	10000	0	100	1000	10000
	Affected	10/50	15/50	16/50	19/50*	18/50	20/50	19/50	25/50*
[redacted] 1997, ASB2012-11493 Crj:CD-1 (ICR)	Dose (ppm)	0	1600	8000	40000	0	1600	8000	40000
	Affected	2/50	2/50	0/50	6/50	6/50	4/50	8/50	7/50
[redacted] 1993, TOX9552382, CD-1 (not further specified)	Dose (mg/kg bw per day)	0	100	300	1000	0	100	300	1000
	Affected**	4/50	2/50	1/50	6/50	14/50	12/50	9/50	13/50

* increase statistically significant, for females based on percentage and not on total number of affected mice
** based on histological examination of lymph nodes with macroscopic changes

COMMENTS:

- Regarding [redacted], **1983**, the different results obtained between the original pathologist and the PWG raise a concern about the reliability of this study in CD-1

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
	mice. It is observed that only in one mouse study; both renal tubule adenoma and carcinoma appear at a higher incidence at the top-dose. The increase is not statistically significant (n.s.s.), and is only flagged positive by IARC because of the borderline significant trend test. Although it is observed that there are marginal increases of adenoma but not carcinoma at the top-doses of two other studies ([redacted] 1997 and [redacted] 2001), it seems debatable, in the absence of renal findings in the other mouse studies, if the renal findings are sufficient to classify for carcinogenicity. - Regarding [redacted] **1993**, It is also a concern that the same strain of mice (CD-1 mice) gives a completely different cancer profile response (renal tumours in the study above and haemangiosarcoma in this study). The reliability of the study is therefore questioned. Increased incidence at top-dose (1000 mkd) considered spurious, in the absence of the same finding in the other mouse studies (except 2 cases in the [redacted] study at the top-dose). If really compound-related, it is unlikely that the same tumour would not have been detected at higher incidence in the studies in CD-1 mice with top-doses >4000 mkd. - Regarding [redacted] **2001**, the increase in malignant lymphoma in Swiss albino mice stands against a very high background level in controls and historical controls. In addition, it has not been reproduced in any other strain of mice (or in rats) questioning its relevance to human cancer hazard. Except for the [redacted] 2001 study, the slightly elevated incidences of lymphoma in ♂at the top-doses are either within HCD, or display poor dose-response. For the study on Swiss Albino (2001), the rationale on the basis of known high spontaneous background levels in this strain by the RMS is supported. Although the top-dose lymphoma findings in 3/5 mouse studies (where trend-tests or pair-wise comparisons were significant) are the most consistent among the observed malignancies in the mouse, the overall weight of evidence would indicate that it is equivocal for classification. - In these studies statistical analysis with the Cochran-Armitage trend test yielded a significant result, whereas the analysis by pair-wise comparisons indicated no statistically	

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
	significant differences. One expert argued that trend tests are more sensitive than e.g. pair-wise comparison methods and as such would be preferable. According to the OECD guidance document on the conduct and design of chronic toxicity and carcinogenicity studies, significance in either kind of test is sufficient to reject the hypothesis that chance accounts for the result. Another view expressed that, according to the OECD 451 guideline for carcinogenicity studies, "the statistical method most appropriate for the analysis of results, given the experimental design and objectives, should be established before commencing the study". - Historical control data are mentioned. The high doses at which positive results were obtained in the trend tests and the fact that IARC has considered only 2 of the 5 mouse studies. There is no pattern of tumours in the studies and the doses are excessive. However, the renal tubular adenomas in the other mouse studies may require further investigation. **PESTICIDES PEER REVIEW TC117** The data should be looked at in an overall prospective. The results reported in p. 90 of the addendum from the RMS were discussed. For two of the mouse studies the tested dose was 4-5 times above the dose levels recommended by the OECD test guideline. The conclusion should not be drawn only on the statistical significance, but as well on the biological significance. For most of the studies HCD are available from the performing lab. The most appropriate statistical test should be decided on before the commencing of the study. Some experts considered that there is, at least, limited evidence for carcinogenicity in tested animals; a concern was raised for the malignant lymphoma in mice due to potential concordance with the human NHL findings. The malignant lymphomas in mice were already discussed in the Pesticides Peer Review expert meeting 125 (February 2015) as they would be the most critical findings. In that meeting the conclusion was "the experts (except one who expressed an uncertainty on this issue because of the lack of in-house HCD for the Wood study and exceedance of HCD in the [redacted] study) consider highly unlikely the carcinogenic potential of glyphosate". The US EPA evaluated 4 of the 5 studies. The [redacted] study was excluded due to the occurrence of viral infection that could influence survival as well as tumour incidence –	

<table>
<tr><th>Subject</th><th>Discussion Pesticides Peer Review Meeting</th><th>Conclusions Pesticides Peer Review Meeting</th></tr>
<tr><td></td><td>especially lymphomas.
Following the revised assessment in the addendum; the RMS no longer supports the conclusion of the 125 meeting.
Therefore the RMS's conclusion is now that there is no evidence of carcinogenicity in either rats or mice in experimental studies according to a weight of evidence (WoE) approach.
Overall, it was concluded that there is no evidence for carcinogenicity in mice due to a WoE approach taking into account lack of statistical significance in pair-wise tests, lack of consistency in multiple animal studies at dose levels at or above the limit dose/MTD, lack of pre-neoplastic lesions, and/or within historical control range.

The RMS's conclusion was supported the majority of experts (with one minority view).</td><td></td></tr>
<tr><td>Experts consultation 3.5:
MSs experts to discuss the carcinogenic profile observed in rats in an experts meeting.

See also 3.13, 2.23, 3.24</td><td>BACKGROUND
ADDENDUM:
[redacted] 1990: 2-yr combined chronic toxicity/carcinogenicity study in Sprague-Dawley rats fed glyphosate at dietary dose levels of 0 (controls), 2000, 8000 and 20000 ppm corresponding to 89/113, 362/457, 940/1183 mg/kg bw per day in males/females).
<table><tr><th>Dose level (ppm):</th><th>0 (control)</th><th>2000</th><th>8000</th><th>20000</th></tr><tr><td>Males</td><td></td><td></td><td></td><td></td></tr><tr><td>Pancreas (islet cell): adenoma</td><td>1/43 (2%)</td><td>8/45 (18%)</td><td>5/49 (10%)</td><td>7/48 (15%)</td></tr><tr><td>Carcinoma</td><td>1/43 (2%)</td><td>0/45</td><td>0/49</td><td>0/48</td></tr><tr><td>Adenoma/carcinoma (combined):</td><td>2/43 (5%)</td><td>8/45 (18%)</td><td>5/49 (10%)</td><td>7/48 (15%)</td></tr><tr><td>Liver: Hepatocellular adenoma</td><td>2/44 (5%)</td><td>2/45 (4%)</td><td>3/49 (6%)</td><td>7/48 (15%)</td></tr><tr><td>Hepatocellular carcinoma</td><td>3/44 (7%)</td><td>2/45 (4%)</td><td>1/49 (2%)</td><td>2/48 (4%)</td></tr><tr><td>Hepatocellular adenoma or carcinoma (combined)</td><td>5/44 (11%)</td><td>4/45 (9%)</td><td>4/49 (8%)</td><td>9/48 (19%)</td></tr></table></td><td>See above (experts consultation 3.1)</td></tr>
</table>

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting

Females				
Pancreas (islet cell): adenoma	5/60 (8%)	1/60 (2%)	4/60 (7%)	0/59
Carcinoma	0/60	0/60	0/60	0/59
Adenoma/carcinoma (combined):	5/60 (8%)	1/60 (2%)	4/60 (7%)	0/59
Thyroid: C-cell adenomas	2/60 (3%)	2/60 (3%)	6/60 (10%)	6/60 (10%)

COMMENTS:

Pancreas: there is definitely no proper dose-response (5,18,10,15% in ♂; 8,2,7,0% in ♀), and no carcinoma. In two other rat studies, the combined incidences also show no dose-response, or are absent. Overall, pancreatic lesions do not trigger any classification.

Liver: only trend in increased adenoma (11,9,8,19%), with a poor dose response, and no carcinoma.

It was also mentioned that the liver adenoma in males was increased at the top dose against a very high background in controls and did not progress to carcinoma.

The thyroid C-cell adenoma in females showed a very flat response and did not progress to carcinoma

C-cell adenoma: slight trend: 3,3,10,10%.

- While there is no clear dose-response relationship in the incidence of pancreatic islet-cell adenomas, liver cell and thyroid C-cell adenomas appear at high dose levels around the limit dose of 1000 mg/kg bw per day
- Regardless of statistics, the biological plausibility of the reported tumours in SD rats in this study points towards chance.
- In rats, positive trends in adenomas are noted in one out of nine valid studies (Stout and Reucker, 1990).
- Six of the 9 rat studies have been considered by IARC.

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The conclusion reached in the discussion above for mice was confirmed for rats.

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
Experts consultation 3.6: MSs experts to discuss the overall weight of evidence and need for classification according to CLP regarding the carcinogenic profile of glyphosate in an experts meeting. See also 3.9, 3.12, 3.14, 3.15, 3.17, 3.18, 3.19, 3.20, 3.23, 3.24, 5.2, 5.3, 5.4	**BACKGROUND** **ADDENDUM: 3. Cancer in Experimental animals** **COMMENTS:** - With so many studies (6 in the mouse and 10 in the rat), consistency and reproducibility are very important factors to take into account in making a decision. The overall WoE indicates that there is no unequivocal evidence of carcinogenicity in animals. - It is obvious that the overall evaluation by RMS and IARC cannot be the same, since a number of studies in the EU-dossier were not available for the IARC workgroup. An overall assessment is in this case justified to put into perspective the observed (non-statistically significant) elevated tumour incidences at the top-doses. - Although the top-dose lymphoma findings in 3/5 mouse studies (where trend-tests or pair-wise comparisons were significant) are the most consistent among the observed malignancies in the mouse, the overall weight of evidence would indicate that it is equivocal for classification. In this addendum to the RAR, RMS has well elucidated the possible causes of a different classification outcome between the EU and IARC. It was unfortunate that IARC did not take into account 3 guideline studies in both mice and rats, since this could have put the overall conclusions in another perspective. Next, relying on significant trends to declare a finding eligible for classification is a policy decision not supported by the EU. Further, CLP-criteria such as spontaneous incidence and excessive toxicity confounders are key elements in the discussion by the RMS, and supported. One important point, perhaps under stressed, is the consistency of outcome, which is poor among the various studies. - The evidence for carcinogenicity in experimental animals is at least limited as compared to the IARC and CLP criteria. Reference to historical control data would not abrogate the positive results from the trend tests. Possibly, the high doses and resulting toxicity may have influenced the tumour outcome in the high dose groups in some of the rodent studies. - Effects do not necessarily have to appear in a consistent dose-dependent manner, in order to be considered as a treatment-related effect. In our opinion, too much weight is given to the factors "progression of lesions to malignancy" as well as "whether responses are in single or both sexes". This will for instance implicate that studies, in which a	The evidence does not support classification with regard to carcinogenicity.

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
	treatment-dependent increase in adenomas in male rats is demonstrated, will not be taken into consideration when evaluating the carcinogenic potential. - Agreement with RMS was expressed based on a weight of evidence approach: considering all available carcinogenicity studies for consistency and reproducibility, lack of statistical significance or dose-relationship and within the range of historical controls. Confounding effect of excessive toxicity cannot be excluded and be the cause of the increased incidence of tumours at the highest dose in life time studies. Thus, based on the data from six carcinogenicity studies in mice and ten chronic toxicity and carcinogenicity in rats, the weight of evidence suggest that no hazard classification for carcinogenicity is warranted for glyphosate according to the CLP criteria. - Additional discussion could be useful on the fact that there are no reports of renal or pancreatic tumours in the epidemiology versus the animal findings. In addition the lack of consistency within the animal studies, and within the epidemiology, could be brought out further. Table 5.3-1 is excellent in displaying the variability between similar studies. **PESTICIDES PEER REVIEW TC117** The RMS stated that there is no need for classification according to the CLP criteria, taking as well into consideration the conclusions under the previous points. Some MSs stated, that the strength of evidence is not sufficient to propose classification One expert proposed to classify the active substance as, at least, carcinogen cat. 2 based on limited evidence of cancer in mice. Conclusion: Based on a weight of evidence approach, the evidence does not support classification with regard to carcinogenicity, (one minority view).	
Experts consultation 4.1: MSs experts to discuss the genotoxic potential of glyphosate	**BACKGROUND** **ADDENDUM:** **4.2.1 Genetic and related effects**: Table 4.2-1 (Glyphosate; mutagenicity tests in mammalian cells or bacteria *in vitro*)/2 (Glyphosate; genotoxicity tests in mammalian cells or bacteria *in vitro*)/3 (Glyphosate; somatic cell mutagenicity tests in mammals, *in vivo*)/4	The experts agreed to the conclusion of the RMS, that classification for mutagenicity is not warranted for glyphosate. In general, it is recognised that the

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
See also 4.2, 4.6, 4.8, 4.9, 4.10, 4.11, 4.12, 4.13, 4.14, 4.15, 5.4	(Glyphosate; further tests on DNA adducts and DNA strand breaks in mammals, in vivo)/5 (Glyphosate; germ cell mutagenicity tests in mammals, *in vivo*) **COMMENTS:** - The *in vitro* and *in vivo* WoE shows that glyphosate is not genotoxic. The active substance glyphosate can be considered as devoid of genotoxic properties and that a classification for mutagenicity is not warranted according to the CLP criteria. - We would be cautious about placing too much reliance on results from new assay types in unusual species (e.g. Comet assay in eels), when there is no indication of a concern from standard regulatory studies. - Agreement with RMS to conclude that, on a WoE basis, glyphosate should not be considered a genotoxic agent. This conclusion is mainly based upon established guideline studies. It was unfortunate that most of the *in-vivo* micronucleus assays submitted in the EU-dossiers were unavailable to IARC, as the result of these could have put into context the few positive published studies, which became decisive in the IARC conclusion. Inconsistent results were obtained in the published studies on indicator genotoxicity endpoints (DNA strand break, DNA adducts). In the IARC monograph, these tests are listed among the other studies on chromosome aberration, without further interpretation. - It should be confirmed by the experts that the few positive results (*in vitro* DNA damage and *in vivo* tests) in the database can be reliably discounted by the (numerous) negative results. - Concerns were expressed on genotoxicity of glyphosate. Some *in vitro* and *in vivo* studies seems to suggest clastogenic effects. Possibly, a modern Comet assay in relevant target tissues such as kidney, liver and bone marrow should be undertaken. Presently, the genotoxicity data would contribute to an increased level of concern in the weight of evidence assessment of glyphosate carcinogenicity. - A number of non-regulatory studies both *in vitro* and *in vivo* investigating glyphosates DNA damaging potential have shown positive results. We suggest that a regulatory *in vivo* mammalian alkaline comet assay (for instance, in the rat liver and kidney) should be conducted according to OECD 489. It would be interesting to know which mouse strains are used in the tests for genotoxicity, since it pointed to a possible strain specific effect in mice (in the conclusion from RMS on section 3 Cancer in experimental animals on page	issue of toxicity of the formulations should be considered further (there are some published studies on the formulation – not GLP and not according to the OECD guidelines – showing positive results).

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
	44). - Based on the results of published data, no firm conclusions can be drawn on the genotoxic potential of the formulations; uncertainty remains about the genotoxicity (comet assay) of glyphosate-based formulation. **PESTICIDES PEER REVIEW TC 117** The RMS refers to the addendum p. 46 ff. The RMS concluded that taking into account all available data and using the weight of evidence approach, glyphosate does not induce mutations *in vivo* and no classification for mutagenicity is warranted. A Comet assay would not change the assessment and the overall conclusion. Human studies have not been evaluated by the RMS, since the exposure was to glyphosate formulations of unknown composition. They were considered weak and would not have changed the overall conclusion. Therefore more weight was given to studies according to GLP. It was discussed whether a Comet assay would add more information to the assessment of mutagenicity. The experts agreed to the conclusion of the RMS, that no classification for mutagenicity is warranted. There are two minority views that considered that further studies should be requested (Comet assay) mostly in order to further inform on potential genotoxicity as a mode of action for carcinogenicity. RMS mentioned that the role of co-formulants was assessed in the RAR, which could explain the effects seen; indeed genotoxicity studies with the formulation would be helpful. In general, it is recognised that the issue of toxicity of the formulations should be considered further (there are some published studies on the formulation – not GLP and not according to the OECD guidelines – showing positive results).	
Experts consultation 4.4: MSs experts to discuss the potential mode of action of glyphosate through oxidative stress	**BACKGROUND** **ADDENDUM:** 4.2.3.1: Oxidative stress **Astiz et al. 2009b**: nine groups of four male Wistar rats were used to investigate the effects of glyphosate, dimethoate and zineb administered alone or in combination on	Considering the lack of evidence for carcinogenic potential of glyphosate, no further consideration regarding the mode of action is required.

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
in an experts meeting. See also 4.16, 5.4	defence systems of the liver, kidney, brain and plasma antioxidant by intraperitoneal injections (3/week for 5 weeks) 10 mg glyphosate/kg bw. Overall, lower antioxidant status in liver, brain, kidney and plasma, higher oxidized protein and glutathione levels in plasma with a decreased concentration of α-tocopherol in brain and liver were observed. SOD was decreased in liver and brain. Glutathione reductase was inhibited in liver while glutathione peroxidase and transferase were unaffected. Plasma lactate dehydrogenase was not affected, but γ-glutamyl transpeptidase activity was increased. In conclusion the IARC statement can be supported that there are indications of oxidative stress in the blood plasma, liver, brain and kidney of rats upon exposure to glyphosate. **COMMENTS:** - Although there are some indications in vitro of oxidative stress, the *in vivo* study in rats (Astiz, 2009b) shows effects that cannot be relied upon as the study was conducted by i.p. administration. By this route of exposure, the normal, physiological detoxification mechanisms of glyphosate are bypassed. On this point, there is disagreement with IARC and RMS that there is significant evidence that glyphosate causes adverse effects through oxidative stress. Further studies by relevant routes of exposure should be performed. - indications of the occurrence of oxidative stress have been observed in one *in vivo* study in combination with cytotoxic/degenerative effects upon intraperitoneal injections to male rats (Astiz et al. 2009b). A parallel could be established with slightly increased tumour incidence in some studies at high dose levels. **PESTICIDES PEER REVIEW TC117** Positive *in vivo* results are available (IP administration) but there is a lack of evidence for carcinogenicity. Due to the lack of carcinogenicity there is no need to further investigate any potential mode of action. There is one minority view.	
Experts consultation 4.5: MSs experts to discuss the immunosuppression	**BACKGROUND** **ADDENDUM:** 4.2.3.2 Inflammation and immunomodulation,	Considering the lack of evidence for carcinogenic potential of glyphosate, no further consideration regarding the mode of action is required.

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
potential of glyphosate in an experts meeting. See also 4.17, 5.4	**Table 4.2-9**: Discussion of studies in chapter 4.2.3 (b) Inflammation and immunomodulation of the IARC monograph **Kumar et al. 2014**: the positive response could be interpreted as qualitative information indicating a potential for airway inflammation. **Chan and Mahler, 1992**: in subchronic studies in rats and mice effects on thymus weight and haematological parameters have been observed. The results are not sufficient to indicate an immunosuppressive effect of glyphosate. More likely they could be interpreted as a nonspecific (toxic) response. Other studies appear to have been performed with glyphosate-based formulations. **COMMENTS:** There is very little evidence to conclude that glyphosate causes immunosuppression. This endpoint has not been evaluated adequately. As the evidence from the available data on immunosuppression is insufficient to conclude on the immunomodulatory action of glyphosate, it should be discussed whether a concern remains that should be addressed regarding this endpoint. **PESTICIDES PEER REVIEW TC117** The RMS concluded that, due to the limited data, there is no evidence for immunosuppressive or immunotoxic properties of glyphosate. A single clear finding of immunosuppression is not supported further by any repeated dose study in the overall data base. <u>Conclusion</u>: All experts agreed that the evidence of immunosuppression is very weak and no further studies are required.	Furthermore the database does not provide any alert regarding an immunosuppressive potential of glyphosate. No further study is required.

0. General

No open points

1. Identity, Physical and chemical properties, Details of uses and further information, Methods of analysis

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Data requirement 1.1 Applicant to submit data for the auto-flammability of the K salt See reporting table 1(9)	RMS: A study on the auto-flammability of the K salt was submitted by the applicant. The study is acceptable for the RMS, and the result is reported in a revised Volume 3.	Not applicable.		Addressed: The auto-flammability of the K salt was submitted and presented in the revised Vol.3
Data requirement 1.2 Applicant to submit information concerning the oxidising properties of MON 52276 See reporting table 1(12)	RMS: A justification according to the UN Recommendations on the Transport of Dangerous Goods (UN no. ST/SG/ AC.10/11/Rev.5) was submitted by the applicant which is considered acceptable for the RMS. The result is reported in a revised Volume 3.	Not applicable.		Addressed: A justification according to the UN Recommendations on the Transport of Dangerous Goods (UN no. ST/SG/ AC.10/11/Rev.5) was submitted and presented in the revised Vol.3
Data requirement 1.3 Applicant to submit a full comparison of the formulation compositions (MON 78043 and MON 78044 vs. MON 52276) See reporting table 1(17)	RMS: The composition of the formulations was submitted by the applicant and was considered as equivalent. The composition of MON 78043, MON 78044 and MON 52276 is included in a revised Volume 4 (Monsanto).	Not applicable.		Addressed: A comparison of the formulation compositions (MON 78043 and MON 78044 vs. MON 52276) was included in a revised Volume 4 (Monsanto)
Data requirement 1.4	RMS: A persistent foam	Not applicable.		Addressed:

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
Applicant to submit the persistent foam study result using the concentration corresponding to the highest rate of use See reporting table 1(20)	study was submitted by the applicant. The result is reported in a revised Volume 3.			The persistent foam study was submitted and presented in the revised Vol.3
Data requirement 1.5 Additional data to address the efficiency and precision of the derivatisation step of the methods using derivatisation. See reporting table 1(29)	RMS: Open point. The applicant (GTF) has provided a short statement, that it is impossible to address the efficiency as required in SANCO/825/00 rev. 8.1. The RMS does not accept the arguments.	Not applicable.		Data gap: A new confirmatory method for residues in soil
Open point 1.1 RMS to amend Vol. 3 B.5 B.5.2.1.1.1, B.5.2.1.1.3, B.5.2.1.1.4, B.5.2.1.2 (two times), and B.5.5. of the RAR and the LoEP replacing ‘lentils’ by ‘sweet corn’ See reporting table 1(30)	RMS: Addressed in revised RAR and LoEP.	Not applicable.		Addressed: ‘lentils’ were replaced by ‘sweet corn’ in the respective parts of the RAR and the LoEP.
Data requirement 1.6	RMS: Open point.	Not applicable.		Data gap:

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
Applicant to submit the additional validation data for the analytical methods for glyphosate in matrices of animal origin. See reporting table 1(38)	The applicant (GTF) has provided a new study (Garrigue, 2014). However, this study requires the same derivatization step, which resulted in data requirement 1.5. Unfortunately, data requirement 1.5 is also not addressed in this new study.			A confirmatory method for glyphosate in fat and liver/kidney as well as a confirmatory method for *N*-acetyl-glyphosate in all animal matrices
Data requirement 1.7 Applicant to submit a confirmatory method for *N*-acetyl-glyphosate in dry plant materials and those with high water and high fat content and a confirmatory method for *N*-acetyl-glyphosate in all kinds of animal matrices. See also comment 3(18) See reporting table 1(48)	RMS: Open point. The applicant (GTF) has provided a short statement, that N-acetyl-glyphosate should not be included in the residue definition for monitoring. The RMS does not accept the arguments.	Not applicable.		Data gap: Applicant to submit a confirmatory method for *N*-acetyl-glyphosate in dry plant materials and those with high water and high fat content and a confirmatory method for *N*-acetyl-glyphosate in all kinds of animal matrices.
Data requirement 1.8 According to Art. 10(3) of Reg. (EU) No 1141/2010 the supplementary complete	RMS: Open point. The applicant (GTF) has not provided the eight studies owned by DuPont. All monitoring methods for food of plant and animal	Not applicable.		Data gap: The studies that are not part of the dossier for renewal and were evaluated in the RAR should be submitted to the COM, MSs and EFSA for

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
dossiers shall contain the full text of each test and study report, as a consequence all the studies that are not part of the dossier for renewal (highlighted in yellow) and were evaluated in the RAR should be submitted to the COM, MSs and EFSA for transparency reasons and to have access to the raw data evaluated. See reporting table 1(53)	origin are based on DuPont studies.			transparency reasons and to have access to the raw data evaluated. (According to Art. 10(3) of Reg. (EU) No 1141/2010 the supplementary complete dossiers shall contain the full text of each test and study report)
Data requirement 1.9 Spectra of relevant impurities. The data requirement has already been identified in the RAR See reporting table 1(54)	RMS: The missing purity of the tested sample was submitted by the applicant.	Not applicable.		Addressed: The missing purity of the tested sample was submitted and presented in a revised RAR
Data requirement 1.10 A confirmatory method for glyphosate in animal fat and kidney/liver.	RMS: Open point. The applicant (GTF) has provided a new study (Garrigue, 2014). However, this study requires the	Not applicable.		Data gap: A confirmatory method for glyphosate in animal fat and kidney/liver

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
Relevant, basic data set for all active substances! The data requirement has already been identified in the RAR See reporting table 1(55)	same derivatization step, which resulted in data requirement 1.5. Unfortunately, data requirement 1.5 is not addressed in this new study.			See also data gap in 1(6)
Open point 1.2 RMS to amend Vol. 3 B.3.1.5 with the cross reference to B.3.2.2 and B.3.2.8 in a corrigendum, or updated RAR. See reporting table public consultation 1(5)	RMS: Accepted. The RAR has been amended.	Not applicable.		Addressed: The RMS amended the cross references in a revised RAR
Open point 1.3 RMS to amend Vol. 3 B.3.2.2 with the cross reference to B.3.1.5 and B.3.2.8 in a corrigendum, or updated RAR. See reporting table public consultation 1(6)	RMS: Accepted. The RAR has been amended.	Not applicable.		Addressed: The RMS amended the cross references in a revised RAR
Open point 1.4 RMS to amend Vol. 3 B.3.2.8 with the cross reference to B.3.1.5 and B.3.2.2 in a corrigendum,	RMS: Accepted. The RAR has been amended.	Not applicable.		Addressed: The RMS amended the cross references in a revised RAR

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
or updated RAR. See reporting table public consultation 1(7)				
Open point 1.5 RMS to update the Vol.3 B.3 with the information from col. 3 of the RT concerning the additional resistance cases and species were added to the database of Heap (2014) in a corrigendum, or updated RAR. See reporting table public consultation 1(8)	RMS: Additional resistance cases and species added to the database of Heap until Nov 2014 were added to the updated RAR.	Not applicable.		Addressed: Additional resistance cases and species added to the database of Heap until Nov 2014 were added to the updated RAR
Open point 1.6 RMS to propose one reference specification, independent from the synthesis pathway, supported by toxicological data based on batches of known composition. It should be noted that one common specification covering all sources would facilitate the registration of PPPs	RMS: The reference specification proposed by the applicant (GTF) was not covered by the available toxicological data. An alternative proposal was derived by RMS's toxicology experts. Several sources are available which are equivalent to this proposed reference specification.	Not applicable.		Addressed: The reference specification proposed by the applicant (GTF) was not covered by the available toxicological data. An alternative proposal was derived by RMS's toxicology experts.

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
containing glyphosate in the EU member states. It should also be emphasised that in the lack of such a specification and taking into account the RMS conclusion in the general Vol.4 : "…it cannot be evaluated, whether the material used in toxicological studies is representative for the proposed specification or the reference specification derived during the previous EU evaluation." "In summary, based on the currently available data and information, safe maximum levels for relevant impurities cannot be derived." , EFSA will have to conclude in the EFSA conclusion that there is no reference specification for this active substance. See general confidential reporting table 1(1)				

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
Data requirement 1.11 Applicant GTF to submit additional data/information to allow to judge whether the impurities are of toxicological relevance or not and to provide data/information demonstrating that the materials used in toxicological studies are representative for the proposed specification. See general confidential reporting table 1(2)	RMS: The submitted data/information is described and evaluated in the revised Vol. 4 (general information).	Not applicable.		Addressed: The submitted data/information was evaluated in the revised Vol. 4 (general information).
Open point 1.7 RMS to amend Vol.4 AFR, C.1.2.4 with the information from col.3 of the RT. See also comment 1(4) See Afrasa confidential reporting table 1(1)	RMS: Volume 4 was revised.	Not applicable.		Addressed: RMS amended Vol.4 AFR, C.1.2.4 with the information from col.3 of the RT in a revised Vol. 4.
Open point 1.8 RMS to update the wording concerning imp.13 in Vol. 4, RAR, AFR, C.1.2.4	RMS: A new reference specification was proposed where impurity 13 is included.	Not applicable.		Addressed: A new reference specification was proposed where impurity 13 was included.

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
Toxicological evaluation, to avoid the misunderstanding that this impurity was also in the reference specification. See Afrasa confidential reporting table 1(2)				
Data requirement 1.12 Applicant Industrias Afrasa to submit the reports : Reverse Mutation Assay using Bacteria (Salmonella typhirium) with Glyphosate (BSL Bioservice Report nr 126159) and Glyphosate: Tier 2: Evaluation of toxicological Properties of Impurities; GABConsulting GmbH, Report nr 616141-A2-0501-01 by Eurotox registred Toxicologist to be evaluated in an addendum. See also comment 1(6) See Afrasa confidential	RMS: The submitted study and the statement are described and evaluated in the revised Vol. 3/B.6 or the revised Vol. 4 (general information), respectively.	Not applicable.		Addressed: The RMS described and evaluated the submitted study and the statement in the revised Vol. 3 and the revised Vol. 4 (general information)

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
reporting table 1(4)				
Open point 1.9 RMS to amend the proposed specification in a revised Vol. 4 of Afrasa See Afrasa confidential reporting table 1(5)	RMS: A new specification was submitted and reported in a revised Volume 4.	Not applicable.		Addressed: A new specification was submitted and reported in a revised Volume 4. (Afrasa)
Data requirement 1.13 Applicant AGRIA to submit data/information concerning the assessment of toxicological relevance of the impurities and data/information demonstrating that the material used in toxicological studies is representative for the proposed specification. See Agria confidential reporting table 1(4)	RMS: The submitted data/information is described and evaluated in the revised Vol. 4 (general information).	Not applicable.		Addressed: The RMS evaluated the submitted data/information in the revised Vol. 4 (general information).
Data requirement 1.14 Applicant Agrichem to submit data/information concerning the assessment of	RMS: The submitted data/information is described and evaluated in the revised Vol. 4 (general information).	Not applicable.		Addressed: The RMS evaluated the submitted data/information in the revised Vol. 4 (general

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
toxicological relevance of the impurities and data/information demonstrating that the material used in toxicological studies is representative for the proposed specification. See Agrichem confidential reporting table 1(3)				information).
Data requirement 1.15 Applicant Agrotrade to submit data/information concerning the assessment of toxicological relevance of the impurities and data/information demonstrating that the material used in toxicological studies is representative for the proposed specification. See Agrotrade confidential reporting table 1(3)	RMS: The submitted data/information is described and evaluated in the revised Vol. 4 (general information).	Not applicable.		Addressed: The RMS evaluated the submitted data/information in the revised Vol. 4 (general information).
Data requirement 1.16 Applicant Albaugh to	RMS: The submitted data/information is described and evaluated in	Not applicable.		Addressed:

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
submit data/information concerning the assessment of toxicological relevance of the impurities and data/information demonstrating that the material used in toxicological studies is representative for the proposed specification. See Albaugh confidential reporting table 1(5)	the revised Vol. 4 (general information).			The RMS evaluated the submitted data/information in the revised Vol. 4 (general information).
Data requirement 1.17 Applicant Arysta to submit data/information concerning the assessment of toxicological relevance of the impurities and data/information demonstrating that the material used in toxicological studies is representative for the proposed specification. See Arysta confidential reporting table 1(6)	RMS: The submitted data/information is described and evaluated in the revised Vol. 4 (general information).	Not applicable.		Addressed: The RMS evaluated the submitted data/information in the revised Vol. 4 (general information).
Data requirement 1.18	RMS: The use of the reaction solution for the	Not applicable.		Addressed: The additional validation data

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
Applicant Arysta to provide additional validation data for the determination of the impurity 2. See Arysta confidential reporting table 1(14)	derivatisation of impurity 2 was provided by the applicant. Volume 4 was amended accordingly.			for the determination of the impurity 2 were presented in the revised Vol.4 (Arysta)
Data requirement 1.19 Applicant Arysta to provide the fortification levels for the determination of the accuracy data for the determination of the impurity 21. See Arysta confidential reporting table 1(15)	RMS: The fortification level were provided by the application. Volume 4 was revised accordingly.	Not applicable.		Addressed: The fortification levels for the determination of the accuracy data for the determination of the impurity were presented in the revised Vol.4 (Arysta)
Data requirement 1.20 Applicant Barclay to submit the manufacturing dates for both sources to be included in a revised RAR See Barclay confidential reporting table 1(4)	RMS: The manufacturing dates for both sources were submitted by the applicant and have been included in the Volume 4.	Not applicable.		Addressed: The manufacturing dates were presented in the revised Vol.4 (Barclay)
Open point 1.10	RMS: An updated Document J was submitted.	Not applicable.		Addressed: The correct maximum content

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
RMS to correct the data for the maximum content of the impurity 20 in a revised Vol.4. See Barclay confidential reporting table 1(8)	The correct maximum content of impurity 20 is given in Volume 4.			of the impurity was presented in the revised Vol. 4. (Barclay)
Data requirement 1.21 Applicant Barclay to submit data/information concerning the assessment of toxicological relevance of the impurities and data/information demonstrating that the material used in toxicological studies is representative for the proposed specification See Barclay confidential reporting table 1(9)	RMS: The submitted data/information is described and evaluated in the revised Vol. 4 (general information).	Not applicable.		Addressed: The RMS evaluated the submitted data/information in the revised Vol. 4 (general information).
Open point 1.11 RMS to correct the typo concerning the mobile phase in a corrigendum. See Barclay confidential reporting table 1(10)	RMS: The typo was corrected.	Not applicable.		Addressed: The typo concerning the mobile phase was corrected in the revised Vol.4 (Barclay)
Open point 1.12	RMS: The typo was	Not applicable.		Addressed:

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
RMS to correct the typo concerning the mobile phase in a corrigendum. See Barclay confidential reporting table 1(11)	corrected.			The typo concerning the mobile phase was corrected in the revised Vol.4 (Barclay)
Open point 1.13 RMS to correct the content of NNG in the table C.1.2-2 in an updated Vol.4 See Barclay confidential reporting table 1(13)	RMS: In Table C.1.2-2 the content of NNG was reported as < 0.2 ppm which corresponds to the LOQ. Furthermore, the maximum limit of NNG was aligned to the LOQ in the table C.1.2.4 by the RMS.	Not applicable.		Addressed: The maximum limit of NNG was aligned to the LOQ in the table C.1.2.4 by the RMS in a revised Vol.4. (Barclay)
Data requirement 1.22 Applicant Barclay to submit representative chromatograms for the determination of the impurity 21, to be evaluated in a revised Vol.4 See Barclay confidential reporting table 1(16)	RMS: The applicability of the method was demon-strated by representative chromatograms. Volume 4 was revised.	Not applicable.		Addressed: The applicability of the method was demonstrated by representative chromatograms. RMS updated the Vol. 4 (Barclay)
Open point 1.14 RMS to include the provided specification for	RMS: The specification provided by Brokden was included in a revised Volume 4.	Not applicable.		Addressed: The specification provided by Brokden was included in a

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
Brokden in an updated Vol.4 See Brokden confidential reporting table 1(1)				revised Vol. 4.
Open point 1.15 RMS to include the information about the starting materials for Brokden in an updated Vol.4 See Brokden confidential reporting table 1(2)	RMS: Information on the commercial availability of the starting materials was provided. This information was included in a revised Volume 4. Information on the purity of the starting materials is still missing.	Not applicable.		Addressed: The information about the starting materials for Brokden was included in an updated Vol.4. (Brokden)
Open point 1.16 RMS to include the information about the date of production of the batches for Brokden in an updated Vol.4 See Brokden confidential reporting table 1(4)	RMS: The date of production of the batches were included in a revised Volume 4.	Not applicable.		Addressed: The information about the date of production of the batches for Brokden was included in an updated Vol.4. (Brokden)
Data requirement 1.23 Applicant Brokden to submit data/information concerning the assessment of toxicological relevance of	RMS: The submitted data/information is described and evaluated in the revised Vol. 4 (general information).	Not applicable.		Addressed: The RMS evaluated the submitted data/information in the revised Vol. 4 (general information).

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
the impurities and data/information demonstrating that the material used in toxicological studies is representative for the proposed specification. See Brokden confidential reporting table 1(7)				
Open point 1.17 RMS to update the LOQ of the NNG method in an updated Vol.4 for Brokden See Brokden confidential reporting table 1(9)	RMS: The LOQ stated by the applicant was included in the revised Volume 4.	Not applicable.		Addressed: The LOQ stated by the applicant was included in the revised Vol. 4. (Brokden)
Open point 1.18 RMS to update the LOQ of the formaldehyde method and values in table C.1.2-1 in an updated Vol.4 for Brokden. See Brokden confidential reporting table 1(10)	RMS: The LOQ stated by the applicant in the batch analysis report A7190 (1.5 g/kg) was included in the revised Volume 4. However, it should be noted that this LOQ exceeds the proposed maximum content of formaldehyde (0.5 g/kg). Therefore, an analytical method with a sufficiently low LOQ is required. Furthermore, the applicant has to demonstrate that the	Not applicable.		Data gap: Applicant Brokden to submit an analytical method for formaldehyde with a sufficiently low LOQ and demonstrate that the technical material meets the proposed maximum content.

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
	technical material meets the proposed maximum content.			
Data requirement 1.24 Applicant Bross to submit additional data/information regarding the validation of the analytical methods used for the quantification of the significant impurities. See also comments 1(7), 1(8), 1(9), 1(10) See Bros S.J. confidential reporting table 1(2)	RMS: The applicant submitted the same statement that was already given in the reporting table. The test for accuracy was conducted with standard solutions which is considered not acceptable for the RMS.	Not applicable.		Data gap: Applicant Bross to submit additional data/information regarding the validation of the analytical methods used for the quantification of the significant impurities
Data requirement 1.25 Applicant Bross to submit an updated technical specification. See Bros S.J. confidential reporting table 1(4)	RMS: A new specification was provided by the applicant. However, the proposed maximum limits of some impurities are still considerably higher than their contents in the representative batches. A justification for the need of the proposed values was not provided.	Not applicable.		Data gap: Applicant Bross to submit justification for the proposed limits of some impurities in the new proposed specification.
Data requirement 1.26	RMS: The submitted	Not applicable.		Addressed:

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
Applicant Bros to submit data/information concerning the assessment of toxicological relevance of the impurities and data/information demonstrating that the material used in toxicological studies is representative for the proposed specification See Bros S.J. confidential reporting table 1(5)	data/information is described and evaluated in the revised Vol. 4 (general information).			The RMS evaluated the submitted data/information in the revised Vol. 4 (general information).
Data requirement 1.27 Applicant Bros to submit for the impurity 15 additional information and results of study on algae addressing the representativeness of the specification. See Bros S.J. confidential reporting table 1(6)	RMS: Additional information on the toxicity of impurity 15 to algae was submitted by the applicant. The result of the evaluation is reported in a revised Volume 4.	Not applicable.		Addressed: Additional information on the toxicity of impurity 15 to algae was submitted and presented in a revised Vol. 4.(Bros)

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
Data requirement 1.28 Applicant Cheminova to submit the missing manufacturing dates of the batches. See Cheminova confidential reporting table 1(4)				Addressed: The manufacturing dates of the batches were presented in the revised Vol.4 (Cheminova)
Data requirement 1.29 Applicant Cheminova to submit data/information concerning the assessment of toxicological relevance of the impurities and data/information demonstrating that the material used in toxicological studies is representative for the proposed specification See Cheminova confidential reporting table 1(6)	RMS: The submitted data/information is described and evaluated in the revised Vol. 4 (general information).	Not applicable.		Addressed: The RMS evaluated the submitted data/information in the revised Vol. 4 (general information).
Open point 1.19 RMS to correct the code of impurity 19 in an updated Vol.4	RMS: Typo in Table C.1.2.2 corrected.	Not applicable.		Addressed: The typo in Table C.1.2.2 was corrected in an updated Vol.4 (Dow)

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
See DOW Agrosciences confidential reporting table 1(1)				
Data requirement 1.30 Applicant Dow to submit the new study in relation to the comment concerning impurity 20. See DOW Agrosciences confidential reporting table 1(4)	RMS: The applicant submitted a non-GLP study in order to justify the original analytical results for impurity obtained in 2007. The data are included in a revised Volume 4. Additional information on the repeatability of the method was not provided.	Not applicable.		Addressed: The data submitted were presented in a revised Vol. 4.(Dow)
Data requirement 1.31 Applicant Dow to submit data/information concerning the assessment of toxicological relevance of the impurities and data/information demonstrating that the material used in toxicological studies is representative for the proposed specification. See DOW Agrosciences confidential reporting table 1(5)	RMS: The submitted data/information is described and evaluated in the revised Vol. 4 (general information).	Not applicable.		Addressed: The RMS evaluated the submitted data/information in the revised Vol. 4 (general information).

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
Open point 1.20 RMS to update the Vol.4 for Dow with the information from the col. 3 of the confidential RT. See DOW Agrosciences confidential reporting table 1(5)	RMS: Two sources are no longer supported by the applicant and Volume 4 is updated accordingly. The submitted data/information is described and evaluated in the revised Vol. 4 (general information) as well.	Not applicable.		Addressed: Vol.4 for Dow was updated with the information from the col. 3 of the confidential RT.
Data requirement 1.32 Applicant Dow to submit an official document, confirming that the respective sources are no longer supported. See also open point in comment 1(5) See DOW Agrosciences confidential reporting table 1(6)	RMS: An official document was submitted by the applicant confirming that the respective sources are no longer supported.	Not applicable.		Addressed: An official document was submitted by the applicant confirming that the respective sources are no longer supported.
Data requirement 1.33 Applicant Excel to submit the new GLP 5 batch data. See Excel confidential reporting table 1(1)	RMS: The new 5-batch analysis is commissioned but not finalised yet.	Not applicable.		Data gap: Applicant Excel to submit the new GLP 5 batch data
Data requirement 1.34	RMS: The submitted	Not applicable.		Addressed:

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
Applicant Excel to submit data/information concerning the assessment of toxicological relevance of the impurities and data/information demonstrating that the material used in toxicological studies is representative for the proposed specification. See Excel confidential reporting table 1(6)	data/information is described and evaluated in the revised Vol. 4 (general information).			The RMS evaluated the submitted data/information in the revised Vol. 4 (general information).
Data requirement 1.35 Applicant Excel to submit additional validation data concerning the method for NNG See Excel confidential reporting table 1(7)	RMS: Additional validation data were submitted in order to demonstrate that the proposed maximum limit can be monitored. The stated LOQ of 1 ppm is included in a revised Volume 4.	Not applicable.		Addressed: Additional validation data concerning the method for NNG was included in the revised Vol.4 (Excel)
Open point 1.21 RMS to include the identity of impurity 11 in a revised Vol.4. See also comment 1(3)	RMS: The identity of impurity 11 was included in a revised Volume 4.	Not applicable.		Addressed: The identity of impurity 11 was included in a revised Vol. 4. (Feinchemie)

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
See Feinchemie confidential reporting table 1(2)				
Data requirement 1.36 Applicant Feinchemie to submit data/information concerning the assessment of toxicological relevance of the impurities and data/information demonstrating that the material used in toxicological studies is representative for the proposed specification. See Feinchemie confidential reporting table 1(5)	RMS: The submitted data/information is described and evaluated in the revised Vol. 4 (general information).	Not applicable.		Addressed: The RMS evaluated the submitted data/information in the revised Vol. 4 (general information).
Data requirement 1.37 Applicant Helm to provide new specification for impurity 3. See also open point 1(1) in the RT for Vol.4 general information See Helm AG confidential reporting table 1(2)	RMS: In table C.1.2.3., the maximum content of impurity 3 was decreased by the applicant. The new value is included in a revised Volume 4.	Not applicable.		Addressed: The new specification value was included in a revised Vol. 4. (Helm)

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
Data requirement 1.38 Applicant Helm to provide new specification for impurity 1. See also open point 1(1) in the RT for Vol.4 general information See Helm AG confidential reporting table 1(3)	RMS: In table C.1.2.4., the mean value was stated in the "thumb rule" column for impurity 1, instead of mean+3SD by mistake. This value, which is now line with the proposed maximum content, is corrected in a revised Volume 4.	Not applicable.		Addressed: The maximum content value of the impurity was corrected in a revised Vol.4 (Helm)
Data requirement 1.39 Applicant Helm to provide new specification for impurity 4. See also open point 1(1) in the RT for Vol.4 general information See Helm AG confidential reporting table 1(4)	RMS: In table C.1.2.7., the maximum content of impurity 4 was decreased by the applicant. The new value is included in a revised Volume 4.	Not applicable.		Addressed: The new content value of the impurity 4 was corrected in a revised Vol.4 (Helm)
Data requirement 1.40 Applicant Helm to submit data/information concerning the assessment of toxicological relevance of the impurities and data/information	RMS: The submitted data/information is described and evaluated in the revised Vol. 4 (general information).	Not applicable.		Addressed: The RMS evaluated the submitted data/information in the revised Vol. 4 (general information).

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
demonstrating that the material used in toxicological studies is representative for the proposed specification. See Helm AG confidential reporting table 1(5)				
Data requirement 1.41 Applicant Helm to submit study on algae according to OECD 201 for Impurity 17. See Helm AG confidential reporting table 1(9)	RMS: Additional information on the toxicity of impurity 15 to algae was submitted by the applicant. The result of the evaluation is reported in a revised Volume 4.	Not applicable.		Addressed: Additional information on the toxicity of impurity 15 to algae was presented in a revised Vol. 4 (Helm)
Data requirement 1.42 Applicant Helm to submit additional validation data for the determination of the impurity 21 (source 3) See Helm AG confidential reporting table 1(11)	RMS: The study submitted to 1(11) of the reporting table (“Evaluation of the mutagenic potential of glyphosate technical”) does not address the data requirement.	Not applicable.		Data gap: Applicant Helm to submit additional validation data for the determination of the impurity 21.
Data requirement 1.43 Applicant Helm to submit	RMS: A statement concerning the specificity of the method was submitted	Not applicable.		Addressed: As the results of the recovery test are reliable, the method is

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
additional validation data for the determination of the impurity 1 (source 4) See also comment 1(14) See Helm AG confidential reporting table 1(12)	by the applicant. As the results of the recovery test are reliable, the method is considered as fit-for-purpose for the RMS.			considered as fit-for-purpose.
Data requirement 1.44 Applicant Helm to submit additional validation data for the method for determination of impurities 1, 3, 5 and 9 found in the 5-batch. See Helm AG confidential reporting table 1(13)	RMS: A statement was submitted by the applicant in which the assessment of the RMS is supported. As already reported in the RAR standard addition calibration was used in order to address the recovery of the method. This means that. It should be noted that the linearity with matrix calibration was >0.99 for each impurity (1, 3, 5 and 9). This option is also in line with SANCO/3030/99: "Where the process of recovery is identical to that used for calibration, for example, if there is no separation of the impurity from the a.s. prior to the determinative step, there is	Not applicable.		Addressed: Standard addition calibration was used in order to address the recovery of the method. Any recovery problem would be seen as a deviation of the linearity.

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
	no measure of recovery. In these cases, an estimate of the accuracy of the analytical technique may be made by an assessment of the linearity of matrix calibration." The RMS is of the opinion that the accuracy of the method is sufficiently tested and additional data are not required.			
Data requirement 1.45 Applicant Helm to submit additional validation data for the method for determination of impurity 21. See Helm AG confidential reporting table 1(15)	RMS: The LOQ for impurity 21 was derived by the applicant in an additional study. The value is considered appropriate to monitor the maximum content of the compound. The result is stated in a revised Volume 4.	Not applicable.		Addressed: The LOQ for impurity 21 was presented in a revised Vol.4 (Helm)
Data requirement 1.46 Applicant Helm to submit additional validation data for the method for determination of impurity 23. See Helm AG confidential reporting	RMS: The applicant submitted a statement which is included in a revised Volume 4. The justification to determine water by loss on drying is accepted by the RMS.	Not applicable.		Addressed: The justification is presented in a revised Vol.4 (Helm)

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
table 1(16)				
Data requirement 1.47 Applicant Helm to submit additional validation data for the method for determination of impurity 20. See Helm AG confidential reporting table 1(17)	RMS: Acceptable repeatability data were submitted by the applicant. The fortification levels for the accuracy are given on p. 78 in the study of Skopec (2009). The data were included in a revised Volume 4.	Not applicable.		Addressed: The additional validation data were presented in the revised Vol.4 (Helm)
Data requirement 1.48 Applicant Helm to submit additional data about the NNG content of of batch '20090506' See Helm AG confidential reporting table 1(20)	RMS: The applicant submitted an internal email correspondence. The outcome is that the stated batches were used indeed in the corresponding tox studies, but the composition given in table C.1.5-1 could not be verified by the applicant. Therefore, table C.1.5-1 was deleted in the revised Volume 4.	Not applicable.		Addressed: The composition given in table C.1.5-1 could not be verified by the applicant Helm.
Open point 1.22 RMS to add the information from the col.3 of the RT (concerning the manufacture as wet cake) in the updated	RMS: The information on the manufacture as wet cake was included in a revised Volume 4 (C.1.2.3).	Not applicable.		Addressed: The information on the manufacture as wet cake was included in a revised Vol. 4 (Monsanto)

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
Vol.4 for Monsanto. See Monsanto confidential reporting table 1(1)				
Open point 1.23 RMS to add the information from the col.3 of the RT (concerning the representativeness of the batches) in the updated Vol.4 for Monsanto See Monsanto confidential reporting table 1(3)	RMS: The information on the representativeness of the batches was included in a revised Volume 4 (C.1.2.3).	Not applicable.		Addressed: The information on the representativeness of the batches was included in a revised Vol. 4 (Monsanto)
Data requirement 1.49 Applicant Monsanto to provide an updated technical specification based on batch data or QC data supporting the proposed limits for impurities. See Monsanto confidential reporting table 1(9)	RMS: QC data have not been submitted by the applicant. Concerning an updated specification the applicant submitted contradictory data. In a document (not dated, not signed) that shall address the data requirement 1(9) of the reporting table, the unchanged specification was provided along with a statement that impurities 6, 7, 8, 10 and 28 shall remain	Not applicable.		Data gap: Applicant Monsanto to provide an updated technical specification based on batch data or QC data supporting the proposed limits for impurities. The RMS assumes that the specification in the “equivalence statement” is to be used for the assessment of the Monsanto sources

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
	specified with upper limits of at least 1 g/kg. In contrast to this document, an “equivalence statement” was provided in order to address the data requirement 1(16) of the reporting table. In the document (dated September 2014, not signed) an updated specification is compared to the new proposed reference specification. The RMS assumes that the specification in the “equivalence statement” is to be used for the assessment of the Monsanto sources. Furthermore, it should be noted that in the “equivalence statement” two different values are stated as the minimum purity (950 g/kg and 972 g/kg). The RMS considers that the value under point A.9 of 950 g/kg is to be used for the evaluation because a purity of 972 g/kg is not achieved in the produced batches.			

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
	Volume 4 was revised according to the updated specification.			
Data requirement 1.50 Applicant Monsanto to submit the analytical method PC-ME-0765 See Monsanto confidential reporting table 1(14)	RMS: Analytical method PC-ME-0765 was submitted by the applicant.	Not applicable.		Addressed: Analytical method PC-ME-0765 was presented in the revised Vol.4 (Monsanto)
Data requirement 1.51 Applicant Monsanto to submit the report Wratten et al (2013) See Monsanto confidential reporting table 1(15)	RMS: The submitted report is described and evaluated in the revised Vol. 4 (general information).	Not applicable.		Addressed: The report Wratten et al (2013) was evaluated in the revised Vol. 4 (general information).
Data requirement 1.52 Applicant Monsanto to provide data/information demonstrating that the material used in toxicological studies is representative for the proposed specification. See Monsanto confidential reporting	RMS: The submitted data/information is described and evaluated in the revised Vol. 4 (general information).	Not applicable.		Addressed: The RMS evaluated the submitted data/information in the revised Vol. 4 (general information).

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
table 1(16)				
Open point 1.24 RMS to include the information from the col.3 of the RT concerning anlytical methods of section C.1.3 in an updated Vol.4 See Monsanto confidential reporting table 1(18)	RMS: The low level accuracy data for impurity [redacted] were already reported in the RAR below table C.1.3-3. The misunderstanding came because of the used abbreviation [redacted] (which is identical to [redacted] see C.1.2.2). The abbreviation [redacted] was added in the revised RAR for clarification.	Not applicable.		Addressed: The abbreviation [redacted] was added in the revised RAR for clarification.
Data requirement 1.53 Applicant Monsanto to submit information detailing with confirmatory methods available for all impurities See Monsanto confidential reporting table 1(19)	RMS: Additional information on the confirmation of the identity of the impurities has not been submitted.	Not applicable.		Data gap: Applicant Monsanto to submit information detailing what confirmatory methods available for all impurities Data gap addressed as in the RAR confidential Vol.4 for Monsanto on p.10 RMS already addressed this point.
Data requirement 1.54 Applicant Monsanto to submit revised evaluation of the precision of method [redacted] with respect	RMS: A revised evaluation of the precision of method [redacted] for the determination of impurity 1 was not submitted by the applicant.	Not applicable.		Data gap: Applicant Monsanto to submit revised evaluation of the precision of method [redacted] with respect to the impurity 1

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
to the impurity 1 See Monsanto confidential reporting table 1(20)				
Data requirement 1.55 Applicant Monsanto to submit MSDSs which are in line with the requirements for REACH for the surfactant [redacted] and its components [redacted] and [redacted] See Monsanto confidential reporting table 1(21)	RMS: The required MSDSs were submitted by the applicant.	Not applicable.		Addressed: The required MSDSs were submitted by the applicant Monsanto
Data requirement 1.56 Applicant Monsanto to clarify the units the values for *N*-nitroso glyphosate are expressed in Table C.1.5. See Monsanto confidential reporting table 1(22)	RMS: The units were clarified by the applicant. The values were corrected in the revised Volume 4.	Not applicable.		Addressed: The units and the values for *N*-nitroso glyphosate were corrected in the revised Vol. 4 (Monsanto)
Data requirement 1.57	RMS: The submitted	Not applicable.		Addressed:

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Applicant Nufarm to submit additional data/information concerning the assessment of toxicological relevance of the impurities and data/information demonstrating that the material used in toxicological studies is representative for the proposed specification See Nufarm confidential reporting table 1(3)	data/information is described and evaluated in the revised Vol. 4 (general information).			The RMS evaluated the submitted data/information in the revised Vol. 4 (general information).
Open point 1.25 RMS to correct the purity of the Mastra batches H05H016A and H95D161A in a revised Vol.4 See Nufarm confidential reporting table 1(6)	RMS: The purity of the batches H05H016A and H95D161A was given by the applicant and the values are included in the revised Volume 4. As the impurity content of the batches H05H016A and H95D161A is not available for the applicant the tables C.1.5-1 and C.1.5-2 were removed in the revised Volume 4.	Not applicable.		Addressed: The purity of the batches H05H016A and H95D161A were corrected in the revised Vol. 4. (Nufarm)
Data requirement 1.58 Applicant Rotam to	RMS: The submitted data/information is	Not applicable.		Addressed:

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submit data/information concerning the assessment of toxicological relevance of the impurities and data/information demonstrating that the material used in toxicological studies is representative for the proposed specification See Rotam confidential reporting table 1(3)	described and evaluated in the revised Vol. 4 (general information).			The RMS evaluated the submitted data/information in the revised Vol. 4 (general information).
Data requirement 1.59 Applicant Sbaro to provide an updated technical specification removing the non significant impurities. See also comment 1(1) See Sabero confidential reporting table 1(2)	RMS: The applicant provided contradictory information concerning the technical specification. In the document submitted to address point 1(2) of the reporting table, the applicant removed the impurities below 1 g/kg as well as the significant impurities 1 and 3. Furthermore, the minimum purity was stated as 994.4 g/kg. In contrast, the applicant provided in the document “equivalence statement” a specification with a stated minimum purity of 950 g/kg	Not applicable.		Data gap: Applicant Sabaro to provide an updated technical specification

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
	(point A.9) and a second value for the minimum purity of 975 g/kg (3 Tier I: Assessment of the equivalence). In this document (dated September 2014), the impurities below 1 g/kg are specified again. According to the document submitted to point 1(2) the impurities below 1 g/kg were removed by the RMS from the specification in the revised Volume 4. The RMS assumes that the impurities 1 and 3 were removed from the specification by mistake by the applicant, and the former maximum limits are retained. However, as the minimum purity is unclear the definite value should be confirmed by the applicant.			
Data requirement 1.60 Applicant Sabero to submit data/information concerning the assessment of	RMS: The submitted data/information is described and evaluated in the revised Vol. 4 (general information).	Not applicable.		Addressed: The RMS evaluated the submitted data/information in the revised Vol. 4 (general

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
toxicological relevance of the impurities and data/information demonstrating that the material used in toxicological studies is representative for the proposed specification. See Sabero confidential reporting table 1(5)				information).
Data requirement 1.61 Applicant Sabero to submit validation data for the determination of impurities 1 and 9. See Sabero confidential reporting table 1(7)	RMS: A study plan was submitted by the applicant. The specificity of the method still needs to be clarified.	Not applicable.		Data gap: Applicant Sabero to submit validation data for the determination of impurities 1 and 9.
Data requirement 1.62 Applicant Sabero to submit validation data for the determination of impurity 2. See Sabero confidential reporting table 1(8)	RMS: New data have not been submitted by the applicant. An explanation for the poor repeatability is still needed.	Not applicable.		Data gap: Applicant Sabero to submit validation data for the determination of impurity 2
Data requirement 1.63 Applicant Sabero to submit validation data for	RMS: New data have not been submitted by the applicant. An explanation for the poor repeatability is	Not applicable.		Data gap: Applicant Sabero to submit validation data for the

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
the determination of impurity 21. See Sabero confidential reporting table 1(9)	still needed.			determination of impurity 21
Data requirement 1.64 Applicant Sabero to submit more specific data for the determination of impurity 23. See Sabero confidential reporting table 1(10)	RMS: A specific method for the determination of impurity 23 was submitted by the applicant. The results were included in a revised Volume 4.	Not applicable.		Addressed: A specific method for the determination of impurity 23 was presented in a revised Vol. 4 (Sabero)
Data requirement 1.65 Applicant Sabero to submit additional data for the determination of impurities [redacted] and [redacted] See Sabero confidential reporting table 1(11)	RMS: A study plan was submitted by the applicant. The specificity of the method still needs to be clarified (see data requirement 1.61).	Not applicable.		Data gap: Applicant Sabero to submit additional data for the determination of impurities [redacted] and [redacted]
Open point 1.26 RMs to correct the typo in a revised Vol.4 See also 1(4) See SAPEC confidential reporting table 1(5)	RMS: The typo was corrected in a revised Volume 4.	Not applicable.		Addressed: The typo was corrected in a revised Vol. 4.(SAPEC)

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
Open point 1.27 RMS to correct the typos in Vol. 4, C.1.3.1 in an updated Vol.4 See SAPEC confidential reporting table 1(8)	RMS: The typo was corrected in a revised Volume 4.	Not applicable.		Addressed: The typo was corrected in a revised Vol. 4.(SAPEC)
Data requirement 1.66 Applicant SAPEC to submit data/information concerning the assessment of toxicological relevance of the impurities and data/information demonstrating that the material used in toxicological studies is representative for the proposed specification. See SAPEC confidential reporting table 1(9)	RMS: The submitted data/information is described and evaluated in the revised Vol. 4 (general information).	Not applicable.		Addressed: The RMS evaluated the submitted data/information in the revised Vol. 4 (general information).
Data requirement 1.67 Applicant SFP to submit data/information demonstrating that the material used in toxicological studies is representative for the	RMS: The submitted data/information is described and evaluated in the revised Vol. 4 (general information).	Not applicable.		Addressed: The RMS evaluated the submitted data/information in the revised Vol. 4 (general information).

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
proposed specification See SPF confidential reporting table 1(2)				
Data requirement 1.68 Applicant SFP to submit report 14-919044-006 See SPF confidential reporting table 1(6)	RMS: Report 14-919044-006 was submitted by the applicant. The validation data were included in a revised Volume 4.	Not applicable.		Addressed: Report 14-919044-006 was presented in a revised Vol. 4.(SPF)
Data requirement 1.69 Applicant Sinon to provide an updated technical specification based on batch data or QC data to support the specification See Sinon confidential reporting table 1(3)	RMS: The applicant provided new batch analysis and an updated specification. These data have been evaluated in a revised Volume 4. An additional “equivalence statement” (dated September 2014) was also submitted. This document contains a contradictory specification and was not taken into account.	Not applicable.		Addressed: Applicant Sinon provided new batch analysis and an updated specification presented in a revised Vol. 4. (Sinon)
Data requirement 1.70 Applicant Sinon to provide manufacturing dates of the batches See Sinon confidential	RMS: A new batch analysis was submitted by the applicant. The results including the manufacturing dates of the batches were reported in a revised Volume 4.	Not applicable.		Addressed: Applicant Sinon provided new batch analysis; the results, including the manufacturing dates, were presented in a revised Vol. 4. (Sinon)

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
reporting table 1(4)				
Data requirement 1.71 Applicant Sinon to submit data/information concerning the assessment of toxicological relevance of the impurities and data/information demonstrating that the material used in toxicological studies is representative for the proposed specification. See Sinon confidential reporting table 1(6)	RMS: The submitted data/information is described and evaluated in the revised Vol. 4 (general information).	Not applicable.		Addressed: The RMS evaluated the submitted data/information in the revised Vol. 4 (general information).
Data requirement 1.72 Applicant Sinon to provide additional validation data for the determination of the impurity 1 See Sinon confidential reporting table 1(7)	RMS: New validation data were provided by the applicant. According to these data the analytical method cannot be regarded as acceptable for the determination of the impurity 1. The results were reported in a revised Volume 4.	Not applicable.		Data gap: Applicant Sinon to provide additional validation data for the determination of the impurity 1
Data requirement 1.73 Applicant Sinon to provide additional validation data for the	RMS: New validation data were provided by the applicant. The results were reported in a revised Volume 4.	Not applicable.		Addressed: The new validation data were reported in a revised Vol. 4 (Sinon)

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
determination of the impurities of the technical material See Sinon confidential reporting table 1(8)				
Data requirement 1.74 Applicant Syngenta to submit the assessment of the relevance/non-relevance of impurities on behalf of the Task Force. See Syngenta confidential reporting table 1(11)	RMS: The submitted data/information is described and evaluated in the revised Vol. 4 (general information).	Not applicable.		Addressed: The RMS evaluated the submitted data/information in the revised Vol. 4 (general information).
Open point 1.28 RMS to update the Vol. 4 with the information presented in col. 3 of the RT concerning impurity 14 See Syngenta confidential reporting table 1(13)	RMS: In the respective table in C.1.5, impurity 14 was changed from “not analysed” to “not detected”.	Not applicable.		Addressed: Table in C.1.5 was updated in a revised Vol. 4 (Syngenta)
Data requirement 1.75 Applicant Syngenta to provide further	RMS: The maximum content of impurity 3 was reduced by the applicant. The value is included in a	Not applicable.		Addressed: The new maximum content of impurity 3 was included in a

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
information concerning impurity 3. See Syngenta confidential reporting table 1(14)	revised Volume 4. In the new submitted document “equivalence statement” the old value for impurity 3 is stated again. This value was not taken into account by the RMS.			revised Vol. 4 (Syngenta)
Open point 1.29 RMS to update Vol.4 with the information from col. 3 of the RT concerning impurity [redacted] See Syngenta confidential reporting table 1(14)	RMS: The updated maximum level of impurity [redacted] is included in a revised Volume 4.	Not applicable.		Addressed: The updated maximum content of impurity [redacted] was included in a revised Vol. 4 (Syngenta)
Data requirement 1.76 Applicant Syngenta to provide additional genotoxicity data to support [redacted] at the level in the proposed specification. See Syngenta confidential reporting table 1(15)	RMS: Open point. No data/information submitted. The applicant (GTF) stated (Anon. (Syngenta), 2014 ASB2014-9302) that an in vitro micronucleus assay in V79 cells conducted with [redacted] existed and that it had initiated a HPRT assay to complete the in vitro genotoxicity battery. However, both studies were not submitted.	Not applicable.		Data gap: Applicant Syngenta to provide additional genotoxicity data to support [redacted] at the level in the proposed specification See Section 2.

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
Open point 1.30 RMS to update the specification for impurity 17 according to col. 3 of the RT in an updated Vol.4 See Syngenta confidential reporting table 1(19)	RMS: The maximum content of impurity 17 was updated according to column 3 of the Reporting Table in a revised Volume 4. In the new submitted document “equivalence statement” the old value for impurity 17 is stated again. This value was not taken into account by the RMS.	Not applicable.		Addressed: The maximum content of impurity 17 was updated according to column 3 of the Reporting Table in a revised Vol. 4. (Syngenta)
Data requirement 1.77 Applicant Syngenta to submit further information related to [redacted] addressing the ecotoxicological representativeness of the specification. See Syngenta confidential reporting table 1(20)	RMS: For further ecotoxicological assessment Syngenta has been given access through a Letter of Access to a OECD 201 test performed on impurity 10. However, this study is not available to the RMS. Therefore, an appropriate conclusion on phytotoxicity is not possible and the specification cannot be regarded as equivalent concerning the content of the impurity 10.	Not applicable.		Data gap: Applicant Syngenta to provide the OECD 201 test performed on impurity 10. See Section 2
Data requirement 1.78 Applicant Syngenta to submit further five batch analysis to substantiate	RMS: Taking the new data into account the removal of impurity 14 is justified for the RMS. The specification was amended in a revised	Not applicable.		Addressed: Based on the new data the specification was amended in a revised Vol.4 (Syngenta)

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
the claim for removal of impurity 14 (Syngenta reference: ASF71_10125) See Syngenta confidential reporting table 1(24)	Volume 4.			
Data requirement 1.79 Applicant Syngenta to submit clarification on the concentration levels in mg/mL used for the linearity test of the impurities impurity 6, impurity 10 and impurity 14. See Syngenta confidential reporting table 1(26)	RMS: The concentration levels were clarified by the applicant. The values were included in a revised Volume 4.	Not applicable.		Addressed: The concentration levels were clarified and the values were included in a revised Vol. 4 (Syngenta)
Data requirement 1.80 Applicant United Phosphorous to submit data/information concerning the assessment of toxicological relevance of the impurities and data/information demonstrating that the	RMS: The submitted data/information is described and evaluated in the revised Vol. 4 (general information).	Not applicable.		Addressed: The RMS evaluated the submitted data/information in the revised Vol. 4 (general information).

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
material used in toxicological studies is representative for the proposed specification See United Phosphorous confidential reporting table 1(1)				
Open point 1.31 RMS to include the new proposed specification for United Phosphorous in an updated Vol.4 See also open point 1(1) in RT for Vol.4 general information See United Phosphorous confidential reporting table 1(2)	RMS: The updated specification provided in the reporting table was included in a revised Volume 4. An additional “equivalence statement” (dated September 2014) was also submitted. This document stating the former maximum limits, but with decreased minimum purity, was not taken into account.	Not applicable.		Addressed: The updated specification provided in the reporting table was included in a revised Vol. 4 (UPL)
Data requirement 1.81 Applicant United Phosphorous to provide additional information on the determination of identity of each impurity. See United Phosphorous	RMS: Additional information on the determination of identity of each impurity has not been submitted by the applicant. The identity was only determined by retention time match with reference standards.	Not applicable.		Addressed.

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
confidential reporting table 1(3)				
Data requirement 1.82 Applicant United Phosphorous to provide additional validation data for the method for the determination of NNG See also comment 1(5) See United Phosphorous confidential reporting table 1(4)	RMS: The submitted document does not address the required validation data for the method for the determination of NNG.	Not applicable.		Data gap: Applicant United Phosphorous to provide additional validation data for the method for the determination of NNG
Data requirement 1.83 Applicant Wynca to submit data/information concerning the assessment of toxicological relevance of the impurities and data/information demonstrating that the material used in toxicological studies is representative for the proposed specification See Wynca confidential reporting table 1(4)	RMS: The submitted data/information is described and evaluated in the revised Vol. 4 (general information).	Not applicable.		Addressed: The RMS evaluated the submitted data/information in the revised Vol. 4 (general information).

2. Mammalian toxicology

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer 0Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
Data requirement 2.1 Applicant to submit the study by Mesnage R, Defarge N, Spiroux de Vendômois J, Séralini G-E. Major pesticides are more toxic to human cells than their declared active principles. Biomedical Research International, 2014. See reporting table 2(14)	RMS: Addressed in revised RAR.	Not applicable.	RMS: The study was not discussed on PRAS 125 meeting. No further amendments needed. Data requirement fulfilled.	Addressed: The study was already included in the original RAR, is reported p. 678, B.6.6.12, Published data (released since 2000) of the revised RAR.
Open point 2.1 RMS to amend table B.6.4-16 in a revised RAR. See reporting table 2(17)	RMS: Addressed in revised RAR.	Not applicable.	RMS: The revised table has been available for PRAS 125 meeting but was not discussed there.	Addressed: The table has been revised (see table B.6.4-17 of the revised RAR).
Open point 2.2 RMS to amend B.6.4.1	RMS: Addressed in revised RAR.	Not applicable.	RMS: Two new (negative) Ames tests were reported in the revised RAR (2015), i.e.,	Addressed: The RMS conclusion of the studies have been revised; EFSA notes

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer 0Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
In vitro genotoxicity testing – Bacterial assays for gene mutation, p. 303, in a revised RAR. See reporting table 2(19)			Schreib (2012, ASB2014-9133) and Thompson (2014, ASB2014-9148) that had not been submitted before. Information has been available for PRAS 125 meeting but was not discussed there.	that these changes should have been reported as well in table B.6.4-1
Open point 2.3 RMS to amend the list of end points with regard to the reproductive toxicity NOAELs. See reporting table 2(37)	RMS: Addressed in revised RAR.	Not applicable.	RMS: See column B. No amendment following PRAS 125 meeting needed.	Addressed: The LoEP has been revised.
Experts' consultation 2.1 The developmental toxicity potential of glyphosate to be discussed in a meeting of experts. See reporting table 2(41)	RMS: Agreement.	Pesticides Peer Review Meeting 125: (25. - 27. February 2015): The majority of the experts (except NO, who confirms the comment based on [redacted] 1991) accepted the evaluation and the conclusion of the RMS and acknowledged that	RMS: In principle, the previous evaluation was confirmed. However, an ARfD was set on this basis (see below).	Addressed: The majority of the experts agreed with the evaluation and the conclusion of the RMS and acknowledged that glyphosate is not considered teratogenic (cardiac effects) taking into account all available studies and no classification regarding developmental toxicity is suggested.

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer 0Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
		glyphosate is not considered teratogenic (cardiac effects) taking into account all available studies. The majority of experts agreed on the conclusions drawn by the RMS on classification and labelling.		
Data requirement 2.2 Applicant to submit the study by Malhotra RC, Ghia DK, Cordato DJ, Beran RG. Glyphosate surfactant herbicide-induced reversible encephalopathy. *J Clin Neurosci* 2010; **17:** 1472–73. See reporting table 2(48)	RMS: Addressed in revised RAR.	Not applicable.	RMS: This paper is briefly addressed in Vol. 3 under B.6.7 and reported under B.6.9.2. It has been available for PRAS 125 but was not discussed there.	Addressed: The study is assessed in the revised RAR: - Page 720, B.6.7 - Published data on neurotoxicity - Page 822, B.6.9.2 - Reports on clinical cases and poisoning incidents
Data requirement 2.3 Applicant to submit the study by reference Samsel et Seneff	RMS: Addressed in revised RAR.	Not applicable.	RMS: See column B. The paper was not discussed on PRAS 125 meeting.	Addressed: The study is assessed in the revised RAR: - Page 803, B.6.8.4 – Further published data

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer 0Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
« Glyphosate's Suppression of Cytochrome P450 Enzyme and amino acid biosynthesis by the gut microbiome : Pathways to modern diseases » *Entropy* **2013**, *15*, 1416-1463. See reporting table 2(55)				
Data requirement 2.4 Applicant to submit *Mink et al, Regulat Toxicol Pharmacol, 63, 440-452, 2012* See reporting table 2(56)	RMS: Addressed in revised RAR.	Not applicable.	RMS: See column B. Was not discussed on PRAS 125 meeting.	Addressed: The study is assessed in the revised RAR: - Page 532, B.6.5.3 – Published data on carcinogenicity
Experts' consultation 2.2 Necessity for deriving an ARfD to be discussed in a meeting of experts.	RMS: Derivation of ARfD is not proposed by RMS. Agreement to discuss it in a meeting of experts.	Pesticides Peer Review Meeting 125: (25. - 27. February 2015): The experts agreed to set an ARfD. The relevant NOAEL is 50 mg/kg bw day from the [redacted] 1996	RMS: An ARfD of 0.5 mg/kg bw was established on PRAS 125 meeting. The RMS had not proposed setting of an ARfD but is fine with that decision. The respective sub-sections in Vol. 1 (2.6.13 and "Overall summary") have been amended following the	Addressed: The ARfD is 0.5 mg/kg bw based on the NOAEL of 50 mg/kg bw per day for mortality and post-implantation losses observed in a rabbit developmental study, 100 UF applied.

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer 0Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
See reporting table 2(63)		study, with an UF of 100 resulting in an **ARfD of 0.5 mg/kg bw**. Open point for section 3; see evaluation table section 3 open point 3.10 Please consider that an ARfD (0.5 mg/kg bw) has been proposed.	PRAS 125 meeting.	
Open point 2.4 RMS to amend the RAR with regard to the use of 0.3% value dermal absorption for exposure assessment. See reporting table 2(81)	RMS: Addressed in revised RAR.	Not applicable.	RMS: Dermal absorption of glyphosate from the representative formulation is 1% and not 0.3%. This has been clearly stated in the revised RAR and considered in exposure calculations. This figure has not been challenged by any party and was not discussed on the PRAS 125 meeting.	Addressed: Dermal absorption of the representative formulation (MON 52276, SL formulation containing 360 g glyphosate/L), concentrate and in-use field dilutions is 1%.
Data requirement 2.5 Applicants to demonstrate the compliance of the batches tested in the mammalian toxicology data package with the proposed specifications.	RMS: The submitted data/information is described and evaluated in Vol. 4 (general information).	Not applicable.	RMS: See column B. Was not an issue for PRAS 125 meeting.	Data gaps: The new proposed reference specification as proposed by the RMS (2014) is supported by the toxicological studies; eight out of the 24 applicants presented specifications that were not supported by the toxicological assessment (Afrasa, Arysta, Bros,

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer 0Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
See reporting table 2(92)				Dow, three out of seven sources of Helm, Monsanto, SPF and one of the two Syngenta manufacturing routes) which is a critical area of concern for the respective applicants/sources. Two relevant impurities were identified, formaldehyde due to its harmonised classification in accordance with the provisions of Regulation (EC) No. 1272/2008 - CLP Regulation as Toxic, Carc 1B and Muta 2 and N-nitro-glyphosate (belonging to a group of impurities of particular concern as they can be activated to genotoxic carcinogens); at the specified levels these impurities are not of concern. Data gaps: All applicants to address the relevance of their respective impurities (except the known relevant ones), in particular impurities that elicited toxicological alerts according to QSAR assessments and the ones specified at higher level than the reference specification.
Experts' consultation	RMS: Agreement.	Pesticides Peer Review	RMS: The proposed ADI and AOEL have been confirmed.	Addressed:

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer 0Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
2.3 ADI and AOEL of glyphosate to be confirmed in a meeting of experts. See reporting table 2(93)		Meeting 125: (25. - 27. February 2015): The experts confirmed the RMS's proposal for the ADI and the AOEL ADI: 0.5 mg/kg bw per day. AOEL: 0.1 mg/kg bw per day.	This was mentioned in the revised Vol. 1 that was produced after the PRAS 125 meeting.	The ADI is confirmed at 0.5 mg/kg bw per day and the AOEL confirmed at 0.1 mg/kg bw per day as proposed by the RMS.
Data requirement 2.6 In the carcinogenicity studies in mice by [redacted] (1997, ASB2012-11493, notifier: Arysta) and by [redacted] (2009, ASB2012-11492, notifier: Nufarm), a certain increase in the incidence of malignant lymphoma in high dose males (6/50 as compared to 2/50 in the control in the first and 5/51 vs. 0/51 in the second study) was noted. The differences did not gain statistical significance. However,	RMS: Addressed in revised RAR. Historical data for the study by [redacted] (1997) have been submitted by the notifier and are reported in the revised RAR.	Not applicable.	RMS: In addition to the historical control data for the study by [redacted] (1997) that cover the observed incidences, historical data for the study by [redacted] (2009) were provided but only after the PRAS 125 meeting. They are reported in the revised RAR now but are not of much use. However, data from the literature is suitable to prove the large variance in lymphoma incidence also in CD-1 mice.	Addressed: Available HCD have been provided by the RMS and considered during the expert meeting under expert consultation 2.5.

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer 0Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
for more reliable assessment, historical control data from the performing laboratories should be provided. The data requirement has already been identifies in the RAR. See reporting table 2(94)				
Data requirement 2.7 Applicant to submit the memorandum of February 4, 2014 that has been made available to the Danish Ministry of Food, Agriculture and Fisheries (http://dca.au.dk/fileadmin/DJF/Notat_gmofoder__uk_version_Memorandum_on_The_feeding_of_genetically_modified_glyphosate_resistant_soy_products_to_livest	RMS: Addressed in revised RAR.	Not applicable.	RMS: See column B. Was not discussed on PRAS 125 meeting.	Addressed: The study is assessed in the revised RAR: - P. 797-798 (cows) and P. 802 (piglets), B.6.8.3.3, Published data

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer 0Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
ock.pdf). See reporting table public consultation 2(3)				
Data requirement 2.8 Applicant to submit the relevant articles as cited in column 2 of the reporting table: - Larsen, K., Najle, R., Lifschitz, A., Virkel, G. (2012). Effects of sub-lethal exposure of rats to the herbicide glyphosate in drinking water: Glutathione transferase enzyme activities, levels of reduced glutathione and lipid peroxidation in liver, kidneys and small intestine. Environmental Toxicology and Pharmacology, 34(3): 811–818. - Mañas, F., Peralta, L., Ugnia, L., Weyers, A., García Ovando, H., & Gorla, N.	RMS: Addressed in revised RAR.	Not applicable.	RMS: See column B. Was not discussed on PRAS 125 meeting.	Addressed: The studies are assessed in the revised RAR: - p. 804, B.6.8.4 - Further published data - p. 404, Table B.6.4-29 - Genetic toxicology studies of glyphosate and glyphosate formulations published on or after 2000 - p. 840, B.6.9.6 - therapeutic regimes

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer 0Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
(2013). Oxidative stress and comet assay in tissues of mice administered glyphosate and ampa in drinking water for 14 days. BAG. Journal of basic and applied genetics, 24(2), 67-75. - Tizhe, E. V., Ibrahim, N. D. G., Fatihu, M. Y., Igbokwe, I. O., George, B. D. J., Ambali, S. F., & Shallangwaa, J. M. (2013a). Haematological changes induced by subchronic glyphosate exposure: ameliorative effect of zinc in Wistar rats. Sokoto Journal of Veterinary Sciences, 11(2), 28-35. - Tizhe, E. V., Ibrahim, N. D. G., Fatihu, M. Y., Igbokwe, I. O., George, B. D. J., Ambali, S. F., & Shallangwa, J. M. (2013b) Serum				

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer 0Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
biochemical assessment of hepatic and renal functions of rats during oral exposure to glyphosate with zinc. Comparative Clinical Pathology, 1-8. - Tizhe, E. V., Ibrahim, N. D. G., Fatihu, M. Y., Onyebuchi, I. I., George, B. D. J., Ambali, S. F., & Shallangwa, J. M. (2013c). Influence of zinc supplementation on histopathological changes in the stomach, liver, kidney, brain, pancreas and spleen during subchronic exposure of Wistar rats to glyphosate. Comparative Clinical Pathology, 1-9. See reporting table public consultation 2(6)				
Open point 2.5	RMS: Addressed in revised	Not applicable.	RMS: See Open Point 2.1! The revised table has been	See open point 2.1

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer 0Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
RMS to amend table B.6.4-16 in Volume 3 of the RAR. See reporting table public consultation 2(7)	RAR.		available for PRAS 125 meeting but was not discussed there.	
Data requirement 2.9 Applicant to provide studies mentioned in the comment by PAN under 2(13) only if they were not taken into account in the assessment made by the RMS: Grisolia, 2002, Sivikova, 2006, Bellé, 2007, Cavas, 2007, Cavalcante, 2008, Guilherme, 2009, Poletta, 2009, Monroy, 2005. See reporting table public consultation 2(13)	RMS: Addressed in revised RAR. (See open point 2.1).	Not applicable.	RMS: See column B. Was not discussed on PRAS 125 meeting.	Addressed: The studies were all assessed in the original RAR, except Guillerme, 2009 (not submitted).
Experts' consultation	RMS: Agreement.	Pesticides Peer Review	RMS: RMS agrees with the	Addressed:

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer 0Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
2.4 MSs to discuss the genotoxicity of glyphosate. See reporting table public consultation 2(13)		Meeting 125: (25. - 27. February 2015): The meeting confirmed that the active substance glyphosate is devoid of any genotoxic potential.	conclusion of the PRAS 125 expert meeting.	Glyphosate did not evidence potential for genotoxicity.
Data requirement 2.10 Applicant to submit all the relevant articles cited in column 2 of the reporting table: - Alvarez-Moya, C., Reynoso Silva, M., Valdez Ramírez, C., Gómez Gallardo, D., León Sánchez, R., Canales Aguirre, A., & Feria Velasco, A. (2014) Comparison of the in vivo and in vitro genotoxicity of glyphosate isopropylamine salt in three different organisms. Genetics and Molecular Biology,	RMS: Addressed in revised RAR.	Not applicable.	RMS: See column B. Was not discussed on PRAS 125 meeting.	Addressed: The studies are assessed in the revised RAR (Heu, 2012a and Heu 2012b were already reported in the original RAR): - P. 403, 404, 405 Table B.6.4-29 - Genetic toxicology studies of glyphosate and glyphosate formulations published on or after 2000 - P. 804, 806, B.6.8.4 - Further published data (released since 2000)

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer 0Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
37(1), 105-110. - Chaufan, G., Coalova, I., & de Molina, M. D. C. R. (2014). Glyphosate Commercial Formulation Causes Cytotoxicity, Oxidative Effects, and Apoptosis on Human Cells Differences With its Active Ingredient. International journal of toxicology, 1091581813517906 - De Souza Filho, J., Sousa, C. C. N., Da Silva, C. C., De Sabóia-Morais, S. M. T., & Grisolia, C. K. (2013). Mutagenicity and Genotoxicity in Gill Erythrocyte Cells of Poecilia reticulata Exposed to a Glyphosate Formulation. Bulletin of environmental contamination and toxicology, 91(5), 583-587.				

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer 0Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
- George, J., & Shukla, Y. (2013) Emptying of Intracellular Calcium Pool and Oxidative Stress Imbalance Are Associated with the Glyphosate-Induced Proliferation in Human Skin Keratinocytes HaCaT Cells. ISRN dermatology, 2013. - Guilherme, S., Santos, M.A., Barroso, C., Gaivão, I., Pacheco, M. (2012) Differential genotoxicity of Roundup® formulation and its constituents in blood cells of fish (Anguilla anguilla): considerations on chemical interactions and DNA damaging mechanisms. Ecotoxicology, 21(5): 1381-1390 - Heu, C., Berquand, A., Elie-Caille, C., Nicod, L. (2012a) Glyphosate-				

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer 0Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
induced stiffening of HaCaT keratinocytes, a Peak Force Tapping study on living cells. Journal of Structural Biology, 178(1): 1- 7. - Heu, C., Elie-Caillea, C., Mougeyc, V., Launayd, S., Nicod, L. (2012b) A step further toward glyphosate-induced epidermal cell death: Involvement of mitochondrial and oxidative mechanisms. Environmental Toxicology and Pharmacology, 34(2): 144–153. - Koller, V.J., Fürhacker, M., Nersesyan, A., Mišík, M., Eisenbauer, M., Knasmueller, S. (2012) Cytotoxic and DNA-damaging properties of glyphosate and Roundup in human-derived buccal epithelial cells. Archives of				

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer 0Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
Toxicology, doi 10.1007/s00204-012-0804-8. - Moreno, N. C., Sofia, S. H., & Martinez, C. B. (2014). Genotoxic effects of the herbicide Roundup Transorb< sup>®</sup> and its active ingredient glyphosate on the fish< i> Prochilodus lineatus</i>. Environmental toxicology and pharmacology, 37(1), 448-454. See reporting table public consultation 2(18)				
Data requirement 2.11 Applicant to submit all the relevant articles published after the date of submission, including the ones mentioned in the comment. - Benachour N,	RMS: Addressed in revised RAR.	Not applicable.	RMS: See column B. Was not discussed on PRAS 125 meeting.	Addressed: The study by Benachour, 2009 was reported already in the original RAR; the study by Alvarez-Moya, 2014 is assessed in the revised RAR (see Data requirement 2.10 above).

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer 0Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
Séralini GE. Chem Res Toxicol. 2009 Jan;22(1):97-105. - Alvarez-Moya et al. 2014 Genet & Molec Biol:37:105-110. See reporting table public consultation 2(20)				
Experts' consultation 2.5 MSs to discuss the carcinogenicity of glyphosate. See reporting table public consultation 2(21)	RMS: Agreement.	Pesticides Peer Review Meeting 125: (25. - 27. February 2015): The experts (except BE expressing an uncertainty on this issue) consider highly unlikely the carcinogenic potential of glyphosate. However the back ground incidences of malignant lymphomas should be further elucidated for the Swiss albino mouse strain in a revised RAR. The reference values are considered to be protective with regard to the dose level where the malignant lymphomas occur.	RMS: RMS agrees with the conclusion of the PRAS 125 meeting. Background incidences have been reported in the literature and were included in the revised RAR after the meeting.	Addressed: The experts (except BE expressing an uncertainty on this issue) consider highly unlikely the carcinogenic potential of glyphosate. However the back ground incidences of malignant lymphomas should be further elucidated for the Swiss albino mouse strain. The reference values are considered to be protective with regard to the dose level where the malignant lymphomas occur.

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer 0Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
		A new open point was proposed, see new open point 2.8. below		
New open point 2.8: RMS to present the information available on the background incidences for the Swiss albino strain in a revised RAR.		Not applicable.	RMS: Background incidences from the literature were included in the revised RAR after the PRAS 125 meeting.	Addressed: Literature review confirmed that a high incidence of malignant lymphomas has been reported 'historically' in Swiss mice; however no valid HCD could be retrieved by the RMS, therefore a treatment-related effect in this study could not be completely excluded, and it was concluded that there is limited evidence of a carcinogenic potential of glyphosate as a high-dose phenomenon in mice of a susceptible strain.
Data requirement 2.12 Applicant to submit the articles mentioned, if not already included in the dossier: - Vandenberg et al. 2012 - Lamb J.C., Boffetta P., Foster	RMS: Addressed in revised RAR.	Not applicable.	RMS: See column B. Not discussed on PRAS 125 meeting.	Addressed: The studies are assessed in the revised RAR: - P. 675, 676 B.6.6.12, Published data (released since 2000)

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer 0Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
W.G., Goodman J.E., Hentz K.L., Rhomberg L.R., Staveley J., Swaen G., Van Der Kraak G. and, Williams A.L. (2014) Critical Comments on the WHO-UNEP State of the Science of Endocrine Disrupting Chemicals – 2012. Regul. Toxicol. Pharmacol. 69(1):22-40. - Rhomberg L.R. and Goodman, J.E. (2012) Low-dose effects and nonmonotonic dose-responses of endocrine disrupting chemicals: Has the case been made? Regul. Toxicol. Pharmacol. 64: 130-133. - Borgert CJ, Baker SP, Matthews JC. (2013) Potency matters: Thresholds govern endocrine activity. Regul. Toxicol.				

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer 0Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
Pharmacol. 67(1):83-8 See reporting table public consultation 2(22)				
Experts' consultation 2.6 MSs to discuss the possible endocrine disrupting properties of glyphosate. See reporting table public consultation 2(22)	RMS: Agreement.	Pesticides Peer Review Meeting 125: (25. - 27. February 2015): The experts agreed with RMS's conclusion that there are no endocrine mediated effects.	RMS: RMS agrees with the conclusion of PRAS 125 meeting.	See data gap in Data requirement 2.15 below: The experts agreed with RMS's conclusion that there are no endocrine mediated effects. EFSA noted that the Apical studies did not show adverse effects on the reproduction, however signs of endocrine activity, even if appearing at parental toxic doses, could not be completely ruled out regarding delay in preputial separation in F1 males and decrease in homogenisation resistant spermatids (*cauda epididymis*) observed in the most recent multigeneration study. The RMS mentions that the results of the first published data from the EDSP (Hershberger, Uterotrophic assays, male and female pubertal assays, steroidogenesis) were negative. However these studies were not submitted for the renewal procedure and a data gap

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer 0Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
				has been identified for the full battery of Tier I screening assays according to the EDSP, or the Level 2 and 3 tests currently indicated in the OECD Conceptual Framework, and analysed in the EFSA Scientific Opinion on the hazard assessment of endocrine disruptors.
Data requirement 2.13 Applicant to submit the articles mentioned in the comment: - Schinasi, L., & Leon, M. E. (2014). Non-Hodgkin Lymphoma and Occupational Exposure to Agricultural Pesticide Chemical Groups and Active Ingredients: A Systematic Review and Meta-Analysis. International journal of environmental research and public health, 11(4), 4449-4527. - Kachuri, L., Demers, P. A., Blair, A.,	RMS: Addressed in revised RAR.	Not applicable.	RMS: See column B. Not discussed on PRAS 125 meeting.	Addressed: The study by Thongprakaisang, 2013 was reported in the initial RAR; the other studies are assessed in the revised RAR: - P. 531, 532, B.6.5.3, Published data on carcinogenicity (released since 2000), Epidemiology studies

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer 0Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
Spinelli, J. J., Pahwa, M., McLaughlin, J. R., ... & Harris, S. A. (2013) Multiple pesticide exposures and the risk of multiple myeloma in Canadian men. International Journal of Cancer - Cocco, P., Satta, G., Dubois, S., Pili, C., Pilleri, M., Zucca, M., ... & Boffetta, P. (2013) Lymphoma risk and occupational exposure to pesticides: results of the Epilymph study. Occupational and environmental medicine, 70(2): 91-98. - Thongprakaisang, S., Thiantanawat, A., Rangkadilok, N., Suriyo, T., & Satayavivad, J. (2013) Glyphosate induces human breast cancer cells growth via estrogen receptors. Food and Chemical Toxicology.				

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer 0Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
See reporting table public consultation 2(31)				
Data requirement 2.14 Applicant to submit the articles mentioned in the comment, if not already included in the dossier: - Hedberg D, Wallin M. Toxicol In Vitro. 2010 Apr;24(3):795-802. - Chan P, Mahler J. Toxic Rep Ser. 1992 Jul;16:1-D3. - De Roos et al. '05 - Hardell et al. '02 See reporting table public consultation 2(32)	RMS: Addressed in revised RAR.	Not applicable.	RMS: See column B. Not discussed on PRAS 125 meeting.	Addressed: The study from Hedberg is assessed in the revised RAR: - P. 805, B.6.8.4, Further published data (released since 2000) The other references were already included in the original RAR.
Experts' consultation 2.7 MSs to discuss the hazard characterisation	RMS: Agreement.	Pesticides Peer Review Meeting 125: (25. - 27. February 2015): The available data are robust	RMS: RMS agrees with the conclusion of PRAS 125 meeting.	Addressed: The experts agreed that the available data are robust enough and carefully considered to conclude on the toxicological

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer 0Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
for glyphosate. See reporting table public consultation 2(33)		enough and always carefully considered to conclude on the toxicological profile of glyphosate including hazard characterisation. The study of Paganelli et al 2010 was performed with extreme exposure conditions with both glyphosate and glyphosate based formulations. Although the study identified a potentially relevant mechanism of action, this does not automatically mean that it is relevant and that it can be considered for a regulatory process. Furthermore higher tier data are available overruling the results of Paganelli et al 2010.		profile of glyphosate, including its hazard characterisation.
Experts' consultation 2.8 MSs to discuss the reprotoxicity of glyphosate. See reporting table	RMS: Agreement.	Pesticides Peer Review Meeting 125: (25. - 27. February 2015): The reproductive toxicity of the active substance glyphosate has been extensively assessed	RMS: RMS agrees with the conclusion of PRAS 125 meeting.	Addressed: The experts agreed that the reproductive toxicity of the active substance glyphosate has been extensively assessed according to internationally recognised and validated protocols and methodologies. The experts considered the available studies

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer 0Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
public consultation 2(35)		according to internationally recognised and validated protocols and methodologies. The experts considered the available studies as sensitive for the definition of the reproductive potential of the active substance glyphosate.		as sensitive for the definition of the reproductive potential of the active substance glyphosate
Experts' consultation 2.9 MSs to discuss the developmental toxicity of glyphosate (see other RT 2(41) See reporting table public consultation 2(37)	RMS: Agreement.	Pesticides Peer Review Meeting 125: (25. - 27. February 2015): The RAR Volume 3, B.6.8.3.3 – published data - has been updated recently. The case reports mentioned have major methodological drawbacks which do not allow any conclusion on the teratogenicity potential.	RMS: RMS agrees with the conclusion of PRAS 125 meeting.	Addressed: See expert consultation 2.1.
Data requirement 2.15 Applicant to submit the Tier 1 screening assays under the US EPA Endocrine Disruptor Screening Program (EDSP).	RMS: First results have been submitted and are reported in the RAR.	Not applicable.	RMS: See column B. No further data available.	Data gap: See Experts' consultation 2.6 above: A data gap has been identified for the full battery of Tier I screening assays according to the EDSP, or the Level 2 and 3 tests currently indicated in the OECD Conceptual Framework, and analysed in the

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer 0Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
See reporting table public consultation 2(40)				EFSA Scientific Opinion on the hazard assessment of endocrine disruptors.
Data requirement 2.16 Applicant to submit the Tier 1 screening assays under the US EPA Endocrine Disruptor Screening Program (EDSP) and the studies mentioned in the comment: - Walsh, 2002 - Romano, 2010 - Benachour, 2005 - Gasnier, 2007 - Hokanson, 2007 - Mose, 2008 See reporting table public consultation 2(41)	RMS: The studies of Romano (2010), Hokanson (2007) and Mose (2008) have been reported in the RAR. Furthermore, studies of Benachour (2007 and 2009) and of Gasnier (2009, 2010, and 2011) have also been reported in the RAR. Studies of Benachour (2005) and Gasnier (2007) have not been submitted and it is questionable to which studies the comment refers.	Not applicable.	RMS: See column B. No amendment can be made.	See data gap in data requirement 2.15 above; The references were reported in the original RAR, however some references are not clear: - A Walsh study is reported in the RAR, but is dated 2000. - If the Benachour (2005) study refers to 'Richard, S. Moslemi, S. Sipahutar, H. Benachour, N. Seralini, G.E., 2005', it is reported in the revised RAR, p. 682. - If the Gasnier (2007) study refers to 'Benachour, N. Sipahutar, H. Moslerni, S. Gasnier, C. Travert, C. Seralini, G. E., 2007', it is reported in the p. 683.
Experts' consultation 2.10 MSs to discuss the	RMS: Agreement.	Pesticides Peer Review Meeting 125: (25. - 27. February 2015):	RMS: RMS agrees with the conclusion of PRAS 125 meeting with regard to the developmental study in	Addressed: See expert consultation 2.1.

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer 0Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
teratogenicity of glyphosate. See reporting table public consultation 2(46)		The RMS concluded that the study has its limitations and did not consider the study reliable. There was no histopathological evidence for the effect of dilated heart. The RMS explained that there was no dose-response seen with the regard to the cleft palate (present at the low dose level). The experts agreed to the RMS's assessment.	rabbits by Suresh (1993).	
Data requirement 2.17 Applicant to submit the articles mentioned in the comment: - Beuret et al (2005) - Rao et al. (1990): J. Nutr. 120:602-609; - Xia et al. (1995): J. Nutr. 125 195-201; - Kim et al.	RMS: The study of Beuret et al. (2005) was reported in the RAR. Additional information was included in the revised RAR. However, the mentioned literature of Rao, Xia and Kim did not refer to glyphosate. This literature was mentioned in comment 2(52) to explain that increased lipid peroxidation is not the result of reduced food consumption. However, the misleading sentence in the	Not applicable.	RMS: See column B.	Addressed: The comment is addressed by the RMS p. 672, B.6.6.12, Published data (released since 2000).

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer 0Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
(1996): Aging 8:123-129 See reporting table public consultation 2(52)	first draft of the RAR was deleted in agreement with the comment 2(52) in the revised RAR. Therefore, the citation of the mentioned literature was not needed in the RAR.			
Data requirement 2.18 Applicant to submit the articles mentioned in the comment, if not already in the dossier: Howe et al 2004, Relyea et al 2012, Lanctot et al 2013. See reporting table public consultation 2(57)	RMS: The mentioned articles refer clearly to ecotoxicology which is not a subject in the chapter on human and mammalian toxicology of the RAR. The spelling of the author Relya is wrong (mentioned as "Relyea" in the reporting table and in column A). Articles of Relya (2005 and 2012) have been reported in the revised RAR.	Not applicable.	RMS: See column B.	Addressed: The study by Relya (2012) is assessed in the revised RAR: - P. 807, B.6.8.4, Further published data (released since 2000) Howe (2004) and Lanctot (2013): Comment transferred to ecotox section 5.
Data requirement 2.19 Applicant to submit the articles mentioned in the comment. - Thongprakaisang, S., Thiantanawat, A., Rangkadilok, N., Suriyo,	RMS: Addressed in revised RAR.	Not applicable	RMS: RMS agrees with the conclusion of PRAS 125 meeting.	Addressed: The study by Thongprakaisan (2013) was reported in the original RAR; the other studies are assessed in the revised RAR: - p. 672, 673, 675, B.6.6.12, Published data (released since 2000)

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer 0Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
T., & Satayavivad, J. (2013) Glyphosate induces human breast cancer cells growth via estrogen receptors. Food and Chemical Toxicology. - Astiz, M., Hurtado de Catalfo, G. E., García, M. N., Galletti, S. M., Errecalde, A. L., Alaniz, M. J. D., & Marra, C. A. (2013) Pesticide-induced decrease in rat testicular steroidogenesis is differentially prevented by lipoate and tocopherol. Ecotoxicology and environmental safety, 91: 129–138 - Basrur, P. K., 2006. Disrupted sex differentiation and feminization of man and domestic animals. Environ. Res. 100, 18–38. - Caglar, S.,				- P. 840, B.6.9.2, Therapeutic regimes - p. 805, B.6.8.4, Further published data (released since 2000)

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer 0Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
Kolankaya, D., 2008. The effect of sub-acute and sub-chronic exposure of rats to the glyphosate-based herbicide Roundup. Environ. Toxicol. Pharmacol. 25, 57–62. - de Liz Oliveira Cavalli, V. L., Cattani, D., Elise Heinz Rieg, C., Pierozan, P., Zanatta, L., Benedetti Parisotto, E., ... & Zamoner, A. (2013) Roundup Disrupted Male Reproductive Functions By Triggering Calcium-Mediated Cell Death In Rat Testis And Sertoli Cells. Free Radical Biology and Medicine. - Omran, N. E., & Salama, W. M. (2013). The endocrine disrupter effect of atrazine and glyphosate on Biomphalaria alexandrina snails. Toxicology and industrial health,				

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer 0Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
0748233713506959. See reporting table public consultation 2(58)				
Experts' consultation 2.11 MSs to discuss the developmental neurotoxicity of glyphosate. See reporting table public consultation 2(59)	RMS: Agreement.	Pesticides Peer Review Meeting 125: (25. - 27. February 2015): From the available data there is no evidence for neurotoxicity and developmental neurotoxicity for the active substance glyphosate, mainly based on both experimental and epidemiological studies.	RMS: There is no evidence of developmental neurotoxicity of glyphosate.	Addressed: Glyphosate did not evidence potential for neurotoxicity or developmental neurotoxicity.
Open point 2.6 RMS to clarify how the assessment of the literature was performed. See reporting table public consultation 2(60)	RMS: In comment 2(60) of the reporting table PAN Europe and further organisations communicate that the assessment of the applicant would be totally inadequate, playing down any adverse effects and using the "Klimisch-axe" to ensure that it is ignored. In a further comment (2(13) by PAN-Europe the commentators	Not applicable.	RMS: See column B. That issue was not discussed on PRAS 125 meeting.	Addressed: The methodology and assessment done by the RMS regarding literature data has been reviewed and agreed by the peer review and EFSA.

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer 0Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
	propose that independent literature "should be qualified as more reliable than industry-sponsored studies with an inherent conflict of interest." The principles of the literature search are described in detail in the RAR. This description was completed in the revised RAR because additional literature was reported. The submitted literature was assigned to the different toxicological end points or to the chapter further studies. Especially important was the assessment of the relevance and of the quality of the submitted literature. A selection of highly relevant studies was reported in detail with an assessment of the quality. For this assessment the Klimisch score was used which is a widely accepted method of assessing the reliability of toxicological studies, mainly for regulatory			

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer 0Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
	purposes (Klimisch, H.J., Andreae, M., Tillmann, U.: "*A systematic approach for evaluating the quality of experimental toxicological and ecotoxicological data*", Regulatory toxicology and Pharmacology, Vol. 25, pp. 1-5 (1997)). However, such detailed description was not possible for every study because approximately 1000 publications have been identified. Therefore, further studies have been reported shorter and more condensed in the RAR in the context of discussion of the different toxicological end points. Mostly, the conclusions of the authors are reported as a short summary. Limiting factors of studies have been reported if considered necessary. The assessment did not follow the proposal of PAN in the above mentioned comments that independent literature should be qualified as more reliable than industry sponsored studies. All			

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer 0Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
	submitted literature was assessed without such ideas of bias. Generally, all available studies have been used by the rapporteur. However, in the case of contradictory results it was necessary to compare also the validity of the submitted data and to conclude on the weight of evidence. For the assessment of the validity of the submitted studies it was especially important to compare if the used methods have really been validated as it was evidenced for the OECD test methods.			
Data requirement 2.20 Applicant to submit the articles mentioned in the comment: - Cattani, D., de Liz Oliveira Cavalli, V. L., Heinz Rieg, C. E., Domingues, J. T., Dal-Cim, T., Tasca, C. I., ... & Zamoner, A. (2014).	RMS: Addressed in revised RAR.	Not applicable.	RMS: See column B. These papers were not discussed on PRAS 125 meeting.	Addressed: The studies are assessed in the revised RAR: - P. 718, B.6.7.1, Published data on neurotoxicity - P. 805, B.6.8.4, Further published data (released since 2000)

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer 0Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
Mechanisms underlying the neurotoxicity induced by glyphosate-based herbicide in immature rat hippocampus: Involvement of glutamate excitotoxicity. Toxicology, 320, 34-45. - El-Shenawy, N.S., 2009. Oxidative stress responses of rats exposed to Roundup and its active ingredient glyphosate. Environ. Toxicol. Pharmacol. 28, 379–385 See reporting table public consultation 2(61)				
Data requirement 2.21 Applicant to submit the articles mentioned in the comment: - Riede et al., ASB2013-14684 - Krüger et al.	RMS: Addressed in revised RAR.	Not applicable.	RMS: The articles by Krüger *et al*. (2012) and Shehata *et al*. (2013) were included. Riede *et al*. (2013) is not an article but a preliminary research report. In the revised RAR, it was described in a more extensive and clear way. A manuscript is in	Addressed: The study by Kruger (2012) was reported in the original RAR; the other studies are assessed in the revised RAR: - P. 801, B.6.8.3.3, Published data - P. 719, B.6.7.1, Published

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer 0Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
(2012) - Shehata et al. (2013) See reporting table public consultation 2(62)			preparation but was not submitted to any journal so far.	data on neurotoxicity
Data requirement 2.22 Applicant to submit the articles mentioned in the comment: - Thongprakaisang et al. 2013. - Larsen K, Najle R, Lifschitz A, Virkel G. Environ Toxicol Pharmacol. 2012 Nov;34(3):811-8 - Cavuşoğlu et al. '11 See reporting table public consultation 2(64)	RMS: Addressed in revised RAR.	Not applicable.	RMS: See column B. These papers were not discussed on PRAS 125 meeting.	Addressed: The study by Thongprakaisang (2013) was reported in the original RAR; the study by Larsen (2012) is assessed in the revised RAR: - P. 804, B.6.8.4, Further published data (released since 2000) The Cavuşoğlu et al. '11 publication is not considered relevant for the current toxicological assessment.
Data requirement 2.23 GTF please submit all articles identified after	RMS: Addressed in revised RAR. Further articles have been submitted by the GTF and	Not applicable.	RMS: See column B.	Addressed. See also Data requirement 2.25 below.

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer 0Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
2011 as offered in your comment in column 3 "All articles identified after December 2011 will be available to EFSA upon request, along with summaries, relevance/reliability evaluations and critiques where appropriate". See reporting table public consultation 2(64)	have been reported in the revised RAR.			
Data requirement 2.24 Applicant to submit the articles mentioned in the comment: - Paganelli A, Gnazzo V, Acosta H, López SL, Carrasco AE. Chem Res Toxicol. 2010;23(10):1586-95. - Antoniou et al. 2012 - Marc J, et al. Toxicol Appl. Pharmacol. 2005	RMS: Addressed in revised RAR.	Not applicable.	RMS: See column B.	Addressed: The studies by Paganelli (2010) and Antoniou (2012) were reported in the initial RAR Several studies from Marc 2002, 2003 and 2004 are reported in the RAR, the 2005 paper 'A glyphosate-based pesticide impinges on transcription' was performed with several formulations and POEA surfactant on sea urchin embryos; the study shows low relevance to the assessment of glyphosate a.s.

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer 0Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
See reporting table public consultation 2(66)				
Open point 2.7 To provide the additional information on variability of the dermal study results in a revised RAR. See reporting table public consultation 2(68)	RMS: Addressed in revised RAR.	Not applicable.	RMS: Amendments have been made in the revised RAR. Dermal absorption of the representative formulation was corrected and is now 1% (concentrate and dilutions). This issue was not discussed on the PRAS 125 meeting.	See Open point 2.4 above.
Data requirement 2.25 Applicant to submit the new articles and the report of the literature research. See reporting table public consultation 2(78)	RMS: Addressed in revised RAR.	Not applicable.	RMS: New published information (submitted by the applicant or from third parties) had been included in the revised RAR (2015) in preparation of the PRAS 125 meeting. Following the PRAS 125 meeting, some more publications were amended reporting the frequency of lymphoma in mice (PRAS 125 homework for RMS).	Addressed: Ref. p. 3 of the revised RAR (vol. 3, B.6)

3. Residues

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
Open point 3.1 RMS to correct in Table B.7.1-68, the unextracted residue value (4.3% instead of 42.9%). See reporting table 3(6)	RMS: Addressed in revised RAR.	Not applicable.	RMS: See column B. No action required.	Addressed Table B.7.1-68 has been amended in the revised RAR of March 2015
Open point 3.2 RMS to considerer in a revised RAR, GTF comments 3(7) to 3(9) on sections B.7.1.1.3 and table B.7.1.1.4 in Vol.3 See reporting table 3(7)	RMS: Addressed in revised RAR.	Not applicable.	RMS: See column B. No action required.	Addressed GTF's comments on section B.7.1.1.3 (Study RIP9600099 none GLP, erroneous values in Table 7.1.-20…) have been taken into account in the revised RAR of March 2015
Open point 3.3 RMS to considerer in a revised RAR the value for milk in table 7.2-14 (0.005 mg eq./kg instead of 0.004). See reporting table	RMS: Addressed in revised RAR.	Not applicable.	RMS: See column B. No action required.	Addressed Value for milk at day 7 (0.005 mg/kg) has been corrected in Table 7B.7.2-14 in the revised RAR of March 2015.

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
3(13)				
Open point 3.4 RMS to reconsider Table 7.3-5 (Overview of glyphosate residues and its metabolites in CP4-EPSPS and GOX modified crops) in a revised RAR, according to applicant comments in column 2. See reporting table 3(15)	RMS: Addressed in revised RAR.	Not applicable.	RMS: See column B. No action required.	Addressed Values in Table B.7.3-5 for study on maize (George, 1995, RIP9700618) have been amended as requested in the revised RAR of March 2015.
Open point 3.5 RMS to amend Table B.7.3-7 in a revised RAR, with the deletion of "lentils" in column "comments". See also comment 3(20) See reporting table 3(16)	RMS: Addressed in revised RAR.	Not applicable.	RMS: See column B. No action required.	Addressed “Lentils” has been deleted from the column “Comments” in Table B.7.3-7 of the revised RAR of March 2015.
Open point 3.6 RMS to correct AMPA	RMS: Addressed in revised RAR.	Not applicable.	RMS: See column B. No action required.	Addressed AMPA value for kidney (4.4% TRR) has been corrected in Table B.7.3-8 of the revised

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
value for hen kidney in Table 7.3-8, in a revised RAR (4.4% TRR instead of 4.2%). See reporting table 3(17)				RAR of March 2015
Data requirement 3.1 A PHI should be provided to define the GAP for olive for oil production, based on the ground fallen fruits (since fruits fallen onto ground are directly exposed to the treatment spray). See reporting table 3(23)	RMS: Open point. Current GAP does not support sufficient trials for an assessment. GAP needs to be reconsidered before an assessment can be conducted.	Not applicable.	RMS: See column B.	Data gap A PHI should be proposed to support the GAPs for olive for oil production (based on ground fallen fruits) and additional residue trials on ground-picked olives conducted according to these GAPs should be provided.
Data requirement 3.2 Four additional trials on ground-picked olives are requested to derive MRL for olives (oil production). A PHI should be proposed to support this uses (see data requirement 3(23)) See also comment	RMS: Addressed in revised RAR, Open Point: GAP needs to be amended with PHI information, data package on olives for oil production needs to be amended accordingly.	Not applicable.	RMS: See column B.	See data gap under Data requirement 3.1

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
3(53) See reporting table 3(26)				
Data requirement 3.3 Additional residue trials on rapeseed conducted according to the supported GAP are requested. Only 3 trials conducted according to the representative uses (2160 g/ha ± 25% tolerance) are available. As the use of the proportionality has not been yet agreed at EU level and since proportionality principle was generally excluded for herbicides by both OECD and CODEX, trials out of the 25% tolerance are not considered. See reporting table 3(30)	RMS: No action. The proportionality principle was generally excluded for herbicides by both OECD and CODEX. Without proportionality, the utilisation of trials with exaggerated application rates is against the ALARA principle in MRL setting. Open point: Additional residue trials on rapeseed conducted according to the supported GAP are requested.	Not applicable.	RMS: See column B.	Data gap Additional residue trials on rapeseed conducted according to the supported GAP are requested.

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
Experts' consultation 3.1 A general approach for the selection of the residue trials relevant for the MRL calculations on cereals, should be discussed in an expert meeting. See also comment 3(31), 3(34), 3(36), 3(52), 3(54), 3(55) and 3(82) See reporting table 3(33)	RMS: Open point. EU consensus needed.	Pesticides Peer Review Meeting 127 (3. – 5 March 2015): The meeting agreed on the following MRL proposals: 20 mg/kg on wheat/rye, 30 mg/kg on barley/oats.	RMS: No action required. MRL proposals in correspondence to RAR.	Addressed MRL proposals in the RAR are agreed as following: - 20 mg/kg on wheat/rye, - 30 mg/kg on barley/oats.
Open point 3.7 RMS to amend section B.7.6.7 on storage stability in a revised RAR, considered applicant comment (not deviation to current guideline). See reporting table 3(35)	RMS: Addressed in revised RAR.	Not applicable.	RMS: See column B. No action required.	Addressed Section B.7.6.7 has been amended according to GTF comments in the revised RAR of March 2015 (storage stability studies were conducted according the guideline into force at the date they were performed).
Experts' consultation 3.2	RMS: Open point. Consensus needed.	Pesticides Peer Review Meeting 127 (3. – 5 March	RMS: No action required	Addressed The Pesticides Peer Review

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
The setting of a conversion factor (CF) for risk assessment on cereals (maize excluded) should be discussed in an expert meeting. See reporting table 3(37)	RMS opinion: CFs are presented in the RAR when possible (e.g. for the cereal grains Vol.3 Tables B.7.6-6 & -7). A general conclusion on a CF of 1.1 for cereals (to be put in the LoEP), based on desiccation uses, is not supported: - In terms of metabolic formation desiccation is the least favourable GAP compared to early applications - Cereal grains should be limited to barley, rye, oats, triticale and wheat, since maize is a GMO - GMO cereal grains (e.g. wheat MON 71800) are currently under development - Besides, it should be discussed whether a CF of 1.1 is a “significant change” or not.	2015): The setting of a conversion factor (CF) for risk assessment on small grain cereals is not required.		Experts’ meeting 127 on residues concluded that the setting of a conversion factor (CF) for risk assessment on small grain cereals is not required. Considering the values where AMPA residues are >LOQ, CF were calculated to be in the range of 1.01 to 0.07, thus with no significant impact on the outcome of the consumer risk assessment. Moreover, the derivation of sound CFs would require taking into account residues in GMO and conventional crops respectively (while representative uses are limited to conventional crops only).
Open point 3.8 RMS to include a	RMS: Addressed in revised RAR´s LoEP.	Not applicable.	RMS: See column B. No action required.	Addressed LoEP has been amended.

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
column "Comment/ Recommendations" in the LoEP summary table on residue trials. See reporting table 3(39)				
Experts' consultation 3.3 MSs to discuss the recoveries after storage under frozen conditions. Note: EFSA remains of the opinion that concurrent recoveries (= fresh or procedural recoveries) **have not** to be used to correct the recovery values observed after storage under frozen conditions and therefore, that the columns "corrected %" should be deleted from the different tables in the RAR. Concurrent recoveries should be used only to confirm that the analytical method has	RMS: Open point. Consensus on data reporting needed. RMS opinion: Both cited documents refer to the generation of studies and their reporting. In all cases the uncorrected values were presented in the studies and given in the RAR. The "% corrected" column was included by the RMS to ease interpretation in spite of OECD 506 (35): "Any decline should take into account the uncorrected residues in stored commodities and procedural recoveries." Especially for analytes difficult to analyse like glyphosate and AMPA identification of a true decline demands	Pesticides Peer Review Meeting 127 (3. – 5 March 2015): Although no harmonised approach could be achieved with regard to the interpretation of the current guideline, the meeting concluded that the uncorrected recoveries and procedural recoveries must always be reported for sake of transparency. For glyphosate, based on the reported data, acceptable storage stability was demonstrated.	RMS: No action required. A paragraph strengthening the case-by-case situation was included in the RAR.	Addressed Although no harmonised approach could be achieved with regard to the interpretation of the current guideline, the meeting concluded that the uncorrected recoveries and procedural recoveries must always be reported for sake of transparency. For glyphosate, based on the reported data, acceptable storage stability was demonstrated. The following sentence has been added in the revised RAR of March 2015 in the section B.7.6.7 on storage stability: *"… it should be noted that the general basis for the*

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
been correctly implemented at the different control time points and that, low storage recovery observed at a certain control point, may be explained by a low procedural recovery. Considering that the rational to support the stability was based on the nominal spiking rates (and not the residue level measured at T0), the RMS conclusion on stability are agreed. See reporting table 3(40)	consideration of the procedural recoveries to get an impression of the overall picture. The impact of the analytical performance was therefore included to help the reader in its assessment.			*interpretation are the uncorrected residue values and their procedural recoveries".*
Experts' consultation 3.4 MSs to discuss the results of the processing studies in soya bean. AMPA residue levels are expressed as AMPA equivalent. Note: In absence of data on acetyl-	RMS: Open point. Consensus needed. RMS opinion: see reporting table.	<u>Pesticides Peer Review Meeting 127 (3. – 5 March 2015):</u> - The derived PFs for glyphosate on soya bean meal (1) and crude oil (0.1) were considered as acceptable. - The meeting was unable to	RMS: No action required. PRAS 127 meeting recommendation confirms RAR.	Addressed The Pesticides Peer Review Experts' meeting 127 on residues concluded that the PFs derived for glyphosate on soya bean meal (1) and crude oil (0.1) are acceptable. In contrast, conversion factors (CF) for risk assessment were

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
glyphosate and acetyl-AMPA, EFSA remains of the opinion that PF and CF should be considered as a "best case" in term of residue transfer in processed commodities. See reporting table 3(43)		derive CFs for risk assessment since the registered US GAPs for comparison with these trials were not reported and also the nature of the crops was not specified (conventional or GMO crop).		not proposed since no information was reported whether the submitted studies were conducted on GMO or on conventional soya bean varieties.
Experts' consultation 3.5 MSs to discuss the results of the processing studies in barley. Note: Processing studies conducted at higher application rates (4300 and 8600 g/ha) and with PHI ≥ 7 days should indeed be taken into account to derive PF and CF (and not only studies conducted at application rates in compliance with the cGAP). A sufficient number of processing studies is therefore	RMS: Open point. Consensus needed. RMS opinion: The suggested processing trials at higher rates were not considered valid due to analytical issues in the study (see revised RAR).	Pesticides Peer Review Meeting 127 (3. – 5 March 2015): PFs and CFs could not be derived from the available processing trials.	RMS: No action required. PRAS 127 meeting recommendation confirms RAR.	Addressed The Pesticides Peer Review Experts' meeting 127 on residues did not derive PF and CF for barley from the submitted processing studies since no validation of the data was reported and significant residue levels of glyphosate were recovered in the control samples (up to 5 mg/kg).

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
available to derive PF and CF for barley malt. See reporting table 3(44)				
Open point 3.9 RMS to amend in a revised RAR, the feeding levels reported in Tables B.7.8-3 and B.7.8-4 (correct values: 0.012, 0.13, 1.44, 7.38 and 19.4 mg eq/kg bw/d). See reporting table 3(48)	RMS: Addressed in revised RAR.	Not applicable.	RMS: See column B. No action required.	Addressed Table B.7.8-4 has been amended in the revised RAR of March 2015.
Open point 3.10 RMS, to insert in a revised RAR (section B.7.8.1 on animal feeding) a statement related to observations on animal health and behaviour. See reporting table 3(49)	RMS: Addressed in revised RAR.	Not applicable.	RMS: See column B. No action required.	Addressed Sentences related to the animal health and behaviour have been added under section B.7.8.1 of the revised RAR of March 2015.

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
Open point 3.11 RMS to reconsider in a revised RAR, the maximum and median animal dietary burdens reported in Table B.7.12-9. See reporting table 3(60)	RMS: Addressed in revised RAR.	Not applicable.	RMS: See column B. No action required.	Addressed Animal burden calculations have been reconsidered in the revised RAR of March 2015.
Open point 3.12 RMS to propose in a revised RAR, extrapolation to the ruminant group, considering the values derived for bovine (values to be added in the consumer risk assessment). See reporting table 3(61)	RMS: Addressed in revised RAR.	Not applicable.	RMS: See column B. No action required.	Addressed In the revised RAR of March 2015, MRL, STMR and HR values derived for bovine have been extrapolated to the ruminant group and considered in the consumer risk assessment.
Open point 3.13 RMS to reconsider in a revised RAR, the title of Table B.7.13-1 (should include CP4-EPSPS	RMS: Addressed in revised RAR.	Not applicable.	RMS: See column B. No action required.	Addressed CP4-EPSPS modification (relevant for maize) has been inserted in the Table B.7.13-1 title.

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
modification, since relevant for maize). See reporting table 3(62)				
Open point 3.14 RMS to corrected active substance content in Appendix B.7.18 (360 g/l instead of 355.7), See reporting table 3(67)	RMS: Addressed in revised RAR.	Not applicable.	RMS: See column B. No action required.	Addressed Active substance content (360 g/l) has been corrected in Appendix B.7.18 of the revised RAR of March 2015.
Open point 3.15 RMS to corrected PPP formulation pages 555, 692, 757 and 942 (WG instead of SG), See reporting table 3(71)	RMS: Open point. Screenshot from study provided in reporting table supporting SG formulation. GTF to clarify statement.	Not applicable.	RMS: See column B.	Addressed PPP formulation type has been amended in the revised RAR of March 2015 (WG instead of SG).
Open point 3.16 RMS to corrected PPP formulation pages 401, 412, 417, 419, 420, 426, 429, 430, 432, 433, 434, 435, 436, 438, 439, 447,	RMS: Addressed in revised RAR.	Not applicable.	RMS: See column B. No action required.	Addressed PPP formulation type has been amended in the revised RAR of March 2015 (SL instead of SC).

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
451, 453, 454, 585, 586, 592, 592, 594, 599, 601, 607, 610, 615, 619, 623, 627, 650, 653, 660, 662, 669, 674, 676, 707, 814, 844, 871, 892, 894, 914, 916, 946 and 960 (SL instead of SC), See reporting table 3(72)				
Open point 3.17 RMS to add PPP name and to correct formulation type in page 574 (MON 52276 and SL formulation). See reporting table 3(74)	RMS: Addressed in revised RAR.	Not applicable.	RMS: See column B. No action required.	Addressed PPP name has been amended in the revised RAR of March 2015 (MON 52276 and SL formulation).
Open point 3.18 RMS to add PPP name in page 578 (MON 44068). See reporting table 3(75)	RMS: Addressed in revised RAR.	Not applicable.	RMS: See column B. No action required.	Addressed PPP name (MON 44068) has been added in the revised RAR of March 2015.
Open point 3.19	RMS: Addressed in revised RAR.	Not applicable.	RMS: See column B. No action required.	Addressed

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
RMS to add PPP name in page 704 and 711 (CHE 3607). See reporting table 3(76)				PPP name (CHE 3607) has been added in the revised RAR of March 2015.
Open point 3.20 RMS to corrected PPP formulation page 771 (WG instead of SG), See reporting table 3(78)	RMS: Addressed in revised RAR.	Not applicable.	RMS: See column B. No action required.	Addressed PPP formulation type has been amended in the revised RAR of March 2015 (WG instead of SG).
Open point 3.21 RMS to add PPP name in page 894 (MON 14478). See reporting table 3(79)	RMS: Addressed in revised RAR.	Not applicable.	RMS: See column B. No action required.	Addressed PPP name (MON 14478) has been added in the revised RAR of March 2015.
Experts' consultation 3.6 Setting of conversion factors for risk assessment in animal matrices, based on the	RMS: Open point. Consensus needed. RMS opinion: No agreement. The study by Cowell et al. involved administration of a 9:1 mix	Pesticides Peer Review Meeting 127 (3. – 5 March 2015): The setting of CFs for risk assessment in commodities of animal origin is not	RMS: No action required. PRAS 127 meeting recommendation confirms RAR.	Addressed Based on the representative uses supported in the framework of the renewal procedure, the Pesticides Peer Review Experts' meeting

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
representative uses, should be discussed in an expert meeting. See reporting table 3(80)	of glyphosate and AMPA. In goat metabolism studies conducted with ^{14}C-glyphosate the formation of AMPA was negligible (<10 %). In addition N-acetyl-glyphosate, which is also included in the RD for enforcement purposes of animal commodities, gave no or negligible residues of AMPA or N-acetyl-AMPA in goat metabolism and feeding studies. On the other hand GOX GMOs contain much higher AMPA levels than other crops. Therefore the composition of the feed itself is relevant for the final CF in the animal tissue. Since the current assessment may not cover all option (conventional burden, high GOX burden, or high NAG burden) the CF may be variable in both directions (near 1 for high NAG, much higher for high GOX). The only option the RMS sees is limiting the CF to European uses without GMO, where the ratio of	required considering the representative uses.		127 on residues concluded that the setting of CF for risk assessment in commodities of animal origin is not required. - Based on the representative uses, residues are not expected in animal matrices (except kidney). - Intakes resulting from the consumption of GMO crops should also be considered to derive sound CF, as the ratio glyphosate/metabolite(s) observed in the feed items has a significant impact on the ratio glyphosate/metabolite(s) finally observed in the animal matrices.

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
	Glyphosate and AMPA in the feed should pass through the animals approximating the CF of 1.2. However, the practical use is not seen by the RMS and a general consensus should be met at an Expert Meeting.			
Experts' consultation 3.7 MSs to discuss this general aspect in an expert meeting. See reporting table 3(83)	RMS: Open point. Consensus needed.	Pesticides Peer Review Meeting 127 (3. – 5 March 2015): The sum up of the LOQ of each compound included in the RD for animal commodities should be considered.	RMS: MRLs amended. MRLs for liver and fat (all species) were elevated from 0.05* mg/kg to 0.1* mg/kg to address for the LOQs of each compound.	Addressed An MRL of 0.1* mg/kg has been proposed for liver and fat (as the sum of the LOQs of 0.05 mg/kg achieved for each individual component).
Data requirement 3.4 Metabolism in GAT-modified crops, metabolism in livestock animals with N-acetyl-glyphosate, hydrolysis stability of N-acetyl-glyphosate and N-acetyl-AMPA. The data requirement has already been identified in the RAR.	RMS: Addressed in revised RAR. Ownership of data required since owner not part of GFT.	Not applicable.	RMS: See column B.	Addressed Livestock metabolism and feeding studies and standard hydrolysis studies using *N*-acetyl-glyphosate have been submitted and assessed by the RMS in the revised RAR.

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
See reporting table 3(86)				
New open point 3.22: Please consider that an ARfD (0.5 mg/kg bw) has been proposed.		Not applicable.	RMS: Assessment of the short-term intake included in the RAR. No acute intake concerns identified.	Addressed An acute consumer risk assessment taking into account the ARfD value of 0.5 mg/kg bw proposed in the course of the peer review has been added in section B.7.15.2 of the revised RAR of March 2015. Highest IESTI using the EFSA PRIMo model: 9% ARfD for barley (NL, adult).

4. Environmental fate and behaviour

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting/EFSA request for RMS' action	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
Open point 4.1 RMS to provide a transparent summary and evaluation of the studies Kesterson & Atkins, 1991 and Honegger (1992) in a revised RAR. See reporting table 4(2)	Addressed.	Not applicable.		Open point closed.
Data requirement 4.1 Applicant to provide a document that sets out the different information available and discusses the pH dependency of biodegradation and adsorption of glyphosate and AMPA. In particular the document should discuss the apparent pH dependence of mineralisation and the likelihood of differential degradation route(s)	Addressed. Information on pH dependency of biodegradation and adsorption of glyphosate and AMPA provided by GTF was implemented in the appropriate chapters in the rev.RAR Vol 3 B8. The argumentation of GTF regarding the pH dependency of degradation rate of glyphosate and AMPA is considered acceptable by the RMS. Therefore the issue of differing degradation pathway is irrelevant in regulatory	Not applicable.		Data requirement fulfilled. See RAR pp 5-13 for the pH dependency of biodegradation and mineralization. See RAR pp 184-187 for the pH dependency of the adsorption to soil.

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting/EFSA request for RMS' action	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
depending on pH. Note the document cited in column 3 of the reporting table at comment 4(3) (pdf icon only present, but not the actual document), may be sufficient to address this request. See reporting table comment 4(3). See reporting table 4(3)	terms. Statistical shown lack of pH dependency of adsorption coefficients of glyphosate and AMPA is supported by literature, by conclusion that sorption of glyphosate and AMPA in soil is not influenced by a single or dominating soil physico-chemical property. The pH dependency of both parameters will not be considered in further risk assessment.			
Open point 4.2 RMS to add information on the study Lewis and Turnball (1992) missing from the last paragraph on page 75 of the RAR in an addendum. An explanation is necessary why a new kinetic analysis was performed by the RMS for this study. See reporting table 4(7)	Addressed.	Not applicable.		Open point closed.

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting/EFSA request for RMS' action	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
Open point 4.3 RMS to provide the visual fits i.e. graphs of the re-evaluated kinetics conducted by the RMS, so the fits to the visual assessment statements presented are clear. Note applicants fits are available to competent authorities as they have access to the complete dossier. Fits completed by the RMS cannot be retrieved from the dossier. See reporting table 4(8)	Addressed.	Not applicable.		Addressed.
Open point 4.4 RMS to perform a kinetic re-evaluation of the Arrow soil (study Dean, 1995) using correctly 'processed' data including presenting the visual	Addressed.	Not applicable.		Open point closed.

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting/EFSA request for RMS' action	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
fits in an addendum. see reporting table comments 4(9), 4(26) and also the related Open point: for another soil at 4 (29)). See reporting table 4(9)				
Open point 4.5 RMS to remove the last sentence on page 81 "the residue data of PMG in soils Speyer 2.1 and Beedon Manor can be used without further processing" and the DT_{50} value related to TMS in the soil Beedon Manor from the Tables B.8.1-91 to and B.8.1-95 in an addendum. and update the DT entries in the list of endpoints consequently. See reporting table 4(12)	Addressed.	Not applicable.		Open point closed.

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting/EFSA request for RMS' action	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
Open point 4.6 RMS to correct DT_{50} value of the study Galicia & Morgenroth, 1993 in Table B.8.1-94 in an addendum. To do this they should present the FOMC and DFOP fits in the addendum (so it is transparent whether the FOMC or DFOP fit is better (current statement on visual fit would indicate that DFOP should be selected (good is better than acceptable) as proposed by applicant where they quote the lower chi2 to justify DFOP.)) Whichever kinetic gives the better fit should be selected resulting in a not normalised endpoint of 83.9 days (DFOP slow phase) or 104.5 days (FOMC DT90/3.32). The list of endpoints to be updated consequently.	Addressed. Persistence endpoint was derived by the RMS selecting best fit kinetics (DFOP) according to FOCUS kinetic recommendations. Since 10% of initial concentration was reached during the study, the DT_{90} FOMC/3.32 (not normalised: 104.5 d and 93.3 d at 20°C and pF2) should be used as modelling endpoint according to FOCUS kinetic recommendations.	Not applicable.		Open point closed.

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting/EFSA request for RMS' action	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
See reporting table 4(14)				
Open point 4.7 RMS to delete DT_{50} and DT_{90} values of the soil Speyer 2.2 (study Galicia & Flückiger, 1993/Mamouni, 2002) from the Tables B.8.1-93 and Tables B.8.1-94 in an addendum and update the list of endpoints consequently. See reporting table 4(15)	Addressed.	Not applicable.		Open point closed.
Open point 4.8 RMS to correct kinetic model in Table B.8.1-96 to 'FOMC_SFO' and correct $\chi 2$ error for soil Speyer 2.3 of the study McLaughlin &, Schanne, (1996) in an addendum and update the list of endpoints	Addressed.	Not applicable.		Open point closed.

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting/EFSA request for RMS' action	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
consequently. See reporting table 4(17)				
Open point 4.9 RMS to correct the days that refer to measured mineralisation days in the LoEP and consider in a corrigendum or amended RAR Volume 1, Level 1 point 2.8.1.1 See reporting table 4(18)	Addressed.	Not applicable.		Open point closed.
Data requirement 4.2 Applicant to submit final reports of the anaerobic soil incubation studies studies of McEwen (2004) and Knoch (2003). See reporting table 4(21)	Addressed.	Not applicable.		Data requirement fulfilled.
Open point 4.10	No calculation of a DT50 in the dark control is provided	Not applicable.		Open point closed.

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting/EFSA request for RMS' action	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
RMS to provide missing information of the study McGahen, 1983 (in particular results of the dark control)and revise the soil photolysis section in an addendum to the RAR. See reporting table 4(22)	by McGahen.			
Data requirement 4.3 Applicant to submit the studies of Esser (1996) and to provide a final report. See reporting table 4(23)	Addressed.	Not applicable.		Data requirement fulfilled.
Open point 4.11 RMS to delete the paragraph cited in reporting table comment 4(28) on page 75 or the RAR in an addendum.	Addressed.	Not applicable.		Open point closed.

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting/EFSA request for RMS' action	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
See reporting table 4(28)				
Open point 4.12 RMS needs to re-do the kinetic re-evaluation of the soil Arrow (soil study Dean, 1995), see Open point: at comment 4(9) and to correct the Tables B.8.1-89, Tables B.8.1-90 and the summary Tables B.8.1-91, B.8.1-93 and B.8.1-94 in an addendum and update the list of endpoints consequently. See reporting table 4(29)	Addressed.	Not applicable.		Open point closed.
Open point 4.13 RMS to present the kinetic fitting of parent glyphosate and AMPA from the field dissipation studies in an addendum , to support the expert discussion	Addressed.	Not applicable.		Open point closed.

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting/EFSA request for RMS' action	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
proposed at reporting table comment 4(37). See reporting table 4(36)				
Experts' consultation 4.1 Member state experts to discuss the field dataset and kinetic fitting for glyphosate and AMPA and agree the way to interpret AMPA dissipation rates from experiments where no decline of AMPA is observed. See reporting table 4(37)	The statement of GTF, that the apparent persistence could also be due to the continuous replenishment of AMPA from the degradation of glyphosate so that the decline phase of AMPA was not reached during the study period, can be supported by RMS. If the rate of formation of AMPA from glyphosate degradation were to be equal to the rate of degradation of AMPA in soil, this will result in an apparent steady state AMPA concentration in soil but it does not mean that AMPA is persistent and is not degrading. The observed residues of AMPA will be the result of simultaneous formation and degradation of AMPA during the study duration. It was shown in the study of Hill 1992 with longer study	Pesticides Peer Review Meeting 126 (24.- 26.2.2015): The experts agreed with the evaluation and endpoint selection of the RMS.	RMS: Addressed.	Experts' consultation completed. The experts agreed with the evaluation and endpoint selection of the RMS.

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	duration that AMPA has been degraded with half lives between 284 and 633 d. The study period in Schulz 1992 a-d is too short to derive reliable half lives compared with the study of Hill, in which a similar residue situation at corresponding sample points like in Schulz 1992 was observed. Only if glyphosate was degraded to less than 10 % during study duration, henceforward the clear decline fit of AMPA could shown because of more than 2 available sampling points. The default values of 1000 d would lead to an overestimation of the persistence of AMPA in the field. This approach is supported by results of laboratory studies, which show clear biological degradation with maximum half life of 301 d at 20 °C for AMPA. According to experience studies with the metabolite as parent result in significant lower half lives compared			

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	with half lives of the metabolite from degradation studies with parent. Therefore the approach of RMS in the RAR should be assessed as conservative.			
Experts' consultation 4.2 Member state experts to discuss the batch adsorption results where calculated 1/n values were <0.7. Experts to conclude on which of the following options to follow with this data set. Should the lower than 1/n values be retained or should the adsorption experiments be considered unreliable and excluded or should a default 1/n of 0.9 be ascribed to soils where 1/n was <0.7? Note the same conclusion does not have to be reached for every soil, it might be dependent on the	The Freundlich slope values were assessed according to the ´Clarification note from EFSA concerning data requirements, study guideline, guidance and consensus of member state fate and behaviour experts on soil adsorption measurements and selection of the slope (1/n value) that describe the Freundlich coefficient (2010)´. Values for 1/n are typically in the range from 0.7 to 1.1, though in some valid experiments values outside this range do sometimes occur. FOCUS guidance indicates that an expected average 1/n when looking at a database of a large number of different compounds is 0.9. The RMS considers that the recommendation of the FOCUS guidance to use the	Pesticides Peer Review Meeting 126 (24.- 26.2.2015): Open point RMS to remove the 4 adsorption results for the soils investigated in the Van Noorloos & Slangen (2001) experiment from the list of agreed endpoints. RMS to remove 3 AMPA default 0.9, 1/n values from Wittig (2002) and replace with the experimentally determined values. Finally recalculate the average KFoc and 1/n values for both glyphosate and AMPA. (adsorption section of the endpoints) Open point: In the PEC groundwater and	RMS: The results from the adsorption study by Van Noorloos & Slangen have been removed from the LoEP and the mean Kfoc and 1/n values for glyphosate have been recalculated. The 1/n values for AMPA from the Wittig study have been replaced with the experimentally determined values. The mean 1/n value in the LoEP has been recalculated. A footnote has been added to the PECgw and PEC_{SW} sections in the LoEP indicating what the correct values for use in any future modelling would be.	Experts' consultation completed.

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results in each batch experiment. See reporting table 4(48)	often referred to 'FOCUS default' Freundlich slope of 0.9 (average value) is applicable when the experiments attempted to investigate the effect of concentration on adsorption, but a reliable 1/n value could not be derived. In cases where no investigations of the relationship between soil solution concentration and adsorption behaviour were conducted by the Notifier, the RMS is of the opinion to use the default 1/n value of 1.0 according to the above mentioned clarification note. Due to the fact that the clarification note is not specific on what to do when the data set is mixed, i.e. only some reliable 1/n values are available, and therefore an established harmonised approach does not exist, the RMS decided not to leave out experimental results (kd values), but to use default 1/n values. Besides the effect of the 1/n value selection on the modelling results, particularly	surface water sections of the list of endpoints RMS to add footnotes indicating what the correct values for use in any future modelling would be.		

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	on PECgw, would probably be marginal as glyphosate and AMPA are strongly adsorbing to soil particles.			
New open point 4.26: RMS to remove the 4 adsorption results for the soils investigated in the Van Noorloos & Slangen (2001) experiment from the list of agreed endpoints. RMS to remove 3 AMPA default 0.9, 1/n values from Wittig (2002) and replace with the experimentally determined values. Finally recalculate the average KFoc and 1/n values for both glyphosate and AMPA. (adsorption section of the endpoints)		Not applicable.		Open point closed.
New open point 4.27: In the PEC groundwater and surface water sections of the list of endpoints RMS to add footnotes indicating		Not applicable.		Open point closed.

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what the correct values for use in any future modelling would be.				
Open point 4.14 RMS to show the values from the text as well as the values from the table and to exclude the sediment systems Bickenbach and Unter-Widdersheim from further evaluation in an addendum and update the list of endpoints consequently. See reporting table 4(54)	Addressed.	Not applicable.		Open point closed.
Data requirement 4.4 Applicant to provide the final study report Heintze (1996). Note an evaluation of the study is already included in the RAR, Vol 3, B.8.4.4 and the	Addressed	Not applicable.		Data requirement fulfilled.

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RMS physically has the study. However the dossier should be updated with the study as all competent authorities may not have the study. The study is not available to EFSA. See reporting table 4(55)				
Open point 4.15 RMS to add information on pH water, clay content etc. in Table B.8.4-2 and Table B.8.4-3 in an addendum. See reporting table 4(65)	Addressed.	Not applicable.		Open point fulfilled.
Open point 4.16 EFSA to indicate in the conclusion that the approval criteria for active substances Art 4.3 (b) of Reg No	-	Not applicable.		Open point fulfilled The criteria for active substances laid down in Art 4.3 (b) of Regulation No 1107/2009 have been appropriately addressed with respect to situations when

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1107/2009 has been appropriately addressed in respect of chemical oxidation of glyphosate and AMPA with Cl_2. See reporting table 4(66)				water, potentially containing residues of glyphosate and AMPA, is abstracted for drinking water and treated by chlorination procedures.
Open point 4.17 RMS to include a groundwater non-relevance assessment for AMPA in an addendum. to the RAR. This assessment should cover consumer exposure as well as risk to aquatic plants. Note that this assessment is only triggered by groundwater monitoring results, that it cannot be excluded result from uses other than the representative uses being assessed in the RAR. It should also be	RMS : In all simulations the 80th percentile PECGW values of glyphosate acid and AMPA at 1 m soil depth were below the groundwater threshold value of 0.1 µg/L indicating that the use of glyphosate as intended is not likely to pose an unacceptable risk to groundwater via direct leaching. The metabolite AMPA was included in risk assessment in chapter B9.2.4, TER values for AMPA, Focus Step 1 arte presented. Glyphosate and AMPA monitored exceeded the predicted environmental	Not applicable.		Open point fulfilled

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questioned whether AMPA in monitoring might originate from sources other than glyphosate. In the literature, it has been documented that AMPA might be also be a degradation product of other phosphonates, particularly ethylene-diamine-tetra-methylenephosphonic acid (EDTMPA) and diethylene-triamine-penta-methylene-phosphonic acid (DTMTPA), that can be components of domestic detergents? See reporting table 4(68)	concentrations for glyphosate acid and AMPA in surface water (PECsw) calculated using the FOCUS (2000) surface water models, even though worst case applications was assumed. Nevertheless, when calculating TER values with the concentrations monitored in the study by Horth (2012, BVL no 2310291), the outcome of the assessment still is covered by that the risk for aquatic organisms.			
Open point 4.18 RMS to summarise information from the VEWIN (Board for the Dutch drinking water companies) in an addendum.	Addressed.	Not applicable.		Open point fulfilled

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See reporting table 4(69)				
Open point 4.19 RMS to add a statement indicating that monitoring in EU indicated occurrence in water resources in the conclusion of PECgw results in an addendum. See reporting table 4(70)	Addressed.	Not applicable.		Open point fulfilled
Open point 4.20 RMS to consider adding a statement on non-professional uses, desiccant use, non-agricultural uses, urban uses and application to time harvest in Critical areas of concern identified in a revised RAR (Volume 1, 3.1.6) Please note: The EFSA conclusion will only	Addressed	Not applicable.		Open point fulfilled

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identify critical areas of concern relating to the representative uses applied for (D1 of the dossier). See reporting table 4(71)				
Open point 4.21 RMS to remove the conclusion « - Denmark: Findings in Denmark appear due to rapid transfer of surface water from nearby surfaces not agricultural use, investigations still ongoing« in an updated RAR or addendum . See reporting table 4(72)	Addressed.	Not applicable.		Open point fulfilled
Data requirement 4.5 Applicant to provide information on the possible runoff of glyphosate and	Addressed (see Point B 8.6.3.1) RMS can follow the argumentation of GTF, that direct (spot) application onto hard surfaces are not part of	Not applicable.		Data gap: Applicants to further assess surface water and ground water exposure for uses on 'all seeded or transplanted

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consequent concentrations of glyphosate and AMPA in surface water, that might result when application occurs indirectly on hard man made surfaces, consequent to the representative uses of 'all seeded or transplanted crops' and 'all seeded crops' (first two rows of the GAP table). See reporting table 4(73)	the representative GAP supporting the glyphosate Annex I renewal submission and that indirect applications on hard man made surfaces are outside the scope the current EU risk assessment paradigms and no guidance is available on what such an assessment should look like or which assumptions such assessment should underpin. Therefore, regarding any hard and man made surface risk assessments, the GTF refers to the re-authorization process of individual company's PPPs containing glyphosate under Article 43 to defend this use at zonal/national level. RMS considers that additional specific information in order to assess the potential contamination of surface water by runoff as well as the potential contamination of groundwater via run-off in surface water with subsequent bank filtration are required, if applications of glyphosate on			crops' and 'all seeded crops' where indirect exposure to hard surfaces and subsequent run off to surface water and bank filtration to groundwater may occur.

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	hard man made surfaces, like railway facilities are intended at the national level.			
Open point 4.22 RMS to update the list of endpoints residues requiring further assessment to update the left hand text to: 'Environmental occurring residues requiring assessment by other disciplines (toxicology and ecotoxicology) and or requiring consideration for groundwater exposure.' and to add in the box glyphosate to the Air definition. Note AMPA was already added regarding groundwater to the list of endpoints 'definitions requiring further assessment' section in the revisions dated 14 July 2014.	Addressed. The LoEP was updated. AMPA is proposed as relevant residue for monitoring following precautionary principles resulting from the frequent detections in groundwater and surface waters, the possible groundwater contamination path via bank filtration and the widespread intended uses of glyphosate in almost all crops (see also Volume 1, 2.13.2 (Definition of residues for monitoring.))	Not applicable.		Open point closed **Note:** in April 2015 EFSA has updated the LoEP in agreement with RMS statement in column B adding AMPA to the monitoring residue definition in groundwater.

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It is unclear how specific AMPA might be to glyphosate. Monitoring result might have other origins? In the literature, it has been documented that AMPA might be also be a degradation product of other phosphonates, particularly ethylene-diamine-tetra-methylenephosphonic acid (EDTMPA) and diethylene-triamine-penta-methylene-phosphonic acid (DTMTPA), that can be components of domestic detergents. See reporting table 4(76)				
Open point 4.23 RMS to provide more details on the search strategy and data bases used for the literature search in an updated RAR or addendum.	Addressed.	Not applicable.		Open point closed

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See reporting table 4(81)				
Data requirement 4.6 Applicant to provide the public literature reference: Mercurio, P., Flores, F., Mueller, J. F., Carter, S., & Negri, A. P. (2014). Glyphosate persistence in seawater. Marine pollution bulletin. See reporting table public consultation 4(4)	-	Not applicable.		Data requirement fulfilled. Further to the considerations already provided by the RMS in the RT and the RAR it should be noted that the study confirms the persistence into the aquatic environment of glyphosate and AMPA already observed in the studies available in the dossier. Whole system DT50: Glyphosate: 13.82 d - > 301.20 d AMPA: 57.61 – 455.72 d The study referred is not applicable to the current risk assessment scheme for modelling fate and behaviour of glyphosate and AMPA in fresh water. From the triggering point of view may be considered supporting information. The values obtained are within the available data and confirm

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				that glyphosate and AMPA should be considered persistent substances.
Open point 4.24 RMS to evaluate newly published literature: Mercurio *et al.* (2014) in an an addendum to the RAR. See reporting table public consultation 4(4)	Addressed.	Not applicable.		Open point fulfilled **Note:** further to the considerations already provided by the RMS in the RT and the RAR it should be noted that the study confirms the persistence into the aquatic environment of glyphosate and AMPA already observed in the studies available in the dossier. Whole system DT50: Glyphosate: 13.82 d - > 301.20 d AMPA: 57.61 – 455.72 d The study referred is not applicable to the current risk assessment scheme for modelling fate and behaviour of glyphosate and AMPA in fresh water. From the triggering point of view may be considered supporting information. The values obtained are within the available data and confirm

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				that glyphosate and AMPA should be considered persistent substances.
Data requirement 4.7 Applicant to provide the public literature references: http://onlinelibrary.wiley.com/doi/10.1002/ps.3724/full and if available " **Occurrence of glyphosate in a stormwater drain due to residential inputs"-** Ting Tang[1,2], Wesley Boënne1, Ann van Griensven[2,3], Piet Seuntjens[1,4,5], Nele Desmet1, Jan Bronders[1]. (1) Flemish Institute for Technological Research, VITO, Mol, Belgium, (2) Department of Hydrology and Hydraulic Engineering, Vrije Universiteit Brussel, Brussels, Belgium, (3) UNESCO-	-	Not applicable.		Data requirement fulfilled. Reference C.T. Ramwell, M. Kah, P. D. Johnson Pest Manag Sci (2014) Published online in Wiley Online Library: (wileyonlinelibrary.com) DOI 10.1002/ps.3724 (http://onlinelibrary.wiley.com/doi/10.1002/ps.3724/full) and published in paper in Pest Management Science Volume 70, Issue 12, pages 1823–1830, December 2014 and it is assessed in appendix to B.8 p 256. Note: reference "*Occurrence of glyphosate in a stormwater drain due to residential inputs"- Ting Tang1,2, Wesley Boënne1, Ann van Griensven2,3, Piet Seuntjens1,4,5, Nele Desmet1, Jan Bronders1. (1) Flemish Institute for Technological Research, VITO, Mol, Belgium, (2)*

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IHE, Delft, The Netherlands, (4) Department of Bioscience Engineering, University of Antwerp, Antwerp, Belgium, (5) Department of Soil Management, Ghent University, Ghent, Belgium See reporting table public consultation 4(5)				*Department of Hydrology and Hydraulic Engineering, Vrije Universiteit Brussel, Brussels, Belgium, (3) UNESCO-IHE, Delft, The Netherlands, (4) Department of Bioscience Engineering, University of Antwerp, Antwerp, Belgium, (5) Department of Soil Management, Ghent University, Ghent, Belgium*" has not been provided. No justification for not providing it is available to EFSA. Note: see also data gap derived from data requirement 4.5.
Open point 4.25 RMS to evaluate newly published literature: http://onlinelibrary.wiley.com/doi/10.1002/ps.3724/full and if available Ting Tang *et al.* in an an addendum to the RAR.	Addressed.	Not applicable.		Open point closed Note: see also data gap derived from data requirement 4.5.

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting/EFSA request for RMS' action	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
See also data requirement at comment 4(73) in the reporting table that compiles comments from the competent authorities. See reporting table public consultation 4(5)				

5. Ecotoxicology

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Open point 5.1 For the representative uses with spot applications, it is clearly stated in the GAP table that the actual application rate per hectare would be 33% to 50% of total application rate per treatment. This should be also reflected in the LoEP in the ecotoxicology section. Therefore RMS is requested to add a footnote in the LoEP for exposure estimations which took into account the 50% of the total application rate. Note: EFSA agrees that harmonisation and further guidance is needed on this issue. See also 5(13), 5(74) See reporting table 5(12)	RMS: Addressed. The footnote was added and reference was also included for the estimates of DDD. RMS appreciates further guidance on this issue.	Not applicable.	RMS: Not applicable.	Open point closed. For the uses in orchards where application is spot or between rows, the risk assessment took into account 50% of the application rate per hectare of treated areas to account for the actual rate per cropped area.
Open point 5.2 RMS to include the details on	RMS: Addressed. Details on the residue data set used to refine the risk assessment to bird	Not applicable.	RMS: Not applicable.	Open point closed. The residue data were included in the revised RAR under the B.9.13.

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the residue data set used to refine the risk assessment to birds in an updated RAR or addendum. See reporting table 5(14)	and mammals are included.			
Open point 5.3 RMS to correct MAF refinement in an updated RAR or addendum. The TERs in LoEP should be amended accordingly. Moreover, the LoEP should also report the refined MAF. See reporting table 5(15)	RMS: MAF values for the application interval of 21 days was calculated using the formula in Appendix H, which results in a MAF of 1.23 for two applications and a MAF of 1.29 for three applications.DDD and TER values are corrected accordingly, as well as in the LoEP.	Not applicable.	RMS: Not applicable.	Open point closed. For the first tier chronic risk assessment the MAF of 1.23 for two applications and a MAF of 1.16 (corrected by EFSA) for three applications were included, where relevant. EFSA has also calculated refined MAF values based on the residue decline DT50 of 2.8 days for the refined risk assessments where relevant.
Open point 5.4 RMS to include for the first tier risk assessment to birds all the scenarios relevant for the representative uses (according to EFSA2009) in a revised RAR or addendum. RMS to also amend the LoEP accordingly. See also 5(19), 5(20), 5(21)	RMS: Addressed. Comment 5(19) For the indication „Oilseed preharvest“ Scenario 122 (BBCH 80-99, late with seeds) is relevant and results in the highest default shortcut values (mean SV= 11.4, 90th centile SV = 24.7). With an application rate 2.16 kg/ha, SCV of 11.4 and ftwa value of	Not applicable.	RMS: Not applicable.	Open point closed. For the representative uses ‘all crop’ pre-planting and post planting, no specific scenarios are available in the EFSA birds & mammals guidance document. All the relevant scenarios related to the early growth stage of several crops were considered in the revised RAR. However, only the worst case

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See reporting table 5(18)	0.53 results in a DDD value of 13.1 and a TER of 7 thus passing the risk assessment. The scenarios 120, 134, and 138 result in a less risk, but were included although they are not worse –case. Please refer to chapter B. 9.1.7.2. Comment 5(20) For the indication “Orchard crops (vines including citrus & tree nuts)/ Post emergence of weeds” sceanrio 142 and 146 are relevant according to the GAP, but 146 presents the worst case and passes the risk assessment. Please refer to chapter B. 9.1.7.2. Comment 5 (21) For the indication“ Vinyard“ it is proposed to include scenario 231 (Small omnivorous bird "lark") considering no interception to take into account an application to the ground for vineyard herbicide uses. A diet composition of 25% grass, 25% weed seeds without interception and 50% ground			scenarios were reported in the LoEP.

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	arthropods without interception was assumed. Please refer to chapter B. 9.1.7.2.			
Experts' consultation 5.1 Mss to discuss and agree the chronic endpoint to be used for risk assessment to mammals. See also 5(25), 5(27), 5(29), 5(36), 5(37), 5(38), 5(40), 5(41). See reporting table 5(24)	RMS: Agreed. RMS considers a decreased body weight gain at 200 mg/kg bw/day and above as well as post-implantation losses to be directly linked to population size. Moreover lower foetal weight and a delay in ossification are considered to be adverse and therefore RMS proposes the NOAEL for developmental effects at 50 mg/kg bw/d. According to EFSA guidance document consideration must also be given to factors that may increase risk: Due to the unique application of glyphosate in various crops and at different seasons during the year in the agricultural landscape the proportion of the population that is exposed is probably remarkable. Any changes in physiology are considered to have the	Pesticides Peer Review Meeting 128 (3. – 5. March 2015): Open point RMS to amend the assessment report by considering all the available data on mammals (reproductive, maternal, and devolpmental toxicity) used to set overall NOAEL.	RMS: Addressed. Assessment was amended by an additional overview upon reproductive, maternal and developmental toxicity.	See new open point 5.18.

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	potential to increase susceptibility and fitness of the animals.			
New open point 5.18: RMS to amend the assessment report by considering all the available data on mammals (reproductive, maternal, and devolpmental toxicity) used to set overall NOAEL.		Not applicable.	RMS: see above.	Open point closed. The information was reported in the revised RAR.
Open point 5.5 RMS to include for the first tier risk assessment to mammals all the scenarios relevant for the representative uses (according to EFSA 2009) in a revised RAR or addendum. RMS to also amend the LoEP accordingly. See reporting table 5(26)	RMS: Addressed. Since voles are not required as focal species in all EU-member states, a more detailed risk assessment with additional generic focal species is added for a possible risk envelope approach. The following Generic focal species were included: Large herbiv. "lagomorph" and Small omniv. "mouse". Please refer to chapter B.9.3.3.2.	Not applicable.	RMS: Not applicable.	Open point closed. For the representative uses ‘all crop’ pre-planting and post planting, no specific scenarios are available in the EFSA birds & mammals guidance document. All the relevant scenarios related to the early growth stage of several crops were considered in the revised RAR. However, only the worst case scenarios were reported in the LoEP.
Open point 5.6 Assuming 50% of 3applications x 2.88 kg a.s./ha	RMS: Addressed. A triple application of 3applications x 2.88 kg a.s./ha	Not applicable.	RMS: Not applicable.	Open point closed. A footnote was added in the LoEP to clarify that the exposure estimates for birds

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with an interval of 28 days (total annual rate of 8.64 kg a.s./ha) for the representative use in ochards, the first tier TER would be >9.3. With the application pattern indicated in the GAP table (total annual rate of 4.32 kg a.s./ha) the TER would be likely above the trigger. However, RMS should clarify this issue in the LoEP (in a footnote). See reporting table 5(35)	was not assessed, because the max. cumulative application rate of 4.32 kg/ha glyphosate in any 12 month period stated in the GAP was related to the application rate/treated area. For the use in orchard a triple application of 3 times max. 1440 g a.s./ha was assumed and a triple application of 2 ×max. 720 g a.s./ha and 1× max. 2880 g a.s./ha. The latter one results in a worst case indicating a risk (TER<10) for small herbivorous mammals due to uptake of contaminated food. The TER is > 10 for the following usage patterns: 1× 2880 kg/ha, 2 × 2160 g/ha and 3× 1440 g/ha. Nevertheless, it can be consider that the calculation of TER is in that case too conservative and the DDD is overestimated. Taking into consideration that the third application differs from the other the use of MAF for the calculation of DDD can be modified. The MAF values for 3 applications and an interval			and mammals scenarios for the representative uses in orchards took into account the actual application rate per cropped area, which was assumed to be 50% of the rate per treated area indicated in the GAP.

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
	of 28 days was calculated using the formula in Appendix H, which results in a MAF of 1.09. The value 1 corresponds to the residues from last application whereas the value 0.09 to the residues level from the first and the second application at time of the third application. The DDD can be calculated as a sum of DDD resulting from the two first applications 0.36x136.4 x 0.09 and the third one 1.44x136.4x1. For the usage scenario 2x720 g a.s./ha + 2880 g a.s./ha the following DDD can be calculated: DDD = (0.72/2)x136.4 x 0.09 + (2.88/2) x 136.4 = 4.4 + 196.4 =200.8 The resulting TER is > 10. Please refer to chapter B.9.3.3.2.			
Open point 5.7 All the valid endpoints should be included in the LoEP. RMS please adds the chronic endpoint for *Daphnia magna* Wüthrich, 1990 (250795).	RMS: Addressed. Endpoints for *Daphnia magna* Wüthrich, 1990 (250795) is included in the LoEP. Endpoint of Wüthrich, 1990 (250795) was not used, endpoint of Magor, Shillabeer,	Not applicable.	RMS: Not applicable.	Open point closed. The chronic endpoint for *Daphnia magna* from Wüthrich, 1990 (250795) was not included in the LoEP. This endpoint was not relevant for the present risk assessment.

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
See reporting table 5(43)	1999 (BL6535/B) was used.			
Open point 5.8 The mortality effect in the study with *Danio rerio* (7 d) clearly followed a dose response relationship. EFSA agrees with SE that the NOEC from this study should be 1.0 mg/L. RMS please amends the chronic TERs for fish based on this endpoint. The amendment has to be reported both in a revised RA/Addendum and in the LoEP. The outcome of the risk assessment would be unchanged. Furthermore, it has to be noted that the dose-response relationship on mortality was not observed in the other two long-term available studies with rainbow trout and fathead minnow.	RMS: Addressed. It was stated during the commenting phase, that "Although not statistically significant, we would hesitate to set the NOEC to 5.6 mg a.s./L since at this treatment level and the level below the NOEC, a mortality of 16.7% and 10% respectively was observed."The following information has been amended In the short term toxicity test on fish larvae, the LC_{50} after 168 hours was determined to be 24.71 mg a.s./L. tThe No-Observed-Effect Concentration (NOEC) and the Lowest-Observed-Effect Concentration (LOEC) for zebra fish (Danio rerio) exposed to glyphosate acid	Not applicable.	RMS: Not applicable.	Open point closed The risk assessment to fish was amended with the NOEC of 1 mg a.s./L

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See reporting table 5(45)	were determined by the author to be 3.2 mg a.s./L and 5.6 mg a.s./L, respectively, based on nominal concentrations. Nevertheless, the mortality effect in the study with *Danio rerio* followed a dose response relationship and in the treatment level at 3.2 mg/L a mortality of 10% was observed. Considering these biological effects as relevant, although not statistically significant, results in a NOEC of 1.0 mg/L. Please refer to chapter B.9.2.1.12. LoEP and risk assessment have been amended as well.			
Open point 5.9 RMS to add NOEC values for algae and aquatic plants and correct reference in an updated RAR or addendum. See reporting table 5(47)	RMS: Addressed. RMS added NOEC values for algae and aquatic plants and corrected reference in an updated RAR or addendum. Please refer to chapter B.9.2.1.6.	Not applicable.	RMS: Not applicable.	Open point closed. The LoEP was amended accordingly
Open point 5.10	RMS: Addressed.	Not applicable.	RMS: Not applicable.	Open point closed.

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RMS to add information in an updated RAR or addendum on the study by Turgut and Fomin (2002) with *Miriophyllum aquaticum*. See reporting table 5(49)	RMS included a Risk assessment with endpoints derived from peer- reviewed literature and the max. PECsw values resulting in TER values. The study by Turgut and Fomin (2002) with Miriophyllum aquaticum was included. Please refer to chapter B.9.2.4.			
Experts' consultation 5.2 Mss to discuss the correction of drift rates as proposed by the RMS for the risk assessment to non-target arthropods and to non-target plants. **Note**: It is acknowledged there is a need to revise the current spray drift rates (see also EFSA PPR opinion on non-target terrestrial plants, EFSA Journal 2014;12(7):3800). However, as recommended by the PPR panel (EFSA Journal 2014;12(7):3800) the use of the current assessment based on FOCUS (2001) should still be followed until the new drift	RMS: RMS still favours modified spray driftability for the scenario siccation. Spray driftability is increased the higher the equipment is distant from the ground level and the higher the canopy level. In general, this issue is reflected by higher drift deposition values. In the case for crop canopy >50cm or special crop heights in vineyards, orchard and hops. Using the basic drift deposition values for field crops would therefore underestimate risk to non target plants, when application in cereals is performed in BBCH 89 before harvest. Therefore, we proposed to	Pesticides Peer Review Meeting 128 (3. – 5 March 2015): RMS to amend the risk assessment to non-target arthropods and to non-target plants using the FOCUS default drift values, highlighting the uncertainties and the possible underestimation of the exposure Additional errors were noted regarding the MAF values for NTA. The RMS should also take into account spray drift values for multiple applications. The amendment should be considered both in a revised	RMS: Addressed. Risk assessment for the scenario siccation was recalculated using the FOCUS default drift values and the uncertainties and the possible underestimation of the exposure is discussed. NTA risk assessment was recalculated.	Open point closed. The LoEP was amended accordingly (relevant only for NTTP).

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curves will be available. See also 5(55), 5(63), 5(61), 5(66), 5(67), See reporting table 5(50)	mirror the height of the crop and the potential higher drift deposition in order to reduce risk to non-target plants in the off-crop habitat. New harmonised values at the EU level are under discussion. In order to respect a precautionary principle in the risk assessment for non-target plants the Ganzelmeier tables have been extended to take into account high crops like e.g. sunflowers by using a modified deposition factor (2.77% *2).	DAR and the LoEP.		
New open point 5.19: RMS to amend the risk assessment to non-target arthropods and to non-target plants using the FOCUS default drift values, highlighting the uncertainties and the possible unersetimation of the exposure Additional errors were noted regarding the MAF values for NTA. The RMS should also take into account spray drift values for multiple		Not applicable.	RMS: see above	see above (Experts' consultation 5.2).

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
applications. The amendment should be considered both in a revised DAR and the LoEP.				
Open point 5.11 RMS to recalculate the MAF value used for risk assessment to non target arthropods by taking into account the application interval in the GAP. The amendment should be considered for in a revised RAR. See reporting table 5(51)	RMS: Addressed. Since glyphosate-containing plant protection products will be applied two times a season at a maximum application rate of 2 x 2160 g a.s./ ha, i.e. 4.32 kg a.s./ha and an application interval indicated in the GAP is a minimum of 21 days the MAF values were calculated on the basis of a 10-day half-life and interval of 21 days (a ratio of 1:2). Please refer to chapter B.9.5.6.	Not applicable.	RMS: Not applicable.	Open point closed.
Data requirement 5.1 GTF to submit new GLP study on microorganisms (N-transformation). See reporting table 5(58)	RMS: Addressed. The study Hutcheson, K , Glyphosate technical (MON 77973): Effect on Soil Microbial Nitrogen Transformations was made available. Please refer to chapter B. 9.8.1 and B 9.8.3.	Not applicable.	RMS: Not applicable.	Addressed. See also data requirement 5.9

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Experts' consultation 5.3 MSs experts to discuss the MAF value to be use for risk assessment to terrestrial non-target plants. See reporting table 5(62)	RMS: Herbicides have the potential to affect non-target plants exposed to spray drift. In the case of non selective herbicides non-target plants should be protected in order to sufficiently protect biodiversity, food web support and habitat for re-colonisation. In order to minimize effects to non-target species application procedures and nozzle equipment can significantly reduce spray drift. Nevertheless, the possibilities for drift reductions can also be achieved by other risk mitigation measures like buffer zones, e.g. in cases where nozzle equipment is not available. The level of drift is mediated by different factors like the wind speed, the crop species and the height or the development of the crop. The spray driftability is increased the higher the equipment is distant from the ground level and the higher the canopy level. In general, this issue is reflected by higher drift deposition values. This is	Pesticides Peer Review Meeting 128 (3. – 5 March 2015): The experts agreed to use the default MAF values to account for effects on NTTP due to multiple applications of glyphosate.	RMS: Agreed.	The default values of 1.7 for 2 applications and 2.3 for three applications were used.

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	the case for crop canopy >50cm (in vegetables, ornamentals and small fruits: drift deposition of 8.02% at 3 m is considered for one application) or special crop heights in vineyards, orchard and hops. Using the basic drift deposition values for field crops would therefore underestimate risk to non target plants, when application in cereals is performed in BBCH 89 before harvest. Therefore, we proposed to mirror the height of the crop and the potential higher drift deposition in order to reduce risk to non-target plants in the off-crop habitat. New harmonised values at the EU level are under discussion. In order to respect a precautionary principle in the risk assessment for non-target plants the Ganzelmeier tables have been extended to take into account high crops like e.g. sunflowers by using a modified deposition factor for field crops (2.77% *2). Upon publication of harmonised drift data, it is proposed new			

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	values in the revised RAR.			
Data requirement 5.2 GTF is given the possibility to submit new GLP study on terrestrial non-target plants. GTF to provide also a new quantitative risk assessment to terrestrial non-target plants. See also 5(50), 5(64), 5(65), 5(66), 5(67) See reporting table 5(63)	RMS: Addressed. The formulation study was made available upon request by the European Food Safety Authority (EFSA) (Bergfield, 2014, BVL no 2716933, GLP, not published). A revised quantitative risk assessment is performed. Please refer to Despite the assumption that the study can be considered to be valid as criteria according to OECD 227 are fullfilled (the seedling emergence is at least 70%; and in the controls the plants do not exhibit visible phytotoxic effects) uncertainties remain concerning the acceptability of the study. For more details lease refer to B.9.9.1.2. Nevertheless, this study displays the only dataset provided for the representative formulation and includes information about the relevance of exclusive representative formulants. In general toxicity studies with	Not applicable.	RMS: Not applicable.	Addressed. See open point 5.12.

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	the commercial product are more appropriate than studies with the active ingredient only for the assessment of the effects on non-target plants. RMS proposes that concerned Member States shall request the submission of additional studies according to OECD227 with the commmercial products particular during product authorziation, in order to evaluate specific sensitive endpoints corresponding to the product to be authorzied and to determine adequate bufferstrips for the protection of non–target plants in off-field areas.			
Open point 5.12 The RMS to consider new data, when available, in an Addendum See reporting table 5(63)	RMS: Addressed. See above.	Not applicable.	RMS: Not applicable.	Open point closed. New studies on non-target plants were evaluated in the revised RAR.
Open point 5.13 RMS to clarify why issues	RMS: RMS devised a new categorisation system, in which studies in category	Not applicable.	RMS: Not applicable.	Open point closed.

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related to the systematic review (SR) were not addressed during the SR protocol development performed by the notifier. See reporting table 5(73)	"UBA2"are reliable with restriction and used as supporting information. This category includes data from the literature or reports, in which the test parameters documented do not totally comply with the respective test guideline, but are sufficient to evaluate the data, as well as studies, in which investigations are described which cannot be subsumed under a testing guideline, but are nevertheless well documented, plausible and scientifically acceptable. In conclusion it is clear that regarding specific evaluations differ between NOT and RMS. RMS agrees that studies with products with unknown formulations cannot take into account at their full rate, when assessing the environmental safety for Annex I renewal of the active substance glyphosate itself.			
Data requirement 5.3 It is acknowledged that the	RMS: Adressed. The study was submitted and	Not applicable.	RMS: Not applicable.	Addressed.

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paper of Marjo Helander, Irma Saloniemi and Kari Saikkonen 2012 was not captured by the systematic literature search because performed for the period 2001-2011. However, the Applicant is given the possibility to provide a summary and full evaluation of the relevance of this paper. See reporting table 5(75)	the relevance was evaluated.			
Open point 5.14 RMS should consider the Applicant's evaluation of the paper Marjo Helander, Irma Saloniemi and Kari Saikkonen 2012 in an addendum. RMS should also clarify whether the systematic literature search report included the references of the papers considered not relevant and the reason for exclusion. See reporting table 5(75)	RMS: Addressed. The study was submitted and is considered in the revised Appendix with the following conclusion: In the review most of the cited literature was addressed in the literature review submitted with the Annex I Renewal of glyphosate (please refer to table below). Other literature cited in this review was either regarding efficacy of the active substance, transgenic plants (not part of the GAP for review), or previous to the evaluation period (pre-2001).	Not applicable.	RMS: Not applicable.	Addressed.
Data requirement 5.4	RMS: Addressed.	Not applicable.	RMS: Not applicable.	Addressed.

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Submission of supplemental studies on acute and chronic toxicity of glyphosate to aquatic organisms cited by FAO specifications and evaluations (2000/2001) for glyphosate. Rationale: For aquatic toxicity additional end points are cited, which were not submitted with the supplementary dossier. The data requirement has already been identified in the RAR. See reporting table 5(79)	The supplemental studies based on which the FAO specifications (2000) to aquatic organisms was generated. Most of the endpoints were derived from studies conducted with the formulation MON 2139 containing POEA. POEA in glyphosate-based products is Known to greatly enhanced toxicity. Please refer to chapter B 9.11 giving detailed information on the surface-active substance. For Annex I Renewal process of Glyphosate, the representative formulation is MON 52276.Nevertheless, endpoints for acute Daphnia and Fish toxicity are lower for the formulation MON 2139 than for the representative formulation MON 52276.			
Data requirement 5.5 Applicant to submit the study from Wagner and Lötters (2013) for procedural reasons: ‘Possible correlation of the worldwide amphibian	RMS: Addressed. The study was submitted and is considered in the revised Appendix. Please refer to chapter B 9.13.10.	Not applicable.	RMS: Not applicable.	Addressed.

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
decline and the increasing use of glyphosate in the agrarian industry. BfN-Skripten 343‘. See reporting table public consultation 5(2)				
Data requirement 5.6 Applicant to submit the following studies for procedural reosans: -Plötner J. & Matschke J. (2012). Akut-toxische, subletale und indirekte Wirkungen von Gly-phosat und glyphosathaltigen Herbiziden auf Amphibien – eine Übersicht. Zeitschrift f. Feldherpetologie 19: 1-20 -Cuhra, M., Traavik, T., & Bøhn, T. (2013). Clone- and age-dependent toxicity of a 587 glyphosate commercial formulation and its active ingredient in Daphnia magna. 588 Ecotoxicology, 22, 251-262. See reporting table public consultation 5(3)	RMS: Addressed. The study was submitted and is considered in the revised Appendix. Please refer to chapter B 9.13.10..	Not applicable.	RMS: Not applicable.	Addressed.
Data requirement 5.7	RMS: Addressed.	Not applicable.	RMS: Not applicable.	Addressed.

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Applicant to submit the following studies for procedural reosans: - Avigliano, L., Fassiano, A. V., Medesani, D. A., de Molina, M. R., & Rodríguez, E. M. (2014). Effects of Glyphosate on Growth Rate, Metabolic Rate and Energy Reserves of Early Juvenile Crayfish, Cherax quadricarinatus M. Bulletin of environmental contamination and toxicology, 1-5. - Fan, J. Y., Geng, J. J., Ren, H. Q., Wang, X. R., & Han, C. (2013). Herbicide Roundup® and its main constituents cause oxidative stress and inhibit acetylcholinesterase in liver of Carassius auratus. Journal of Environmental Science and Health, Part B, 48(10), 844-850. - Mona, M. H., Gaafar, R. M., Helal, I. B., Omran, N. E., & Salama, W. M. (2013).	The studies were submitted and are considered in the revised Appendix, mainly in chapter and B 9.13.9.and B 9.13.10.			

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Evaluation of cytotoxic effects of atrazine and glyphosate herbicides on< i> Biomphalaria glabrata</i> snails. The Journal of Basic & Applied Zoology, 66(2), 68-75. - Nwani, C. D., Nagpure, N. S., Kumar, R., Kushwaha, B., Kumar, P., & Lakra, W. S. (2013). Induction of micronuclei and nuclear lesions in Channa punctatus following exposure to carbosulfan, glyphosate and atrazine. Drug and chemical toxicology, (0), 1-8. - Richard, S., Prévot-D'Alvise, N., Bunet, R., Simide, R., Couvray, S., Coupé, S., & Grillasca, J. P. (2014). Effect of a Glyphosate-Based Herbicide on Gene Expressions of the Cytokines Interleukin-1β and Interleukin-10 and of Heme Oxygenase-1 in European Sea Bass, Dicentrarchus labrax L. Bulletin of environmental contamination and toxicology, 1-6.				

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- Sandrini, J. Z., Rola, R. C., Lopes, F. M., Buffon, H. F., Freitas, M. M., Martins, C. D., & da Rosa, C. E. (2013) Effects of glyphosate on cholinesterase activity of the mussel Perna perna and the fish Danio rerio and Jenynsia multidentata: In vitro studies. Aquatic toxicology (Amsterdam, Netherlands), 130, 171. - Brodeur, J. C., Poliserpi, M. B., & Sánchez, M. (2014). Synergy between glyphosate-and cypermethrin-based pesticides during acute exposures in tadpoles of the common South American Toad< i> Rhinella arenarum</i>. Chemosphere, 112, 70-76. - Syedkolaei, S. J. G., Shiri, N., Mirvaghefi, A. R., Rafiee, G. R., & Makhdomi, C. (2013). Toxicity evaluation of Malathion, Carbaryle and Glyphosate in common carp fingerlings (Cyprinus carpio,				

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Linnaeus, 1758). Journal of Veterinary Research, 68(3), 257-267. - Erhunmwunse, N. O., Alohan, F. I., Enuneku, A., Tongo, I., Ainerua, M., & Idugboe, S. (2013). Pathological alterations in the liver of post-juvenile African Catfish (Clarias gariepinus) exposed to sublethal concentrations of the herbicide Glyphosate. Journal of Natural Sciences Research, 3(15), 87-91. - Moreno, N. C., Sofia, S. H., & Martinez, C. B. (2014). Genotoxic effects of the herbicide Roundup Transorb< sup>®</sup> and its active ingredient glyphosate on the fish< i> Prochilodus lineatus</i>. Environmental toxicology and pharmacology, 37(1), 448-454. - dos Santos, K. C., & Martinez, C. B. (2014). Genotoxic and biochemical effects of atrazine and				

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Roundup< sup>®</sup>, alone and in combination, on the Asian clam< i> Corbicula fluminea</i>. Ecotoxicology and environmental safety, 100, 7-14. - Uren Webster, T. M., Laing, L. V., Florance, H., & Santos, E. M. (2013). Effects of glyphosate and its formulation, Roundup®, on reproduction in zebrafish (Danio rerio). Environmental science & technology. - Dornelles, M. F., & Oliveira, G. T. (2013). Effect of Atrazine, Glyphosate and Quinclorac on Biochemical Parameters, Lipid Peroxidation and Survival in Bullfrog Tadpoles (Lithobates catesbeianus). Archives of environmental contamination and toxicology, 1-15. - Gholami-Seyedkolaei, S. J., Mirvaghefi, A., Farahmand, H., & Kosari, A. A. (2013). Effect of a glyphosate-based herbicide				

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
in< i> Cyprinus carpio:</i> Assessment of acetylcholinesterase activity, hematological responses and serum biochemical parameters. Ecotoxicology and environmental safety, 98, 135-141. - Yadav, S. S., Giri, S., Singha, U., Boro, F., & Giri, A. (2013). Toxic and genotoxic effects of Roundup on tadpoles of the Indian skittering frog (< i> Euflictis cyanophlyctis</i>) in the presence and absence of predator stress. Aquatic Toxicology, 132, 1-8. - Janssens, L., & Stoks, R. (2013). Synergistic effects between pesticide stress and predator cues: Conflicting results from life history and physiology in the damselfly< i> Enallagma cyathigerum</i>. Aquatic Toxicology, 132, 92-99. - De Souza Filho, J., Sousa, C. C. N., Da Silva, C.				

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
C., De Sabóia-Morais, S. M. T., & Grisolia, C. K. (2013). Mutagenicity and Genotoxicity in Gill Erythrocyte Cells of Poecilia reticulata Exposed to a Glyphosate Formulation. Bulletin of environmental contamination and toxicology, 91(5), 583-587. - Güngördü, A. (2013). Comparative toxicity of methidathion and glyphosate on early life stages of three amphibian species:< i> Pelophylax ridibundus</i>,< i> Pseudepidalea viridis</i>, and< i> Xenopus laevis</i>. Aquatic Toxicology. - Lanctôt, C., Robertson, C., Navarro-Martín, L., Edge, C., Melvin, S. D., Houlahan, J., & Trudeau, V. L. (2013). Effects of the glyphosate-based herbicide Roundup WeatherMax® on metamorphosis of wood frogs (< i> Lithobates sylvaticus</i>) in natural wetlands. Aquatic Toxicology.				

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- Wagner, N., Reichenbecher, W., Teichmann, H., Tappeser, B., & Lötters, S. (2013) Questions concerning the potential impact of glyphosate-based herbicides on amphibians. Environmental Toxicology and Chemistry. - Kumar, A., Jahavar Ali, A. (2013) Toxic impacts of two organophosphorus pesticides on the acetylcholinesterase activity and biochemical composition of freshwater fairy shrimp streptocephalus dichotomus. International Journal of Pharma and Bio Sciences, 4(2): 966 – 972. - Meza-Joya, F.L., Ramírez-Pinilla, M.P., Fuentes-Lorenzo, J.L. (2013) Toxic, cytotoxic, and genotoxic effects of a glyphosate formulation (roundup®SL–cosmoflux®411F) in the direct-developing frog eleutherodactylus johnstonei. Environmental and Molecular Mutagenesis, DOI:				

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10.1002/em.21775. t - Akinsorotan, A., Zelibe, S., & Olele, N. (2013) Acute Toxicity And Behavioural Changes On African Catfish (Clarias gariepinus) Exposed To Dizensate (Glyphosate Herbicide). International Journal of Scientific & Engineering Research 4(3). - de Castilhos Ghisi, N., & Cestari, M. M. (2012). Genotoxic effects of the herbicide Roundup® in the fish Corydoras paleatus (Jenyns 1842) after short-term, environmentally low concentration exposure. Environmental Monitoring and Assessment, 185(4): 3201-3207. - Lajmanovich, R. C., Junges, C. M., Attademo, A. M., Peltzer, P. M., Cabagna-Zenklusen, M. C., & Basso, A. (2013). Individual and Mixture Toxicity of Commercial Formulations Containing Glyphosate, Metsulfuron-				

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
Methyl, Bispyribac-Sodium, and Picloram on Rhinella arenarum Tadpoles. Water, Air, & Soil Pollution, 224(3), 1-13. - Vera-Candioti, J., Soloneski, S., Larramendy, M.L. (2013) Evaluation of the genotoxic and cytotoxic effects of glyphosate-based herbicides in the ten spotted live-bearer fish Cnesterodon decemmaculatus (Jenyns, 1842). Ecotoxicology and environmental safety, 89(1): 166–173. - Yadav, S.S., Giri, S., Singha, U., Boro, F., Giri, A. (2013) Toxic and genotoxic effects of Roundup on tadpoles of the Indian skittering frog (Euflictis cyanophlyctis) in the presence and absence of predator stress. Aquatic Toxicology, 132–133: 1–8. - Guilherme, S., Santos, M.A., Barroso, C., Gaivão, I., Pacheco, M. (2012) Differential genotoxicity of				

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
Roundup® formulation and its constituents in blood cells of fish (Anguilla anguilla): considerations on chemical interactions and DNA damaging mechanisms. Ecotoxicology, 21(5): 1381-1390. - Hued, A. C., Oberhofer, S., de los Ángeles Bistoni, M. (2012) Exposure to a Commercial Glyphosate Formulation (Roundup®) Alters Normal Gill and Liver Histology and Affects Male Sexual Activity of Jenynsia multidentata (Anablepidae, Cyprinodontiformes). Archives of environmental contamination and toxicology, 62(1): 107-117. - Moore LJ, Fuentes L, Rodgers JH Jr, Bowerman WW, Yarrow GK, Chao WY, Bridges WC Jr. (2012) Relative toxicity of the components of the original formulation of Roundup to five North American anurans. Ecotoxicol Environ Saf;78:				

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
128-33. - Relyea, R.A. (2012) New effects of Roundup on amphibians: Predators reduce herbicide mortality; herbicides induce antipredator morphology. Ecological Applications, 22(2), 634-647. - Guilherme, S., Santos, M. A., Gaivão, I., & Pacheco, M. (2014). DNA and chromosomal damage induced in fish (Anguilla anguilla L.) by aminomethylphosphonic acid (AMPA)—the major environmental breakdown product of glyphosate. Environmental Science and Pollution Research, 1-10. - Armiliato, N., Ammar, D., Nezzi, L., Straliotto, M., Muller, Y. M., & Nazari, E. M. (2014). Changes in Ultrastructure and Expression of Steroidogenic Factor-1 in Ovaries of Zebrafish Danio rerio Exposed to Glyphosate. Journal of Toxicology and Environmental Health, Part A,				

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
77(7), 405-414. - Lajmanovich, R. C., Junges, C. M., Attademo, A. M., Peltzer, P. M., Cabagna-Zenklusen, M. C., & Basso, A. (2013). Individual and mixture toxicity of commercial formulations containing glyphosate, metsulfuron-methyl, bispyribac-sodium, and picloram on Rhinella arenarum tadpoles. Water, Air, & Soil Pollution, 224(3), 1-13. - Glusczak, L., Loro, V.L., Pretto, A., Moraes, B.S., Raabe, A., Duarte, M.F., de Sousa Valladão, D.M. (2011) Acute exposure to glyphosate herbicide affects oxidative parameters in Piava (*Leporinus obtusidens*). Archives of environmental contamination and toxicology, 61(4): 624-630 (PENDING ON THE OPEN POINT BELOW). See reporting table public consultation 5(4)				
Open point 5.15 RMS to clarify if the following	RMS: Addressed. The study is considered in the	Not applicable.	RMS: Not applicable.	Addressed.

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
study was considered in the systematic literature search alredy available in the dossier: -Glusczak, L., Loro, V.L., Pretto, A., Moraes, B.S., Raabe, A., Duarte, M.F., de Sousa Valladão, D.M. (2011) Acute exposure to glyphosate herbicide affects oxidative parameters in Piava (*Leporinus obtusidens*). Archives of environmental contamination and toxicology, 61(4): 624-630. See also 5(3) See reporting table public consultation 5(4)	revised Appendix and the following Environmental Relevance was concluded: Based on modelling assumptions, the concentrations expected in surface waters exposed to drift lie around 0.1 mg a.i./L. Test was conducted with a unknown commercial formulation exceeding the expected drift values . Nevertheless, the testing showed that high concentrations of glyphosate-based herbicides can cause changes in oxidative stress parameters in Piava.			
Data requirement 5.8 Applicant tot submit the following study for procedural reasons: Relyea RA. 2009. A cocktail of contaminants: how mixtures of pesticides at low concentrations affect aquatic communities. *Oecologia* **159**, 363-376.	RMS: Addressed. The study was submitted and is considered in the revised Appendix.	Not applicable.	RMS: Not applicable.	Addressed.

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
See also 5(3) See reporting table public consultation 5(5)				
Open point 5.16 RMS to provide in an addendum a new detailed summary of the conclusions regarding endocrine disruption potential of the active ingredient glyphosate based on the data available alredy with the dossier. See tox… See reporting table public consultation 5(6)	RMS: Addressed. RMS provided a chapter (B9.12) on the endocrine disruption potential of the active ingredient glyphosate based on the data available already with the dossier.	Not applicable.	RMS: Not applicable.	Open point closed. The issue was addressed in the revised RAR.
Data requirement 5.9 Applicant to liase with the RMS and to submit the studies under consideration by the RMS for procedural reasons. A new systematic literature search would be appreciated **Note**: for the risk assessment to microorganisms, the	RMS: Addressed. The studies were submitted and are considered in the revised Appendix.	Not applicable.	RMS: Not applicable.	Addressed. The new study on N-transformation was submitted and evaluated in the revised RAR.

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
nitrogen transformation and carbon mineralisation was considered, according to the current requirements. A data requirement was set for a valid N-transformation study in the other reporting table point 5(58) See reporting table public consultation 5(7)				
Data requirement 5.10 Applicant to submit the following study for procedural season: - Mesnage et al. 2013 See reporting table public consultation 5(13)	RMS. Addressed. The study is submitted and is considered in the revised Appendix.	Not applicable.	RMS: Not applicable.	Addressed. The study is mentioned in the RAR.
Open point 5.17 RMS to amend the classification of the active substance in the LoEP (the classification of the formulated products is not considered in the LoEP).	RMS: Addressed. The following classification and labelling is proposed : Chronic 2, H411, GHS09; P273; P391, P501.	Not applicable.	RMS: Not applicable.	Open point closed. The classification of the active substance was amended. The classification of the formulated products was deleted.

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
See reporting table public consultation 5(16)				

PEER REVIEW REPORT ON **GLYPHOSATE** OCTOBER 2015

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00	Cover page
01	Comments on the assessment report and addendum 1
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06	Comments on the draft EFSA conclusion and updated EFSA conclusion

Report of Pesticides Peer Review written procedure on additional information

GLYPHOSATE

Rapporteur Member State: DE

Comments on the assessment report are listed in the relevant reporting table. Comments submitted during the written procedure on the points for clarification are listed in Appendix 1.

Documents submitted for written procedure:

Date	Supplier	File Name
14.07.2014	DE/EFSA	Glyphosate_reporting table_rev 0__2014-07-14.doc
July 2014	DE/EFSA	_Glyphosate reporting table_public consultation.doc
29.01.2015	DE	Glyphosate_evaluation table_AIR II_section 1_2015-01_29.doc
29.01.2015	DE	Glyphosate_evaluation table_AIR II_section 2_2015-01_29.doc
29.01.2015	DE	Glyphosate_evaluation table_AIR II_section 3_2015-01_29.doc
29.01.2015	DE	Glyphosate_evaluation table_AIR II_section_4_2015-01_29.doc
29.01.2015	DE	Glyphosate_evaluation table_AIR II_section_5_2015-01_29.doc
29.01.2015	DE	Glyphosate_RAR_12_LoEP_CA-CP_rev 2015-01_29.docx
14.07.2014	DE/EFSA	Glyphosate confidential reporting tables (zip-file)
29.01.2015	DE	Glyphosate_RAR_01_Volume1_2015-01_29.docx
29.01.2015	DE	Glyphosate_RAR_04_Volume3CA-CP_B-2_2015-01_29.doc
29.01.2015	DE	Glyphosate_RAR_05_Volume3CA-CP_B-3_2015_01-29.docx
29.01.2015	DE	Glyphosate_RAR_05_Volume3CA-CP_B-3_Appendix_2015-01-29.docx
29.01.2015	DE	Glyphosate_RAR_06_Volume3CA-CP_B-4_2015-01-29.docx
29.01.2015	DE	Glyphosate_RAR_07_Volume3CA-CP_B-5_2015-01-29.docx
29.01.2015	DE	Glyphosate_RAR_08_Volume3CA-CP_B-6_2015-01-29.doc
29.01.2015	DE	Glyphosate_RAR_09_Volume3CA-CP_B-7_2015-01-29.docx
10.02.2015	DE	Glyphosate_RAR_10_Volume3CA-CP_B-8_2015-02-10.docx
10.02.2015	DE	Glyphosate_RAR_10_Volume3CA-CP_B-8_Appendix_2015-02-10.docx
29.01.2015	DE	Glyphosate_RAR_11_Volume3CA-CP_B-9_2015-01-29.docx
29.01.2015	DE	Glyphosate_RAR_22_Volume4_Afrasa_2015-01-29.doc
29.01.2015	DE	Glyphosate_RAR_22_Volume4_Agria_2015-01-29.doc
29.01.2015	DE	Glyphosate_RAR_22_Volume4_Agrichem_2016-01-29.doc
29.01.2015	DE	Glyphosate_RAR_22_Volume4_Agro_2015-01-29.doc
29.01.2015	DE	Glyphosate_RAR_22_Volume4_Albaugh_2015-01-29.doc
29.01.2015	DE	Glyphosate_RAR_22_Volume4_Arysta_2015-01-29.doc
29.01.2015	DE	Glyphosate_RAR_22_Volume4_Barclay_2015-01-29.doc
29.01.2015	DE	Glyphosate_RAR_22_Volume4_Brokden_2015-01-29.doc
29.01.2015	DE	Glyphosate_RAR_22_Volume4_Bros_2015-01-29.doc

Date	Supplier	File Name
29.01.2015	DE	Glyphosate_RAR_22_Volume4_Cheminova_2015-01-29.doc
29.01.2015	DE	Glyphosate_RAR_22_Volume4_Dow_2015-01-29.doc
29.01.2015	DE	Glyphosate_RAR_22_Volume4_Excel_2015-01-29.doc
29.01.2015	DE	Glyphosate_RAR_22_Volume4_Feinchemie_2015-01-29.doc
29.01.2015	DE	Glyphosate_RAR_22_Volume4_General information_2015-01-29.docx
29.01.2015	DE	Glyphosate_RAR_22_Volume4_Helm_2015-01-29.doc
29.01.2015	DE	Glyphosate_RAR_22_Volume4_Monsanto_2015-01-29.doc
29.01.2015	DE	Glyphosate_RAR_22_Volume4_Nufarm_2015-01-29.doc
29.01.2015	DE	Glyphosate_RAR_22_Volume4_Rotam_2015-01-29.doc
29.01.2015	DE	Glyphosate_RAR_22_Volume4_Sabero_2015-01-29.doc
29.01.2015	DE	Glyphosate_RAR_22_Volume4_Sapec_2015-01-29.doc
29.01.2015	DE	Glyphosate_RAR_22_Volume4_SFP_2015-01-29.doc
29.01.2015	DE	Glyphosate_RAR_22_Volume4_Sinon_2015-01-29.doc
29.01.2015	DE	Glyphosate_RAR_22_Volume4_Syngenta_2015-01-29.doc
29.01.2015	DE	Glyphosate_RAR_22_Volume4_UPL_2015-01-29.doc
29.01.2015	DE	Glyphosate_RAR_22_Volume4_Wynca_2015-01-29.doc

Appendix 1: Discussion table written procedure: GLYPHOSATE

Appendix 1: Discussion Table Written Procedure, Glyphosate

1. Identity, Physical and chemical properties, Details of uses and further information, Methods of analysis

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
1	Data requirement 1.1 Applicant to submit data for the auto-flammability of the K salt See reporting table 1(9)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
2	Data requirement 1.2 Applicant to submit information concerning the oxidising properties of MON 52276 See reporting table 1(12)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
3	Data requirement 1.3 Applicant to submit a full comparison of the formulation compositions (MON 78043 and MON 78044 vs. MON 52276) See reporting table 1(17)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
4	Data requirement 1.4 Applicant to submit the persistent foam study result using the concentration corresponding to the highest rate of use See reporting table 1(20)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
5	Data requirement 1.5 Additional data to address the efficiency and precision of the derivatisation step of the methods using derivatisation. See reporting table 1(29)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
6	Data requirement 1.6 Applicant to submit the additional validation data for the analytical methods for glyphosate in matrices of animal origin. See reporting table 1(38)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
7	Data requirement 1.7 Applicant to submit a confirmatory method for *N*-acetyl-glyphosate in dry	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	plant materials and those with high water and high fat content and a confirmatory method for *N*-acetyl-glyphosate in all kinds of animal matrices. See also comment 3(18) See reporting table 1(48)		
8	Data requirement 1.8 According to Art. 10(3) of Reg. (EU) No 1141/2010 the supplementary complete dossiers shall contain the full text of each test and study report, as a consequence all the studies that are not part of the dossier for renewal (highlighted in yellow) and were evaluated in the RAR should be submitted to the COM, MSs and EFSA for transparency reasons and to have access to the raw data evaluated. See reporting table 1(53)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
9	Data requirement 1.9 Spectra of relevant	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	impurities. The data requirement has already been identified in the RAR See reporting table 1(54)		
10	Data requirement 1.10 A confirmatory method for glyphosate in animal fat and kidney/liver. Relevant, basic data set for all active substances! The data requirement has already been identified in the RAR See reporting table 1(55)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
11	Data requirement 1.11 Applicant GTF to submit additional data/information to allow to judge whether the impurities are of toxicological relevance or not and to provide data/information demonstrating that the materials used in toxicological studies are representative for the	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	proposed specification. See general confidential reporting table 1(2)		
12	Data requirement 1.12 Applicant Industrias Afrasa to submit the reports : Reverse Mutation Assay using Bacteria (Salmonella typhirium) with Glyphosate (BSL Bioservice Report nr 126159) and Glyphosate: Tier 2: Evaluation of toxicological Properties of Impurities; GABConsulting GmbH, Report nr 616141-A2-0501-01 by Eurotox registred Toxicologist to be evaluated in an addendum. See also comment 1(6) See Afrasa confidential reporting table 1(4)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
13	Data requirement 1.13 Applicant AGRIA to submit data/information concerning the assessment of toxicological relevance of	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	the impurities and data/information demonstrating that the material used in toxicological studies is representative for the proposed specification. See Agria confidential reporting table 1(4)		
14	Data requirement 1.14 Applicant Agrichem to submit data/information concerning the assessment of toxicological relevance of the impurities and data/information demonstrating that the material used in toxicological studies is representative for the proposed specification. See Agrichem confidential reporting table 1(3)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
15	Data requirement 1.15 Applicant Agrotrade to submit data/information concerning the assessment of toxicological relevance of	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	the impurities and data/information demonstrating that the material used in toxicological studies is representative for the proposed specification. See Agrotrade confidential reporting table 1(3)		
16	Data requirement 1.16 Applicant Albaugh to submit data/information concerning the assessment of toxicological relevance of the impurities and data/information demonstrating that the material used in toxicological studies is representative for the proposed specification. See Albaugh confidential reporting table 1(5)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
17	Data requirement 1.17 Applicant Arysta to submit data/information concerning the assessment of toxicological relevance of	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	the impurities and data/information demonstrating that the material used in toxicological studies is representative for the proposed specification. See Arysta confidential reporting table 1(6)		
18	Data requirement 1.18 Applicant Arysta to provide additional validation data for the determination of the impurity 2. See Arysta confidential reporting table 1(14)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
19	Data requirement 1.19 Applicant Arysta to provide the fortification levels for the determination of the accuracy data for the determination of the impurity 21. See Arysta confidential reporting table 1(15)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
20	Data requirement 1.20 Applicant Barclay to submit the manufacturing dates for both sources to be included in a revised RAR See Barclay confidential reporting table 1(4)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
21	Data requirement 1.21 Applicant Barclay to submit data/information concerning the assessment of toxicological relevance of the impurities and data/information demonstrating that the material used in toxicological studies is representative for the proposed specification See Barclay confidential reporting table 1(9)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
22	Data requirement 1.22 Applicant Barclay to submit representative chromatograms for the determination of the	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	impurity 21, to be evaluated in a revised Vol.4 See Barclay confidential reporting table 1(16)		
23	Data requirement 1.23 Applicant Brokden to submit data/information concerning the assessment of toxicological relevance of the impurities and data/information demonstrating that the material used in toxicological studies is representative for the proposed specification. See Brokden confidential reporting table 1(7)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
24	Data requirement 1.24 Applicant Bross to submit additional data/information regarding the validation of the analytical methods used for the quantification of the significant impurities. See also comments 1(7),	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	1(8), 1(9), 1(10) See Bros S.J. confidential reporting table 1(2)		
25	Data requirement 1.25 Applicant Bross to submit an updated technical specification. See Bros S.J. confidential reporting table 1(4)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
26	Data requirement 1.26 Applicant Bros to submit data/information concerning the assessment of toxicological relevance of the impurities and data/information demonstrating that the material used in toxicological studies is representative for the proposed specification See Bros S.J. confidential reporting table 1(5)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
27	Data requirement 1.27 Applicant Bros to submit for	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	the impurity 15 additional information and results of study on algae addressing the representativeness of the specification. See Bros S.J. confidential reporting table 1(6)		
28	Data requirement 1.28 Applicant Cheminova to submit the missing manufacturing dates of the batches. See Cheminova confidential reporting table 1(4)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
29	Data requirement 1.29 Applicant Cheminova to submit data/information concerning the assessment of toxicological relevance of the impurities and data/information demonstrating that the material used in toxicological studies is representative for the proposed specification	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	See Cheminova confidential reporting table 1(6)		
30	Data requirement 1.30 Applicant Dow to submit the new study in relation to the comment concerning impurity 20. See DOW Agrosciences confidential reporting table 1(4)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
31	Data requirement 1.31 Applicant Dow to submit data/information concerning the assessment of toxicological relevance of the impurities and data/information demonstrating that the material used in toxicological studies is representative for the proposed specification. See DOW Agrosciences confidential reporting table 1(5)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
32	Data requirement 1.32	AT: not considered	Noted. for the conclusion, please refer to the evaluation table.

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	Applicant Dow to submit an official document, confirming that the respective sources are no longer supported. See also open point in comment 1(5) See DOW Agrosciences confidential reporting table 1(6)	NL: not reviewed	
33	Data requirement 1.33 Applicant Excel to submit the new GLP 5 batch data. See Excel confidential reporting table 1(1)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
34	Data requirement 1.34 Applicant Excel to submit data/information concerning the assessment of toxicological relevance of the impurities and data/information demonstrating that the material used in toxicological studies is representative for the	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	proposed specification. See Excel confidential reporting table 1(6)		
35	Data requirement 1.35 Applicant Excel to submit additional validation data concerning the method for NNG See Excel confidential reporting table 1(7)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
36	Data requirement 1.36 Applicant Feinchemie to submit data/information concerning the assessment of toxicological relevance of the impurities and data/information demonstrating that the material used in toxicological studies is representative for the proposed specification. See Feinchemie confidential reporting table 1(5)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
37	Data requirement 1.37	AT: not considered	Noted. for the conclusion, please refer to the evaluation table.

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	Applicant Helm to provide new specification for impurity 3. See also open point 1(1) in the RT for Vol.4 general information See Helm AG confidential reporting table 1(2)	NL: not reviewed	
38	Data requirement 1.38 Applicant Helm to provide new specification for impurity 1. See also open point 1(1) in the RT for Vol.4 general information See Helm AG confidential reporting table 1(3)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
39	Data requirement 1.39 Applicant Helm to provide new specification for impurity 4. See also open point 1(1) in the RT for Vol.4 general information See Helm AG confidential reporting table 1(4)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
40	Data requirement 1.40 Applicant Helm to submit data/information concerning the assessment of toxicological relevance of the impurities and data/information demonstrating that the material used in toxicological studies is representative for the proposed specification. See Helm AG confidential reporting table 1(5)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
41	Data requirement 1.41 Applicant Helm to submit study on algae according to OECD 201 for Impurity 17. See Helm AG confidential reporting table 1(9)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
42	Data requirement 1.42 Applicant Helm to submit additional validation data for the determination of the impurity 21 (source 3)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	See Helm AG confidential reporting table 1(11)		
43	Data requirement 1.43 Applicant Helm to submit additional validation data for the determination of the impurity 1 (source 4) See also comment 1(14) See Helm AG confidential reporting table 1(12)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
44	Data requirement 1.44 Applicant Helm to submit additional validation data for the method for determination of impurities 1, 3, 5 and 9 found in the 5-batch. See Helm AG confidential reporting table 1(13)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
45	Data requirement 1.45 Applicant Helm to submit additional validation data for the method for determination of impurity 21.	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	See Helm AG confidential reporting table 1(15)		
46	Data requirement 1.46 Applicant Helm to submit additional validation data for the method for determination of impurity 23. See Helm AG confidential reporting table 1(16)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
47	Data requirement 1.47 Applicant Helm to submit additional validation data for the method for determination of impurity 20. See Helm AG confidential reporting table 1(17)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
48	Data requirement 1.48 Applicant Helm to submit additional data about the NNG content of of batch '20090506' See Helm AG confidential	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	reporting table 1(20)		
49	Data requirement 1.49 Applicant Monsanto to provide an updated technical specification based on batch data or QC data supporting the proposed limits for impurities. See Monsanto confidential reporting table 1(9)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
50	Data requirement 1.50 Applicant Monsanto to submit the analytical method PC-ME-0765 See Monsanto confidential reporting table 1(14)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
51	Data requirement 1.51 Applicant Monsanto to submit the report Wratten et al (2013) See Monsanto confidential reporting table 1(15)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
52	Data requirement 1.52	AT: not considered	Noted. for the conclusion, please refer to the evaluation table.

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	Applicant Monsanto to provide data/information demonstrating that the material used in toxicological studies is representative for the proposed specification. See Monsanto confidential reporting table 1(16)	NL: not reviewed	
53	Data requirement 1.53 Applicant Monsanto to submit information detailing with confirmatory methods available for all impurities See Monsanto confidential reporting table 1(19)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
54	Data requirement 1.54 Applicant Monsanto to submit revised evaluation of the precision of method [redacted] with respect to the impurity 1 See Monsanto confidential reporting table 1(20)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
55	Data requirement 1.55	AT: not considered	Noted. for the conclusion, please refer to the evaluation table.

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	Applicant Monsanto to submit MSDSs which are in line with the requirements for REACH for the [redacted] See Monsanto confidential reporting table 1(21)	NL: not reviewed	
56	Data requirement 1.56 Applicant Monsanto to clarify the units the values for *N*-nitroso glyphosate are expressed in Table C.1.5. See Monsanto confidential reporting table 1(22)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
57	Data requirement 1.57 Applicant Nufarm to submit additional data/information concerning the assessment of toxicological relevance of the impurities and data/information demonstrating that the material used in toxicological studies is representative for the proposed specification	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	See Nufarm confidential reporting table 1(3)		
58	Data requirement 1.58 Applicant Rotam to submit data/information concerning the assessment of toxicological relevance of the impurities and data/information demonstrating that the material used in toxicological studies is representative for the proposed specification See Rotam confidential reporting table 1(3)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
59	Data requirement 1.59 Applicant Sbaro to provide an updated technical specification removing the non significant impurities. See also comment 1(1) See Sabero confidential reporting table 1(2)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
60	Data requirement 1.60 Applicant Sabero to submit data/information concerning the assessment of toxicological relevance of the impurities and data/information demonstrating that the material used in toxicological studies is representative for the proposed specification. See Sabero confidential reporting table 1(5)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
61	Data requirement 1.61 Applicant Sabero to submit validation data for the determination of impurities 1 and 9. See Sabero confidential reporting table 1(7)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
62	Data requirement 1.62 Applicant Sabero to submit validation data for the determination of impurity 2.	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	See Sabero confidential reporting table 1(8)		
63	Data requirement 1.63 Applicant Sabero to submit validation data for the determination of impurity 21. See Sabero confidential reporting table 1(9)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
64	Data requirement 1.64 Applicant Sabero to submit more specific data for the determination of impurity 23. See Sabero confidential reporting table 1(10)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
65	Data requirement 1.65 Applicant Sabero to submit additional data for the determination of [redacted] See Sabero confidential reporting table 1(11)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
66	Data requirement 1.66	AT: not considered	Noted. for the conclusion, please refer to the evaluation table.

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	Applicant SAPEC to submit data/information concerning the assessment of toxicological relevance of the impurities and data/information demonstrating that the material used in toxicological studies is representative for the proposed specification. See SAPEC confidential reporting table 1(9)	NL: not reviewed	
67	Data requirement 1.67 Applicant SFP to submit data/information demonstrating that the material used in toxicological studies is representative for the proposed specification See SPF confidential reporting table 1(2)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
68	Data requirement 1.68 Applicant SFP to submit report 14-919044-006	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	See SPF confidential reporting table 1(6)		
69	Data requirement 1.69 Applicant Sinon to provide an updated technical specification based on batch data or QC data to support the specification See Sinon confidential reporting table 1(3)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
70	Data requirement 1.70 Applicant Sinon to provide manufacturing dates of the batches See Sinon confidential reporting table 1(4)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
71	Data requirement 1.71 Applicant Sinon to submit data/information concerning the assessment of toxicological relevance of the impurities and data/information demonstrating that the material used in	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	toxicological studies is representative for the proposed specification. See Sinon confidential reporting table 1(6)		
72	Data requirement 1.72 Applicant Sinon to provide additional validation data for the determination of the impurity 1 See Sinon confidential reporting table 1(7)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
73	Data requirement 1.73 Applicant Sinon to provide additional validation data for the determination of the impurities of the technical material See Sinon confidential reporting table 1(8)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
74	Data requirement 1.74 Applicant Syngenta to submit the assessment of the relevance/non-relevance of impurities on behalf of	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	the Task Force. See Syngenta confidential reporting table 1(11)		
75	Data requirement 1.75 Applicant Syngenta to provide further information concerning impurity 3. See Syngenta confidential reporting table 1(14)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
76	Data requirement 1.76 Applicant Syngenta to provide additional genotoxicity data to support [redacted] at the level in the proposed specification. See Syngenta confidential reporting table 1(15)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
77	Data requirement 1.77 Applicant Syngenta to submit further information related to [redacted] addressing the ecotoxicological representativeness of the specification.	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	See Syngenta confidential reporting table 1(20)		
78	Data requirement 1.78 Applicant Syngenta to submit further five batch analysis to substantiate the claim for removal of impurity 14 (Syngenta reference: ASF71_10125) See Syngenta confidential reporting table 1(24)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
79	Data requirement 1.79 Applicant Syngenta to submit clarification on the concentration levels in mg/mL used for the linearity test of the impurities impurity 6, impurity 10 and impurity 14. See Syngenta confidential reporting table 1(26)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
80	Data requirement 1.80 Applicant United Phosphorous to submit data/information concerning	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	the assessment of toxicological relevance of the impurities and data/information demonstrating that the material used in toxicological studies is representative for the proposed specification See United Phosphorous confidential reporting table 1(1)		
81	Data requirement 1.81 Applicant United Phosphorous to provide additional information on the determination of identity of each impurity. See United Phosphorous confidential reporting table 1(3)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
82	Data requirement 1.82 Applicant United Phosphorous to provide additional validation data for the method for the determination of NNG See also comment 1(5)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	See United Phosphorous confidential reporting table 1(4)		
83	Data requirement 1.83 Applicant Wynca to submit data/information concerning the assessment of toxicological relevance of the impurities and data/information demonstrating that the material used in toxicological studies is representative for the proposed specification See Wynca confidential reporting table 1(4)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.

2. Mammalian toxicology

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
1	Data requirement 2.1 Applicant to submit the	AT: Generic comment. For this AI, a large number of studies of varying scientific validity are available. Non-systematic, arbitratry assessment of selected publications is considered time consuming and will not result in a comprehensive overview of the available data on this substance.	Noted. for the conclusion, please refer to the evaluation table.

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	study by Mesnage R, Defarge N, Spiroux de Vendômois J, Séralini G-E. Major pesticides are more toxic to human cells than their declared active principles. Biomedical Research International, 2014. See reporting table 2(14)	NL: not reviewed	
2	Data requirement 2.2 Applicant to submit the study by Malhotra RC, Ghia DK, Cordato DJ, Beran RG. Glyphosate surfactant herbicide-induced reversible encephalopathy. *J Clin Neurosci* 2010; **17:** 1472–73. See reporting table 2(48)	AT: - NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
3	Data requirement 2.3 Applicant to submit the study by reference Samsel et Seneff « Glyphosate's Suppression of Cytochrome P450 Enzyme and amino acid biosynthesis by the gut microbiome : Pathways to	AT: - NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	modern diseases » *Entropy* **2013**, *15*, 1416-1463. See reporting table 2(55)		
4	Data requirement 2.4 Applicant to submit *Mink et al, Regulat Toxicol Pharmacol, 63, 440-452, 2012* See reporting table 2(56)	AT: - NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
5	Data requirement 2.5 Applicants to demonstrate the compliance of the batches tested in the mammalian toxicology data package with the proposed specifications. See reporting table 2(92)	AT: According to the RMS evaluation in part C, the detailed composition of the tested material is available only for a small fraction of the toxicological studies. In addition to that, not a single tested material contained all impurities Thus, it is considered impossible to conclude that a theoretical 'worst case' material containing critical impurities at the maximum specified levels would be covered by the toxicological testing performed. We support limiting the [redacted] and Impurity 20, N-Nitroso-Glyphosate) to below 1 mg/kg as suggested in (SANCO/10597/2003 –rev. 10.1). It is unclear whether the sum of both impurities should be below 1 mg/kg? We support with setting the threshold for formaldehyde (Impurity 21) to below 1g/kg.	Data gaps: The new proposed reference specification as proposed by the RMS (2014) is supported by the toxicological studies; eight out of the 24 applicants presented specifications that were not supported by the toxicological assessment (Afrasa, Arysta, Bros, Dow, three out of seven sources of Helm, Monsanto, SPF and one of the two Syngenta manufacturing routes) which is a critical area of concern for the respective applicants/sources. Two relevant impurities were identified, formaldehyde due to its harmonised classification in accordance with the provisions of Regulation (EC) No. 1272/2008 - CLP Regulation as Toxic, Carc 1B and Muta 2 and N-nitro-glyphosate (belonging to a group of

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
			impurities of particular concern as they can be activated to genotoxic carcinogens); at the specified levels these impurities are not of concern. [redacted] has been deleted from the specification (see section 1). Data gaps: All applicants to address the relevance of their respective impurities (except the known relevant ones), in particular impurities that elicited toxicological alerts according to QSAR assessments and the ones specified at higher level than the reference specification.
6	Data requirement 2.6 In the carcinogenicity studies in mice by [redacted] (1997, ASB2012-11493, notifier: Arysta) and by [redacted] (2009, ASB2012-11492, notifier: Nufarm), a certain increase in the incidence of malignant lymphoma in high dose males (6/50 as compared to 2/50 in the control in the first and 5/51 vs. 0/51 in the second study) was noted. The differences did not gain statistical significance. However, for more reliable	AT: Historical control data have been provided, the tumor incidence in male animals at the highest dose group of 40000ppm is within the range o the historical control data provided. NL: not reviewed	Addressed: Available HCD have been provided by the RMS and considered during the expert meeting under expert consultation 2.5.

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	assessment, historical control data from the performing laboratories should be provided. The data requirement has already been identifies in the RAR. See reporting table 2(94)		
7	Data requirement 2.7 Applicant to submit the memorandum of February 4, 2014 that has been made available to the Danish Ministry of Food, Agriculture and Fisheries (http://dca.au.dk/fileadmin/DJF/Notat_gmofoder__uk_version_Memorandum_on_The_feeding_of_genetically_modified_glyphosate_resistant_soy_products_to_livestock.pdf). See reporting table public consultation 2(3)	AT: No comment NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
8	Data requirement 2.8	AT: No comment	Noted. for the conclusion, please refer to the evaluation table.

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	Applicant to submit the relevant articles as cited in column 2 of the reporting table: Larsen, K., Najle, R., Lifschitz, A., Virkel, G. (2012). Effects of sub-lethal exposure of rats to the herbicide glyphosate in drinking water: Glutathione transferase enzyme activities, levels of reduced glutathione and lipid peroxidation in liver, kidneys and small intestine. Environmental Toxicology and Pharmacology, 34(3): 811–818. Mañas, F., Peralta, L., Ugnia, L., Weyers, A., García Ovando, H., & Gorla, N. (2013). Oxidative stress and comet assay in tissues of mice administered glyphosate and ampa in drinking water for 14 days. BAG. Journal of basic and applied genetics, 24(2), 67-75. Tizhe, E. V., Ibrahim, N. D. G., Fatihu, M. Y., Igbokwe, I. O., George, B. D. J., Ambali, S. F., &	NL: not reviewed	

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	Shallangwaa, J. M. (2013a). Haematogical changes induced by subchronic glyphosate exposure: ameliorative effect of zinc in Wistar rats. Sokoto Journal of Veterinary Sciences, 11(2), 28-35. Tizhe, E. V., Ibrahim, N. D. G., Fatihu, M. Y., Igbokwe, I. O., George, B. D. J., Ambali, S. F., & Shallangwa, J. M. (2013b) Serum biochemical assessment of hepatic and renal functions of rats during oral exposure to glyphosate with zinc. Comparative Clinical Pathology, 1-8. Tizhe, E. V., Ibrahim, N. D. G., Fatihu, M. Y., Onyebuchi, I. I., George, B. D. J., Ambali, S. F., & Shallangwa, J. M. (2013c). Influence of zinc supplementation on histopathological changes in the stomach, liver, kidney, brain, pancreas and spleen during subchronic exposure of Wistar rats to glyphosate. Comparative Clinical Pathology, 1-9.		

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	See reporting table public consultation 2(6)		
9	Data requirement 2.9 Applicant to provide studies mentioned in the comment by PAN under 2(13) only if they were not taken into account in the assessment made by the RMS: Grisolia, 2002, Sivikova, 2006, Belle, 2007, Cavas, 2007, Cavalcante, 2008, Guilherme, 2009, Poletta, 2009, Monroy, 2005. See reporting table public consultation 2(13)	AT: No comment NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
10	Data requirement 2.10 Applicant to submit all the relevant articles cited in column 2 of the reporting table: Alvarez-Moya, C., Reynoso Silva, M., Valdez Ramírez, C., Gómez Gallardo, D., León Sánchez, R., Canales Aguirre, A., & Feria Velasco, A. (2014) Comparison of the	AT: - NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	in vivo and in vitro genotoxicity of glyphosate isopropylamine salt in three different organisms. Genetics and Molecular Biology, 37(1), 105-110. Chaufan, G., Coalova, I., & de Molina, M. D. C. R. (2014). Glyphosate Commercial Formulation Causes Cytotoxicity, Oxidative Effects, and Apoptosis on Human Cells Differences With its Active Ingredient. International journal of toxicology, 1091581813517906 De Souza Filho, J., Sousa, C. C. N., Da Silva, C. C., De Sabóia-Morais, S. M. T., & Grisolia, C. K. (2013). Mutagenicity and Genotoxicity in Gill Erythrocyte Cells of Poecilia reticulata Exposed to a Glyphosate Formulation. Bulletin of environmental contamination and toxicology, 91(5), 583-587. George, J., & Shukla, Y. (2013) Emptying of Intracellular Calcium Pool and Oxidative Stress		

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	Imbalance Are Associated with the Glyphosate-Induced Proliferation in Human Skin Keratinocytes HaCaT Cells. ISRN dermatology, 2013. Guilherme, S., Santos, M.A., Barroso, C., Gaivão, I., Pacheco, M. (2012) Differential genotoxicity of Roundup® formulation and its constituents in blood cells of fish (Anguilla anguilla): considerations on chemical interactions and DNA damaging mechanisms. Ecotoxicology, 21(5): 1381-1390 Heu, C., Berquand, A., Elie-Caille, C., Nicod, L. (2012a) Glyphosate-induced stiffening of HaCaT keratinocytes, a Peak Force Tapping study on living cells. Journal of Structural Biology, 178(1): 1- 7. Heu, C., Elie-Caillea, C., Mougeyc, V., Launayd, S., Nicod, L. (2012b) A step further toward glyphosate-induced epidermal cell death: Involvement of mitochondrial and oxidative		

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	mechanisms. Environmental Toxicology and Pharmacology, 34(2): 144–153. Koller, V.J., Fürhacker, M., Nersesyan, A., Mišík, M., Eisenbauer, M., Knasmueller, S. (2012) Cytotoxic and DNA-damaging properties of glyphosate and Roundup in human-derived buccal epithelial cells. Archives of Toxicology, doi 10.1007/s00204-012-0804-8. Moreno, N. C., Sofia, S. H., & Martinez, C. B. (2014). Genotoxic effects of the herbicide Roundup Transorb< sup>®</sup> and its active ingredient glyphosate on the fish< i> Prochilodus lineatus</i>. Environmental toxicology and pharmacology, 37(1), 448-454. See reporting table public consultation 2(18)		

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
11	Data requirement 2.11 Applicant to submit all the relevant articles published after the date of submission, including the ones mentioned in the comment. Benachour N, Séralini GE. Chem Res Toxicol. 2009 Jan;22(1):97-105. Alvarez-Moya et al. 2014 Genet & Molec Biol:37:105-110. See reporting table public consultation 2(20)	AT: No comment NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
12	Data requirement 2.12 Applicant to submit the articles mentioned, if not already included in the dossier: Vandenberg et al. 2012 Lamb J.C., Boffetta P., Foster W.G., Goodman J.E., Hentz K.L., Rhomberg L.R., Staveley J., Swaen G., Van Der Kraak G. and,Williams A.L. (2014) Critical Comments on the	AT: No comment NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	WHO-UNEP State of the Science of Endocrine Disrupting Chemicals –2012. Regul. Toxicol. Pharmacol. 69(1):22-40. Rhomberg L.R. and Goodman, J.E. (2012) Low-dose effects and nonmonotonic dose-responses of endocrine disrupting chemicals: Has the case been made? Regul. Toxicol. Pharmacol. 64: 130-133. Borgert CJ, Baker SP, Matthews JC. (2013) Potency matters: Thresholds govern endocrine activity. Regul. Toxicol. Pharmacol. 67(1):83-8 See reporting table public consultation 2(22)		
13	Data requirement 2.13 Applicant to submit the articles mentioned in the comment: Schinasi, L., & Leon, M. E. (2014). Non-Hodgkin Lymphoma and	AT: No comment. NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	Occupational Exposure to Agricultural Pesticide Chemical Groups and Active Ingredients: A Systematic Review and Meta-Analysis. International journal of environmental research and public health, 11(4), 4449-4527. Kachuri, L., Demers, P. A., Blair, A., Spinelli, J. J., Pahwa, M., McLaughlin, J. R., ... & Harris, S. A. (2013) Multiple pesticide exposures and the risk of multiple myeloma in Canadian men. International Journal of Cancer Cocco, P., Satta, G., Dubois, S., Pili, C., Pilleri, M., Zucca, M., ... & Boffetta, P. (2013) Lymphoma risk and occupational exposure to pesticides: results of the Epilymph study. Occupational and environmental medicine, 70(2): 91-98. Thongprakaisang, S., Thiantanawat, A., Rangkadilok, N., Suriyo, T., & Satayavivad, J. (2013) Glyphosate induces human		

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	breast cancer cells growth via estrogen receptors. Food and Chemical Toxicology. See reporting table public consultation 2(31)		
14	Data requirement 2.14 Applicant to submit the articles mentioned in the comment, if not already included in the dossier: Hedberg D, Wallin M. Toxicol In Vitro. 2010 Apr;24(3):795-802. Chan P, Mahler J. Toxic Rep Ser. 1992 Jul;16:1-D3. De Roos et al. '05 Hardell et al. '02 See reporting table public consultation 2(32)	AT: No comment NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
15	Data requirement 2.15 Applicant to submit the Tier 1 screening assays under the US EPA Endocrine Disruptor Screening Program (EDSP). See reporting table public	AT: No comment NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	consultation 2(40)		
16	Data requirement 2.16 Applicant to submit the Tier 1 screening assays under the US EPA Endocrine Disruptor Screening Program (EDSP) and the studies mentioned in the comment: Walsh, 2002 Romano, 2010 Benachour, 2005 Gasnier, 2007 Hokanson, 2007 Mose, 2008 See reporting table public consultation 2(41)	AT: No comment NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
17	Data requirement 2.17 Applicant to submit the articles mentioned in the comment: Beuret et al (2005) Rao et al. (1990): J. Nutr. 120:602-609; Xia et al. (1995): J. Nutr. 125 195-201; Kim et al. (1996): Aging	AT: No comment NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	8:123-129 See reporting table public consultation 2(52)		
18	Data requirement 2.18 Applicant to submit the articles mentioned in the comment, if not already in the dossier: Howe et al 2004, Relyea et al 2012, Lanctot et al 2013. See reporting table public consultation 2(57)	AT: No comment NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
19	Data requirement 2.19 Applicant to submit the articles mentioned in the comment. Thongprakaisang, S., Thiantanawat, A., Rangkadilok, N., Suriyo, T., & Satayavivad, J. (2013) Glyphosate induces human breast cancer cells growth via estrogen receptors. Food and Chemical Toxicology. Astiz, M., Hurtado de Catalfo,	AT: No comment NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	G. E., García, M. N., Galletti, S. M., Errecalde, A. L., Alaniz, M. J. D., & Marra, C. A. (2013) Pesticide-induced decrease in rat testicular steroidogenesis is differentially prevented by lipoate and tocopherol. Ecotoxicology and environmental safety, 91: 129–138 Basrur, P. K., 2006. Disrupted sex differentiation and feminization of manand domestic animals. Environ. Res. 100, 18–38. Caglar, S., Kolankaya, D., 2008. The effect of sub-acute and sub-chronic exposure of rats to the glyphosate-based herbicide Roundup. Environ. Toxicol. Pharmacol. 25, 57–62. de Liz Oliveira Cavalli, V. L., Cattani, D., Elise Heinz Rieg, C., Pierozan, P., Zanatta, L., Benedetti Parisotto, E., ... & Zamoner, A. (2013) Roundup Disrupted Male Reproductive Functions By Triggering Calcium-Mediated Cell Death In Rat Testis And Sertoli Cells. Free Radical		

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	Biology and Medicine. Omran, N. E., & Salama, W. M. (2013). The endocrine disrupter effect of atrazine and glyphosate on Biomphalaria alexandrina snails. Toxicology and industrial health, 0748233713506959. See reporting table public consultation 2(58)		
20	Data requirement 2.20 Applicant to submit the articles mentioned in the comment: Cattani, D., de Liz Oliveira Cavalli, V. L., Heinz Rieg, C. E., Domingues, J. T., Dal-Cim, T., Tasca, C. I., ... & Zamoner, A. (2014). Mechanisms underlying the neurotoxicity induced by glyphosate-based herbicide in immature rat hippocampus: Involvement of glutamate excitotoxicity. Toxicology, 320, 34-45. El-Shenawy, N.S., 2009. Oxidative stress responses	AT: No comment NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	of rats exposed to Roundup and its active ingredient glyphosate. Environ. Toxicol. Pharmacol. 28, 379–385 See reporting table public consultation 2(61)		
21	Data requirement 2.21 Applicant to submit the articles mentioned in the comment: Riede et al., ASB2013-14684 Krüger et al. (2012) Shehata et al. (2013) See reporting table public consultation 2(62)	AT: No comment NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
22	Data requirement 2.22 Applicant to submit the articles mentioned in the comment: Thongprakaisang et al. 2013. Larsen K, Najle R, Lifschitz A, Virkel G. Environ Toxicol Pharmacol. 2012 Nov;34(3):811-8 Cavuşoğlu et al. '11	AT: No comment NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	See reporting table public consultation 2(64)		
23	Data requirement 2.23 GTF please submit all articles identified after 2011 as offered in your comment in column 3 "All articles identified after December 2011 will be available to EFSA upon request, along with summaries, relevance/reliability evaluations and critiques where appropriate". See reporting table public consultation 2(64)	AT: No comment NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
24	Data requirement 2.24 Applicant to submit the articles mentioned in the comment: Paganelli A, Gnazzo V, Acosta H, López SL, Carrasco AE. Chem Res Toxicol. 2010;23(10):1586-95. Antoniou et al. 2012 Marc J, et al. Toxicol Appl Pharmacol. 2005	AT: No comment NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	See reporting table public consultation 2(66)		
25	Data requirement 2.25 Applicant to submit the new articles and the report of the literature research. See reporting table public consultation 2(78)	AT: No comment NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.

3. Residues

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
1	Data requirement 3.1 A PHI should be provided to define the GAP for olive for oil production, based on the ground fallen fruits (since fruits fallen onto ground are directly exposed to the treatment spray). See reporting table 3(23)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
2	Data requirement 3.2 Four additional trials on ground-picked olives are requested to derive MRL for olives (oil production). A PHI should be proposed to support this uses (see data requirement 3(23)) See also comment 3(53) See reporting table 3(26)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.
3	Data requirement 3.3 Additional residue trials on rapeseed conducted according to the supported GAP are requested. Only 3 trials conducted according to the representative uses (2160 g/ha ± 25% tolerance) are available. As the use of the proportionality has not been yet agreed at EU level and since proportionality principle was generally excluded for herbicides by both OECD and CODEX, trials out of the 25% tolerance are not considered.	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	See reporting table 3(30)		
4	Data requirement 3.4 Metabolism in GAT-modified crops, metabolism in livestock animals with N-acetyl-glyphosate, hydrolysis stability of N-acetly-glyphosate and N-acetyl-AMPA. The data requirement has already been identified in the RAR. See reporting table 3(86)	AT: not considered NL: not reviewed	Noted. for the conclusion, please refer to the evaluation table.

4. Environmental fate and behaviour

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
1	Data requirement 4.1 Applicant to provide a document that sets out the different information available and discusses the pH dependency of	AT: No comment NL: No overall information from this document seems to have been included in the RAR (neither Volume 3 nor Volume 1). The embedded pdf document that was convincing to the RMS indeed cannot be read. Hence although the data requirement has been fulfilled formally we would like to see the outcome of the evaluation reflected in the RAR or LoEP	Data requirement fulfilled See RAR pp 5-13 for the pH dependency of biodegradation and mineralization. See RAR pp 184-187 for the pH dependency of the adsorption to soil.

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	biodegradation and adsorption of glyphosate and AMPA. In particular the document should discuss the apparent pH dependence of mineralisation and the likelihood of differential degradation route(s) depending on pH. Note the document cited in column 3 of the reporting table at comment 4(3) (pdf icon only present, but not the actual document), may be sufficient to address this request. See reporting table comment 4(3). See reporting table 4(3)	somewhere. It seems (from the text in column 3) there was an indication of pH dependent mineralisation however no remarks were made in the LoEP. It also seems that the apparent relation was due to CO2 solubility differences, but this did not explain the onbservations fully. Maybe it could be stated in the EFSA conclusion that based on argumentation provided by the applicant and evaluated by RMS during the review process it is shown that there was no apparent pH dependency for degradation or sorption?	
2	Data requirement 4.2 Applicant to submit final reports of the anaerobic soil incubation studies studies of McEwen (2004) and Knoch (2003). See reporting table 4(21)	AT: No comment NL: No comments. RMS states this has been addressed. The studies are evaluated in the RAR and included in the updated List of studies relied on (B8.10).	Data requirement fulfilled

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
3	Data requirement 4.3 Applicant to submit the studies of Esser (1996) and to provide a final report. See reporting table 4(23)	AT: No comment NL: RMS states this has been addressed. The Esser 1996 photolysis study is evaluated in the RAR and included in the updated List of studies relied on. Please note that there are various Esser 1996 studies discussed in the RAR which makes transparent reading of the List of references relied on difficult.	Data requirement fulfilled
4	Data requirement 4.4 Applicant to provide the final study report Heintze (1996). Note an evaluation of the study is already included in the RAR, Vol 3, B.8.4.4 and the RMS physically has the study. However the dossier should be updated with the study as all competent authorities may not have the study. The study is not available to EFSA. See reporting table 4(55)	AT: No comment NL: No comments. RMS states this has been addressed. For EFSA to check.	Data requirement fulfilled
5	Data requirement 4.5 Applicant to provide information on the possible runoff of glyphosate and consequent concentrations of glyphosate and AMPA in	AT: No comment NL: RMS and GTF seem to agree that the direct use on hardened surfaces is not within the scope of the substance review. This is also agreed by NL. These kind of applications should be assessed on a national level. This potential emission route cannot be properly addressed in a harmonised (zonal) way as no harmonised EU methodology is available.	Data gap: Applicants to further assess surface water and ground water exposure for uses on ‘all seeded or transplanted crops’ and ‘all seeded crops’ where indirect exposure to hard surfaces and

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	surface water, that might result when application occurs indirectly on hard man made surfaces, consequent to the representative uses of 'all seeded or transplanted crops' and 'all seeded crops' (first two rows of the GAP table). See reporting table 4(73)	In relation to this point of the reporting table NL would like to point out that there are many data on glyphosate/AMPA exceedance of drinking water criteria based on monitoring data, and plausible cause analysis has revealed that this is mainly due to the use on hardened surfaces [based on analysis of STP effluent in The Netherlands] - see many (annual) reports of the International Rhine Committee and/or RIWA-Rhine/Meuse (also reporting to Vewin which is the board of Dutch drinking water companies). The applicant could have submitted those data. Just as national background: To NL's opinion it is not certain or proven that only the *non*-professional (mis)use of glyphosate on pavements is responsible. Analysis on the Dutch monitoring data seem to indicate that (also in terms of absolute sales figures) that the professional use contributes most to the exceedance. This is why the Dutch authorisations for professional use on hardened surfaces have been restricted to a specific protocol in 2006. See also NL comment 4(69) which was addressed by RMS but only by including a very small summary (as sent by Ctgb but not explored further in-depth). The applicant could probably have had access to more national or European/ catchment level water quality reports.	subsequent run off to surface water and bank filtration to groundwater may occur.
6	Data requirement 4.6 Applicant to provide the public literature reference: Mercurio, P., Flores, F., Mueller, J. F., Carter, S., & Negri, A. P. (2014). Glyphosate persistence in seawater. Marine pollution bulletin.	AT: No comment NL: the RMS has addressed this in an addendum to the RAR. It was not included in the List of references relied on, but RMS evaluated the study in the update RAR at B.8.4.5.2 (page 348) (as less relevant). No comments.	Data requirement fulfilled Further to the considerations already provided by the RMS in the RT and the RAR it should be noted that the study confirms the persistence into the aquatic environment of glyphosate and AMPA already observed in the studies available in the dossier. Whole system DT50:

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	See reporting table public consultation 4(4)		Glyphosate: 13.82 d - > 301.20 d AMPA: 57.61 – 455.72 d The study referred is not applicable to the current risk assessment scheme for modelling fate and behaviour of glyphosate and AMPA in fresh water. From the triggering point of view may be considered supporting information. The values obtained are within the available data and confirm that glyphosate and AMPA should be considered persistent substances.
7	Data requirement 4.7 Applicant to provide the public literature references: http://onlinelibrary.wiley.com/doi/10.1002/ps.3724/full and if available " **Occurrence of glyphosate in a stormwater drain due to residential inputs"-** Ting Tang[1,2], Wesley Boënne1, Ann van Griensven[2,3], Piet Seuntjens[1,4,5], Nele Desmet1, Jan Bronders[1]. (1) Flemish Institute for Technological Research, VITO, Mol, Belgium, (2) Department of Hydrology and Hydraulic Engineering,	AT: No comment NL: this is not addressed (or at least it appears to be not reflected by RMS in the amended RAR).	Data requirement fulfilled. Reference C.T. Ramwell, M. Kah, P. D. Johnson Pest Manag Sci (2014) Published online in Wiley Online Library: (wileyonlinelibrary.com) DOI 10.1002/ps.3724 (http://onlinelibrary.wiley.com/doi/10.1002/ps.3724/full) and published in paper in Pest Management Science Volume 70, Issue 12, pages 1823–1830, December 2014 and it is assessed in appendix to B.8 p 256. Note: reference "*Occurrence of glyphosate in a stormwater drain due to residential inputs"- Ting Tang1,2, Wesley Boënne1, Ann van Griensven2,3,*

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	Vrije Universiteit Brussel, Brussels, Belgium, (3) UNESCO-IHE, Delft, The Netherlands, (4) Department of Bioscience Engineering, University of Antwerp, Antwerp, Belgium, (5) Department of Soil Management, Ghent University, Ghent, Belgium See reporting table public consultation 4(5)		*Piet Seuntjens1,4,5, Nele Desmet1, Jan Bronders1. (1) Flemish Institute for Technological Research, VITO, Mol, Belgium, (2) Department of Hydrology and Hydraulic Engineering, Vrije Universiteit Brussel, Brussels, Belgium, (3) UNESCO-IHE, Delft, The Netherlands, (4) Department of Bioscience Engineering, University of Antwerp, Antwerp, Belgium, (5) Department of Soil Management, Ghent University, Ghent, Belgium*" has not been provided. No justification for not providing it is available to EFSA. Note: see also data gap derived from data requirement 4.5. (entry 5 in this table)

5. Ecotoxicology

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
1	Data requirement 5.1 GTF to submit new GLP study on microorganisms (N-transformation). See reporting table 5(58)	AT: not considered NL: No comments. RMS states this has been addressed. The study is evaluated in the RAR and included in the updated List of studies relied on.	Addressed See also data requirement 5.9
2	Data requirement 5.2 GTF is given the possibility to submit new GLP study on terrestrial non-target plants. GTF to provide also a new quantitative risk assessment to terrestrial non-target plants. See also 5(50), 5(64), 5(65), 5(66), 5(67) See reporting table 5(63)	AT: not considered NL: No comments. RMS states this has been addressed. The study is evaluated in the RAR and included in the updated List of studies relied on.	Addressed See open point 5.12 in the evaluation table.
3	Data requirement 5.3 It is acknowledged that the paper of Marjo Helander, Irma Saloniemi and Kari Saikkonen 2012 was not	AT: not considered NL: No comments.	Noted. for the conclusion, please refer to the evaluation table.

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	captured by the systematic literature search because performed for the period 2001-2011. However, the Applicant is given the possibility to provide a summary and full evaluation of the relevance of this paper. See reporting table 5(75)		
4	Data requirement 5.4 Submission of supplemental studies on acute and chronic toxicity of glyphosate to aquatic organisms cited by FAO specifications and evaluations (2000/2001) for glyphosate. Rationale: For aquatic toxicity additional end points are cited, which were not submitted with the supplementary dossier. The data requirement has already been identified in the RAR. See reporting table 5(79)	AT: not considered NL: No comments.	Noted. for the conclusion, please refer to the evaluation table.

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
5	Data requirement 5.5 Applicant to submit the study from Wagner and Lötters (2013) for procedural reasons: 'Possible correlation of the worldwide amphibian decline and the increasing use of glyphosate in the agrarian industry. BfN-Skripten 343'. See reporting table public consultation 5(2)	AT: not considered NL: No comments. RMS states this has been addressed. The study is mentioned in the RAR and included as reference.	Addressed.
6	Data requirement 5.6 Applicant to submit the following studies for procedural reosans: -Plötner J. & Matschke J. (2012). Akut-toxische, subletale und indirekte Wirkungen von Gly-phosat und glyphosathaltigen Herbiziden auf Amphibien – eine Übersicht. Zeitschrift f. Feldherpetologie 19: 1-20 -Cuhra, M., Traavik, T., & Bøhn, T. (2013). Clone- and age-dependent toxicity of a 587 glyphosate commercial	AT: not considered NL: no comments.	Noted. for the conclusion, please refer to the evaluation table.

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	formulation and its active ingredient in Daphnia magna. 588 Ecotoxicology, 22, 251-262. See reporting table public consultation 5(3)		
7	Data requirement 5.7 Applicant to submit the following studies for procedural reosans: Avigliano, L., Fassiano, A. V., Medesani, D. A., de Molina, M. R., & Rodríguez, E. M. (2014). Effects of Glyphosate on Growth Rate, Metabolic Rate and Energy Reserves of Early Juvenile Crayfish, Cherax quadricarinatus M. Bulletin of environmental contamination and toxicology, 1-5. Fan, J. Y., Geng, J. J., Ren, H. Q., Wang, X. R., & Han, C. (2013). Herbicide Roundup® and its main constituents cause oxidative	AT: not considered NL: no comments.	Noted. for the conclusion, please refer to the evaluation table.

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	stress and inhibit acetylcholinesterase in liver of Carassius auratus. Journal of Environmental Science and Health, Part B, 48(10), 844-850. Mona, M. H., Gaafar, R. M., Helal, I. B., Omran, N. E., & Salama, W. M. (2013). Evaluation of cytotoxic effects of atrazine and glyphosate herbicides on< i> Biomphalaria glabrata</i> snails. The Journal of Basic & Applied Zoology, 66(2), 68-75. Nwani, C. D., Nagpure, N. S., Kumar, R., Kushwaha, B., Kumar, P., & Lakra, W. S. (2013). Induction of micronuclei and nuclear lesions in Channa punctatus following exposure to carbosulfan, glyphosate and atrazine. Drug and chemical toxicology, (0), 1-8. Richard, S., Prévot-D'Alvise, N., Bunet, R., Simide, R., Couvray, S., Coupé, S., & Grillasca, J. P. (2014). Effect		

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	of a Glyphosate-Based Herbicide on Gene Expressions of the Cytokines Interleukin-1β and Interleukin-10 and of Heme Oxygenase-1 in European Sea Bass, Dicentrarchus labrax L. Bulletin of environmental contamination and toxicology, 1-6. Sandrini, J. Z., Rola, R. C., Lopes, F. M., Buffon, H. F., Freitas, M. M., Martins, C. D., & da Rosa, C. E. (2013) Effects of glyphosate on cholinesterase activity of the mussel Perna perna and the fish Danio rerio and Jenynsia multidentata: In vitro studies. Aquatic toxicology (Amsterdam, Netherlands), 130, 171. Brodeur, J. C., Poliserpi, M. B., & Sánchez, M. (2014). Synergy between glyphosate-and cypermethrin-based pesticides during acute exposures in tadpoles of the common South American		

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	Toad< i> Rhinella arenarum</i>. Chemosphere, 112, 70-76. Syedkolaei, S. J. G., Shiri, N., Mirvaghefi, A. R., Rafiee, G. R., & Makhdomi, C. (2013). Toxicity evaluation of Malathion, Carbaryle and Glyphosate in common carp fingerlings (Cyprinus carpio, Linnaeus, 1758). Journal of Veterinary Research, 68(3), 257-267. Erhunmwunse, N. O., Alohan, F. I., Enuneku, A., Tongo, I., Ainerua, M., & Idugboe, S. (2013). Pathological alterations in the liver of post-juvenile African Catfish (Clarias gariepinus) exposed to sublethal concentrations of the herbicide Glyphosate. Journal of Natural Sciences Research, 3(15), 87-91. Moreno, N. C., Sofia, S. H., & Martinez, C. B. (2014). Genotoxic effects of the herbicide Roundup Transorb< sup>®</sup>		

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	and its active ingredient glyphosate on the fish< i> Prochilodus lineatus</i>. Environmental toxicology and pharmacology, 37(1), 448-454. dos Santos, K. C., & Martinez, C. B. (2014). Genotoxic and biochemical effects of atrazine and Roundup< sup>®</sup>, alone and in combination, on the Asian clam< i> Corbicula fluminea</i>. Ecotoxicology and environmental safety, 100, 7-14. Uren Webster, T. M., Laing, L. V., Florance, H., & Santos, E. M. (2013). Effects of glyphosate and its formulation, Roundup®, on reproduction in zebrafish (Danio rerio). Environmental science & technology. Dornelles, M. F., & Oliveira, G. T. (2013). Effect of Atrazine, Glyphosate and Quinclorac on Biochemical Parameters, Lipid		

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	Peroxidation and Survival in Bullfrog Tadpoles (Lithobates catesbeianus). Archives of environmental contamination and toxicology, 1-15. Gholami-Seyedkolaei, S. J., Mirvaghefi, A., Farahmand, H., & Kosari, A. A. (2013). Effect of a glyphosate-based herbicide in< i> Cyprinus carpio:</i> Assessment of acetylcholinesterase activity, hematological responses and serum biochemical parameters. Ecotoxicology and environmental safety, 98, 135-141. Yadav, S. S., Giri, S., Singha, U., Boro, F., & Giri, A. (2013). Toxic and genotoxic effects of Roundup on tadpoles of the Indian skittering frog (< i> Euflictis cyanophlyctis</i>) in the presence and absence of predator stress. Aquatic Toxicology, 132, 1-8. Janssens, L., & Stoks, R. (2013). Synergistic effects		

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	between pesticide stress and predator cues: Conflicting results from life history and physiology in the damselfly< i> Enallagma cyathigerum</i>. Aquatic Toxicology, 132, 92-99. De Souza Filho, J., Sousa, C. C. N., Da Silva, C. C., De Sabóia-Morais, S. M. T., & Grisolia, C. K. (2013). Mutagenicity and Genotoxicity in Gill Erythrocyte Cells of Poecilia reticulata Exposed to a Glyphosate Formulation. Bulletin of environmental contamination and toxicology, 91(5), 583-587. Güngördü, A. (2013). Comparative toxicity of methidathion and glyphosate on early life stages of three amphibian species:< i> Pelophylax ridibundus</i>,< i> Pseudepidalea viridis</i>, and< i> Xenopus laevis</i>. Aquatic Toxicology.		

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	Lanctôt, C., Robertson, C., Navarro-Martín, L., Edge, C., Melvin, S. D., Houlahan, J., & Trudeau, V. L. (2013). Effects of the glyphosate-based herbicide Roundup WeatherMax® on metamorphosis of wood frogs (< i> Lithobates sylvaticus</i>) in natural wetlands. Aquatic Toxicology. Wagner, N., Reichenbecher, W., Teichmann, H., Tappeser, B., & Lötters, S. (2013) Questions concerning the potential impact of glyphosate-based herbicides on amphibians. Environmental Toxicology and Chemistry. Kumar, A., Jahavar Ali, A. (2013) Toxic impacts of two organophosphorus pesticides on the acetylcholinesterase activity and biochemical composition of freshwater fairy shrimp streptocephalus dichotomus. International Journal of Pharma and Bio Sciences,		

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	4(2): 966 – 972. Meza-Joya, F.L., Ramírez-Pinilla, M.P., Fuentes-Lorenzo, J.L. (2013) Toxic, cytotoxic, and genotoxic effects of a glyphosate formulation (roundup®SL–cosmoflux®411F) in the direct-developing frog eleutherodactylus johnstonei. Environmental and Molecular Mutagenesis, DOI: 10.1002/em.21775. t Akinsorotan, A., Zelibe, S., & Olele, N. (2013) Acute Toxicity And Behavioural Changes On African Catfish (Clarias gariepinus) Exposed To Dizensate (Glyphosate Herbicide). International Journal of Scientific & Engineering Research 4(3). de Castilhos Ghisi, N., & Cestari, M. M. (2012). Genotoxic effects of the herbicide Roundup® in the fish Corydoras paleatus (Jenyns 1842) after short-term, environmentally low concentration exposure.		

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	Environmental Monitoring and Assessment, 185(4): 3201-3207. Lajmanovich, R. C., Junges, C. M., Attademo, A. M., Peltzer, P. M., Cabagna-Zenklusen, M. C., & Basso, A. (2013). Individual and Mixture Toxicity of Commercial Formulations Containing Glyphosate, Metsulfuron-Methyl, Bispyribac-Sodium, and Picloram on Rhinella arenarum Tadpoles. Water, Air, & Soil Pollution, 224(3), 1-13. Vera-Candioti, J., Soloneski, S., Larramendy, M.L. (2013) Evaluation of the genotoxic and cytotoxic effects of glyphosate-based herbicides in the ten spotted live-bearer fish Cnesterodon decemmaculatus (Jenyns, 1842). Ecotoxicology and environmental safety, 89(1): 166–173. Yadav, S.S., Giri, S., Singha, U., Boro, F., Giri, A. (2013) Toxic and genotoxic effects		

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	of Roundup on tadpoles of the Indian skittering frog (Euflictis cyanophlyctis) in the presence and absence of predator stress. Aquatic Toxicology, 132–133: 1–8. Guilherme, S., Santos, M.A., Barroso, C., Gaivão, I., Pacheco, M. (2012) Differential genotoxicity of Roundup® formulation and its constituents in blood cells of fish (Anguilla anguilla): considerations on chemical interactions and DNA damaging mechanisms. Ecotoxicology, 21(5): 1381-1390. Hued, A. C., Oberhofer, S., de los Ángeles Bistoni, M. (2012) Exposure to a Commercial Glyphosate Formulation (Roundup®) Alters Normal Gill and Liver Histology and Affects Male Sexual Activity of Jenynsia multidentata (Anablepidae, Cyprinodontiformes). Archives of environmental contamination and toxicology, 62(1): 107-117.		

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	Moore LJ, Fuentes L, Rodgers JH Jr, Bowerman WW, Yarrow GK, Chao WY, Bridges WC Jr. (2012) Relative toxicity of the components of the original formulation of Roundup to five North American anurans. Ecotoxicol Environ Saf;78: 128-33. Relyea, R.A. (2012) New effects of Roundup on amphibians: Predators reduce herbicide mortality; herbicides induce antipredator morphology. Ecological Applications, 22(2), 634-647. Guilherme, S., Santos, M. A., Gaivão, I., & Pacheco, M. (2014). DNA and chromosomal damage induced in fish (Anguilla anguilla L.) by aminomethylphosphonic acid (AMPA)—the major environmental breakdown product of glyphosate. Environmental Science and Pollution Research, 1-10.		

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	Armiliato, N., Ammar, D., Nezzi, L., Straliotto, M., Muller, Y. M., & Nazari, E. M. (2014). Changes in Ultrastructure and Expression of Steroidogenic Factor-1 in Ovaries of Zebrafish Danio rerio Exposed to Glyphosate. Journal of Toxicology and Environmental Health, Part A, 77(7), 405-414. Lajmanovich, R. C., Junges, C. M., Attademo, A. M., Peltzer, P. M., Cabagna-Zenklusen, M. C., & Basso, A. (2013). Individual and mixture toxicity of commercial formulations containing glyphosate, metsulfuron-methyl, bispyribac-sodium, and picloram on Rhinella arenarum tadpoles. Water, Air, & Soil Pollution, 224(3), 1-13. Glusczak, L., Loro, V.L., Pretto, A., Moraes, B.S., Raabe, A., Duarte, M.F., de Sousa Valladão, D.M. (2011) Acute exposure to		

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	glyphosate herbicide affects oxidative parameters in Piava (*Leporinus obtusidens*). Archives of environmental contamination and toxicology, 61(4): 624-630 (PENDING ON THE OPEN POINT BELOW). See reporting table public consultation 5(4)		
8	Data requirement 5.8 Applicant tot submit the following study for procedural reasons: Relyea RA. 2009. A cocktail of contaminants: how mixtures of pesticides at low concentrations affect aquatic communities. *Oecologia* **159**, 363-376. See also 5(3) See reporting table public consultation 5(5)	AT: not considered NL: No comments. RMS states this has been addressed. The study is mentioned in the RAR and included as reference.	Addressed.
9	Data requirement 5.9 Applicant to liase with the	AT: not considered NL: no comments.	Addressed The new study on N-transformation was submitted and evaluated in the revised RAR

No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	RMS and to submit the studies under consideration by the RMS for procedural reasons. A new systematic literature search would be appreciated **Note**: for the risk assessment to microorganisms, the nitrogen transformation and carbon mineralisation was considered, according to the current requirements. A data requirement was set for a valid N-transformation study in the other reporting table point 5(58) See reporting table public consultation 5(7)		
10	Data requirement 5.10 Applicant to submit the following study for procedural season: Mesnage et al. 2013 See reporting table public consultation 5(13)	AT: not considered NL: No comments. RMS states this has been addressed. The study is mentioned in the RAR and included as reference.	Addressed The study is mentioned in the RAR

PEER REVIEW REPORT ON **GLYPHOSATE** OCTOBER 2015

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06	**Comments on the draft EFSA conclusion and updated EFSA conclusion**

List of all comments on the draft EFSA conclusion and updated EFSA conclusion

	Document
28.07.2015	_Glyphosate comments on draft EFSA Conclusion_28-07-2015.doc
20.10.2015	_Glyphosate all comments on (updated) draft EFSA Conclusion.doc

Background			
No.	**Reference** (e.g. conclusion text, list of endpoints, evaluation table etc)	**Member State comment**	**EFSA response to comment**
1		DE: No comment.	
2	p. 6, third paragraph	COM: The reference to July 2015 may have to be amended pending the publication of the IARC monograph and subsequent evaluation.	Thank you for your comment, the conclusion will be amended accordingly, as soon as the further deadlines can be calculated.
3	p. 6, fifth paragraph	COM: The reference to July 2015 may have to be amended pending the publication of the IARC monograph and subsequent evaluation.	Thank you for your comment, the conclusion will be amended accordingly, as soon as the further deadlines can be calculated.

Identity, physical/chemical/technical properties and methods of analysis			
No.	**Reference** (e.g. conclusion text, list of endpoints, evaluation table etc)	**Member State comment**	**EFSA response to comment**
1	Conclusion text, Section 1, page 7	DE: It is proposed that the sentence: "*N-nitroso-glyphosate and formaldehyde were considered relevant impurities at a maximum content of 1 mg/kg and 1 g/kg respectively (see Section 2).*" is modified to: "*N-nitroso-glyphosate and formaldehyde were considered relevant impurities at a maximum content of **less than** 1 mg/kg and 1 g/kg respectively (see Section 2).*" Justification: According to the Regulation (EC) No 1272/2008 substances with a content of 1 g/kg formaldehyde has to be classified with Carc. 1B (H350).	Agreed, the sentence has been updated accordingly.
2	Conclusion text, Section 1, page 8	DE: It is proposed to further clarify that *"Residues of glyphosate and N-acetyl-glyphosate in food and feed of*	Agreed, the modification of the sentence has been made accordingly.

Identity, physical/chemical/technical properties and methods of analysis			
No.	**Reference** (e.g. conclusion text, list of endpoints, evaluation table etc)	**Member State comment**	**EFSA response to comment**
		plant origin can be monitored by HPLC-MS/MS methods with LOQs of 0.05 mg/kg for both compounds in each commodity group…", when additional analytical methods evaluated by the RMS which are not provided with the dossier of the Glyphosate Task Force are considered. Therefore, the sentence: "*Residues of glyphosate and N-acetyl-glyphosate in food and feed […]*' should be modified to: "***Considering additional analytical methods evaluated by the RMS which are not provided with the dossier of the GTF, residues*** *of glyphosate and N-acetyl-glyphosate in food and feed […]*'.	
3	p. 7, second paragraph of section 1	COM: The sentence "The RMS […] concluded that in 17 cases the proposed specification was regarded as equivalent […]." appears to conflict with other statements in the draft Conclusion referring to eight out of 24 applicants presenting specifications not supported by the tox assessment (p. 8, third paragraph of section 2; p. 24, last paragraph of section 9.2). Please correct or clearly explain discrepancy.	The RMS made the comparison of the individual specifications based on the Guidance Document SANCO/10597/2003 rev 10.1 which differentiates between chemical equivalence (tier I) and toxicological equivalence (tier II). In Section 1 of the EFSA conclusion the tier 1 equivalence is discussed as mentioned in the cited sentence, while in Section 2 the toxicological equivalence is concluded on. This is the reason why the cases of non- compliance can differ in these two cases.
4	p. 7/8, list of data gaps	COM: The data gap on a revised evaluation of the precision of method PC-ME-0554-02 with respect to one impurity, mentioned in section 7 on p. 22, is not reflected in section 1.	Agreed. This data gap was considered to be covered by the general data gap requesting additional information from Monsanto concerning the methods for impurities, however for more clarity the data gap that you have

Identity, physical/chemical/technical properties and methods of analysis			
No.	**Reference** (e.g. conclusion text, list of endpoints, evaluation table etc)	**Member State comment**	**EFSA response to comment**
			referred to in section 7 has now been explicitly mentioned in Section 1.
5	The draft EFSA conclusion – section 1 Identity, physical/chemical/technical properties and methods of analysis, p8	FR: In the third paragraph, it is indicated that residues of glyphosate and *N*-acetyl-glyphosate in food and feed of plant origin are monitored by HPLC-MS/MS methods for both compounds in "each commodity group". For better clarity, please specify in detail the validated matrice groups.	Agreed. The sentence has been modified to "all representative commodity groups".
6	List of end point – food/feed of plant origin	FR: In the part monitoring/Enforcement methods, methods for the determination of glyphosate residue in animal matrice are reported. Could you please clarify?	As the residue definition in animal matrices was defined as sum of glyphosate and *N*-acetyl-glyphosate, expressed as glyphosate, methods have been presented accordingly with the indication of the respective data gaps.
7	Conclusion on the evaluation of the text.	UK: This section should outline the nature of the TGAI manufactured e.g. the majority are manufactured as a TC, but one applicant manufactures glyphosate as a wet cake.	Agreed. A sentence has been added to the conclusion clarifying that TGAI can be also manufactured as a TK.
8	Conclusion on the evaluation of the text.	UK: For Monsanto, as well as a data gap for further batch data and QC data, a specification for the material manufactured should still be provided. Although it is not a critical area of concern it should be included as a data gap. It is appreciated that the RMS has updated vol 4 of the RAR and it now clearly indicates that this source is manufactured as a wet cake. However, the reasoning that a specification for what is actually manufactured is not required is not acceptable. The same argumentation about analysing the solvent level would also be applicable to TK but clearly a specification for what is manufactured is still required for a TK. Hence a material manufactured with a significant	Agreed. The additional data gap concerning the TK has been added.

Identity, physical/chemical/technical properties and methods of analysis			
No.	**Reference** (e.g. conclusion text, list of endpoints, evaluation table etc)	**Member State comment**	**EFSA response to comment**
		amount of solvent present should also have a specification for the manufactured material.	
9	Conclusion on the evaluation of the text.	UK: It is noted in section 7 (list of studies to be generated) the following data gap is listed: • Additional information concerning confirmatory methods for all impurities (see confidential RT) (relevant for applicant Monsanto Europe N.V./S.A, for all representative uses evaluated; submission date proposed by the applicant: unknown; see Section 1) This data gap is not listed in section 1. This data gap arises as a result of comment from FR. The UK made a similar comment for all the vol 4 provided with regards to how the identity of the impurities had been addressed. Monsanto responded that they could provide confirmatory methods for all impurities to address the confirmation of the identities of the impurities and hence the reason for the data gap. However, it is not clear that the confirmation of identity of the impurities has been addressed by all applicants. Consistency on how this is assessed for each source is required. Hence the need to confirm the identities of the impurities (e.g. by confirmatory methods of analysis as proposed by Monsanto) appears to be a data gap for other applicants and not just Monsanto.	As this point can be considered addressed by the statement of the RMS in the confidential Vol.4 for Monsanto (p.10), the data gap was removed from the EFSA conclusion and an explanation has been given in the evaluation table.
10	Conclusion on the evaluation of the text.	UK: For the monitoring methods for food of plant and animal origin the determination of the extraction efficiency	Disagreed. The extraction efficiency was described in the RAR Vol. B5 and the EFSA

Identity, physical/chemical/technical properties and methods of analysis			
No.	**Reference** (e.g. conclusion text, list of endpoints, evaluation table etc)	**Member State comment**	**EFSA response to comment**
		is an important requirement and as such it should be stated if this was adequately addressed.	conclusions concerning the monitoring methods would contain such details only if this would have been a data gap.
11	Conclusion on the evaluation of the text.	UK: As a derivatisation was used for the soil method then it should be stated whether or not the efficiency and precision of the derivatisation step was adequately addressed.	The RMS considered method B.5.3.1.1 (Schneider, V., 2001) acceptable as the analytical procedure used stable isotope labelled internal standards added to the test portion. In such cases, the demonstration of sufficient efficiency and precision of the derivatisation step was considered unimportant and methods were considered acceptable without additional tests of efficiency and precision of the derivatisation step. However a data gap was identified for the confirmatory method.
12	List of endpoints: Methods of analysis	UK: In the section for monitoring methods for plants reference is made to liver, kidney, fat , milk and eggs. In addition it should be stated here that the confirmatory methods missing (according to the text) for N-acetyl glyphosate is specifically missing for only crops of a high water and high fat content.	Agreed. The monitoring methods for plants section of the LoEP has been corrected.
13	List of endpoints: Methods of analysis	UK: In the section for the monitoring methods for food/feed of animal origin it should be stated (in accordance with the text) that the LOQ validated for milk and eggs is 0.025 mg/kg and 0.05 mg/kg for liver, kidney and fat.	Agreed. The LOQs of the methods for animal matrices have been updated in the LoEP.

Mammalian toxicity			
No.	**Reference** (e.g. conclusion text, list of endpoints, evaluation table etc)	**Member State comment**	**EFSA response to comment**
1	Summary, page 2	DE: The U.S. EPA submitted on June 29, 2015 the conclusions on a full battery of Tier 1 assays on endocrine disruption on glyphosate. Therefore, the following paragraph should be added: "***Glyphosate was selected by the U.S. EPA Endocrine Disruptor Screening Program's (EDSP) to undergo a full battery of Tier I screening assays for evaluation of glyphosate's potential to interact with the oestrogen, androgen and thyroid endocrine pathways. The weight of evidence conclusions have been submitted by the U.S. EPA on June 29, 2015 and should be considered in the EU peer review process, although could not been considered in the RAR. The U.S. EPA concluded that there was no convincing evidence of potential interaction with oestrogen, androgen or thyroid pathways. The conclusions of the U.S. EPA on the weight of evidence analysis confirm the previous EU assessment of available data and the conclusions of the Pesticides Peer Review Experts' Meeting 125 in February 2015.***" The sentences: "*The full battery of Tier I screening assays according to the EDSP, or Level 2 and 3 tests currently indicated in the OECD Conceptual Framework, and analysed in the EFSA Scientific Opinion on the hazard assessment of endocrine disruptors are needed to address the potential for*	The US EPA EDSP is already mentioned in the conclusion, together with the preliminary results mentioned by the RMS; however the studies are not available to the peer review. It is noted that the US EPA criteria for assessing ED properties may differ from the EU criteria and therefore the studies should be submitted before reaching a final conclusion.

Mammalian toxicity			
No.	**Reference** (e.g. conclusion text, list of endpoints, evaluation table etc)	**Member State comment**	**EFSA response to comment**
		endocrine-mediated mode of action regarding delay in preputial separation in F1 males and decrease in homogenisation resistant spermatids (cauda epididymis) in F0 observed in the most recent multigeneration study to address the ED assessment of glyphosate." should be deleted.	
2	Conclusion text, Section 2	DE: It is recommended to mention the exceptionally large database and the principle that the toxicological evaluation of all endpoints relies on a magnitude of valid studies rather than on one "key study".	Agreed. An introductory sentence has been added.
3	Conclusion text, Section 2	DE: It should be mentioned that the toxicity of formulations might be higher than that of the active substance, due to the relatively low toxicity of glyphosate and to the toxic properties of certain co-formulants. MS should care about that when granting national/zonal authorisations.	EFSA has been mandated by the European Commission to give its view on the evaluation of the POE tallowamine as presented in the RAR. This will not be included in the EFSA conclusion but in an EFSA statement under preparation, which will be finalised and available together with the EFSA conclusion.
4	Conclusion text, Section 2, page 11	DE: The U.S. EPA submitted on June 29, 2015 the conclusions on a full battery of Tier 1 assays on endocrine disruption on glyphosate. However, the original Tier 1 studies were not submitted. It is proposed to amend the section on endocrine disruption as follows: "*Glyphosate is not classified or proposed to be classified […], androgen and thyroid endocrine pathways.* ***The weight of evidence conclusions have been submitted by the U.S. EPA on June 29, 2015. The EPA assessment considers additionally to the new results***	See response to comment 1.

Mammalian toxicity			
No.	**Reference** (e.g. conclusion text, list of endpoints, evaluation table etc)	**Member State comment**	**EFSA response to comment**
		of the Tier 1 assays on endocrine disruption also other scientifically relevant information (OSRI), including general toxicity data and open literature studies in the weight of evidence assessment. The U.S. EPA concluded that there was no convincing evidence of potential interaction with oestrogen, androgen or thyroid pathways. Therefore, EDSP Tier 2 testing was not recommended for glyphosate. The conclusions of the U.S. EPA on the weight of evidence analysis of potential interaction of glyphosate with the oestrogen, androgen or thyroid pathways confirm the previous EU assessment of available data and the conclusions of the Pesticides Peer Review Experts' Meeting 125 in February 2015. However the Tier 1 studies of the U.S. EPA program were not submitted. No potential for neurotoxicity or immunotoxicity was detected in glyphosate-administered rats."	
5	Conclusion text, Section 2, page 9	DE: The sentence: "*In Swiss albino mice, a statistically significant increased incidence of malignant lymphomas was observed at the top dose of 1460 mg/kg bw per day, above the (limited) historical control data in one study (not reproduced in four other valid long term studies) that was discussed at length during the experts meeting.*" should be modified to: "*In Swiss albino mice, a statistically significant increased incidence of malignant lymphomas was observed at the top dose of 1460 mg/kg bw per day,* ***which***	Agreed, the text has been revised accordingly.

Mammalian toxicity			
No.	**Reference** (e.g. conclusion text, list of endpoints, evaluation table etc)	**Member State comment**	**EFSA response to comment**
		exceeded the "limit" dose of 1000 mg/kg bw/day recommended for the oral route of exposure in chronic toxicity and carcinogenicity studies (OECD, 2012a) and was *above the (limited) historical control data in one study (not reproduced in four other valid long term studies) that was discussed at length during the experts meeting."* The statement is then more precisely. Accordingly the following reference has to be added to the list of References: "***OECD (Organisation for Economic Co-operation and Development), 2012a. Series on Testing and Assessment: No 116: Guidance document 116 on the conduct and design of chronic toxicity and carcinogenicity studies, supporting test guidelines 451, 452 and 453 2nd edition. ENV/JM/MONO(2011)47, 156 pp.***"	
6	Conclusion text, Section 2, page 10	DE: The sentence: "*For those references, which have not been submitted under the EU peer review, […]*" should be modified to: "*For* ***the references relating to carcinogenicity and mutagenicity****, which have not been submitted under the EU peer review, […].*" for further clarification.	The references are not exclusively related to carcinogenicity and mutagenicity. This part of the conclusion has been revised after the TC117 on glyphosate.
7	Conclusion text, Section 2, page 10	DE: The sentences: "*Pregnant rabbits were found to be particularly vulnerable to glyphosate administration and developmental effects were linked to severe maternal toxicity, including maternal deaths.*" should be modified to: "*Pregnant rabbits were found to be particularly vulnerable to*	As this issue has not been raised during the peer review and isn't critical to the risk assessment, it hasn't been considered by EFSA and should be considered under the pertinent forum.

Mammalian toxicity			
No.	**Reference** (e.g. conclusion text, list of endpoints, evaluation table etc)	**Member State comment**	**EFSA response to comment**
		glyphosate administration and developmental effects were linked to severe maternal toxicity, including maternal deaths ***at dose levels from 100 mg/kg bw/day onwards.*** *"* for further clarification. Moreover, the sentence: "***Therefore Germany as the rapporteur Member State proposed STOT RE Cat 2 but this proposal has not been discussed on community level so far***." should be added subsequently.	
8	Conclusion text, Section 2, page 11	DE: The sentence: "*A postulated effect of glyphosate on microbial communities present in the gut of mammals […].*" Should be modified to: "*A postulated* ***adverse*** *effect of glyphosate on* ***quantitative composition of ruminal microflora or ruminal metabolism in ruminants*** *could not be substantiated by* ***means of the "Rumen Simulation Technique"***. ***In particular****, there was* ***no*** *evidence of Clostridium botulinum overgrowth.*" for further clarification.	Agreed, the text has been revised accordingly.
9	Conclusion text, Section 2, page 11	DE: The section on the ADI should be revised accordingly: "***The acceptable daily intake (ADI) of glyphosate is 0.5 mg/kg bw, based on the maternal and developmental NOAEL of 50 mg/kg bw per day from the developmental toxicity study in rabbits and applying a standard uncertainty factor (UF) of 100. The previous EU evaluation had set an ADI of 0.3 mg/kg bw based on the four long term toxicity studies in rats that were available at that time. An overall NOEL of about 30 mg/kg bw/day was***	Agreed, the text has been revised accordingly.

Mammalian toxicity			
No.	**Reference** (e.g. conclusion text, list of endpoints, evaluation table etc)	**Member State comment**	**EFSA response to comment**
		established."	
10	Conclusion text, Section 2, page 12	DE: The section on the AOEL should be revised accordingly: "***The acceptable operator exposure level (AOEL) is 0.1 mg/kg bw per day on the same basis as the ADI and ARfD, applying a correction factor to account for the limited oral absorption of 20%. The previous EU evaluation had set an AOEL of 0.2 mg/kg bw per day that was based on maternal toxicity in a rabbit developmental study but assumed an NOAEL of 75 mg/kg bw per day, an UF of 100 and 30% oral absorption.***"	The suggestion is in line with the text already in the conclusion; clarification regarding the use of NOEL/NOAEL has been added.
11	Conclusion text, Section 7, page 23	DE: The U.S. EPA submitted on June 29, 2015 the conclusions on a full battery of Tier 1 assays on endocrine disruption on glyphosate. However, the original Tier 1 studies were not submitted. It is proposed that EFSA decides to include the U.S. EPA conclusion on endocrine disruption of glyphosate in the outstanding peer review on the IARC monograph. Therefore the point on endocrine disruption should be amended as follows: "***Glyphosate was selected by the U.S. EPA Endocrine Disruptor Screening Program's (EDSP) to undergo a full battery of Tier I screening assays for evaluation of glyphosate's potential to interact with the oestrogen, androgen and thyroid endocrine pathways. The weight of evidence conclusions have been submitted by the U.S. EPA on June 29, 2015. The U.S. EPA concluded that there***	See response to comment 1.

Mammalian toxicity			
No.	**Reference** (e.g. conclusion text, list of endpoints, evaluation table etc)	**Member State comment**	**EFSA response to comment**
		was no convincing evidence of potential interaction with oestrogen, androgen or thyroid pathways. The conclusions of the U.S. EPA on the weight of evidence analysis confirm the previous EU assessment of available data and the conclusions of the Pesticides Peer Review Experts' Meeting 125 in February 2015."	
12	Conclusion text, Section 9, page 24	DE: Point 1 should be amended as follows: "***Glyphosate is not classified or proposed to be classified as carcinogenic or toxic for the reproduction category 2 in accordance with the provisions of Regulation (EC) No. 1272/2008 (harmonised classification supported by the present assessment) and therefore the conditions of the interim provisions of Annex II, Point 3.6.5 of Regulation (EC) No 1107/2009 concerning human health for the consideration of endocrine disrupting properties are not met. Glyphosate was selected by the U.S. EPA Endocrine Disruptor Screening Program's (EDSP) to undergo a full battery of Tier I screening assays for evaluation of glyphosate's potential to interact with the oestrogen, androgen and thyroid endocrine pathways. The weight of evidence conclusions have been submitted by the U.S. EPA on June 29, 2015. The U.S. EPA concluded that there was no convincing evidence of potential interaction with oestrogen, androgen or thyroid pathways. The conclusions of***	See response to comment 1.

Mammalian toxicity			
No.	**Reference** (e.g. conclusion text, list of endpoints, evaluation table etc)	**Member State comment**	**EFSA response to comment**
		the U.S. EPA on the weight of evidence analysis confirm the previous EU assessment of available data and the conclusions of the Pesticides Peer Review Experts' Meeting 125 in February 2015."	
13	Conclusion text, Section 2, page 9	DE: The sentence: "*Malignant lymphomas observed in mice are not mentioned in this article.*" should be modified to: "***Not all relevant data and references*** *are mentioned in this article.*"	This part of the conclusion has been revised after the TC117 on glyphosate.
14	p. 8, third paragraph of section 2	COM: The sentence "[…] eight out of the 24 applicants presented specifications that were not supported by the toxicological assessment […]."appears to conflict with the statement on p. 7, second paragraph of section 1. Please correct or clearly explain discrepancy.	Section 1compares the technical specifications with the respective representative analytical batches; section 2 compares the reference specification with the batches used in toxicity testing.
15	List of endpoints – section 2 mammalian toxicology, entry on classification and proposed labelling with regard to toxicological data	COM: Please consider whether the recent submission of a new intention by the RMS to ECHA for classification of glyphosate as STOT RE 2 (in addition to the existing classifications for Serious Eye Damage 1 and Aquatic Chronic 2) should be reflected here. It is an RMS proposal that was made after the peer review, hence not a peer review proposal.	Thank you for the information. As correctly stated, the proposal was not submitted for the peer review and can therefore not be taken into consideration at this late stage.
16	general	BE: Agrees with the conclusion of EFSA on the toxicology part.	Thank you for your agreement.
17	Second paragraph, page 9	BE suggested change in the wording: "not ***clearly*** reproduced in four other valid long term studies", as in 2/4 studies a slight increase was seen in the ♂ top-dose mice. It is acknowledged that the incidences were within the in-house HCD, but a slight trend existed.	Considering the outcome of the TC 117, this comment appears to be obsolete; therefore the text has not been revised. This part of the conclusion has been revised

Mammalian toxicity			
No.	**Reference** (e.g. conclusion text, list of endpoints, evaluation table etc)	**Member State comment**	**EFSA response to comment**
		The conclusion *"…there is limited evidence of a carcinogenic potential of glyphosate as a high-dose phenomenon in mice of a susceptible strain;…*", should be supplemented by: "***because of the discutable biological relevance of the mouse lymphoma findings**, (this conclusion would not alter the harmonised classification of glyphosate regarding carcinogenicity*)."	after the TC117 on glyphosate.
18	Paragraph p.10 on the IARC proposal	BE: The sentence: "*The IARC assessment is based on public literature only"* is potentially misleading. Formally, all references in the Lancet Oncology are publically available. However, the most relevant paper (the JMPR monograph of 2004, cited in EFSA's conclusion) encloses a number of primary studies which are based upon guideline studies from the industry (amongst which early carcinogenicity studies on Glyphosate, which were also submitted for the DAR). Such studies are not published as peer-reviewed open literature, thus one can hold the opinion that the IARC monograph is not supported by "public literature" only, since reviewers should refer to primary references in the first place. The context is explained in the paragraph, but on top of that, the abovementioned phrase should be adapted accordingly to avoid misunderstandings.	This part of the conclusion has been revised after the TC117 on glyphosate.
19	Paragraph p.10 on the IARC proposal	BE: agrees that on the basis of published studies and the short explanation in the Lancet Oncology, it is difficult to fully understand the basis of the IARC position. Hence, the conclusion "*At the moment, no further assessment can be made…"* is supported, and all interested parties are awaiting	This part of the conclusion has been revised after the TC117 on glyphosate.

Mammalian toxicity			
No.	**Reference** (e.g. conclusion text, list of endpoints, evaluation table etc)	**Member State comment**	**EFSA response to comment**
		the proper publication of the IARC monograph.	
20	EFSA Conclusion text – Tox parts	FR: Pending the publication of the IARC monograph, no further assessment can be made and FR supports the conclusion reached by EFSA regarding carcinogenicity.	This part of the conclusion has been revised after the TC117 on glyphosate.
21	Summary, page 2. Repeated top of page 11 and 4th bullet of page 23 and section 9.1	UK: Given the extensive database available on glyphosate, there is no reason to demand the full set of tests for endocrine disruption. Especially as it is noted at the bottom of page 10 that the ED effects appeared at parentally toxic doses.	As explained in the text, endocrine mediated adverse effects could not be ruled out; the lack of mechanistic data does not allow to differentiate between effects due to general toxicity from the ones that may be endocrine-mediated.
22	Section 2, Mammalian Toxicity – Bottom of page 9	UK: Any changes to the text following the review of the IARC decision must be clearly separated from the text describing the conclusions of the PRAPeR meeting. There was very extensive and detailed discussion at PRAPeR before the conclusion on carcinogenicity was reached.	Noted.
23	Section 2, Mammalian Toxicity – Bottom of page 11 – AOEL derivation	UK: In the derivation of the AOEL it is mentioned that this is a change from the previous value. The basis for the 50 mg/kg bw/d is described in the report of PRAPeR 125 and whilst UK considers this value precautionary it was the conclusion of PRAPeR. The reason for the change to the oral absorption value is not explained in the conclusion or the meeting report. The 20% is very conservative and is not based on data for rabbits. As this is a change to the original value, the basis needs to be transparent.	The oral absorption value was not discussed during the experts meeting as it was already proposed by the RMS in the RAR and agreed during the commenting period. Please refer to volume 1, p. 37 and reporting table comments 2(1), 2(2) and 2(3).
24	Section 9.1	UK: See comment 1. The ED assessment cannot be finalised until the EU has agreed its criteria for ED assessments. Until this	EFSA is asked to give its view on the approval criteria in which endocrine disruption is one of the key elements. An assessment of the criteria

Mammalian toxicity			
No.	**Reference** (e.g. conclusion text, list of endpoints, evaluation table etc)	**Member State comment**	**EFSA response to comment**
		documentation is available it is uncertain which, if any, studies are critical to the ED decision for glyphosate. If the company performs studies now, these might not be required for the decision and be an unjustified use of animals. This should be brought out in the EFSA conclusion.	in place is detailed in several chapters of the conclusion (summary, main text and area not finalised).
25	LOEP – toxicologically relevant compounds	UK: In the main text of the conclusions outstanding issues were raised in respect of N-acetyl AMPA and N-acetyl glyphosate. However these have been removed (or were already absent from) the LOEP. The two documents need to be consistent. As the requirements appear to relate specifically to imported GMOs, not the use of glyphosate in the EU, the UK proposes that N-acetyl AMPA and N-acetyl glyphosate are addressed at the stage of an import tolerance for the GMOs.	As AMPA is considered to present a similar toxicological profile as glyphosate, and not more toxic, it is not considered as toxicologically relevant. As the toxicological profile of N-acetyl AMPA and N-acetyl glyphosate has not been addressed, it is unknown whether they are relevant or not; therefore they are not reported as such in the LoEP.
26	2. Mammalian toxicity	NL: Although not essential for the renewal of glyphosate as an active substance, it would be very informative, and useful for national/zonal preparation assessments, if in the EFSA conclusion a few words on the POE-tallowamine surfactant are added, just like in the RAR.	EFSA has been mandated by the European Commission to give its view on the evaluation of the POE tallowamine as presented in the RAR. This will not be included in the EFSA conclusion but in an EFSA statement under preparation, which will be finalised and available together with the EFSA conclusion.

Residues			
No.	**Reference** (e.g. conclusion text, list of endpoints, evaluation table etc)	**Member State comment**	**EFSA response to comment**
1	LoEP, Residues from livestock feeding studies	DE: The proposal comment made by EFSA is supported.	Thank you for your support.
2	LoEP, Summary of residues data according to the representative uses on raw agricultural commodities	DE: The introduction paragraph is not completely correct, since not ALL trials in the Table were analysed for AMPA. Therefore, the paragraph should be amended as follows: "***Unless otherwise stated**, all samples […].*"	Agreed LoEP amended accordingly
3	LoEP, Summary of residues data according to the representative uses on raw agricultural commodities	DE: To avoid a future generalization of the broad extrapolation, the comments given in the Table should be amended by mentioning that glyphosate was applied pre-sowing/-planting or to the soil beneath trees. For example for the root and tuber vegetables the following amendment should be done: "*Based on the **pre-sowing** trials conducted on potato and carrots where residue levels were all <LOQ, a MRL of 0.05* mg/kg is proposed for the root and tuber vegetable group (including potato).*" Otherwise people may wonder why a deviating approach to the Guidance Documents is conducted.	Agreed LoEP amended accordingly
4	Conclusion on the evaluation of the text.	UK: Although an overall residue definition for risk assessment to cover conventional crops and GMO crops has been set it should be made clearer that residue data for N-acetyl-glyphosate and N-acetyl-AMPA are not required for conventional crops . (Clearly the residues data assessed for the conventional crops for the renewal only included glyphosate and AMPA).	It has been added that "the N-acetyl glyphosate and N-acetyl-AMPA metabolites are relevant for the GM crops containing the GAT modification."
5	List of endpoints: Residues	UK: For the conversion factor for non-tolerant crops it should make it clearer that N-acetyl-glyphosate and N-acetyl-AMPA are not relevant.	See point 6

Residues			
No.	**Reference** (e.g. conclusion text, list of endpoints, evaluation table etc)	**Member State comment**	**EFSA response to comment**
6	List of endpoints: Residues	UK: In the summary of the residue trials alongside the statement that all the samples were analysed for glyphosate and AMPA it should state that as the crops are conventional crops the inclusion of N-acetyl-glyphosate and N-acetyl-AMPA are not relevant.	Agreed It has been added in the LoEP that all trials were conducted on conventional crops and therefore that the residue definition for risk assessment is limited to sum glyphosate and AMPA..
7	List of Endpoints	NL: A note below the box with endpoints regarding 'residues from livestock feeding studies' explaining what 'gly-MAX' means, would be helpful. Furthermore, it would be appreciated if a note would be added below this box, which mentions that the calculations in this box are based on the representative uses limited to conventional crops.	Agreed LoEP has been amended to mention that values refer to the maximum residue levels observed in the feeding studies
8	List of Endpoints	NL: Regarding the 'summary of residue data…': Shouldn't the residue trials on rape seed be analysed according to the residue definition for monitoring which contains N-acetyl-glyphosate (although the representative use is on non-tolerant rape seed, the residue definition for monitoring for rape seed is described as 'sum of glyphosate and N-acetyl-glyphosate' for both tolerant as well as non-tolerant rape seed)?	See comments 4 and 6 It has been added that all trials were conducted on conventional crops and therefore that the residue definition for risk assessment is limited to sum glyphosate and AMPA.

Environmental fate and behaviour			
No.	**Reference** (e.g. conclusion text, list of endpoints, evaluation table etc)	**Member State comment**	**EFSA response to comment**
1	Conclusion, Environmental fate and behaviour/List of studies to be generated...	DE: RMS highly appreciates that the need for additional information on the groundwater entry path bank filtration was recognized and included into the list of studies to be generated.	Thank you for your supporting comment.
2	Conclusion text, Section 4, page 14,	UK: Since the text relates to the fate and behaviour of glyphosate in the environment perhaps the phrase "*physiologically typical pH 5-9 values*" could be amended to "***environmentally relevant*** *pH 5-9 values*".	Agreed an improvement to the wording was warranted. The text has been updated to: 'although the di-anion predominates at the typical environmental pH range of 5-9.'
3	Conclusion text, Section 4, various paragraphs.	UK: A minor typographical error, but in various parts of Section 4 the word "*extend*" is used whereas the correct term should be "***extent***".	Thank you, the conclusion text has been amended accordingly.
4	Conclusion text, Section 4, page 16	UK: We agree that the conclusion correctly highlights the uncertainty in the use of the standard FOCUSgw models for glyphosate and AMPA, due to the specific ionic characteristics of these molecules. This was an issue that the meeting of experts cited as being important information to communicate to risk managers. However we wonder whether this should be given slightly greater prominence in the conclusion? We are not sure if this is sufficient to warrant inclusion in the 'critical areas of concern' but suggest that it does need to be made clearer (maybe as a footnote to the table in Section 9.3?).	Thank you for your suggestion. A footnote has been added to the table in section 6.2. The footnote says: 'Note there is uncertainty in the assessment, as the standard FOCUSgw models, scenarios and approach do not account for the specific ionic characteristics of glyphosate and AMPA.' As this issue has not led to an assessment not finalised for individual uses or a critical area of concern (that applies to all uses) or a critical concern for a subset of uses it cannot be indicated in section 9.3.
5	List of studies to be generated	UK: For clarity, the medium of pH measurement should be cited in the data gap for degradation rate of AMPA in soils with pH 5-6. For consistency with how the pH values are expressed in the LOEP, this should be probably be in H_2O.	Thank you, the conclusion text has been amended accordingly.

Environmental fate and behaviour			
No.	**Reference** (e.g. conclusion text, list of endpoints, evaluation table etc)	**Member State comment**	**EFSA response to comment**
6	Conclusion text	NL: the conclusion text is very factual, for instance a wide range in persistence in soil or water is found (for both a.s. and AMPA), however it does not explain why or how choices for model input are made When looking at the LoEP (eg. Surface water PEC calculation) it becomes clear that geomean (of DT50 whole system) was used. The same holds true for groundwater (DT50 soil). It could be stated that a wide range of DT50 is observed but in view of the large data set (or: because there were no clear reasons as to why this range was so large) the geomean is considered appropriate for use in modelling	The conclusion has not been updated. It is the objective of the EFSA conclusion that it should be factual, thank you for recognising that we have been factual. The conclusion cites the relevant FOCUS guidance that has been followed. This is the usual approach in all EFSA conclusions. It is clear from the list of endpoints what input values have been used in modelling. The list of endpoints is the place to find this detail. It is clear from the comment of the NL that they were able to locate this information in the list of endpoints. The EFSA style for its conclusions is that we would only describe the reasons why it was decided not to use a mean approach, due to an identified soil property correlation. No correlation was identified in this case.
7	Conclusion text	NL: in the conclusion text considering monitoring data should "*….subsequent surface contamination and bank filtration to groundwater*" not read "*….subsequent surface* ***water*** *contamination and bank filtration to groundwater*"? See also the correct wording in the last column of the evaluation table. This data gap originates from data requirement 4(5) which was not discussed in the expert meeting. Although NL agrees that attention is needed for run-off of hard surfaces, NL also considers that the currently defended	The conclusion has been updated to add the missing word (water). The relevant wording has also been expanded to explain why hard surfaces can be an issue related to some of the uses in the representative use GAPs. The new text is: 'In particular, further information is needed to assess the contamination route through run off (especially for in situations where applications to hard surfaces might occur) and subsequent

Environmental fate and behaviour			
No.	**Reference** (e.g. conclusion text, list of endpoints, evaluation table etc)	**Member State comment**	**EFSA response to comment**
		EU gap does not include hard surfaces. The intended use as pre-emergence or post-harvest application (on transplanted or seeded crops) is indeed on at that time uncultivated land, but this does not mean that this consists of hard surfaces such as gravel, concrete etc. or that it is always located next to permanent concrete strips. In evaluation table 4(20) it is stated that the EFSA conclusion would only reflect the intended uses. Therefore the data gap seems to be a bit of a long shot. Furthermore it is not clear how the applicant should address this issue since no EU harmonised guidance or exposure models exist for this route as also stated by RMS in the evaluation table (see also earlier NL comments during the written procedure).	surface water contamination and bank filtration to groundwater. This route was considered relevant for the representative uses on 'all seeded or transplanted crops' and 'all seeded crops' as horticultural practices can mean that containers or seed trays can be placed on hard surfaces.' This inclusion came from commenting during the peer review. By consulting the reporting and evaluation tables the reasoning for including the data gap becomes clear. Data requirement responses are subject to a written consultation with member states, so it is quite usual that they are not on the agenda for discussion in a meeting of experts. It is impossible for there to be agreed EU guidance for every issue. However the absence of guidance is not a reason not to identify issues as data gaps.
	Conclusion text	NL: With regard to the max observed for AMPA it could be stated at the field study section in the EFSA conclusion text that this reached 53.8%, since this is higher than in lab (50.1%) and was used for further exposure assessment for soil organisms (see PECsoil calculations in LoEP).	Thank you for this comment. EFSA agrees there would be utility in adding this fact in the conclusion's text. The new text is: 'AMPA was also captured as being formed at a comparable (but numerically higher) proportion of the precursor glyphosate (53.8% on a molar basis) to that which was observed in the available laboratory soil incubations.'

Environmental fate and behaviour			
No.	**Reference** (e.g. conclusion text, list of endpoints, evaluation table etc)	**Member State comment**	**EFSA response to comment**
	Conclusions text	NL see table 6.2 typo/mix-up: *Monitoring data: equivocal results. Exceedances are reported for which it is not possible to rule out that contamination was caused **under** by uses following GAP*	Agreed the text has been corrected as proposed.
	List of endpoints	NL: in the sorption box a mean (or median? Please clarify) of 20 values is given after 4 values have been omitted (result of peer review). However just below a mean (or median?) of 24 values is still given. Please adapt and/or clarify.	Agreed the value from 24 studies had been removed. The retained values are arithmetic means. This has been clarified.

Ecotoxicology			
No.	**Reference** (e.g. conclusion text, list of endpoints, evaluation table etc)	**Member State comment**	**EFSA response to comment**
1	Conclusion, page 16 , paragraph 5; indirect effects (biodiversity)	DE: RMS believes that against the background of the former and the current legislative framework for PPP risk regulation it is the explicit remit of the risk assessment for an active substance to include all kinds of effects in the risk assessment that are considered to have a relevant impact on the diversity and abundance of non-target organisms. The risk from indirect effects resulting from extensively used herbicides such as glyphosate was therefore addressed in order to provide the best available scientific base for necessary decisions at the level of the	EFSA acknowledged the effort of the RMS to provide information and argumentation on the indirect effects (biodiversity) on non-target organisms via trophic interaction of glyphosate. EFSA also acknowledged the relevance of considering indirect effects, as reflected in the Conclusion. It is however, noted that there was a general agreement to consider this as an important risk management issue. Indeed, it is difficult to take into account in the prospective

Ecotoxicology			
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		subsequent risk management. Nevertheless in the current draft EFSA conclusion, RMS is missing the recognition that indirect effects are an integral part of a transparent risk characterization contributing to the risk of PPP. RMS therefore kindly asks EFSA to reconsider the issue of indirect effects on non-target organisms at higher trophic level and proposes the following "amendment" to the paragraph 3 in chapter 5 and chapter 9 (concerns): *Some aspects of the risk assessment of glyphosate were discussed at the Pesticides Peer Review Meeting 128 (03 – 05 March 2015).* *RMS raised concerns regarding the indirect effects (biodiversity) on non-target organisms via trophic interaction of extensively used herbicides such as glyphosate. At the meeting there was an exchange of views on this issue and experts acknowledged that the overall risk of an respective PPP for non-target organisms might under certain circumstances require the consideration of indirect effects depending on the specific landscape setting such as e.g. availability of alternative food habitats for farmland species and the spatial and temporal intensity of use of herbicidal or insecticidal active PPP at this landscape.* *The appropriate characterization of the overall risk can therefore not ignore aspects such as indirect effects of PPP. The risk from indirect effects resulting from extensively used herbicides such as glyphosate was addressed by RMS*	risk assessment for an active substance '*landscape setting such as e.g. availability of alternative food habitats for farmland species and the spatial and temporal intensity of use of herbicidal or insecticidal active PPP at this landscape'.* The Conclusion was not changed.

Ecotoxicology			
No.	**Reference** (e.g. conclusion text, list of endpoints, evaluation table etc)	**Member State comment**	**EFSA response to comment**
		in order to provide the best available scientific base for necessary decisions at the level of the subsequent risk management. Experts acknowledged that there exist so far no guidance for the consideration of indirect effects in risk assessment. Nevertheless, the experts considered this as an important risk management issue.	
2	Conclusion , Aquatic organisms	DE: RMS proposes to add the following information to the paragraph: *Moreover, peer-reviewed relevant articles have been considered as supporting and critical information in risk assessment. Endpoints deriving out of these publications were used for an additional risk assessment and indicated a low risk to aquatic organisms with the highest FOCUS step 2 $PEC_{sw.}$*	EFSA acknowledged the effort of the RMS to consider additional information from literature. However, since there are no indications of diverging outcome of the risk assessment, it is considered not needed to change the Conclusion.
3	List of endpoints; Toxicity/exposure ratios for aquatic species	DE: Toxicity/exposure ratios were amended for the metabolites AMPA and HMPA in the list of endpoints.	Thank you for the updated document.
4	Conclusion; Birds	DE: EFSA identified a data gap to further address the risk to insectivorous birds for the representative use in cereals (pre-harvest application). RMS stated that for the scenario "Cereals pre harvest /crop maturity" the GAP indicates that cereal applications are made for pre-harvest uses and desiccation (starting with BBCH 89), which is why the Late season- seed heads scenario was considered the most relevant. Nevertheless, including the scenario which takes into account BBCH 71 - 89, the "Small insectivorous bird "passerine" does not	EFSA disagrees No data or information were available to further address the risk to insectivorous birds for the representative use in cereals (pre-harvest application), even on the basis on a weight of evidence approach. The Conclusion was not changed.

Ecotoxicology			
No.	**Reference** (e.g. conclusion text, list of endpoints, evaluation table etc)	**Member State comment**	**EFSA response to comment**
		achieve the acceptability criteria TER ≥ 5. for long-term effects. In those cases an assessment might consider the following: - Birds are highly mobile and often travel considerable distances between breeding habitat and feeding habitat. Hence, a refinement of PT to 0.5 can be proposed. - Particularly in the case of pre-harvest application it must be assumed that habitat loss due to harvest takes place inbetween a short period and therefore, long-term feeding on contaminated foliar insects displays a worse case. In conclusion RMS considers the long-term risk resulting from an exposure of birds to glyphosate according to the intended use in the scenario "all crops (all seeded or transplanted crops) " and "Cereals pre harvest /crop maturity, to be acceptable. This comment refers also to the Overview of the concerns identified for each representative use considered in chapter 9.3.	
5	Conclusion; Mammals acute risk	DE: The acute risk to mammals was assessed as low at the first tier level for all the representative uses, except for the worst-case scenario 'small herbivorous mammals (e.g. common vole, *Microtus arvalis*)' for the uses in 'grassland". For the scenario "All crops (all seeded or transplanted crops)/ Pre-planting of crop" the Generic focal species with a worse case short cut of 40,9 and a DDD of 100 mg/kg	The short cut value proposed by the RMS of 40.9 is not worst-case for application on early growth stage of "All crops (all seeded or transplanted crops)/ Pre-planting of crop". The Conclusion was not changed.

Ecotoxicology			
No.	**Reference** (e.g. conclusion text, list of endpoints, evaluation table etc)	**Member State comment**	**EFSA response to comment**
		resulted in an acceptable acute risk. This comment refers also to the Overview of the concerns identified for each representative use considered in chapter 9.3.	
6	Conclusion; Mammals long term risk	DE: The long-term risk to mammals was indicated as high for the representative uses 'grassland", in particular, to small herbivorous mammals. Nevertheless, for the scenario "All crops (all seeded or transplanted crops)/ Pre-planting of crop" a worse case short cut of 21 and a DDD of 9 mg/kg was assumed resulting in an acceptable long term risk.	The short cut value proposed by the RMS of 21 (i.e. 21.7) is not worst-case for application on early growth stage of "All crops (all seeded or transplanted crops)/ Pre-planting of crop". The Conclusion was not changed.
7	Conclusion ; NTA, NTTP Drift values for the pre-harvest applications	DE: RMS proposes to amend the paragraph as follows: *For the risk assessment for non-target arthropods and for terrestrial non target plants, the use of modified drift values was proposed by the RMS for the pre-harvest applications, because the scenario "pre-harvest" is currently not considered by the FOCUS default drift values. RMS proposed to mirror the height of the crop during pre-harvest by higher drift deposition in order to reduce risk to non-target arthropods in the off-crop habitat. The experts considered it more appropriate to use the FOCUS default drift values rather than the corrected values, but it was also agreed to highlight that the drift depositions might be underestimated with the default values for these particular uses of glyphosate.*	The Conclusion was not changed as proposed, except for the sentence '*RMS proposed to mirror the height of the crop during pre-harvest by higher drift deposition in order to reduce risk to non-target arthropods in the off-crop habitat?,* because considered redundant
8	p. 17, last paragraph	COM: In the sentence "For the risk assessment for non-target-arthropods and for terrestrial non target plants, the use of modified drift values as proposed by the RMS for the	Thank you for your comment. The conclusion has been amended accordingly.

Ecotoxicology			
No.	**Reference** (e.g. conclusion text, list of endpoints, evaluation table etc)	**Member State comment**	**EFSA response to comment**
		pre-harvest applications (i.e. representative uses in cereals and oilseeds was discussed at the experts' meeting).", the closing bracket should be moved after the word "oilseeds" to preserve the meaning of the sentence.	
9	p. 24, last paragraph of section 9.2	COM: The sentence "Eight out of the 24 applicants presented specifications that were not supported by the toxicological assessment […]."appears to conflict with the statement on p. 7, second paragraph of section 1. Please correct or clearly explain discrepancy.	See response to comment 14 in mammalian toxicity section.
10	p. 25, section 9.3, header row of table	COM: Please consider adding "pre-planting" and "post-planting" to the representative uses on 'all seeded or transplanted crops' and 'all seeded crops', respectively, for improved clarity, as these terms are also used in other sections of the draft Conclusion.	Thank you for your comment, the table has been amended.
11	p. 25, section 9.3, header row of table	COM: did not find a post-harvest representative use on cereals in the GAP table in the list of endpoints. Please correct table in section 9.3.	The post-harvest use is not mentioned in the GAP table, but was introduced in the list of endpoints for the section on fate and behaviour for unknown reasons. This use will anyway be covered by the calculations for the pre-emergence and pre-planting use. The list of end points and the conclusion have been amended accordingly.
12	Conclusions of the evaluation 6. Ecotoxicology, P.16	HELLAS: Regarding "*the indirect effects (biodiversity) on non-target organisms via trophic interaction of extensively used herbicides such as glyphosate*", we acknowledge that there is an explicit risk assessment scheme that takes into account Biodiversity and Ecosystem Services in Risk	Noted Please consider that 'an explicit risk assessment scheme that takes into account Biodiversity and Ecosystem Services in Risk Assessment' is not available. However, in the on-going revision of

Ecotoxicology			
No.	**Reference** (e.g. conclusion text, list of endpoints, evaluation table etc)	**Member State comment**	**EFSA response to comment**
		Assessment and we agree on the importance of this issue for risk management.	the ecotoxicology guidance document, EFSA first identifies the Specific Protection Goal (SPG), taking into account the ecosystem services. Once the SPGs will be agreed by the risk managers, EFSA will develop risk assessment schemes which should ensure the protection of ecosystem services and biodiversity.
13	Conclusions of the evaluation 6. Ecotoxicology, P.17	HELLAS: "*For the risk assessment for non-target arthropods and for terrestrial non target plants, the use of modified drift values as proposed by the RMS for the pre-harvest applications (i.e. representative uses in cereals and oilseeds was discussed at the experts' meeting)*." Please complete or modify the sentence for clarity reasons.	See comment 8
14	Conclusions of the evaluation 6. Ecotoxicology, P.18	HELLAS: agrees with the conclusions for non-target terrestrial plants and drift deposition rates of particular uses of glyphosate as well as that, plants are to be affected at single application event since they are immobile. With respect to the future consideration of multiple exposure events, please also consider that testing of residual effects and root uptake would facilitate testing of cumulative exposure.	Noted EFSA agrees that effect from cumulative exposure should be considered with proper testing.
15	LOEP table-toxicity/exposure ratios for terrestrial vertebrates	UK: <u>General comment:</u> There are a number of discrepancies between the RAR and the LOEP risk assessment for birds and mammals. The UK evaluator has commented on these below however has not commented past the tier 1 mammal assessment. The correct endpoints have been used in these assessments but	As explained in the Conclusion no specific scenarios are available in the EFSA(2009) for the spraying applications against emerged annual, perennial and biennial weeds for the representative use "all crops, pre-planting and post planting".

Ecotoxicology			
No.	**Reference** (e.g. conclusion text, list of endpoints, evaluation table etc)	**Member State comment**	**EFSA response to comment**
		the RMSs risk assessment appears to differ considerable from that presented in the LOEP table. EFSA have clearly made extensive changes to the LOEP table however it is very difficult for other MS to follow the reasoning behind these changes as they are not documented in the RAR or the evaluation table. It is not easy to get a clear picture of the bird or mammal assessment, ideally the RAR needs to be updated to reflect the risk assessment present in the LOEP table. As a result of this other MS's are unable to check whether the conclusions/data gaps stated in the ecotoxicology summary section of the EFSA conclusion are in line with the assessment. The conclusions stated are in line with the changes made by EFSA, highlighted in purple, however they are not in line with the RMS conclusions.	Worst case scenarios related to the early stage of several crops were therefore considered. The LoEP was extensive changed by EFSA to make transparent the risk assessment against the approach followed. However, for improving the transparency, the parameters used to calculate the DDD values were added to the LoEP. By doing this, typo were noted and corrected. As a general rule, the RMSs'conclusions in the RARs should be considered as superseded by the EFSA Conclusions, as result of the peer review of the preliminary risk assessments. It is rather common that the final LoEP differs from the one submitted with the RAR.
16	LOEP table-toxicity/exposure ratios for terrestrial vertebrates	UK: <u>Screening step (acute) -birds</u> For the worst case use pattern and scenario for orchard crops (vines, including citrus and tree nuts), it is unclear why an application rate of 1-3 applications e.g. 2 x 720 g a.s/ha + 1 x 2880 g a.s/ha was not considered to be the worst case for the generic focal species small omnivorous bird. The TER for this exposure scenario is 24.	Combination of possible use patterns, which included worst case situations were considered for risk assessment. For orchards, applications are made intra-rows, therefore it was assumed that the actual application rates per hectare of cropped areas were the 50% of the rates per hectare of treated areas (i.e. 2.16 kg a.s. /ha of cropped areas) On the basis of this assumption, the combination mentioned by the UK, was not considered as

Ecotoxicology			
No.	**Reference** (e.g. conclusion text, list of endpoints, evaluation table etc)	**Member State comment**	**EFSA response to comment**
			worst –case.
17	LOEP table-toxicity/exposure ratios for terrestrial vertebrates	UK: Screening step and tier 1 assessment for birds For all worst case scenarios in which 2 applications of the active substance are assessed, it would be useful if the application interval was stated. For some scenarios this is stated (e.g. long term risk to bird's tier 1, all crops (pre planting), interval of 21 d stated. However for others it is not.	Noted. LoEP amended accordingly
18	LOEP table-toxicity/exposure ratios for terrestrial vertebrates	UK: Tier 1 long term assessment for birds. For all crops (all seeded crops), post planting/pre emergence of crop-the worst case scenario for 1 x 1080 g a.s/ha is stated as: Medium herbiv.graniv. bird "pigeon" Wood pidgeon (*Columba palumbus*)/ with a DDD of 13 and a TER of 8. In the RAR, the lowest TER is 7 (DDD of 12.99) for the reproductive risk to the medium herbivorous bird on oilseed rape (BBCH 10-19). Therefore the values stated in the LOEP table need amending to 12.99 and 7 instead of 13 and 8.	Noted The LoEP was amended as follows: TER 7.41. The DDD of 12.99 was left as 13.
19	LOEP table-toxicity/exposure ratios for terrestrial vertebrates	UK: Tier 1 long term assessment for birds It is unclear how the worst case use pattern and scenarios for orchards crops, post emergence of weeds have been determined. In the RAR, the lowest TER is 9 (DDD 10.21) for the reproductive risk to the small omnivorous bird 'lark' in vineyards, 1 x max 2880 g a.s/ha. The next lowest TER is	Noted The scenario small granivorous bird 'finch' was considered the most relevant for not crop directed application, all season. However, some corrections were needed for the TER values in the LoEP: -a result of an application of 1 x max 2880 g

Ecotoxicology			
No.	**Reference** (e.g. conclusion text, list of endpoints, evaluation table etc)	**Member State comment**	**EFSA response to comment**
		10 (DDD 9.6) for the reproductive risk to the small granivorous bird 'finch' in orchards, 1 x max 2880 g a.s/ha. The LOEP table states the TER of 11(DDD 8.8) for the reproductive risk to the small granivorous bird as a result of an application of 1 x max 2880 g a.s/ha. The RAR states that this risk is to the small insectivorous bird 'redstart'. The LOEP table also states the TER of 19 (DDD 5.10) for the reproductive risk to the small granivorous bird as a result of an application of 3 x 1440 g a.s/ha. The RAR states that this risk is to the small omnivorous bird 'lark'.	a.s/ha., the DDD is 9.6 and the TER 10; -as a result of an application of 3 x 1440 g a.s/ha the DDD is 5.6 and the TER is 17. It is noted that the application rates were divided by two, for considering the inter-row area only.
20	LOEP table-toxicity/exposure ratios for terrestrial vertebrates	UK: <u>Tier 1 acute assessment for mammals</u> The worst case use pattern and scenarios for all crops (all seeded or transplanted crops), pre planting of crop- is not consistent with the RAR. Table B 9.3-7 in the RAR states the worst case TER of >19 for the reproductive risk to both the large herbivorous and small herbivorous mammal (DDD of 103.35 and 100.40 respectively). The LOEP table states a TER of >6 (DDD 335.9) for the small herbivorous mammal. A TER of 19.2 (DDD 103.67) is stated for the large herbivorous mammal. The MAF in the LOEP table is also stated as 1.1 whereas in the assessment a MAF of 1.14 was used.	See comment 15 The TER of >6 (DDD 335.9) for the small herbivorous mammal and the TER of 19.2 (DDD 103.67) for the large herbivorous mammal were related to the acute risk assessment.

Ecotoxicology			
No.	**Reference** (e.g. conclusion text, list of endpoints, evaluation table etc)	**Member State comment**	**EFSA response to comment**
21	LOEP table-toxicity/exposure ratios for terrestrial vertebrates	UK: Tier 1 acute assessment for mammals It is not clear where the values stated for the all crops (all seeded crops), post planting/pre emergence of crop come from. This scenario is not considered in the RAR.	See comment 15
22	LOEP table-toxicity/exposure ratios for terrestrial vertebrates	UK: Tier 1 acute assessment for mammals It is unclear how the worst case use pattern and scenarios for orchards crops, post emergence of weeds have been determined. In the RAR, the lowest TER is >8 (DDD 249.3) for the acute risk to the small herbivorous mammal 'vole' in orchards, 1-3 applications (e.g. 2 x 720 g as/ha + 1 x 2880 g as/ha). The next lowest TER is >10 (DDD 196.42) for the acute risk to the small herbivorous mammal 'vole' in orchards, 1 x max 2880 g a.s/ha. The LOEP table does states the TER of >10 (DDD 196.42) however the lowest TER of >8 (as stated above) is not stated. Instead a TER of >18.5 (DDD 108.03) for the acute risk to the small herbivorous mammal 'vole' in orchards as a result of 3 x 1440 g a.s/ha (MAF 1.1) is stated. In the RAR, the acute risk to the small herbivorous mammal 'vole' in orchards as a result of 3 x 1440 g a.s/ha is considered with a MAF of 1.09, which produces a DDD of 107.05 and a TER of >18. It is acknowledged that some of these changes are minor but the RAR should be in line with the LOEP table and if it is not then this it should be clearly stated why in the evaluation table.	See comment 15

Ecotoxicology			
No.	**Reference** (e.g. conclusion text, list of endpoints, evaluation table etc)	**Member State comment**	**EFSA response to comment**
23	LOEP table-toxicity/exposure ratios for terrestrial vertebrates	UK: Tier 1 reproductive assessment for mammals The worst case use pattern and scenarios for all crops (all seeded or transplanted crops), pre planting of crop- is not consistent with the RAR. Table B 9.3-8 in the RAR states the worst case TER of 1.6 for the reproductive risk to both the large herbivorous and small herbivorous mammal (DDD of 30.45, 31.29 and 30.45). These have been calculated using a different MAF to that stated in the LOEP table. The LOEP table states a TER of 0.49 (DDD 101.8) for the small herbivorous mammal. A TER of 4.55 (DDD 10.98) is stated for the small omnivorous mammal 'wood mouse'.	See comment 15
24	LOEP table-toxicity/exposure ratios for terrestrial vertebrates	UK: Tier 1 reproductive assessment for mammals It is not clear where the values stated for the all crops (all seeded crops), post planting/pre emergence of crop come from. This scenario is not considered in the RAR.	See comment 15
25	LOEP table-toxicity/exposure ratios for terrestrial vertebrates	UK: Tier 1 reproductive assessment for mammals It is unclear how the worst case use pattern and scenarios for orchards crops, post emergence of weeds have been determined. In the RAR, the lowest TER is 0.7 (DDD 70.79) for the reproductive risk to the small herbivorous mammal 'vole' in orchards, 1-3 applications (e.g. 2 x 720 g as/ha + 1 x 2880 g as/ha). The next lowest TER is 0.9 (DDD 55.17) for the reproductive risk to the small herbivorous mammal 'vole' in orchards, 1 x max 2880 g a.s/ha. The LOEP table does states the TER of 0.9 (DDD 55.17) however the lowest TER of 0.7 (as stated above) is not	See comment 15

Ecotoxicology			
No.	**Reference** (e.g. conclusion text, list of endpoints, evaluation table etc)	**Member State comment**	**EFSA response to comment**
		stated. Instead a TER of 1.51 (DDD 33.06) for the reproductive risk to the small herbivorous mammal 'vole' in orchards as a result of 3 x 1440 g a.s/ha (MAF 1.29) is stated. In the RAR, the reproductive risk to the small herbivorous mammal 'vole' in orchards as a result of 3 x 1440 g a.s/ha produces a DDD of 31.75 and a TER of 1.6. It is acknowledged that some of these changes are minor but the RAR should be in line with the LOEP table and if it is not then this it should be clearly stated why in the evaluation table.	
26	Toxicity data for aquatic species	UK: Why are the toxicity endpoints for glyphosate IPA-salt and glyphosate K-salt not stated in this table for all aquatic organisms? All valid endpoints should be stated in the LOEP table.	Noted. The endpoints which are the most relevant for risk assessment were included in the LoEP. No changes are needed
27	Toxicity data for aquatic species	UK: For the *Myriophyllum* toxicity study for AMPA the EC50 (dry weight) is stated as 63 mg/L. In the RAR the endpoint for this study (CHE-022/4-80/A Wenzel, 2012 BVL no 2310997) is stated as 63.2 mg/L. Furthermore the lowest endpoint from this study should be an EC50 for root length of 31.1 mg/L.	Noted. The LoEP was corrected
28	Toxicity/exposure ratios for the most sensitive aquatic organisms	UK: The table with the FOCUS step 1 and 2 TER vales in states a TER of 303 for the fish prolonged risk (NOEC 1000 ug/L) for FOCUS step 2 (PEC 18.49). This should be a TER of 54. This is already reflected in the RAR.	Noted. The LoEP was corrected
29	Toxicity/exposure ratios for the most sensitive	UK: There are no tables to show the aquatic risk assessment for the metabolites.	Noted. The LoEP was amended

Ecotoxicology			
No.	**Reference** (e.g. conclusion text, list of endpoints, evaluation table etc)	**Member State comment**	**EFSA response to comment**
	aquatic organisms		
30	Effects on other arthropod species	UK: The UK evaluator agrees with the comment box included by EFSA regarding the worst case application rate as 2 x 2160 g a.s/ha for the risk assessment for non target arthropods. The UK made a comment at the expert meeting regarding this as it is unclear why an application to orchards of 3 x 1440 g a.s/ha, taking account of the 0.5% reduction (28 day interval) was not assessed. The application rate assessed does appear to be worst case but it needs to be explained as to why this is the case.	Noted The use pattern of 2 x 2160 g represents the worst case for exposure estimations (in-field and off field rate
31	Effects on earthworms, other soil macro-organisms and soil micro-organisms	UK: The acute earthworm endpoint for the a.s is stated as an LC_{50} of 5770 mg/kg d.w soil in the LOEP table. In the RAR this is stated as 5600 mg/kg d.w soil. This is therefore not consistent with the TER of 846 stated in the toxicity/exposure ratios table which has been calculated using the correct endpoint of 5600 mg/kg d.w soil.	Noted. The LoEP was amended
32	Effects on earthworms, other soil macro-organisms and soil micro-organisms	UK: For soil micro organisms the study results for the effect of the a.s on carbon mineralisation are stated as: '9.3% effect at day 28 at 6.4 mg /kg d.w.soil (4.8kg /ha)' This results is from a study by Franco Perina, 2000. In the RAR a study submitted for the EU review of glyphosate (2002) is also referenced in which no effects up to 28.8 mg a.s/kg d.w soil were observed for carbon mineralisation. Why wasnt this endpoint stated in the LOEP table?	Noted Only the most relevant endpoints on carbon mineralisation and nitrogen transformation were included in the LoEP.
33	Effects on earthworms, other soil macro-organisms and soil micro-organisms	UK: For soil micro organisms, the effect of the a.s (code name MON 77973) to nitrogen mineralisation (Hutcheson, K 2014) is stated as a 6% effect after 28 days at 33.1 mg	The 2.13% effect was observed at 14-28 days. The relevant percentage of effects observed at 28 days was 5.73% (reported in the LoEP as

Ecotoxicology			
No.	**Reference** (e.g. conclusion text, list of endpoints, evaluation table etc)	**Member State comment**	**EFSA response to comment**
		a.e/kg d.w soil. The study summary states a 2.13% effect for the transformation rate.	6%). No changes are needed.
34	Effects on biological methods for sewage treatment	UK: The EC_{50} in the LOEP table is stated as >1000 mg/L. In the RAR the EC_{50} is stated as >100 mg/L.	Noted The LoEP was corrected
35	5. Ecotoxicology	UK: For endocrine disruption it is concluded: 'On the basis of the available data in the area of ecotoxicology, there was no indication of endocrine disrupting adverse effects.' It should note that there are currently no defined criteria for identifying endocrine disruptors or interpreting the significance of any affects in these or similar studies under 1107/2009. As a result of this, it can not be concluded whether endocrine disruptive effects are/are not taking place.	It the Conclusion the following was concluded: 'On the basis of the available data in the area of ecotoxicology, there was no indication of endocrine disrupting adverse effects. However, pending on the outcome of the data gaps identified in section 2, further ecotoxicology data may be needed'. No further changes were considered needed.
36	Conclusions of the evaluation, 5 Ecotoxicology, terrestrial non-target plants	NL: In case of the application 'Orchard crops, vines including citrus & tree nuts, Intrarow & Spot treatments' the RMS calculates the TER with 50% of the application rate. NL can agree with that in case of e.g. chronic risk to birds and mammals (not in case of the acute risk assessment!!), but considers this not acceptable for non-target plants. Plants which are standing next to the row or spot where the application is made with the full dose, get the full off-crop dose and are affected by this dose. Hence, NL is of the opinion that the full dose rate should be used for TER calculation.	The maximum cumulative application rate of 4.32 kg a.s./ha was divided by 2 for the uses in orchards to account of the amount per cropped area, due to the application intra-rows. Therefore, all the risk assessments for orchards were performed by considering the actual dose per cropped area (i.e. half of the total amount) This was clearly reported in the LoEP and in the GAP table. The Conclusion was not changed.

Ecotoxicology			
No.	**Reference** (e.g. conclusion text, list of endpoints, evaluation table etc)	**Member State comment**	**EFSA response to comment**
37	General	NL: Why the List of Endpoints is not added to the EFSA conclusion?	For technical reasons the documents are kept separately and will be merged once the EFSA conclusion is final and ready for adoption.

Other			
No.	**Reference** (e.g. conclusion text, list of endpoints, evaluation table etc)	**Member State comment**	**EFSA response to comment**
38		DE: No comment.	Noted

Member States' comments on the draft EFSA Conclusion on glyphosate – updated mammalian toxicology section (RMS: DE) (20.10.2015) 1/5

Pesticides Peer Review Written Procedure: October 2015

Background			
No.	**Reference** (e.g. conclusion text, list of endpoints, evaluation table etc.)	**Member State comment**	**EFSA response to comment**
1	p. 26, section 9.3, header row of table	COM: Thank you for amending the header row of the table in response to the earlier comments, however for the first two representative uses, there has been a misunderstanding, since the headers still do not unambiguously identify the different representative uses. Please consider using "All seeded or transplanted crops – Pre-planting" for the first column, and "All seeded crops – Post-planting/pre-emergence" for the second column, as these terms are also used in other sections of the draft Conclusion and notably in the GAP table.	Apologies for the misunderstanding, the document has been amended.
2	EFSA Conclusion	NL: For this (updated) version of the EFSA Conclusion, we are only commenting on the mammalian toxicology section.	Noted.
3	EFSA Conclusion	UK: For this (updated) version of the EFSA Conclusion, we are only commenting on the carcinogenicity issue.	Noted.

Mammalian toxicity			
No.	**Reference** (e.g. conclusion text, list of endpoints, evaluation table etc.)	**Member State comment**	**EFSA response to comment**
1	**EFSA Conclusion text** Mammalian toxicity, page 11	DK has a comment regarding the sentence: "No evidence of carcinogenicity was confirmed by the majority of the experts in either rats or mice due to a lack of statistical significance in pair-wise comparison tests, lack of consistency in multiple animal studies at dose levels at or above the limit dose/MTD, lack of pre-neoplastic lesions and/or being within historical control range." The lack of statistical significance in pair-wise comparison tests should not be listed explicitly in the text since positive results of the trend analysis were also considered when assessing the carcinogenic potential of glyphosate. It was particularly emphasized during the expert meeting that the overall conclusion was based not only on statistical significance alone, regardless of the statistical analysis used (pair-wise comparison or trend analysis), but rather on the overall weight of evidence considering lack of biological plausibility, consistency in animal studies, levels of doses tested and statistical significance. We suggest the following: "No evidence of carcinogenicity was confirmed by the majority of the experts in either rats or mice. The experts based this on the overall weight of evidence considering a lack of biological plausibility, i.e. lack	Partially (dis)agreed. It is important to mention the different statistical methods considered, such as the lack of statistical significance in a pair-wise comparison. As mentioned during the teleconference, statistical analysis should primarily be performed according to the protocol of the study agreed before initiating a study. Furthermore, the statistical analysis is part of the overall weight of evidence. However it is agreed to add a sentence to mention the results obtained in a trend analysis.

Mammalian toxicity			
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		of pre-neoplastic findings, lack of consistency in animal studies, findings being within the historical control range, findings at or above the limit dose/MTD level. The statistical significance in trend analysis (but not in pair-wise comparison) *per se* was balanced against the former consideration.	
2	Carcinogenicity	NL: No comments. The EFSA conclusion properly reflects the discussions in the TC 117.	Noted.
3	EFSA Conclusion and LOEP.	UK: We agree with the revised conclusions on carcinogenicity. The additional text in the EFSA conclusion on the carcinogenicity discussions is clear and concise, and accurately reflects the agreed minutes of the TC117.	Noted.
4		FR: No comment.	Noted.
5	Conclusions of the evaluation, 2. Mammalian toxicity, Page 11, 3rd paragraph, last sentence	DE: It is proposed that the sentence: "*No evidence of carcinogenicity was confirmed by the majority of the experts in either rats or mice due to a lack of statistical significance in pair-wise comparison tests, lack of consistency in multiple animal studies at dose levels at or above the limit dose/MTD, lack of pre-neoplastic lesions and/or being within historical control range.*" is modified to: "*No evidence of carcinogenicity was confirmed by the majority of the experts* ***(with the exception of one minority view)*** *in either*	Agreed, the text has been revised accordingly.

Mammalian toxicity			
No.	**Reference** (e.g. conclusion text, list of endpoints, evaluation table etc.)	**Member State comment**	**EFSA response to comment**
		rats or mice due to a lack of statistical significance in pair-wise comparison tests, lack of consistency in multiple animal studies ***and slightly increased incidences only*** *at dose levels at or above the limit dose/MTD, lack of pre-neoplastic lesions and/or being within historical control range.*"	
6	Conclusions of the evaluation, 2. Mammalian toxicity, Pages 10 and 11	DE: With regard to both animal studies (in particular lymphoma in mice) and epidemiological studies, it is stated that a (large) majority of experts concluded that there was no carcinogenic risk to humans. For transparency reasons it might be useful to explain the minority views a bit more in detail.	Agreed, this has been done taking into consideration the comments made by the respective MSs comments (see comments 5, 7, 11 and 12 in this chapter)
7	Conclusions of the evaluation, 2. Mammalian toxicity, Page 11, 3rd paragraph	DE: For a more detailed description and for transparency reasons the following two sentences should be added: "*During the teleconference 117, the experts also agreed to the conclusion of the RMS, that for the active substance glyphosate no classification for mutagenicity is warranted. However, there were two minority views, that a Comet assays should be requested for confirmation.*"	Agreed, the text has been added (see also comment 12 below).
8	List of studies to be generated, still ongoing or available but not peer reviewed Page 24, 2nd point	DE: It is proposed that the 2nd point: "*Relevance of all individual impurities present in the technical specification (except the two already known relevant ones), […]*" is modified to: "***For technical test materials which do not meet the proposed specification,*** *relevance of all*	Disagreed, the relevance of all individual impurities has to be addressed, even the ones that were tested (in some studies) at the levels reported in the batches used in toxicological studies. Nevertheless it is acknowledged that

Mammalian toxicity			
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		individual impurities present in the technical specification (except the two already known relevant ones) […]'	this data gap is more critical for the technical specifications that do not meet the newly proposed reference specification.
9	Conclusions of the evaluation, 2. Mammalian toxicity, Page 11, 2nd paragraph	DE: It should be clearly stated that with respect to positive results (*in vivo* and *in vitro*) for different formulations supplementary data/information on the genotoxicity of the products should be required for product authorisation. In order to get a legal basis for these data requirements on formulated products a general discussion at European level should be initiated.	Agreed, a sentence has been added.
10	2. Mammalian toxicity	ES: We are in agreement with EFSA conclusion that glyphosate is unlikely to pose a carcinogenic hazard to humans and the evidence does not support classification with regard to its carcinogenic potential according to CLP Regulation. This was also the view of the majority of the EU peer review experts in contrast to the IARC evaluation.	Noted.
11	Yellow highlighted text reflecting TC117 of 29 Sept 2015.	SE: No comments. The text reflects our deviating view that the CLP criteria for limited evidence of cancer in humans are fulfilled.	Noted, thank you. Nevertheless, more details have been added regarding minority views as requested by other MSs, including the RMS.
12	EFSA Conclusion	NO: According to minutes of the TC117 there are two minority views that considered that further studies should be requested (Comet assay). This is not reflected in the conclusion regarding the genotoxicity of glyphosate.	Agreed, this has been added in the text (see also comment 7 above).