REPORT OF PESTICIDE PEER REVIEW TC 80

GLYPHOSATE – AIR V
Rapporteur Member State: Assessment Group on Glyphosate (AGG) consisting of FR, HU, NL, SE

2. Mammalian toxicity

Date: 25 November 2022

List of participants:

Institute	**Member States Country code**
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Federal Institute for Risk Assessment (BfR)	DE
Ministry of Environment and Food of Denmark, Environmental Protection Agency	DK
TRAGSATEC	ES
Ministerio de Sanidad	ES
Finnish Safety and Chemicals Agency (Tukes)	FI
Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail (ANSES)	FR
National Food Chain Safety Office (NEBIH)	HU
Pesticide Control Division, Department of Agriculture, Fisheries & Food	IE
Board for the Authorisation of Plant Protection Products and Biocides (Ctgb)	NL
Eko-Futura Sp. Z o.o. , an external unit of The Ministry of Agriculture and Rural Development	PL
Swedish Chemicals Agency (KemI)	SE
National Institute of Public Health	SI
External experts (11)	EFSA

Institute	Member States Country code
Observer	CH

In accordance with EFSA's Policy on Independence[1] and the Decision of the Executive Director on Competing Interest Management[2,] EFSA screened the Annual Declarations of Interest filled out by the participants invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process, and no interests were declared orally by the members at the beginning of this meeting.

[1] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf
[2] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf

Discussion points/Outcome

2. Mammalian toxicity

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Minutes might be revised due to pending data gaps at the time of the meeting and /or eventual need for further follow up consultation after the meeting. If needed, the final agreement will be made available in the meeting report published at the end of the peer review process.

Subject	Conclusions Pesticide Peer Review Meeting
Experts' consultation 2.1 Experts to discuss the **absorption, distribution, metabolism and excretion** of glyphosate acid in mammals and to agree on an overall oral absorption value. Toxicokinetic behaviour and **potential accumulation** of glyphosate in bone matrix should also be discussed.	The oral absorption value is 20% as proposed during the previous renewal assessment (EFSA, 2015[3]). The highest levels of glyphosate acid were measured in bone, followed by kidney and liver. There was no evidence of a potential for accumulation in animal tissues. **Open point**: RMS to provide a revised RAR reporting the agreement of the meeting.
Experts' consultation 2.2 Experts to discuss and agree on the overall no observed adverse effect levels (NOAELs) for **short-term toxicity studies** conducted in dogs, rats and mice.	The relevant short-term oral **NOAEL** in **rats is 79 mg/kg bw per day** derived from a 90-day repeated dose study (Report No. 434/016) and based on effects of caecum (i.e. mucosal atrophy) and increased alkaline phosphatase (ALP) reported at the lowest observable adverse effect level (**LOAEL**) of **730 mg/kg bw per day**. This NOAEL also covers for other critical effects observed at higher doses, i.e., soft stool, diarrhoea, reduction in body weight gain and food consumption, and liver effects (increased weight, changes in blood chemistry).

[3] EFSA (European Food Safety Authority), 2015. Conclusion on the peer review of the pesticide risk assessment of the active substance glyphosate. EFSA Journal 2015; 13(11):4302, 107 pp. doi:10.2903/j.efsa.2015.4302.

Subject	Conclusions Pesticide Peer Review Meeting
For findings on **salivary glands**, see also experts' consultation 2.15.	The relevant short-term oral **NOAEL** in **mice** is **1221 mg/kg bw per day** derived from a 90-day repeated study (Report No. IET 94-0136) based on decreased food consumption, liver effects (blood chemistry), caecum (distension not accompanied by histopathological changes), and increased incidence of cystitis in the urinary bladder reported at the **LOAEL** of **6295 mg/kg bw per day**. The relevant short-term oral **NOAEL** in **dog** is **53 mg/kg bw per day** derived from a 90-day repeated toxicity study (Report No. 1816) and based on decreased food consumption, increased gamma-glutamyl transferase (GGT), increased ALP and bilirubin at the **LOAEL of 252/253 mg/kg bw per day**. The relevant short-term **dermal NOAEL** in **rat** (systemic) is **1000 mg/kg bw per day** derived from 21-day studies (Report No. CTL/P/4985 and Report No. 7839). A LOAEL for local effects of 1000 mg/kg bw per day was derived from a 21-day study and based on the mild skin irritation observed at the only dose tested. The relevant short-term **dermal NOAEL** in **rabbit** (systemic) is **2000 mg/kg bw per day** derived from 28-day studies (Report No. CTL/P/4985 and Report No. 7839). A NOAEL of 1000 mg/kg bw per day is set for local effects. **Open point:** RMS to correct the value on the increased bilirubin observed in male dogs in Table 6.3.26-5 (Report No. 1816).
Experts' consultation 2.3 Experts to discuss the impact of the following **deviations** for **genotoxicity studies** on glyphosate (major vs minor deviation): • Absence of metabolic activation in *in vitro* genotoxicity studies, given	The experts agreed that the absence of metabolic activation in *in vitro* genotoxicity studies, given the limited metabolism of glyphosate, is a minor deviation. The experts agreed that a lack of positive control data alone, where positive results are obtained, would not lead to a score of 3 "reliability insufficient or unreliable" (using the Klimisch score). The experts agreed that the lack of historical control data (HCD) alone, provided positive results are observed, would not lead to a reliability

Subject	Conclusions Pesticide Peer Review Meeting
the limited metabolism of glyphosate. • Lack of positive control data where positive results are observed. • Lack of historical control data, provided that the study includes proper concurrent negative control data without high variability.	score of 3 "reliability insufficient or unreliable" (using the Klimisch score).
Experts' consultation 2.4 Experts to discuss the outcome of the RMS' assessment of the data submitted following the data requirements set in the genotoxicity section of the reporting tables (Member States and Public) also taking into account the outcome of the ECHA RAC committee assessment.	This experts' consultation point has been discussed under **Experts' consultation 2.2, 2.3, 2.4 identified following comments by public** (see further down in this report).
Experts' consultation 2.5 Experts to discuss the reliability and relevance of the bacterial gene mutation assay CA 5.4.1/012; Report no. RL3393/2007-2.0AM-B (2007).	This experts' consultation point has been discussed under **Experts' consultation 2.2 identified following comments by public** (see further down in this report).
Experts' consultation 2.6 Experts to discuss the reliability and relevance of the bacterial gene mutation assay	This experts' consultation point has been discussed under **Experts' consultation 2.2 identified following comments by public** (see further down in this report).

Subject	Conclusions Pesticide Peer Review Meeting
CA 5.4.1/015; Report no. IET 94-0142 (1995).	
Experts' consultation 2.7 Experts to discuss the reliability and relevance of the bacterial gene mutation assay CA 5.4.1/018; Report no. 887-MUT.AMES (1993).	This experts' consultation point has been discussed under **Experts' consultation 2.2 identified following comments by public** (see further down in this report).
Experts' consultation 2.8 Experts to discuss the reliability and relevance of the *in vitro* chromosome aberration (CA) test (1998) CA 5.4.1/025.	This experts' consultation point has been discussed under **Experts' consultation 2.3 identified following comments by public** (see further down in this report).
Experts' consultation 2.9 Experts to discuss the reliability and relevance of the *in vitro* CA test, 1996, CA 5.4.1/026.	This experts' consultation point has been discussed under **Experts' consultation 2.3 identified following comments by public** (see further down in this report).
Experts' consultation 2.10 Experts to discuss the reliability and relevance of the *in vitro* CA test, 1995, CA 5.4.1/027.	This experts' consultation point has been discussed under **Experts' consultation 2.3 identified following comments by public** (see further down in this report).
Experts' consultation 2.11 Experts to discuss the reliability and relevance of the *in vitro* CA test, 1995, CA	This experts' consultation point has been discussed under **Experts' consultation 2.3 identified following comments by public** (see further down in this report).

Subject	Conclusions Pesticide Peer Review Meeting
5.4.1/028 (Report No. 141918).	
Experts' consultation 2.12 The reliability and relevance of the *in vitro* micronucleus (MN) test by Roustan, A. et al, 2014[4] to be discussed by the experts.	This experts' consultation point has been discussed under **Experts' consultation 2.3 identified following comments by public** (see further down in this report).
Experts' consultation 2.13 MSs experts to discuss the NOAEL from the 2-year rat study 2 (Report No. CTL/PR1111, 2001) in an experts' meeting.	The **NOAEL** of the **2-year rat** study 2 (Report No. CTL/PR1111) is 121 mg/kg bw per day, based on decreased adrenal weight in females and increased ALP (>50% compared with controls) observed at 361 mg/kg bw per day.
Experts' consultation 2.14 MSs experts to discuss the NOAEL of the 2-year rat study 5 (Report No. 886.C.C-R, 1996) in an experts' meeting.	The **NOAEL** of the **2-year rat** study 5 (Report No. 886.C.C-R) is 59.4 mg/kg bw per day, based on increased incidence of liver lesions (small livers, focal haemorrhage, small cyst and a pale and mottled appearance), lung lesions (increased incidence of emphysema, collapse, petechiae, ecchymoses), cataracts and increased ALP observed at 595.2 mg/kg bw per day. **Open point** The RMS is kindly asked to revise the RAR based on the outcome of the discussion.
Experts' consultation 2.15 MSs experts to discuss the relevance of the **salivary gland findings** observed in	The experts concluded that the salivary gland effects are likely to be a local effect. It was agreed to apply a margin of safety (MOS) approach based on a local effect. To this aim the local LOAEL of 100 mg/kg bw per day derived from the 2-year rat study 7 (Report No. 7867 from 1993) was compared with the acceptable daily intake (ADI) of 0.5 mg/kg bw per day, resulting in a MOS of 200. This margin was

[4] Roustan A, Aye M, De Meo M, Di Giorgio C. Genotoxicity of mixtures of glyphosate and atrazine and their environmental transformation products before and after photoactivation. Chemosphere. 2014 Aug;108:93-100. doi: 10.1016/j.chemosphere.2014.02.079. Epub 2014 Apr 12. PMID: 24875917

Subject	Conclusions Pesticide Peer Review Meeting
- Oral 90-day toxicity study in rats – study 6, Report No. 7136,1991; p. 106; - Oral 90-day toxicity in mice – study 1, Report No. IET 94-0136, 1995; p. 133; - 1-year rat study 6 (Report No. CTL/P/5143, 1996, p. 61); - 2-year rat study 7 (Report No. 7867, 1993, p. 84-85); - Parental toxicity in the 2-generation reproductive toxicity study in rat Report No. CHV 47/911129, 1992: p. 73 And referencing: - 8-week oral rat study of citric acid (B.6.8.2.2, Report No. WIL-50361, 2010, p. 326) in an experts' meeting.	considered sufficiently protective for local effects of glyphosate upon exposure at the ADI level. Overall, the experts concluded that the salivary gland effects are not relevant to derive toxicological reference values.
Experts' consultation 2.16 MSs experts to discuss the reliability of the **18-month mouse study** 2 (Report No. Toxi: 1559.CARC-M, 2001, p. 111-121) in an experts' meeting.	In the **18-month mouse** study 2 (Report No. Toxi: 1559.CARC-M), the NOAEL is revised at 149.7 mg/kg bw per day based on increased mortality and the increased incidence of stomach cysts at the top dose level of 1454 mg/kg bw per day. The study was assessed as reliable with restrictions. **Open point** RMS to include in the RAR more information regarding the distribution of ecto/endoparasites among controls and treated groups. **Open point** The RMS is kindly asked to revise the RAR based on the outcome of the discussion.

Subject	Conclusions Pesticide Peer Review Meeting
Experts' consultation 2.17 MSs experts to discuss the potential for glyphosate to induce **oxidative stress** in an experts' meeting.	Glyphosate may induce oxidative stress, but increased oxidative stress was not consistently demonstrated in the available studies. Regarding epidemiological studies investigating oxidative stress endpoints, it was agreed that no conclusion can be drawn on the possible relationship between glyphosate exposure and changes in oxidative stress parameters on the basis of the limited database and outcome from human observational studies available. Overall, no clear conclusion can be reached. **Open point** New studies identified after the public consultation period (see experts' consultation 2.37) to be considered by the RMS in a revised RAR: • Robin Mesnage, Mariam Ibragim, Daniele Mandrioli, Laura Falcioni, Eva Tibaldi, Fiorella Belpoggi, Inger Brandsma, Emma Bourne, Emanuel Savage, Charles A Mein, Michael N Antoniou, Comparative Toxicogenomics of Glyphosate and Roundup Herbicides by Mammalian Stem Cell-Based Genotoxicity Assays and Molecular Profiling in Sprague-Dawley Rats, Toxicological Sciences, Volume 186, Issue 1, March 2022, Pages 83–101, https://doi.org/10.1093/toxsci/kfab143 **Open point** RMS to consider three epidemiological studies investigating oxidative stress in a revised RAR (new studies identified after the public consultation period, see experts' consultation 2.37): • Makris et al. 2022: Oxidative stress of glyphosate, AMPA and metabolites of pyrethroids and chlorpyrifos pesticides among primary school children in Cyprus. Environ Res 212, 113316. doi: 10.1016/j.envres.2022.113316. • Eaton et al. 2022: The association between urinary glyphosate and aminomethyl phosphonic acid with biomarkers of oxidative stress among pregnant women in the PROTECT birth cohort study. Ecotoxicology and Environmental Safety, 233, 113300. doi: 10.1016/j.ecoenv.2022.113300.

Subject	Conclusions Pesticide Peer Review Meeting
	• Sidthilaw et al. 2022: Effects of exposure to glyphosate on oxidative stress, inflammation, and lung function in maize farmers, Northern Thailand. BMC Public Health, 22, 1343. doi: 10.1186/s12889-022-13696-7.
Experts' consultation 2.18 MSs experts to discuss the NOAEL of the **2-year rat** study 8 (Report No. MSL-10495, 1990) in an experts' meeting.	The **NOAEL** of the 2-year rat study 8 (Report No. MSL-10495) is 89 mg/kg bw per day based on stomach mucosal irritation observed at higher dose levels (362 mg/kg bw per day and higher).
Experts' consultation 2.19 MSs experts to discuss the weight of evidence on the relationship between glyphosate exposure and risk of lymphohematopoietic cancer (LHC), including non-Hodgkin's lymphoma (NHL), Hodgkin's lymphoma (and other subtypes), multiple myeloma (MM), and leukemia from **epidemiological studies** and the outcome of the newly reported studies in an experts' meeting. Also taking into account the outcome of the ECHA RAC meeting and their opinion on classification.	The available epidemiological studies currently do not provide sufficient indication that glyphosate exposure is associated with any cancer-related health effect. **Open point** RMS to consider in a revised RAR the study by De Roos et al. 2022 identified after the public consultation period (see experts' consultation 2.37): Herbicide use in farming and other jobs in relation to non-Hodgkin's lymphoma (NHL) risk. Occupational and Environmental Medicine, 79(12), 795-806.
Experts' consultation 2.20 MS experts to discuss the **relevance and reliability** of all the available studies (both	All the experts agreed with the RMS on the **relevance and reliability** of all the available studies included in the revised RAR. These include both regulatory studies as well as the studies from the open literature including the parameters assessed and used in the weight of evidence for reproductive and developmental toxicity assessment. The experts

Subject	Conclusions Pesticide Peer Review Meeting
regulatory and from literature) and assessed parameters for their use in the weight of evidence for **reproductive and developmental toxicity assessment**. Also taking into account the outcome of the ECHA RAC meeting and their opinion on classification.	also agreed on the inclusion of the considerations made by the ECHA Risk Assessment Committee (RAC) meeting and of their opinion on the inclusion of this evidence for classification[5].
Experts' consultation 2.21 MS experts to discuss the human relevance and use of rabbit in the **developmental toxicity** assessment of glyphosate.	The **human relevance** of the effects observed in the rabbit developmental toxicity studies could not be dismissed for the derivation of the reference values for human risk assessment. An **overall rabbit developmental NOAEL** was set at 150 mg/kg per day based on increased incidence of post-implantation loss at 450 mg/kg bw per day and reduced foetal weight at 300 mg/kg bw per day in the study Report No. CHV 45 & 39 & 40/901303 (1991). An **overall rabbit maternal NOAEL** was set at 50 mg/kg bw per day based on reduced body weight gain (gestation day (GD) 7-19) by 24-29% in dams administered 200 mg/kg bw per day. Since gastrointestinal irritation is observed in several species, also following administration via diet, it is appropriate to set an acute reference dose (ARfD) based on a NOAEL for the most sensitive species. Using the developmental NOAEL set at 150 mg/kg bw per day in the rabbit developmental toxicity study (Report No. CHV 45 & 39 & 40/901303) as point of departure and a standard uncertainty factor of 100, results in an ARfD of 1.5 mg/kg bw which would also protect from the post-implantation loss observed in rabbits. All experts agreed that the rabbit developmental toxicity study (Report No. 434/020) is considered as supplementary information only because of the excessive mortality observed at the high dose, compromising the dose-response analysis. **Open point**

[5] ECHA RAC, 2022. Committee for Risk Assessment (RAC) Opinion proposing harmonised classification and labelling at EU level of glyphosate (ISO); N-(phosphonomethyl)glycine. Adopted on 30 May 2022.

Subject	Conclusions Pesticide Peer Review Meeting
	RMS to revise the reliability of the rabbit developmental toxicity study (Report No. 434/020) in a revised RAR.
Experts' consultation 2.22 MS experts to agree on values for **NOAEL/LOAEL reproductive** in the reproductive toxicity studies and agree on the overall NOAEL/LOAEL reproductive considering all comments/concerns raised during the commenting period. Reference is made to the following comments: - MS experts to discuss the reduced number of homogenisation resistant spermatid in cauda epididymis observed in F0 for the reproductive toxicity study B.6.6.1/01 (Report number 2060/0013). - MS experts to discuss the findings of increased large follicles and increased number of animals with irregular cycle observed in the reproductive toxicity study B.6.6.1/01 (2060/0013). - MS experts to discuss the toxicological significance of the ano-genital distance (AGD) values normalised to the cube root of pup weight	**Overall reproductive NOAEL** is 351 mg/kg bw per day, based on decrease in homogenisation resistant spermatid count in F0 males observed at limit dose in Report No. 2060/0013. **Overall NOAEL** for **offspring toxicity** is 293 mg/kg bw per day, based on reduced body weight observed at 985 mg/kg bw per day in Report No. CTL/P/6332. **Overall NOAEL/LOAEL** for **parental toxicity** is 417 mg/kg bw per day, based on increased liver and kidney weights at 2151 mg/kg bw per day observed in study Report No. IET 96-0031. **Open point** RMS to provide a revised RAR reporting the agreement of the meeting.

Subject	Conclusions Pesticide Peer Review Meeting
for the study B.6.6.1/001 (2060/0013). - MS experts to discuss the limitations of oestrus cyclicity assessments conducted in reproductive toxicity studies. MS experts to agree on values for **NOAEL/LOAEL offspring** in the reproductive toxicity studies and agree on the overall NOAEL/LOAEL offspring considering all comments/concerns raised during the commenting period. Reference is made to the following comments: - MS experts to discuss the setting of NOAEL offspring based on delayed preputial separation observed in F1 offspring for the reproductive toxicity study B.6.6.1/01 (2060/0013). - MS experts to discuss the setting of NOAEL offspring based on reduction in pup body weight observed in the reproductive toxicity studies. MS experts to agree on values for **NOAEL/LOAEL parental** in the reproductive toxicity studies and agree on the overall NOAEL/LOAEL parental considering all comments/concerns raised	

Subject	Conclusions Pesticide Peer Review Meeting
during the commenting period. See expert consultation 2.29 regarding the endocrine disruption (ED) assessment of glyphosate.	
Experts' consultation 2.23 MS experts to discuss the endocrine disruption (**ED**) **potential** of the active substance glyphosate and the toxicological relevance of the effects on estrus cyclicity.	*Please refer to the Pesticide Peer Review TC 84 Mammalian toxicology – Ecotoxicology joint ED session (1-2 December 2022)*
Experts' consultation 2.24 Experts to discuss **the relevance and reliability** of the available historical control data for **developmental toxicity** parameters and the impact on the assessment of developmental toxicity effects.	All experts agreed that historical control data (HCD) are correctly reported and contextualized in the revised RAR and there is no remaining concern.
Experts' consultation 2.25 Experts to discuss the **setting of maternal and developmental NOAEL/LOAEL** values in the rat developmental toxicity studies.	In the **rat developmental toxicity studies**, - the **overall maternal NOAEL** is 300 mg/kg bw per day based on the findings in study Report No. CHV 43 & 41/90716 (clinical signs, reduced bodyweight gain in dams) and Report No. IET 94-0152 (clinical signs) at 1000 mg/kg bw per day; - the **overall developmental NOAEL** is 300 mg/kg bw per day based on the findings in study Report No. CHV 43 & 41/90716 (reduced ossification, skeletal variations in foetuses) at 1000 mg/kg bw per day.

Subject	Conclusions Pesticide Peer Review Meeting
	Open point RMS to provide a revised assessment of the study Report No. CHV 43 & 41/90716 considering the body weight gain (BWG) change between gestation day (GD) 6 and GD 20.
Experts' consultation 2.26 Experts to discuss the assessment of the retro-oesophageal right subclavian artery also in the context of a **non-monotonic dose-response** (NMDR) effect.	The retro-oesophageal right subclavian artery finding is not treatment related and not consequent to a non-monotonic dose-response (NMDR).
Experts' consultation 2.27 Experts to discuss in an experts' meeting the **neurotoxic potential** of glyphosate by taking carefully into consideration all the available evidence from the applicants, literature and epidemiological studies in a weight of evidence approach. Particular consideration should be given to the discussion of the: • systemic NOAEL of the 90-day neurotoxicity study in rats Report No. 2060-0010, 2006; • possible effect of glyphosate on the concentrations of several neurotransmitters in various regions of the brain in rodents and relevance of the findings;	1) The NOAEL for systemic toxicity is 395 mg/kg bw per day in males, based on reduced body weight gain and food consumption in the 90-day neurotoxicity study in rat (Report No. 2060-0010); in the absence of neurotoxicity findings, the NOAEL for sub-chronic neurotoxicity is confirmed to be ≥ 1499 mg/kg bw per day in males. This is in line with the conclusion reached in Report No. CTL/P/4867 (additional 90-day neurotoxicity study in rats). 2) There is no sufficient evidence of an effect of glyphosate active substance and/or glyphosate-based herbicides (GBH) on neurotransmitters. 3) Limited data are available from *in vitro* and *in vivo* studies regarding the potential relationship between exposure to glyphosate and parkinsonism/Parkinson's disease; the integration of the epidemiological studies with the experimental evidence is not triggering a concern for parkinsonism. No relevant indication of neurodegenerative changes in the pivotal neurotoxicity studies conducted up to 1499 mg/kg bw per day was observed. 4) There is no sufficient evidence on the association between glyphosate exposure and autism spectrum disorder (ASD). 5) There is no sufficient evidence on the association between glyphosate exposure and amyotrophic lateral sclerosis (ALS); no relevant indication of neurodegenerative changes in the pivotal

Subject	Conclusions Pesticide Peer Review Meeting
• the possible relationship between long-term exposure to glyphosate and developing chronic and neurodegenerative diseases such as Parkinson's disease by taking into consideration all the available evidence and epidemiological studies; • potential relationship between autism spectrum disorder and exposure to glyphosate by taking into consideration all the available evidence and epidemiological studies; • potential relationship between amyotrophic lateral sclerosis and exposure to glyphosate by taking into consideration all the available evidence and epidemiological studies.	neurotoxicity studies conducted up to 1499 mg/kg bw per day was observed. 6) Developmental Neurotoxicity (DNT). A specific DNT study on glyphosate acid is not available. Some non-guideline studies on glyphosate and glyphosate-based herbicide (GBH) formulations indicated isolated DNT findings only observed with the GBH. It was noted that in a guideline DNT study, performed with the glyphosate trimesium, positive effects were reported. Overall (considering that glyphosate trimesium is not representing glyphosate from the qualitative toxicological profile perspective), based on the available data on glyphosate acid and GBH and on the fact that it is not possible to identify a pattern of effects suggesting DNT liabilities for glyphosate acid using the available dataset, it is considered that the current toxicological reference values (TRVs) are protective. The residual uncertainties (coming from the studies performed with GBH) are considered of having no impact on the TRVs. However, a data gap can be identified to further refine the toxicological profile and assessment of glyphosate acid for DNT endpoints. **Open point** RMS to include in the revised RAR an assessment of the following studies on DNT potential for glyphosate, identified after the public consultation (see experts' consultation 2.37): • Glyphosate Trimesium. Study type: developmental neurotoxicity study - rat; MRID 45539801 [6] • Luna et al., 2021: Glyphosate exposure induces synaptic impairment in hippocampal neurons and cognitive deficits in developing rats. Arch Toxicol 95(6):2137-2150 • Del Castilo et al. 2022: Lifelong exposure to a low-dose of the glyphosate-based herbicide RoundUp causes intestinal damage, gut dysbiosis, and behavioural changes in mice. Int J Mol Sci, 23(10):5583. • Ojiro et al., 2023: Comparison of the effect of glyphosate and glyphosate-based herbicide on hippocampal neurogenesis after developmental exposure in rats. Toxicol 483:153369

[6] U.S. EPA: Data evaluation Record. Glyphosate Trimesium. Study type: developmental neurotoxicity study - rat; MRID 45539801. 2005. Accessed from: https://www.regulations.gov/document/EPA-HQ-OPP-2016-0093-0183

Subject	Conclusions Pesticide Peer Review Meeting
	• US EPA ToxCast/Tox21 Dashboard[7] **Open point** RMS to include in the revised RAR an assessment of the following studies on neurotoxic potential for glyphosate, identified after the public consultation (see experts' consultation 2.37): • Moser et al., 2022: Glyphosate and neurological outcomes: a systematic literature review of animal studies. J Toxicol Environ Health, part B, 25(4):162-209. • Winstone et al., 2022: Glyphosate infiltrates the brain and increases pro-inflammatory cytokine TNFα: implications for neurodegenerative disorders. J of inflammation, 19:193.
Experts' consultation 2.28 Experts to discuss the relevance of inappropriate **immunostimulation findings** and the impact of this on the overall risk assessment (including a potential definition of a NOAEL).	No evidence of immunosuppression was reported in the available immunotoxicity study (Report No. WIL-50393) which is designed to investigate a suppression of the humoral immune response and no conclusions can be drawn on the toxicological relevance of the apparent increase in Total Spleen Activity IgM/potential immunostimulation by glyphosate. Based on this study, the agreed NOAEL is 1448 mg/kg bw per day (highest dose tested). **Open point** RMS to correct the measures used to assess the variability in the results from the study Report No. WIL-50393 in Table B.6.8.2.1-3 (to be presented as mean +/- standard error of the mean (SEM)).
Experts' consultation 2.29 Experts to discuss • The relevance and reliability of the available studies (both regulatory and from literature) and assessed parameters for their use in the weight of	*Please refer to the Pesticide Peer Review TC 84 Mammalian toxicology – Ecotoxicology joint ED session (1-2 December 2022)*

[7] Available at this link: https://comptox.epa.gov/dashboard/chemical/invitrodb/DTXSID1024122 [accessed in November 2022].

Subject	Conclusions Pesticide Peer Review Meeting
evidence for **ED assessment**; • The information that can be derived from the available studies based on: tested item, test system (including species, where necessary), study design and parameters assessed; • The weight of evidence for ED leading to the overall conclusion on whether the criteria as laid down in point 3.6.5 of Annex II to Regulation 1107/2009 are met.	
Experts' consultation 2.30 Experts to discuss the weight-of-evidence assessment of the available data regarding - the potential effect of glyphosate on the **gut microbiota** (in animals and humans) and possible consequences; - the potential impact of glyphosate on the health of **livestock** and **pet** animals. (it should be considered if this assessment would change the previous EFSA assessment of the impact of glyphosate on animal health (https://www.efsa.europa.eu/en/efsajournal/pub/5283)).	Studies on potential effects of glyphosate on the human and animal gut microbiome are not expected to impact the risk assessment, based on the current state of knowledge; the available data for the mammalian toxicity assessment were sufficiently protective for any health impact for livestock and pet animals (in line with the conclusions of the EFSA scientific report, 2018[8]). The impact of glyphosate on the microbiome was also discussed in the Pesticide Peer Review Experts' TC 82 on ecotoxicology (see Expert consultation point 5.1 identified following comments from the public) and similar conclusions were achieved. **Open point** RMS to include the assessment of 7 additional articles (identified after the public consultation, see also experts' consultation 2.37) in the revised RAR (see below): • Barnett JA, Bandy ML, Gibson DL (2022). Is the Use of Glyphosate in Modern Agriculture Resulting in Increased Neuropsychiatric Conditions Through Modulation of the Gut-brain-microbiome Axis?

[8] EFSA (European Food Safety Authority), 2018. Scientific Report on evaluation of the impact of glyphosate and its residues in feed on animal health. *EFSA Journal* 2018;16(5):5283, 22 pp. https://doi.org/10.2903/j.efsa.2018.5283

Subject	Conclusions Pesticide Peer Review Meeting
It is acknowledged that, due to the absence of validated guidelines and criteria to assess the impact of gut microbiome modifications on human health, the relevance of the related studies and reliability of the results may not be conclusive from a regulatory perspective. It is however noted that the ongoing gut microbiome research is expected to play a relevant role in regulatory science in the future, with potential implications for risk assessments and predictive risk models.	Front Nutr. 9: 827384. https://doi.org/10.3389%2Ffnut.2022.827384 • Del Castilo I, Neumann AS, Lemos FS, De Bastiani MA, Oliveira FL, Zimmer ER, Rêgo AM, Hardoim CCP, Antunes LCM, Lara FA (2022). Lifelong Exposure to a Low-Dose of the Glyphosate-Based Herbicide RoundUp® Causes Intestinal Damage, Gut Dysbiosis, and Behavioral Changes in Mice. Int. J. Mol. Sci. 23, 5583 https://doi.org/10.3390/ijms23105583 • Hu J, Lesseur C, Miao Y, Manservisi F, Panzacchi S, Mandrioli D, Belpoggi F, Chen J, Petrick L (2021). Low-dose exposure of glyphosate-based herbicides disrupt the urine metabolome and its interaction with gut microbiota. Sci Rep 11, 3265 https://doi.org/10.1038/s41598-021-82552-2 • Huch M, Stoll DA, Kulling SE, Souku ST (2022). Metabolism of glyphosate by the human fecal microbiota. Toxicology Letters, 358: 1-5 https://doi.org/10.1016/j.toxlet.2021.12.013 • Liu JB, Chen K, Li ZF, Wang ZY, Wang L. (2022). Glyphosate-induced gut microbiota dysbiosis facilitates male reproductive toxicity in rats. Sci Total Environ 20;805:150368. https://doi.org/10.1016/j.scitotenv.2021.150368 • Mesnage R, Calatayud M, Duysburgh C, Marzorati, M, Antoniou M (2022). Alterations in infant gut microbiome composition and metabolism after exposure to glyphosate and Roundup and/or a spore-based formulation using the SHIME technology. Gut Microbiome, 3, E6 https://doi.org/10.1017/gmb.2022.5 • Puigbò P, Leino LI, Rainio MJ, Saikkonen K, Saloniemi I, Helander M (2022). Does Glyphosate Affect the Human Microbiota? Life 2022, 12, 707 https://doi.org/10.3390/life12050707
Experts' consultation 2.31 Experts to discuss the toxicity profile of the following **metabolites** (other	**AMPA (M02)** The experts unanimously concluded that AMPA is unlikely to be genotoxic and that it has a similar toxicity profile as glyphosate. The majority of the experts agreed with the RMS' proposal to apply glyphosate's reference values to this metabolite.

Subject	Conclusions Pesticide Peer Review Meeting
metabolites could also be discussed depending on the outcome of the residues discussion: - general toxicity and genotoxicity data: AMPA, N-acetyl glyphosate, N-acetyl AMPA. - Genotoxicity data for: N-methyl AMPA, N-glyceryl AMPA, N-malonyl AMPA.	**N-methyl AMPA (M03)** The experts unanimously concluded that N-methyl AMPA is unlikely to be genotoxic. **Open point**: RMS to include the negative Ames test present in the confidential RAR also in the non-confidential RAR after asking for and getting the permission from the applicants. **N-acetyl glyphosate (M04)** The experts unanimously concluded that the genotoxicity of N-acetyl glyphosate was insufficiently investigated as far as aneugenicity is concerned (**data gap**), whereas general toxicity was sufficiently investigated. The data gap for aneugenicity is not critical because it involves a threshold mechanism. The metabolite does not appear to be of greater toxicity than glyphosate. The majority of the experts agreed with the RMS' proposal to apply glyphosate's reference values to this metabolite. **N-acetyl AMPA (M05)** The experts unanimously concluded that N-acetyl AMPA is unlikely to be genotoxic and that it has a similar toxicity profile as glyphosate. The majority of the experts agreed with the RMS' proposal to apply glyphosate's reference values to this metabolite. **N-glyceryl AMPA (M06)** The experts unanimously concluded that the available quantitative structure–activity relationship (QSAR) analysis does not raise concern for genotoxicity. Nevertheless, the QSAR analysis is not considered sufficiently reliable for the endpoints "clastogenicity/aneugenicity" and the experts agreed that an *in vitro* micronucleus (MN) test will be needed to address the metabolite's clastogenic/aneugenic potential (**data gap**). **N-malonyl AMPA (M07)** The experts unanimously concluded that the available QSAR analysis does not raise concern for genotoxicity. Nevertheless, the QSAR analysis is not considered sufficiently reliable for the endpoints "clastogenicity/aneugenicity" and the experts agreed that an *in vitro*

Subject	Conclusions Pesticide Peer Review Meeting
	MN test will be needed to address the metabolite's clastogenic/aneugenic potential (**data gap**). **<u>Methylphosphonic acid (M08)</u>** The experts unanimously concluded that the available QSAR analysis does not raise concern for genotoxicity. Nevertheless, the QSAR analysis is not considered sufficiently reliable for the endpoints "clastogenicity/aneugenicity" and the experts agreed that an *in vitro* MN test will be needed to address the metabolite's clastogenic/aneugenic potential (**data gap**). **<u>N-methyl glyphosate (M09)</u>** The experts unanimously concluded that N-methyl glyphosate is unlikely to be genotoxic.
Experts' consultation 2.32 MS experts to discuss in an experts' meeting the case reports/literature studies and epidemiological data dealing with possible relationship between exposure to glyphosate and **respiratory health** issues. Classification as respiratory irritant of glyphosate is under the remit of ECHA, the applicants should refer to that process too.	Overall, there are no concerns regarding respiratory health effects (i.e., irritation and sensitisation) and glyphosate exposure. This is in line with the ECHA RAC assessment.
Experts' consultation 2.33 MS experts to discuss in an experts' meeting **biomonitoring** data and their relevance in relation to the reference values, ADME (adsorption-distribution-	The estimated human exposure levels to glyphosate (dietary or para-occupational) extrapolated from human biomonitoring data do not raise a concern for adults, children and/or operators. **Open point** RMS to update in a revised RAR the calculations based on biomonitoring data, including:

Subject	Conclusions Pesticide Peer Review Meeting
metabolism-excretion) data, and non-dietary exposure estimates.	- a comparison of the 95th percentile or maximum value (depending on the data available) for urinary glyphosate concentration with the acute acceptable operator exposure level (AAOEL)/ARfD as appropriate; - consideration of an oral absorption value of 1% for the data from dietary exposure, while 20% is still applicable for occupational exposure; - calculations for combined exposure with AMPA where available. **Open point** RMS to consider the additional studies evaluated by the EFSA WG for the revised calculations in the revised RAR (identified after the public consultation period, see experts' consultation 2.37): • Kougias et al., 2021: Risk Assessment of Glyphosate Exposures from Pilot Study with Simulated Heavy Residential Consumer Application of Roundup® using a Margin of Safety (MOS) Approach. Risk Analysis, 41(9), 1693-1715; doi:10.1111/risa.13646 • Buekers et al., 2022a: Glyphosate and AMPA in Human Urine of HBM4EU Aligned Studies: Part A Children. Toxics, 10(8), 470. https://doi.org/10.3390/toxics10080470 • Buekers et al., 2022b:Glyphosate and AMPA in Human Urine of HBM4EU-Aligned Studies: Part B Adults. Toxics, 10(10), 552. https://doi.org/10.3390/toxics10100552 • NHANES, 2022 : National Health and Nutrition Examination Survey (NHANES), 2022 (weblink) (and Ospina M. et al, 2022: Exposure to Glyphosate in the United States: Data from the 2013–2014 National Health and Nutrition Examination Survey. Environment International, 107620. https://doi.org/10.1016/j.envint.2022.107620); • Connolly et al. 2022: A Human Biomonitoring Study Assessing Glyphosate and Aminomethylphosphonic Acid (AMPA) Exposures among Farm and Non-Farm Families. Toxics, 10(11), 690. DOI: 10.3390/toxics10110690

Subject	Conclusions Pesticide Peer Review Meeting
Experts' consultation 2.34 Derivation of the **toxicological reference values** (ADI, ARfD, AOEL and AAOEL) to be discussed by the experts.	**The acceptable daily intake (ADI) is 0.5 mg/kg bw per day** based on the NOAEL of 53 mg/kg bw per day from a 90-day dog study, supported by the NOAEL of 59.4 mg/kg bw per day from a 2-year rat study and covering the NOAEL of 50 mg/kg bw per day for maternal toxicity in the rabbit developmental toxicity studies (for which human relevance was considered questionable). **The acceptable operator exposure level (AOEL) is 0.1 mg/kg bw per day**, based on the same considerations as for the ADI, and applying an additional correction for the limited oral absorption of 20%. **The acute reference dose (ARfD) is 1.5 mg/kg bw** based on the overall rabbit developmental NOAEL of 150 mg/kg bw per day and applying a standard uncertainty factor of 100. **The acute AOEL (AAOEL) is 0.3 mg/kg bw** based on the same point of departure as for setting the ARfD, and applying a standard uncertainty factor of 100 and a correction for the limited oral absorption of 20%. **Open point** RMS to clarify the NOAEL (value for the most sensitive sex) for the 2-year rat study (study 5; report No 886.C.C.-R of 1996) in a revised RAR. **Open point** RMS to communicate with the Residue section the agreed revised ADI (ARfD has not been changed with regard to the RMS proposal in the initial RAR 2021) for consumer risk assessment. **Open point** RMS to provide an amendment of the Section 2.6.10 of the RAR Vol. 1 to reflect the agreed toxicological reference values and related results of non-dietary exposure estimates.
Experts' consultation 2.35	Based on the *in vitro* dermal absorption study with human skin, the agreed **dermal absorption values** are

Subject	Conclusions Pesticide Peer Review Meeting
Experts to discuss the **dermal absorption** values and the **non-dietary exposure estimates** for the representative uses of glyphosate.	- for the concentrate (360 g/L): 0.096% - for the dilution 1 (28.8 g/L): 0.23% - for the dilution 2 (2.4 g/L): 0.68% For the **non-dietary exposure estimates**, - for the workers re-entering the vegetable crops treated for cereal volunteers, the task of "inspection" is considered appropriate; - for the workers re-entering orchards and vineyards (for an exposure duration of 8h), the task of "inspection" is considered appropriate as well; - for the bystanders and residents' exposure estimates for the uses in orchards and vineyards, the scenario for cereals is applicable to provide appropriate spray drift values; - for the workers re-entering the vegetables after inter row application, the exposure estimates for the task "reaching, picking" are considered covered by the other uses on vegetables (with a maximum application rate of 2.16 kg as/ha); - for the use on railway tracks, it can be considered that there is no re-entry of workers; - for the uses on invasive species, the dermal absorption value of 0.23% can be used for the dilution in 5L water/ha. **Open point** RMS to provide the updated BfR template with the revised RAR, excluding the outliers for the *in vitro* dermal absorption study of glyphosate through human epidermis (Report No. JV2084-REG). **Open point** RMS to provide revised non-dietary exposure estimates (including for bystander children) for all representative uses with the agreed AOEL/AAOEL, agreed dermal absorption values and agreed input parameters to be used in the EFSA calculator. RMS to report consistent numbers of the uses for clear reference to the GAP table. RMS to provide an overview table showing how scenarios can be grouped differently for all categories (Operators, Workers, Residents, Bystanders) and provide revised exposure estimates to demonstrate transparently which ones are the worst-case scenarios.

Subject	Conclusions Pesticide Peer Review Meeting
New experts' consultation point 2.36 proposed by EFSA for completeness of discussion (October 2022): Experts to discuss the relevance of the identified **impurities** and the toxicological profile of the **co-formulants**.	**Impurities:** Four **relevant impurities** were identified in the reference specification. A **data gap** was identified for another impurity (of unclear toxicological relevance) that showed a potential for clastogenicity in an *in vitro* chromosome aberration study that was not followed up *in vivo*. This is a concern for the sources that contain this impurity in their reference specification. **Open point for EFSA** to identify in its conclusion to which sources this data gap is applicable. **Co-formulants:** All co-formulants have been discussed. All the MSs agreed that the available toxicological information is enough to conclude on their safety. However, EFSA noted that for one of them no repeated-dose toxicity data (e.g., over short and long-term) are available. **Post-meeting note**: EFSA is of the opinion that a data gap needs to be set to address potential issues upon repeated exposure. **Open point** RMS to integrate substance identification, content in the formulation, toxicological and ecotoxicological information on the co-formulants in the revised RAR. **Post-meeting note:** **Open point** The RMS is kindly requested to clarify the meaning of the function 'active' in the table on the composition on page 41 of Volume 4 (not for applicants). This is to avoid confusion with the function attributed to co-formulants as listed in Regulation (EU) 284/2013 (pages 11 and 12) and the function of glyphosate, as the only active substance in the formulation.

Subject	Conclusions Pesticide Peer Review Meeting
New experts' consultation point 2.37 proposed by EFSA for completeness of discussion (October 2022): Experts to consider some **potentially relevant newly available publications** arisen after the public consultation/reporting table stage. EFSA identified a number of publications that might be considered potentially relevant and therefore it was agreed to share these selected studies with MSs to allow a peer review and further consideration in the expert meetings. In particular, MS experts are asked to share their views whether these potentially relevant articles might be considered more critical or may alter the weight of evidence in the current assessment and to determine if any eventual follow up would be needed.	Formally, in line with the legislation, there is no legal obligation to consider newly available data submitted outside of the dedicated public and targeted consultations or after the deadline of the window for providing the additional information within the clock stop period, unless they constitute adverse data (cf Article 56 of Regulation (EC) No 1107/2009 regarding information on potentially harmful or unacceptable effects). For this reason, although a systematic review of the literature has not been carried out by EFSA or the RMS, EFSA has identified newly available papers on glyphosate even outside of the legal requirements and collected a list of studies as a result. **Open point** New studies identified after the public consultation on glyphosate to be considered for their potential relevance and impact on the overall risk assessment. See specific open points at expert consultation points 2.17, 2.19, 2.27, 2.30, 2.33. Additionally, the following studies should be considered further in a revised RAR: - Gerona et al., 2022: Glyphosate exposure in early pregnancy and reduced fetal growth: a prospective observational study of high-risk pregnancies. Environmental Health, 21(1), 1-12 doi: 10.1186/s12940-022-00906-3 - Bai et al., 2022: Perinatal exposure to glyphosate-based herbicides impairs progeny health and placental angiogenesis by disturbing mitochondrial function. Environment International, 170, 107579 https://doi.org/10.1016/j.envint.2022.107579.
Expert consultation points identified following comments by public	
Experts' consultation 2.1 identified following comments by public: Experts to discuss the **overall weight of evidence** for **genotoxicity** on glyphosate	Glyphosate is unlikely to be genotoxic or mutagenic based on a weight of evidence approach. The formulation for the representative uses is unlikely to be genotoxic or mutagenic based on a weight of evidence approach.

Subject	Conclusions Pesticide Peer Review Meeting
once the data requirements set have been addressed and discussed, and specific experts' consultations on specific endpoints (e.g. clastogenicity) and studies (e.g. Ames test) are fulfilled also taking into account the outcome of the **ECHA RAC meeting and their opinion on classification.**	
Experts' consultation 2.2 identified following comments by public: Experts to discuss the weight of evidence for **gene mutation** for glyphosate.	The following agreement was reached on **acceptability** for the following studies: • Report no. RL3393/2007-2.0AM-B (2007), CA 5.4.1/012 in RAR B.6.4.1.12. supportive based on relevance and reliability criteria: less relevant and reliable with restrictions. • Report no. IET 94-0142 (1995), CA 5.4.1/015 in RAR B.6.4.1.15. acceptable based on relevance and reliability criteria: relevant and reliable with restrictions. • Report no. 887-MUT.AMES (1993), CA 5.4.1/018 in RAR B.6.4.1.18. supportive based on relevance and reliability criteria: less relevant, reliable with restrictions. The following agreement was reached on the **weight of evidence for gene mutation**: Glyphosate does not have the potential to induce gene mutations based on a weight of evidence approach. The formulation for the representative uses does not have the potential to induce gene mutations based on a weight of evidence approach.

Subject	Conclusions Pesticide Peer Review Meeting
Experts' consultation 2.3 identified following comments by public: Experts to discuss the weight of evidence for **clastogenicity and aneugenicity** for glyphosate.	The following agreement was reached on **acceptability** for the following studies: • Report No. CTL/P/6050, CA 5.4.1/025 in RAR B.6.4.1.27 supportive based on relevance and reliability criteria: less relevant, reliable with restrictions. • Report No. 434/015, CA 5.4.1/026 in RAR B.6.4.1.28 supportive based on relevance and reliability criteria: less relevant, reliable with restrictions. • Report No. IET 94-0143, CA 5.4.1/027 in RAR B.6.4.1.29 acceptable based on relevance and reliability criteria: relevant and reliable with restrictions. • Report No. 141918, CA 5.4.1/028 in RAR B.6.4.1.30 Supportive based on relevance and reliability criteria: less relevant, reliable with restrictions. • Roustan, A. et al. 2014[9], RAR B.6.4.4.11 Not acceptable based on relevance and reliability criteria: less relevant, not reliable (lack of purity). • Report No. 830083, CA 5.4.2/016 in RAR B.6.4.2.17 Supplementary based on relevance and reliability criteria: less relevant, reliable with restrictions. • Report No. 300/3, CA 5.4.2/011 in RAR B.6.4.2.11 Not acceptable based on relevance and reliability criteria: less relevant, not reliable (lack of purity). • Report No. CTL/P/4954, CA 5.4.2/009 in RAR B.6.4.2.9 Acceptable based on relevance and reliability criteria: relevant and reliable with restrictions. • Report No. RF-G12.79/99, CA 5.4.2/008 in RAR B.6.4.2.8

[9] Roustan, A., Aye, M., De Meo, M., & Di Giorgio, C. (2014). Genotoxicity of mixtures of glyphosate and atrazine and their environmental transformation products before and after photoactivation. Chemosphere, 108, 93-100.

Subject	Conclusions Pesticide Peer Review Meeting
	Supplementary based on relevance and reliability criteria: less relevant and reliable with restrictions. • Report No. 889-MUT.MN, CA 5.4.2/010 in RAR B.6.4.2.10 Acceptable based on relevance and reliability criteria: relevant and reliable with restrictions. • Report No.2060/014, CA 5.4.2/007 in RAR B.6.4.2.7 Supplementary based on relevance and reliability criteria: less relevant and reliable with restrictions. • Mañas, F. et al. 2009[10] in RAR B.6.4.4.35 *In vivo* micronucleus (MN) part, supplementary based on relevance and reliability criteria: less relevant and reliable with restrictions. • Ilyushina, N. et al. 2018b[11], CA 5.4/005 in RAR B.6.4.4.5 Not acceptable based on relevance and reliability criteria: relevant, reliability not assignable. • Paz-y-Mino et al., 2011[12] in RAR B.6.4.4.40. Not acceptable based on relevance and reliability criteria: less relevant, reliability not assignable. • Bolognesi et al., 2009[13] in RAR B.6.4.41. Supplementary based on relevance and reliability criteria: less relevant/reliable with several restrictions. Evidence of **bone marrow exposure** for all *in vivo* MN studies:

[10] Mañas, F., Peralta, L., Raviolo, J., Ovando, H. G., Weyers, A., Ugnia, L., ... & Gorla, N. (2009). Genotoxicity of glyphosate assessed by the comet assay and cytogenetic tests. Environmental toxicology and pharmacology, 28(1), 37-41.
[11] Ilyushina, N. A., Averianova, N., Masaltsev, G., & Revazova, Y. U. (2018). Comparative investigation of genotoxic activity of glyphosate technical products in the micronucleus test in vivo. Toksikologicheskiy vestnik, 151(4), 24-8.
[12] Paz-y-Miño, C., Muñoz, M. J., Maldonado, A., Valladares, C., Cumbal, N., Herrera, C., ... & López-Cortés, A. (2011). Baseline determination in social, health, and genetic areas in communities affected by glyphosate aerial spraying on the northeastern Ecuadorian border.
[13] Bolognesi, C., Carrasquilla, G., Volpi, S., Solomon, K. R., & Marshall, E. J. P. (2009). Biomonitoring of genotoxic risk in agricultural workers from five Colombian regions: association to occupational exposure to glyphosate. Journal of Toxicology and Environmental Health, Part A, 72(15-16), 986-997.

Subject	Conclusions Pesticide Peer Review Meeting
	It is concluded that glyphosate reaches the bone marrow in the available *in vivo* MN tests based on sufficient evidence. The following agreement was reached on the **weight of evidence for chromosome aberration (clastogenicity/aneugenicity)**: Glyphosate is unlikely to be clastogenic or aneugenic based on a weight of evidence approach. The formulation for the representative uses is unlikely to be clastogenic or aneugenic based on a weight of evidence approach. **Open point** RMS to check the revised RAR regarding the cycle time as it seems to be a typo for the study CA 5.4.1/0025 (1998, Report No. CTL/P/6050) in RAR B.6.4.1.27. **Open point** RMS to assess the method of analysis used in the plasma analysis in the study CA 5.4.2/015 (Report No. 14613.402.078.14) in RAR B.6.4.2.15.
Experts' consultation 2.4 identified following comments by public: Experts to discuss the weight of evidence for **DNA damage** for glyphosate.	The following agreement was reached on **acceptability** for the following studies: • Mañas, T et al. 2013[14], CA 5.4/012 in RAR B.6.4.4.12 Supplementary based on the following relevance and reliability criteria: less relevant and reliable with restrictions. • Milic, M. et al. 2018[15], CA 5.3.1/010 in RAR B.6.4.4.14 Not acceptable based on the following relevance and reliability criteria: less relevant and not reliable.

[14] Mañas, Fernando Javier; Peralta, Laura; Ugnia, Laura; Weyers, Alicia; García Ovando, Hugo; et al.; 2013. Oxidative stress and comet assay in tissues of mice administered glyphosate and ampa in drinking water for 14 days; Sociedad Argentina de Genética; Journal of basic and applied genetics; 24; 2; 12-2013; 67-75

[15] Milić, M., Žunec, S., Micek, V., Kašuba, V., Mikolić, A., Tariba Lovaković, B., ... & Želježić, D. (2018). Oksidacijski stres, aktivnost kolinesteraza i primarna oštećenja u jetri, krvi i plazmi Wistar štakora nakon 28-dnevnog izlaganja glifosatu. Arhiv za higijenu rada i toksikologiju, 69(2), 154-168.

Subject	Conclusions Pesticide Peer Review Meeting
	• Paz-y-Mino et al., 2007[16], in RAR B.6.4.4.39 (discussed under experts' consultation 2.3. public). Not acceptable based on the following relevance and reliability criteria: less relevant, not reliable. • Koureas et al., 2014[17] in B.6.4.4.42 (discussed under experts' consultation 2.3. public). Supplementary based on the following relevance and reliability criteria: less relevant, reliable with restrictions. The following agreement was reached on the **weight of evidence for DNA damage:** Glyphosate may have the potential to induce DNA damage. The evidence is weak. **Open point** RMS to further clarify the information available on the toxicity of mice in other toxicity studies in the dossier to complement the assessment of Mañas, T et al. 2013, CA 5.4/012 in RAR B.6.4.4.12.
Experts' consultation 2.5 identified following comments by public: MSs experts to discuss the statistical analysis approach to be taken into account in **carcinogenicity studies**. MSs experts to discuss the use of HCD in the long-term/carcinogenicity studies. MSs experts to discuss the appropriateness of the high	The methodology used by the RMS in the weight of evidence (WoE) assessment of the carcinogenic potential of glyphosate was agreed by all experts. Based on all the available evidence, the experts agreed that glyphosate is not considered carcinogenic in rats up to the highest dose level tested of 1214 mg/kg bw per day in males and 1498 mg/kg bw per day in females. The experts agreed that in the mouse studies no carcinogenic effects were seen up to 988 mg/kg bw per day in males and 1081 mg/kg bw per day in females. **Open point**

[16] Paz-y-Miño, C., Sánchez, M. E., Arévalo, M., Muñoz, M. J., Witte, T., De-la-Carrera, G. O., & Leone, P. E. (2007). Evaluation of DNA damage in an Ecuadorian population exposed to glyphosate. Genetics and Molecular Biology, 30, 456-460.
[17] Koureas, M., Tsezou, A., Tsakalof, A., Orfanidou, T., & Hadjichristodoulou, C. (2014). Increased levels of oxidative DNA damage in pesticide sprayers in Thessaly Region (Greece). Implications of pesticide exposure. Science of the Total Environment, 496, 358-364.

Subject	Conclusions Pesticide Peer Review Meeting
doses used in the long-term/carcinogenicity studies. MSs experts to discuss the relevance of the malignant lymphomas observed in male mice. MSs experts to discuss the relevance of the kidney tumours observed in male mice. MSs experts to discuss the relevance of the hemangiosarcomas observed in male and female mice. MSs experts to discuss the relevance of the skin keratoacanthomas observed in male mice. MSs experts to discuss the relevance of the skin basal cell tumours observed in male mice. MSs experts to discuss the relevance of the hepatocellular adenomas observed in male mice.	RMS to include the missing findings, WoE assessment and conclusion on the toxicological relevance of haemangiomas observed in female mice in a revised RAR. **Open point** RMS to revise the List of Endpoints (LoEP) regarding the carcinogenic potential of glyphosate in rats and mice.
Experts' consultation 2.6 identified following comments by public: MSs experts to discuss the outcome of the **2-year rat** study 1 (Report No. 2060-0012) in an experts' meeting.	The NOAEL of the 2-year rat study 1 (Report No. 2060-0012) is 285.2 mg/kg bw per day, based on the increase in alkaline phosphatase, adipose infiltration of the bone marrow and kidney findings which are of equivocal relevance in both sexes, and the skin effects including areas of necrosis/giant cell reaction to keratin and keratoacanthoma observed in high dose males. **Open point** RMS to provide the incidences of adrenal adenomas, mammary gland adenocarcinomas, and combined adenocarcinomas and adenomas

Subject	Conclusions Pesticide Peer Review Meeting
	(which are reported in Portier, 2020[18]), and respective assessment in a revised RAR.
Experts' consultation 2.7 identified following comments by public: MS experts to discuss in an experts' meeting the **epidemiological data** dealing with possible relationship between exposure to glyphosate and **reproductive toxicity**, also taking into account the outcome of the ECHA RAC meeting and their opinion on classification.	No conclusion can be drawn on any potential causal association between glyphosate exposure and reproductive endpoints on the basis of the available epidemiological studies. **Open point** RMS to update the RAR by including the agreement of the meeting.
Experts' consultation 2.8 identified following comments by public: MS experts to discuss the possible relationship between exposure to glyphosate and non-Hodgkin's lymphoma in an experts' meeting by taking into consideration all the available literature and epidemiological data.	See expert's consultation 2.19

[18] Portier, C. J. (2020). A comprehensive analysis of the animal carcinogenicity data for glyphosate from chronic exposure rodent carcinogenicity studies. Environmental Health, 19(1), 1-17.

REPORT OF PESTICIDE PEER REVIEW TC 84

GLYPHOSATE – AIR V

Rapporteur Member State: Assessment Group on Glyphosate (AGG) consisting of FR, HU, NL, SE

2. Mammalian toxicity (endocrine disruption (ED) properties)

Date: 02 December 2022

List of participants:

Institute	**Member States Country code**
Austrian Agency for Health and Food Safety (AGES)	AT
Federal Public Service Health	BE
Federal Institute for Risk Assessment (BfR)	DE
Federal Environmental Agency (UBA)	DE
Ministry of Environment and Food of Denmark, Environmental Protection Agency	DK
TRAGSATEC	ES
Finnish Safety and Chemicals Agency (Tukes)	FI
Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail (ANSES)	FR
National Food Chain Safety Office (NEBIH)	HU
Board for the Authorisation of Plant Protection Products and Biocides (Ctgb)	NL
Swedish Chemicals Agency (KemI)	SE
National Institute of Public Health	SI
External experts (2)	EFSA

In accordance with EFSA's Policy on Independence[1] and the Decision of the Executive Director on Competing Interest Management[2,] EFSA screened the Annual Declarations of Interest filled out by the

[1] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf
[2] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf

participants invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process, and no interests were declared orally by the members at the beginning of this meeting.

Discussion points/Outcome

2. Mammalian toxicity

Please note that information part of this report may have been masked by EFSA in accordance with Article 63 of Regulation (EC) No 1107/2009 as well as EFSA's Practical Arrangements concerning confidentiality in accordance with Articles 7 and 16 of Regulation (EC) No 1107/2009, or EFSA's Practical Arrangements concerning transparency and confidentiality as a consequence of confidentiality requests submitted by the applicant on application dossiers for pesticides active substances or Maximum Residue Levels, respectively. Please note that information disclosed in this report is without prejudice to pre-existing intellectual property rights and data exclusivity clauses set out in Union law, and particularly in Article 62 of Regulation (EC) No 1107/2009.
Minutes might be revised due to pending data gaps at the time of the meeting and /or eventual need for further follow up consultation after the meeting. If needed, the final agreement will be made available in the meeting report published at the end of the peer review process.

Subject	Conclusions Pesticide Peer Review Meeting
Experts' consultation 2.23 MS experts to discuss the endocrine disruption (**ED**) **potential** of the active substance glyphosate and the toxicological relevance of the effects on oestrus cyclicity.	**Thyroid (T)-modality:** The dataset for the T-modality is considered sufficiently investigated for the active substance glyphosate. No T-mediated adversity and activity were observed in a sufficiently investigated dataset consisting of several studies of different duration and multiple doses administered in mouse, rat, rabbit and dog. **Oestrogen, androgen and steroidogenesis modalities (EAS)-modalities:** The dataset for the EAS-modalities is considered sufficiently investigated for the active substance glyphosate. There is no evidence of EAS-mediated adversity and activity in a sufficiently investigated dataset consisting of several studies of different duration and multiple doses administered in mouse, rat, rabbit and dog. It was concluded that the ED criteria according to point 3.6.5 of Annex II to Regulation (EC) No 1107/2009, as amended by Commission Regulation (EU) 2018/605, are not met for the EAS- and T-modalities for the active substance glyphosate.
Experts' consultation 2.29 Experts to discuss:	The RMS provided updated information in the revised RAR for the reliability and relevance assessment of studies included in the ED properties assessment.

Subject	Conclusions Pesticide Peer Review Meeting
• The relevance and reliability of the available studies (both regulatory and from literature) and assessed parameters for their use in the weight of evidence for ED assessment; • The information that can be derived from the available studies based on: tested item, test system (including species, where necessary) study design and parameters assessed; • The weight of evidence for ED leading to the overall conclusion on whether the criteria as laid down in point 3.6.5 of Annex II to Regulation 1107/2009 are met.	The EFSA ED Working Group (WG) conducted an independent reliability and relevance assessment, and this was presented to the experts in the peer review meeting. When applying both approaches (by RMS and EFSA) for the quality assessment of the evidence in the public literature, there are no factual differences, and the results are in agreement when using the outcome of the studies in a weight of evidence (WoE) approach for the assessment of the ED properties of glyphosate active substance. It was however noted that the level of details for assessing the risk of bias of the endpoints measured in the public literature studies is different. During the discussion, EFSA informed the RMS and the MSs that the EFSA ED WG Weight of Evidence report will be published by EFSA as a supporting documentation to the regulatory assessment of the active substance glyphosate. As a matter of transparency and completeness and taking into account that many comments were received during the public consultation on the methods and results of this quality assessment, EFSA suggested the RMS to consider and make reference to the EFSA ED WG WoE report and related appendices in the revised RAR. **Open points** 1. RMS to revise the ED assessment and include the missing studies. 1.1. RMS to conduct the reliability and relevance and uncertainty analysis of the endpoints measured in the studies. 2. RMS to make a reference to the EFSA ED WG WoE report.

REPORT OF PESTICIDE PEER REVIEW TC 83

GLYPHOSATE – AIR V

Rapporteur Member State: Assessment Group on Glyphosate (AGG) consisting of FR, HU, NL, SE

3. Residues

Date: 2 December 2022

List of participants:

Institute	**Member States Country code**
Austrian Agency for Health and Food Safety (AGES)	AT
Federal Institute for Risk Assessment (BfR)	DE
Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail (ANSES)	FR
National Food Chain Safety Office (NEBIH)	HU
Department of Agriculture, Food & Marine (DAFM) Ireland	IE
Board for the authorisation of plant protection products and biocides (Ctgb)	NL
Swedish Food Agency	SE
External experts (2)	EFSA

In accordance with EFSA's Policy on Independence[1] and the Decision of the Executive Director on Competing Interest Management[2,] EFSA screened the Annual Declarations of Interest filled out by the participants invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process, and no interests were declared orally by the members at the beginning of this meeting.

[1] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf
[2] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf

Discussion points/Outcome

3. Residues

Please note that information part of this report may have been masked by EFSA in accordance with Article 63 of Regulation (EC) No 1107/2009 as well as EFSA's Practical Arrangements concerning confidentiality in accordance with Articles 7 and 16 of Regulation (EC) No 1107/2009, or EFSA's Practical Arrangements concerning transparency and confidentiality as a consequence of confidentiality requests submitted by the applicant on application dossiers for pesticides active substances or Maximum Residue Levels, respectively. Please note that information disclosed in this report is without prejudice to pre-existing intellectual property rights and data exclusivity clauses set out in Union law, and particularly in Article 62 of Regulation (EC) No 1107/2009.
Minutes might be revised due to pending data gaps at the time of the meeting and /or eventual need for further follow up consultation after the meeting. If needed, the final agreement will be made available in the meeting report published at the end of the peer review process.

Subject	Conclusions Pesticide Peer Review Meeting
Experts' consultation 3.1 Experts to discuss the validity and the results of the storage stability studies in plant matrices and to conclude on the maximal storage time for which acceptable frozen storage stability has been demonstrated for all compounds included in the agreed plant residue definitions for monitoring and risk assessment. Special emphasis should be given to the following points: -Acceptable storage stability of glyphosate, AMPA and other compounds in the different plant matrices, - the use of mixed spiking solution of glyphosate, N-acetyl-glyphosate and AMPA	Based on the available information and considering the OECD test guideline 506, the following frozen storage stability periods were agreed: For **glyphosate**: High water content commodities: 24 months High protein content commodities: 18 months Oilseeds: 12 months - no extrapolation proposed across the category of high oil content commodities High starch content commodities: 24 months Citrus fruit: 24 months – no extrapolation proposed across the category of high acid content commodities Straw and stover: 12 months, or longer for individual matrices An overall extrapolation was confirmed for the frozen storage stability of glyphosate of at least 12 months for all commodities, including processed commodities. Individual commodities or categories are covered by longer storage stability periods. For **AMPA**: High water content commodities**:** at least 6 months across the commodities in this category due to decline observed in stored clover samples, while for several individual commodities in this category longer storage periods are supported by the data.

Subject	Conclusions Pesticide Peer Review Meeting
in several storage stability studies, -the representativeness of sample preparation in the storage stability studies for the metabolism studies and the field residue trials, -the suitability of the analytical methods including extraction efficiency used.	High protein content commodities: 12 months (based on a study submitted after the public consultation) Oilseeds: 12 months – no extrapolation proposed across the category of high oil content commodities High starch content commodities: 12 months Citrus fruit: 24 months – no extrapolation proposed across the category of high acid content commodities In "other commodities", sample storage stability was matrix dependent. An overall extrapolation was confirmed for the storage stability of AMPA of at least 6 months for all commodities, including processed commodities. Individual commodities or categories are covered by longer storage stability periods. The conclusions reached on the frozen storage stability on AMPA and glyphosate do not trigger a reassessment of the rotational crop residue trials, while they did for primary crops trials. The processing trials should also be reviewed in that context. **Open point:** RMS to assess the residue trials in primary crops and the processing trials in the light of the conclusions reached in the meeting on the storage stability of AMPA and glyphosate in frozen samples.
Experts' consultation 3.2 Experts to discuss the results and validity of the storage stability studies in animal matrices (study 1 and 2/3) and conclude on the maximal storage time for which stability has been demonstrated especially for AMPA in fat matrices (poultry, pig and ruminant) and glyphosate in milk. Special	Based on the available storage stability and analytical methods data, considering also the sample preparation, study 1 was agreed as fully acceptable, and study 3 with the limitation to milk only. Study 2 is not acceptable. Satisfactory frozen sample storage stability was demonstrated as agreed by the meeting as follows: **For AMPA:** Pig fat: 15 months Cow fat: 24 months Chicken fat: 25 months

Subject	Conclusions Pesticide Peer Review Meeting
emphasis should be given to the representativeness of sample preparation in the storage stability studies for the metabolism and feeding studies and the suitability/validity of the analytical methods used.	**For glyphosate:** Milk: 22 months Data on other commodities and analytes were not requested to be further discussed, and for them the assessment in the RAR is considered agreed.
Experts' consultation 3.3 Experts to discuss the potential impact of the use of trimesium salt in glyphosate plant studies (metabolisation, uptake through leaves and from soil, magnitude of residues) and the representativeness of such studies to inform on the uptake and metabolism of glyphosate acid and isopropylamine salt (representative technical and formulation). In case these studies are not considered fully representative, MSs to discuss if additional studies performed with the representative active substance and formulation need to be provided.	Metabolism studies in plants conducted with glyphosate trimesium can be used to support the assessment of the metabolism of glyphosate in plants. Studies conducted with the trimesium, diammonium and isopropylamine salt formulations showed that no differences - neither in the rate nor the amount absorbed – were observed when compared. The plant species is much more decisive for the absorbed and translocated amount than the salt present in the formulation used.
Experts' consultation 3.4 MSs experts: -to discuss if sufficient and reliable metabolism studies	*In the remit of this report the term 'conventional crop' refers to a traditionally bred variety that dies when treated with glyphosate, and 'glyphosate tolerant crop' to a crop variety, that maintains agronomic yield when treated with glyphosate; currently this is achieved by genetic modification.*

Subject	Conclusions Pesticide Peer Review Meeting
are available to support all the representative uses. -to propose a residue definition for risk assessment and monitoring for the representative uses, considering also potential residues in rotational crops to the representative uses. -to decide if the information available allows to extend the residue definitions proposed to other crop groups and if general residue definitions (RD) can be proposed (including monitoring RD to enforce MRLs in imported crops).	The experts agreed that the data selected as reliable were sufficient to use to elucidate the metabolic pathway and the nature of residues in plants to cover all crop categories. Based on the evidence submitted in the metabolism studies with conventional and glyphosate tolerant crops, separate **residue definitions for risk assessment** were set: 1) Conventional crops: Sum of glyphosate, AMPA, expressed as glyphosate. 2) Glyphosate tolerant crops: Sum of glyphosate, AMPA, N-acetyl glyphosate and N-acetyl AMPA, expressed as glyphosate. Glyphosate tolerant crops are currently not grown in the EU; however, imports of such crops are possible. For **monitoring**, two options were proposed for risk management consideration. Both options address crops with glyphosate tolerant modifications that were identified as being on the market in 2019 and consider specific metabolites that prevail in the crops. **Option 1 - According to Codex (FAO-WHO, 2019)[3]:** 1) For soya bean, oilseed rape (OSR), maize (including sweet corn): Sum of glyphosate and N-acetyl glyphosate, expressed as glyphosate 2) All other crops: Glyphosate only **Option 2- According to the proposal in the EFSA MRL Art.12 Reasoned Opinion of 2019[4]**, including also the metabolite AMPA: 1) For soya bean, OSR, cotton, maize (including sweet corn), sugar beet: Sum of glyphosate, AMPA and N-acetyl glyphosate, expressed as glyphosate 2) All other crops: Glyphosate only **Open point:**

[3] FAO and WHO. 2019. *Pesticide residues in food 2019 – Extra Joint FAO/WHO Meeting on Pesticide Residues Evaluation Part I: Residues*. Rome. https://www.fao.org/publications/card/en/c/CA6010EN/
[4] EFSA (European Food Safety Authority), 2019. Review of the existing maximum residue levels for glyphosate according to Article 12 of Regulation (EC) No 396/2005 – revised version to take into account omitted data. EFSA Journal 2019;17(10):5862 doi:10.2903/j.efsa.2019.5862

Subject	Conclusions Pesticide Peer Review Meeting
	RMS to cross-check the publications Eaton et al., 2022 (doi: 10.1016/j.ecoenv.2022.113300) and the therein referenced article Grandcoin, et al., 2017 (doi.org/10.1016/j.waters.2017.03.055), and other relevant literature sources given there in the context of assessing the evidence of other sources of AMPA from phosphonate detergents passing through sewage treatment and the practice of sewage sludge used as agricultural fertilizer.
Experts' consultation 3.5 Experts to discuss the validity of all animal metabolism studies with special emphasis on the tested materials (suitability of mixtures and equivalence of trimesium glyphosate), the overall extraction rate and the characterisation/identification. Special attention should be given to the characterisation/identification in milk and shortcomings of the studies. Experts should conclude on the suitability of the studies to elucidate the metabolism in animals. On the basis of the valid studies experts to discuss and agree on the animal residue definition for risk assessment and monitoring.	It was agreed that qualitatively the glyphosate trimesium data could be relied on to derive residue definitions. The experts agreed that the available data were sufficient to elucidate the metabolic pathway and the nature of residues present in animal commodities. The following residue definitions were agreed: **Residue definition for risk assessment in animal commodities:** **Considering the representative uses only**: sum of glyphosate and AMPA, expressed as glyphosate. In the context of **future MRL-setting procedures**: sum of glyphosate, AMPA, N-acetyl glyphosate and N-acetyl AMPA, expressed as glyphosate. **Residue definition for monitoring of animal commodities:** **Considering also future MRL-setting procedure**: sum of glyphosate and N-acetyl glyphosate, expressed as glyphosate.
Experts' consultation 3.6	The "risk envelope approach"[5] is not applicable in the context of the risk assessment of the active substance. The experts discussed and

[5] Guidance document SANCO/11244/2011 rev. 5 of 14 March 2011 on the preparation and submission of dossiers for plant protection products according to the "risk envelope approach".

Subject	Conclusions Pesticide Peer Review Meeting
Experts to discuss whether the reported residue trials can be considered as acceptable to support the representative uses despite the deviations noted for these trials compared to the Good Agricultural Practices (GAPs) regarding the number of applications, the pre-harvest interval (PHI) values at harvest, and the deficiencies identified as regards the lack of storage stability data on metabolites and validation data of the analytical methods. The results of the available metabolism studies in primary and rotational crops should also be considered as a support to this discussion as regards the potential soil uptake, translocation and accumulation of the residues throughout the plants following glyphosate application. Based on the overall discussion and agreement reached under this point, the applicability of the "risk envelope approach" to adequately address the magnitude of residues for all crops and crop groups according to the	agreed the approach for the assessment of the residue trials data set on the basis of the technical guideline SANTE/2019/12752[6]. It was agreed that the data indicated that residues were in the category between the limit of detection (LOD) and the limit of quantification (LOQ). The experts identified some situation where wider extrapolation between crops might be accepted based on whether the GAP have crops present at the time of application or not. Except for these situations, overall the outcome resulted in the following open points and data gap: **Data gap:** A sufficient number of residue trials for table olives in Northern EU (NEU). Note: Data gap identified in the RAR and confirmed by the meeting. **Open point:** RMS to update the RAR with the assessment of residue trials for olives picked from the ground. **Open point:** RMS to clarify the method used in the residue trials in olives with regard to the extraction solvent used, because there is a mismatch for the extraction solvent reported in RAR Vol.3 B.5 and B.7, and therefore it may not be the same method. **Open point:** RMS to assess the available trials with pre-sowing / pre-planting, pre-emergence uses a) taking into account the decision on storage stability data for the different commodities and categories b) identify where additional trials would be necessary for the different crops and zones requested in the GAP table, when assessed in line with the technical guidelines SANTE/2019/12752.

[6] Technical guidelines on data requirements for setting maximum residue levels, comparability of residue trials and extrapolation of residue data on products from plant and animal origin (Repealing and replacing the existing Guidance Document SANCO 7525/VI/95 Rev. 10.3).

Subject	Conclusions Pesticide Peer Review Meeting
representative uses, as proposed by the RMS, should be further discussed.	It is noted that all MS experts including the RMS disagreed with step b) of this open point and only EFSA considered step b) in this open point necessary. **Open point:** RMS to assess the available trials with inter-row uses a) taking into account the decision on storage stability data for the different commodities and categories b) identify where additional trials would be necessary for the different crops and zones requested in the GAP table, when assessed in line with the technical guidelines SANTE/2019/12752. It is noted that the RMS and the majority of MS experts disagreed with step b) of this open point while there was a minority opinion of EFSA and one MS expert considering step b) in this open point necessary.
Experts' consultation 3.7 Experts to discuss the relevance of all presented feeding studies (poultry, ruminant and swine) with respect to the administered substance(s) and in relation to the agreed animal residue definition and conclude on the validity of these feeding studies. Special emphasis should be given to the analytical methods used and the updated dietary burden calculation.	**Feeding studies** - **with N-acetyl glyphosate:** The studies are scientifically acceptable but were not used for the risk assessment because the metabolite is not formed in conventional crops that are assessed by the renewal review. - **with glyphosate-trimesium:** The study in poultry was not acceptable. The ruminant study was acceptable with the limitation to the milk commodity but should only be used if it is demonstrated that absorption, distribution and residue quantities in the study with the trimesium salt do not differ compared to glyphosate ion. - **with glyphosate : AMPA mixture (9:1):** The study is acceptable to assess the representative uses. Future use of the study would depend on the contribution of glyphosate and AMPA calculated in the animal diet consequent to the uses being assessed in the future. A minor update is requested for the dietary burden calculation and a change of the conclusions reached on residue levels is not expected. **Open point:**

Subject	Conclusions Pesticide Peer Review Meeting
	Dietary burden calculation should be repeated not including primary crop residue levels for cereal commodities. **Open point:** RMS to assess the data in the poultry feeding study 3 in terms of the duration of frozen sample storage for eggs to confirm that the sample storage time was less than 14 months. Residues in animal commodities with regard to the representative uses were assessed to be below the LOQ of the analytical method, pending confirmation that the data for eggs are reliable (see sample storage duration clarification task in the open point above).
Experts' consultation 3.8 Experts to discuss whether the nature of residues at the standard hydrolysis conditions for processing has been sufficiently investigated according to the data requirements for all compounds (glyphosate, AMPA, N-acetyl AMPA and N-acetyl glyphosate) that may potentially be included in the monitoring and risk assessment residue definitions for plants in view of the deviations/deficiencies identified in Study 1 CA 6.5.1/001 and in Study 3 CA 6.5.1/003.	Based on the available 3 studies (assessed as acceptable following justification provided by the applicants), the stability of the 4 compounds (glyphosate, AMPA, N-acetyl glyphosate and N-acetyl AMPA) included in the different residue definitions for monitoring and risk assessment under the standard hydrolysis conditions had been demonstrated.
Experts' consultation 3.9 Experts to discuss if the available information (metabolism studies and field	The experts agreed that the data selected as reliable were sufficient to use to elucidate the metabolic pathway and the nature of residues in rotational crops. Based on the evidence submitted in the metabolism studies with conventional crops, the following

Subject	Conclusions Pesticide Peer Review Meeting
residue trials) is sufficient to characterise the nature and magnitude of the residues expected in rotational crops from the representative uses and if any additional component needs to be added to the residue definitions in plants (risk assessment and monitoring) to inform the potential residues in rotational crops.	**Residue definition for risk assessment in rotational crops were derived for** all conventional rotational crops: Sum of glyphosate and AMPA, expressed as glyphosate. For glyphosate tolerant rotational crops, additional data would have to be submitted to address the potential relevance of additional metabolites (e.g. N-acetyl glyphosate and N-acetyl AMPA), should glyphosate tolerant crops be authorised in the EU in the future. **Residue definition for monitoring in rotational crops is proposed as:** Glyphosate by default. With regard to the studies on the magnitude of residues in rotational crops, data gaps were identified as the data package is still to be completed in view of the data requirements. **Data gap:** The ongoing two trials in rotational crops should be completed. **Data gap:** Two additional trial sites should be investigated for rotational crops. In order to increase the variety of crops tested it is suggested that the applicants test different crops to those already investigated.
Experts' consultation 3.10 Experts to discuss the residue definition in honey and bee products and the MRL derived for honey and bee products for the representative uses from the field trials available and information from the scientific literature.	The residue definitions derived for plant commodities (see expert consultation point 3.4) should also be applicable to honey in line with the guidance SANCO 11956/2016 rev. 9[7]. To establish MRLs in honey, the available four supervised trials (analysing glyphosate and AMPA) in Phacelia fields should be used in line with the guidance SANCO 11956/2016 rev. 9.

[7] Technical guidelines Sante/11956/2016 rev. 9 from 14 September 2018- Technical guidelines for determining the magnitude of pesticide residues in honey and setting Maximum Residue Levels in honey.

Subject	Conclusions Pesticide Peer Review Meeting
New experts' consultation point 3.11 proposed by EFSA for completeness of discussion (October 2022): Experts to consider some potentially relevant newly available publications arisen after the public consultation/reporting table stage. EFSA identified a number of publications that might be considered potentially relevant and therefore it was agreed to share these selected studies with MSs to allow a peer review and further consideration in the expert meetings. In particular, MS experts are asked to share their views whether these potentially relevant articles might be considered more critical or may alter the weight of evidence in the current assessment and to determine if any eventual follow up would be needed.	Formally, in line with the legislation, there is no legal obligation to consider newly available data submitted outside of the dedicated public and targeted consultations or after the deadline of the window for providing the additional information within the clock stop period, unless they constitute adverse data (cf Article 56 of Regulation (EC) No 1107/2009 regarding information on potentially harmful or unacceptable effects). For this reason, although a systematic review of the literature has not been carried out by EFSA or RMS, EFSA has identified newly available papers on glyphosate even outside of the legal requirements and collected a list of studies as a result. The experts agreed that none of the publications identified in the area of Residues were relevant for the assessment of the renewal of glyphosate.
	Based on the discussions and conclusions in the meeting, a general follow-up action for the RMS was identified as necessary: **Open point**: RMS to systematically update Vol.1, Vol.3 of the RAR and the list of endpoints in line with the agreements of the peer review experts' meeting. **Open point**:

Subject	Conclusions Pesticide Peer Review Meeting
	RMS to provide a screening assessment for the existing MRLs for glyphosate in the light of the conclusions of the peer review experts' meetings in residues and in mammalian toxicology, considering changes in terms of residue definitions and the toxicology of glyphosate and its metabolites.

REPORT OF PESTICIDE PEER REVIEW TC 81

GLYPHOSATE (AIR V)
Rapporteur Member State: Assessment Group on Glyphosate (AGG) consisting of FR, HU, NL, SE

4. Environmental fate and behaviour

Date: 21 November 2022

List of participants:

Institute	**Member States Country code**
Austrian Agency for Health and Food Safety (AGES)	AT
Federal Public Service Health, Food Chain Safety and Environment	BE
Umweltbundesamt / Federal Environmental Agency (UBA)	DE
Ministry of Environment and Food of Denmark, Environmental Protection Agency	DK
Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail (ANSES)	FR
National Food Chain Safety Office (NÉBIH)	HU
Pesticide Registration Division, Department of Agriculture, Food and the Marine Laboratories	IE
Board for the Authorisation of Plant Protection Products and Biocides (Ctgb)	NL
Swedish Chemicals Agency (KemI)	SE
External experts (3)	EFSA
External expert - Chair (1)	CH
Observers (2)	CH

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[1] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf
[2] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf

Discussion points/Outcome

4. Environmental fate and behaviour

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Subject	Conclusions Pesticide Peer Review Meeting
Experts' consultation 4.1 Experts to discuss and agree on: - the use of trigger/modelling endpoints for testing pH-dependence of glyphosate and AMPA - the way to handle pH dependence of the biphasic degradation rates of glyphosate (use of DT50/DT90/kinetic parameters) - the selection of modelling endpoints for glyphosate, when pH-dependence is confirmed, including endpoints derived from field dissipation studies. This discussion to take into account the RMS assessment	On balance the experts agreed with the RMS conclusion that pH dependent degradation in soil of glyphosate and its metabolite AMPA cannot be excluded considering the available soil DT90 values, the fast phase DT50 values and the slow phase DT50 values for glyphosate. For AMPA the pH dependency was indicated on the basis of SFO DT50 values. The experts agreed that the approach of the RMS for modelling endpoints at the first tier was appropriate and can be used for the approval / RAR exposure assessment. However, they agreed that for uses where refinement would be needed (future assessments), geomeans for acidic and alkaline soils be used. The experts agreed that the available dataset of kinetic values should be split in relation to soils having a pH above or below 6.5, measured in water. They also agreed that the kinetic formation fraction from glyphosate to AMPA from the available dataset should be the arithmetic mean of all soils independent of their pH. **Open point** RMS to correct the distance to the weather station indicated on page 485 of the amended RAR to 42 km and update the conclusion to indicate that it was concluded as correct to use the information (regarding temperature) as it had been erroneously indicated on page 429 and 585 that the data from the distant weather station should not

Subject	Conclusions Pesticide Peer Review Meeting
of the additional information submitted by the applicants.	be considered reliable. RMS to add a note that for the other weather data (precipitation) there was on-site information available. **Open point** RMS to amend the RAR page 674 to correct the Kendall test results for the pathway fit. **Open point** RMS to update the RAR including the CP product Vol3 and list of endpoints (LoEP) to include the soil geomean DegT50 results for glyphosate and AMPA when the dataset is split for soils with a pH in water above and below 6.5. **Data gap** Reliable AMPA soil DegT50 endpoints from at least 3 field trial sites were not available.
Experts' consultation 4.2 Experts to discuss and agree on the definition of the residue for exposure/risk assessment taking into account the RMS evaluation of the information provided consequent to the data requirements. In particular whether the definition for sediment needs to include "chromatographic fraction P1a" and/or 1-oxo-AMPA / M3.3.	The RMS proposed the inclusion of the metabolites P1a and M3.3 in the residue definition for sediment based on a rough estimation of max. occurrence of each unknown fraction in the related AMPA-dosed study, considering that AMPA is formed up to 27% of the applied radioactivity (AR) in glyphosate dosed study. The rough estimation showed that in sediment P1a has a max. estimated occurrence of 14.4% AR and M3.3 has a max. estimated occurrence of 6.2% AR from glyphosate. The applicants provided a kinetic approach to determine the max. occurrence of fractions P1a and M3.3 using the entire metabolic pathway from glyphosate, showing similar results and demonstrating that both metabolites would trigger their inclusion in the residue definition for risk assessment in the sediment compartment. It was discussed whether the fractions P1a and M3.3 should be included also in the residue definition for the risk assessment in the surface water compartment. Since metabolite HMPA was clearly appearing only in the water compartment, but was quantified in the glyphosate-dosed water/sediment study, the experts discussed also the inclusion of metabolite HMPA in the residue definition for sediment.

Subject	Conclusions Pesticide Peer Review Meeting
	Both PEC surface water and PEC sediment were calculated for HMPA using a default Koc value of 10 mL/g, resulting in potentially not appropriate PEC for the sediment compartment. The experts agreed on the inclusion of P1a and M3.3 in the residue definition for risk assessment in the sediment compartment. The experts agreed on the PEC sediment calculated by the RMS using the max occurrence of 14.4%, considered as worst-case occurrence between P1a and M3.3. The experts agreed to not include the two unknown fractions P1a and M3.3 in the residue definition for risk assessment for the surface water. The experts agreed on the inclusion of metabolite HMPA in the residue definition for sediment and on the need for PEC sediment calculated with a default Koc value of 10000 mL/g. The experts also agreed on the RMS conclusion that the unknown fraction M3.3 cannot be formally identified as 1-oxo-AMPA and that both fractions P1a and M3.3 cannot be identified as the same compound. The final agreed **definition for residues requiring further assessment** is: Soil (Glyphosate, AMPA), Groundwater (Glyphosate, AMPA), Surface Water (Glyphosate, AMPA, HMPA), Sediment (Glyphosate, AMPA, HMPA, P1a, M3.3). **Open point:** RMS to delete from the LoEP the PEC surface water calculated using a default Koc value of 10000 mL/g for the fractions P1a and M3.3. RMS to indicate in the RAR that only the PECsed are acceptable and required. **Open point:** RMS to update the PEC sediment calculations for HMPA using a default Koc value of 10000 mL/g and to include the metabolite HMPA in the residue definition for sediment in both an update to the RAR and the list of endpoints.

Subject	Conclusions Pesticide Peer Review Meeting
Experts' consultation 4.3 MSs to discuss in a meeting of experts the groundwater monitoring data from public survey reported in the public monitoring data assessment and interpretation study CA 7.5/002 (2020) in light of the additional information required to the applicants, and to agree if/how to use these data for EU regulatory purpose. MS to also discuss the published groundwater monitoring information associated with railway sites in Sweden and, as for the other groundwater monitoring information, to agree if/how to use these data for EU regulatory purpose.	Overall, for the period 1995-2020, a total of 251755 data for glyphosate analysed samples and 228453 data for AMPA analysed samples from 40031 and 35909 sampling sites, respectively, were assessed from groundwater monitoring in the updated RAR. The experts discussed and agreed with the RMS assessment of the outlier analysis and although the method applied appeared robust, it was considered not adapted to the specific case. The comparison against the threshold values, reported as exceedances of glyphosate concentration of drinking water standards resulted in only few cases, mostly sampled once. The RMS assessment that the results of the applicant's vulnerability evaluation should be taken with caution was endorsed by the experts for the reasons identified by the RMS in their assessment in the RAR. The experts discussed the topic of surface water becoming groundwater as a result of bank infiltration / the connectivity of surface water bodies to groundwater aquifers. In the published groundwater monitoring exercise carried out in Sweden from use on railways, the monitored levels provide reassurance that groundwater exposure above the parametric value generally did not occur in the monitored situations. However, for limited durations, concentrations above the parametric value can occur in individual samples. These monitoring results confirm that for the representative use of a single application per year to railways, groundwater exposure above the parametric limit of short duration under the Swedish conditions monitored is possible (1% exceedance in the down gradient wells, 6% (glyphosate) 4% (AMPA) exceedance of 0.1 µg/L in wells beneath the tracks where preferential connection to groundwater might have occurred). But for longer temporal exposure assessment goals, exposure above the parametric limit was not indicated. Overall, the experts agreed with the conclusion of the RMS that this groundwater monitoring dataset for glyphosate and AMPA was insufficient to use for regulatory groundwater exposure assessment and results need to be taken with caution. In relation to the bank infiltration / the connectivity of surface water bodies to groundwater aquifers, the experts acknowledged that the large proportion of agricultural land treated with glyphosate may make this a more important issue than for other active substances and their

Subject	Conclusions Pesticide Peer Review Meeting
	metabolites, but the route of entry to groundwater from surface water is in practice common to all uses of substances that have significant surface water exposure potential. In the published groundwater monitoring exercise carried out in Sweden from use on railways, the representative use of two applications per year was not covered by the monitoring exercise. The results of the monitoring would not be representative of conditions in the whole of the EU. However, it was concluded that this information is useful for the exposure assessment for the single use application pattern and Swedish conditions monitored. **Open point** The applicant's latest aquifer type analysis (one aspect of the applicant's vulnerability assessment) to be added to the amended RAR as this information is currently missing. **Open point** RMS to add references to publications and databases referenced in the updated groundwater public monitoring data assessment and interpretation study (2022) that are not in the RAR to the Vol. 3CA B.8 (AS) monitoring addendum at the end of the RMS study summary on page 145. **Open point** RMS to update Volume 1 of the RAR to discuss the issue of connectivity of surface water and groundwater and the potential for bank infiltration of glyphosate, AMPA and HMPA, considering the information in the study Sanchis *et al.* (2012)[3] and their conclusion on it. **Open point**

[3] Sanchís, J., Kantiani, L., Llorca, M. 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 402, 2335–2345 (2012). https://doi.org/10.1007/s00216-011-5541-y; (ERRATUM) Sanchís, J., Kantiani, L., Llorca, M. et al. Erratum to: 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 404, 617 (2012). https://doi.org/10.1007/s00216-012-5992-9

Subject	Conclusions Pesticide Peer Review Meeting
	EFSA to present in its conclusion the issue of connectivity of surface water to groundwater (including so called bank infiltration) and indicate in its conclusion that information to further address this route for groundwater exposure is a data gap. I.e. in a way comparable to what had been done in the previous peer review at EU level of glyphosate. **Open point** RMS to provide a summary and assessment of the groundwater monitoring associated with the use of glyphosate on railways in Sweden (publication Cederlund, 2022)[4] considering the discussion in the expert meeting in an amended RAR and include the results in the list of endpoints.
Experts' consultation 4.4 MSs to discuss in a meeting of experts if the general methodology of data collection of public monitoring data and the minimum quality criteria based on existing guideline documents for groundwater monitoring programs are applicable to surface water (SW) and sediment monitoring data. Experts also to agree if/how to use these data for EU regulatory purpose also in light of the additional information required to the applicants. In addition, the approach used by the RMS in the	For the period 1995-2020, a total of 308134 data for glyphosate analysed samples and 270813 data for AMPA analysed samples from 15004 and 12689 sampling sites, respectively, from public monitoring data were assessed for surface water in the updated RAR. The experts discussed and agreed that the general methodology of data collection proposed by the applicants, including the minimum quality criteria, were of limited applicability for the assessment of the data for regulatory purposes. The experts discussed and agreed with the RMS assessment of the outlier analysis and although the method applied appeared robust, it was considered not adapted to the specific case. The comparison against the threshold values, reported as exceedances of glyphosate concentration against the regulatory acceptable concentration (RAC) resulted in only few cases, mostly sampled once, while only two sites had consecutive exceedances. The RMS assessment that the results of the applicant's vulnerability evaluation should be taken with caution was endorsed by the experts for the reasons identified by the RMS in their assessment in the RAR. Above all, due to the very limited number of exceedances provided with the analysis, the experts concluded that there is no need in carefully scrutinising the factors used in the applicant's analysis.

[4] Cederlund, 2022. Environmental fate of glyphosate used on Swedish railways — Results from environmental monitoring conducted between 2007–2010 and 2015–2019. Science of The Total Environment Volume 811, 10 March 2022, https://doi.org/10.1016/j.scitotenv.2021.152361

Subject	Conclusions Pesticide Peer Review Meeting
assessment of SW monitoring data against the Drinking Water Directive (DWD) threshold for raw SW should be discussed.	Regarding the sediment monitoring data provided, the experts agreed with the RMS conclusion that the spatial/temporal distribution of the dataset is limited (i.e., 1272 samples for glyphosate and 1224 samples for AMPA from three EU MSs and for the period 2003-2019). The experts also agreed that the minimum quality criteria set in the FOCUS Groundwater Report (European Commission, 2014)[5] cannot be directly applicable to the sediment compartment. Overall, the experts agreed with the conclusion of the RMS that the surface water monitoring dataset for glyphosate and AMPA was insufficient to use for regulatory surface water exposure assessment and the results need to be taken with caution. Monitoring results from public survey cannot be assimilated to concentrations that can be used for regulatory exposure assessment and be assessed against a regulatory exposure assessment goal without additional information. For the sediment monitoring, the experts agreed that the limited dataset provided is not representative of the EU and a comparison of sediment concentrations with the RAC values is of limited use. **Open point** RMS to add references to publications and databases referenced in the updated surface water public monitoring data assessment and interpretation study (2022) that are not in the RAR to the Vol. 3CA B.8 (AS) monitoring addendum at the end of the RMS study summary on page 347.
Experts' consultation 4.5 MSs to discuss in a meeting of experts the available information on the drinking water monitoring data in light of the additional information requested to the applicants, and to agree if/how to use	Unaggregated drinking water monitoring data were only available from 4 member states regarding glyphosate and 3 for AMPA and the data were limited. The experts noted that a proportion of the data reported are not recent. No information was available in the study regarding the origin of raw data for drinking water. The experts noted that the findings of glyphosate exceeding the pesticide standard for drinking water of 0.1 µg/L in some samples, reflects a legal breach of the drinking water regulation.

[5] European Commission, 2014. Assessing potential for movement of active substances and their metabolites to ground water in the EU. Report of the FOCUS Workgroup. EC Document Reference SANCO/13144/2010-v. 3, 613 pp.

Subject	Conclusions Pesticide Peer Review Meeting
these data for EU regulatory purpose.	Overall, the experts considered that the available data from individual drinking water samples were of limited value for assessment for the whole EU, as unaggregated values only originated from a few countries. The member state experts agreed with the RMS statement in the RAR that the data discussed here should be considered with caution and further information might be requested at MS level for product registration. **Open point** RMS to carry out the action that was indicated at open point 4.125 in the evaluation table.
Experts' consultation 4.6 MSs to discuss in a meeting of experts the relevance of the available monitoring data for glyphosate in the air compartment and to agree if/how this information can be used in the EU regulatory exposure assessment.	The experts discussed the assessment of the monitoring data for glyphosate and the metabolite AMPA that was reported in the updated RAR in relation to the air compartment. In particular, the discussion focused on the public monitoring raw data originated only from France covering the period 2018-19 (381 samples from 8 sites) and the additional information provided from literature review with monitoring studies in Germany and France. The experts noted that despite the few data available and the intrinsic properties of glyphosate and AMPA, there is a high frequency of quantified samples with values > the limit of detection (LOD) for glyphosate, with the frequency for AMPA being lower. The experts agreed that for the design of the studies, the concentrations detected are proposed to mainly be related to the particulate-bound concentration, as a result of wind-eroded particle transportation, rather than volatilisation. Overall, the experts agreed with the conclusion of the RMS that this very limited air monitoring dataset for glyphosate and AMPA was insufficient to use for regulatory air exposure assessment and the results need to be taken with caution.
New experts' consultation point 4.7 proposed by EFSA for completeness of discussion (October 2022):	Formally, in line with the legislation, there is no legal obligation to consider newly available data submitted outside of the dedicated public and targeted consultations or after the deadline of the window for providing the additional information within the clock stop period, unless they constitute adverse data (cf Article 56 of Regulation (EC) No

Subject	Conclusions Pesticide Peer Review Meeting
Experts to consider some potentially relevant newly available publications arisen after the public consultation/reporting table stage. EFSA identified a number of publications that might be considered potentially relevant and therefore it was agreed to share these selected studies with MSs to allow a peer review and further consideration in the expert meetings. In particular, MS experts are asked to share their views whether these potentially relevant articles might be considered more critical or may alter the weight of evidence in the current assessment and to determine if any eventual follow up would be needed.	1107/2009 regarding information on potentially harmful or unacceptable effects). For this reason, although a systematic review of the literature has not been carried out by EFSA or RMS, EFSA has identified newly available papers on glyphosate even outside of the legal requirements and collected a list of studies as a result. As an outcome of this exercise, after a preliminary assessment, EFSA identified a publication on groundwater monitoring associated with railway sites in Sweden as potentially relevant: Cederlund, H. (2022) Environmental fate of glyphosate used on Swedish railways results from 2007-2010 and 2015-2019. Science of the Total Environment 811 (2022) 152361. Conclusions from the discussion on this paper can be found earlier in this meeting report at experts' consultation point 4.3.

REPORT OF PESTICIDE PEER REVIEW TC 82

GLYPHOSATE – AIR V

Rapporteur Member State: Assessment Group on Glyphosate (AGG) consisting of FR, HU, NL, SE

5. Ecotoxicology

Date: 2 December 2022

List of participants:

Institute	**Member States Country code**
Austrian Agency for Health and Food Safety (AGES)	AT
Umweltbundesamt / German Environment Agency (UBA)	DE
Federal Research Centre for Cultivated Plants Institute for Bee Protection	DE
DEPA	DK
Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail (ANSES)	FR
National Food Chain Safety Office (NEBIH)	HU
Department of Agriculture, Food and The Marine	IE
Ctgb	NL
Swedish Chemicals Agency	SE
Kmetijski Inštitut Slovenije / Agricultural Institute of Slovenia	SI
External experts (4)	EFSA
Hearing expert in private capacity	N/A
Observers (4)	CH

Pesticide Peer Review TC 82 (21 November – 2 December 2022)
Glyphosate

In accordance with EFSA's Policy on Independence[1] and the Decision of the Executive Director on Competing Interest Management[2,] EFSA screened the Annual Declarations of Interest filled out by the participants invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process, and no interests were declared orally by the members at the beginning of this meeting.

[1] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf
[2] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf

Discussion points/Outcome

5. Ecotoxicology

Please note that information part of this report may have been masked by EFSA in accordance with Article 63 of Regulation (EC) No 1107/2009 as well as EFSA's Practical Arrangements concerning confidentiality in accordance with Articles 7 and 16 of Regulation (EC) No 1107/2009, or EFSA's Practical Arrangements concerning transparency and confidentiality as a consequence of confidentiality requests submitted by the applicant on application dossiers for pesticides active substances or Maximum Residue Levels, respectively. Please note that information disclosed in this report is without prejudice to pre-existing intellectual property rights and data exclusivity clauses set out in Union law, and particularly in Article 62 of Regulation (EC) No 1107/2009.
Minutes might be revised due to pending data gaps at the time of the meeting and /or eventual need for further follow up consultation after the meeting. If needed, the final agreement will be made available in the meeting report published at the end of the peer review process.

Subject	Conclusions Pesticide Peer Review Meeting
Experts' consultation 5.1 The appropriate endpoint for the reproductive risk assessment to wild mammals should be discussed and agreed.	The experts discussed the most appropriate reproductive endpoint for the risk assessment for wild mammals considering all of the data available in the toxicology section B.6 of the RAR. Overall, the experts at the meeting decided that, further to the assessment of the RMS, the ecological relevance of the endpoints should be considered. When the ecological relevance is considered, the most appropriate endpoint is 150 mg a.s./kg bw per day from the rabbit developmental toxicity study and is based on observed developmental and maternal effects occurring at 200 mg a.s./kg bw per day. All experts were in agreement with the endpoint. The meeting agreed that this endpoint should be used for all wild mammal species. The meeting agreed that there was no additional information from the open literature which should be further considered for the selection of the appropriate endpoint. **Open point** RMS to reflect the outcome of the discussion in the RAR for the selection of the reproductive endpoint to be used for the assessment of wild mammals and to update the risk assessment in the RAR and list of endpoints (LoEP).

Subject	Conclusions Pesticide Peer Review Meeting
Experts' consultation 5.2 The appropriate reproductive toxicity endpoint for birds should be discussed and agreed. This discussion should be combined with the discussion under expert consultation point 5.4 where information from the literature studies should be considered.	The experts discussed the appropriate reproductive toxicity endpoint for birds considering the 4 reproduction studies available in the RAR and whether there were any suitable data from the literature (the latter was discussed under expert consultation point 5.4). Overall, all experts agreed with the RMS' proposal that the endpoint for risk assessment should be the no observed adverse effect level (NOAEL) of 117 mg a.s./kg bw per day based on the mallard duck study. **Open point** RMS to reflect in the RAR (and to update the list of endpoints (LoEP) accordingly) that the endpoint from study CA 8.1.1.3/005 (1978) on the mallard duck is not valid, considering the lack of analytical verification. The RMS may also reflect that the peer review expert meeting agreed to use a NOAEL of 117 mg a.s./kg bw per day based on the mallard duck study (1999, CA 8.1.1.3/004).
Experts' consultation 5.3 The appropriate acute toxicity endpoint to be used in the risk assessment for wild mammals should be discussed and agreed.	The experts discussed the appropriate acute toxicity endpoint to be used in the risk assessment for wild mammals considering all of the data available in the toxicology section B.6 of the RAR. Overall, considering the following: - The unusually large body of evidence showing the occurrence of sublethal effects in acute mammal studies - consideration that the overall risk assessment is not driven by acute effects (i.e., the reproductive risk assessment for wild mammals is what drives the outcome of the assessment) - acknowledgement that this is not a standard approach for acute risk assessment considering that the risk assessment methodology is calibrated against lethal effects - the geomean approach was proposed to account specifically for the observed sublethal effects The meeting agreed with the new proposal by the RMS specifically for glyphosate. Therefore, the geomean LD_{50} (3447 mg/kg bw) should be used for the screening and Tier-1 assessment.

Subject	Conclusions Pesticide Peer Review Meeting
	Open point RMS to reflect the outcome of the discussion for the selection of the acute toxicity endpoint for wild mammals and update the risk assessment in the RAR and LoEP by using the geomean endpoint (3447 mg/kg bw) in the screening and Tier-1 assessment.
Experts' consultation 5.4 The experts should discuss the study of 'Ruuskanen S. et al. (2020), Female Preference and Adverse Developmental Effects of Glyphosate-Based Herbicides on Ecologically Relevant Traits in Japanese Quails' and any other relevant literature which provide information on the effects of glyphosate to birds. The discussion should focus on two aspects: i) Firstly, the experts should discuss whether the literature studies provide any reliable standard endpoints (i.e., those mentioned in EFSA (2009)[3] and in OECD 223, OECD 206 or the EPA OCSPP 850.2300) to be used in the acute and reproductive risk assessment. ii) Secondly, the experts should discuss and reflect whether there are additional endpoints coming from the literature which are not	The experts at the meeting considered the assessment of the RMS of the literature data for birds. The meeting agreed that some of the endpoints assessed in the three studies by Ruuskanen et al, 2020[1, 2, 3] (see references below) may be of ecological relevance, such as those relating to reproductive output and embryonic development. The experts agreed with the RMS that the relevance criteria for the tested formulation discussed under expert consultation point 5.10, will mean that the relevance classification for these studies will be amended to "less relevant but supplementary". Overall, the experts agreed that the reliability assessment for the three studies by Ruuskanen S. et al. 2020 should be updated considering the reliability criteria agreed under expert consultation point 5.12 and the additional reliability criteria for food consumption and timing of exposure. **Open points** RMS to reflect the outcome of the discussion on bird literature studies in a revised RAR. Additionally, the RMS is requested to update the reliability assessment (three studies by Ruuskanen S. et al., 2020[1, 2, 3]) considering the reliability criteria agreed under expert consultation point 5.12 and the additional reliability criteria for food consumption and timing of exposure. The RMS will also need to update the relevance assessment for these studies. RMS to move the exposure criterion of exposure duration from table 3 to table 1 in the RAR CA Appendix literature and to clarify that the criterion also considers the timing of the exposure related to the endpoint being measured.

[3] EFSA (European Food Safety Authority), 2009. Guidance on Risk Assessment for Birds and Mammals on request from EFSA. EFSA Journal 2009;7(12):1438, 358 pp. doi:10.2903/j.efsa.2009.1438

Subject	Conclusions Pesticide Peer Review Meeting
normally assessed in the standard regulatory studies.	**References cited from the open literature** [1] Ruuskanen S. *et al.* 2020. Female Preference and Adverse Developmental Effects of Glyphosate-Based Herbicides on Ecologically Relevant Traits in Japanese Quails Environmental science & technology (2020), Vol. 54, No. 2, pp. 1128-1135 [2] Ruuskanen, S., Rainio, M.J., Uusitalo, M. et al. Effects of parental exposure to glyphosate-based herbicides on embryonic development and oxidative status: a long-term experiment in a bird model. Sci Rep 10, 6349 (2020). https://doi.org/10.1038/s41598-020-63365-1 [3] Ruuskanen S, Rainio MJ, Gómez-Gallego C, Selenius O, Salminen S, Collado MC, Saikkonen K, Saloniemi I, Helander M. Glyphosate-based herbicides influence antioxidants, reproductive hormones and gut microbiome but not reproduction: A long-term experiment in an avian model. Environ Pollut. 2020 Nov;266(Pt 1):115108. doi: 10.1016/j.envpol.2020.115108. Epub 2020 Jul 5. PMID: 32768925.
Experts' consultation 5.5 Experts to discuss and agree on the risk assessment for birds and mammals from plant metabolites.	The experts discussed and agreed on the risk assessment for birds and mammals from plant metabolites. The discussion considered the risk from metabolite AMPA and also whether there were additional metabolites which require assessment. Overall, the meeting agreed with the assessment from the RMS that the risk to birds and wild mammals from the plant metabolite AMPA in primary crops is covered by the assessment for the parent. In addition, the risk from AMPA in rotational crops is considered to be addressed considering that the concentration in plant would not exceed that of the parent in primary crops. In addition, assuming it was confirmed that there are no additional metabolites in plants above 10% (other than those discussed above), the experts agreed that the risk to birds and mammals from plant metabolites is addressed**.** **Open points** - RMS to include an assessment in the B.9 section of the RAR confirming that there are no additional plant metabolites exceeding 10%, considering the valid data presented in the residues section.

Subject	Conclusions Pesticide Peer Review Meeting
	- RMS to reflect in a revised RAR the meeting discussion on the risk assessment for birds and mammals from plant metabolites.
Experts' consultation 5.6 Experts to discuss the refined risk assessment for mammals. This discussion may include a risk assessment using a refined DT_{50} in plants and/or population modelling.	The discussion was separated into three mains points: i) reliability of the refined DT_{50} value, ii) the available population modelling and iii) the final reproductive risk assessment for small herbivorous mammals. i) <u>Reliability of refined DT_{50} value</u> Overall, the experts agreed that, since only a single reliable DT_{50} value was available, a quantitative refinement of the DT_{50} in risk assessment was not appropriate. However, it was concluded that a qualitative use of the residue dissipation studies may be appropriate, i.e., to note that some data were available suggesting that the dissipation is faster than the default value of 10 days. ii) <u>Reliability of the population modelling</u> Overall, the experts agreed with the evaluation as performed by the RMS, noting several additional aspects as outlined in the open points below. Therefore, the experts concluded that the modelling could not be used to refine the risk to small herbivorous mammals for the representative uses under assessment. iii) <u>Overall outcome of the reproductive risk assessment for small herbivorous mammals</u> Overall, the experts agreed that the RMS should update their assessment reflecting on the relevance of the exposure scenarios for small herbivorous mammals by considering their likely presence. In addition, the RMS should reflect that a quantitative reduction of the exposure estimate cannot be done for the spot applications without suitable data. Instead, the RMS should reflect that the spot application should be considered as a qualitative argumentation. **Open points** - The RMS should update the study evaluations of the 4 GLP trials (IF-93/04572-01, AS/1911/CN, IF-93/13842-01, AS/1912/CN) to provide an evaluation of the geographical independence of the

Subject	Conclusions Pesticide Peer Review Meeting

	study sites, in accordance with the recommendations of EFSA (2019)[4].
	- The RMS should also reflect the outcome of the discussion regarding the reliability of the refined DT_{50} value in the revised RAR. The endpoint should not be included in the LoEP.
	- RMS to update the risk assessment taking into account the exposure scenarios where the presence of small herbivorous mammals was considered unlikely.
	- In addition, the RMS should reflect that a quantitative reduction of the exposure estimate cannot be done for the spot applications without suitable data. Instead, the RMS should reflect that the spot application should be considered as a qualitative argumentation.
	
	Open points
	
	- RMS to include the applicants' summaries on the population model in the revised RAR.
	- RMS to include the evaluation of the model and model study in the Appendix of the RAR.
	- RMS to update the study evaluation of the population modelling in the RAR including that the exposure modification factor (EMF) of 5 shall be considered as a positive control.
	- RMS to reflect the additional concerns and uncertainties identified in the meeting regarding the suitability of the available modelling for the current risk assessment, in the study evaluation in the Appendix of the RAR:
	
	  - There is a need for justification that the modelled spp. (common vole) is appropriate for the EU GAPs under assessment
	  - problem formulation: relevance of the modelling GAPs in comparison to the GAPs under assessment
	  - geographical relevance of the model to the EU territory
	  - an updated reliability assessment for the toxicology data package in the context of the evaluation of the model
	  - The modelling should have explored the consequences of structural uncertainty due to the implemented way of density regulation in the model. In particular, the assumption of less

[4] EFSA (European Food Safety Authority), 2019. Technical report on the outcome of the Pesticides Peer Review Meeting on general recurring issues in ecotoxicology. EFSA supporting publication 2019:EN-1673. 117pp. doi:10.2903/sp.efsa.2019.EN-1673

Subject	Conclusions Pesticide Peer Review Meeting
	resources for maintaining than for establishing home-range. (A question that could be replied is "Why is population density not decreasing when food resources significantly decrease due to glyphosate application?") - Considering the specificity to the GAP uses under assessment, a consideration should be given to the realism and conservativeness of the landscape scenario in relation to the assumptions on spray drift, mowing events, timing, rate and frequency of application, dissipation of the active substance in plant matrices, assumption of the complete wilting after 10 days.
Experts' consultation 5.7 Experts to discuss the assumptions that have been made for the bird and mammals risk assessment for the uses to railway tracks and for invasive species.	The experts discussed the assumptions that have been made for the bird and mammals risk assessment for the uses to railway tracks and for invasive species. Overall, the meeting agreed with the principles of the RMS assessment for the railway track uses but considered that some additional reflections should be made in the RAR (see open points). Overall, the experts agreed with the assessment by the RMS for the use to invasive species with the additional note that the high interception value would not be suitable in the case of the cut-stem (included in the GAP) or treatment of less established plants. Nevertheless, in these cases a qualitative argumentation can be made considering that the application is via spot treatment and applications to cut-stem and young plants are not expected to be made to extensive areas of the field. However, should application be made to more extensive treatment areas, the available assessment would not cover this situation. **Open points** - The RMS should clarify in the RAR that the underlying assumption for the exposure assessment for the use to railways is that spray direction is downward and that the embankments are not treated with a side-ward sprayer.

Subject	Conclusions Pesticide Peer Review Meeting
	- The RMS should update the risk assessment by assuming the worst-case drift value of 0.47% from HardSPEC (Hollis et al, 2017[5]). - RMS to reflect the additional argumentations for invasive species including consideration of cut stem and young plants and the additional qualitative arguments concluded at the meeting. RMS to perform updated calculations for the spot treatment using the revised endpoint for mammals.
Experts' consultation 5.8 Experts to discuss the endpoints obtained from studies where pH was (potentially) lowered by high concentrations of glyphosate in its acid form along with their use in the risk assessment.	When glyphosate active substance is tested in its acid form at high concentrations, it may significantly lower pH of the test medium if not buffered. There is evidence that, in some experiments, the observed effects on aquatic organisms are not linked to direct toxicity of glyphosate, but rather to the induced acid conditions. To disentangle true effect of glyphosate from pH alteration, it was agreed that the approach taken by the RMS is appropriate in terms of excluding data points obtained under conditions of pH being outside the range recommended in the relevant OECD guidance. It was also agreed that for literature studies in which pH was not measured and glyphosate acid was tested at concentration > 10 mg/L, the reliability score will be impacted (refer to expert consultation point 5.12 for the dedicated discussion and related open points).
Experts' consultation 5.9 Experts to agree on the classification of literature aquatic studies where analytical verification of the tested concentrations is completely lacking or incomplete.	Analytical verification of the tested concentration is an important quality-related aspect of ecotoxicological tests with aquatic organisms that ensures the accuracy of the endpoints derived from such studies. The database available for glyphosate presents different situations in terms of analytical verification, with different levels of associated uncertainty. Four categories were agreed to identify the reliability of dossier and literature studies and the related usability in the risk assessment:

[5] Hollis, Ramwell, Holman and Whelan, HardSPEC A First-tier Model for Estimating Surface- and Ground-Water Exposure resulting from Herbicides applied to Hard Surfaces. Updated Technical Guidance on Model Principles and Application for version 1.4.3.2. Version 2.1, April 2017.
https://www.hse.gov.uk/pesticides/pesticides-registration/data-requirements-handbook/fate/hardspec/HardSPEC_Guidance.pdf

Subject	Conclusions Pesticide Peer Review Meeting
	1. Verification of test item in solution throughout the experiment according to OECD. Reliable. Can be used for endpoint setting (quantitative risk assessment). 2. Verification of test item at the beginning of the test. Reliable with restrictions. Can be used for EP setting (quantitative risk assessment). 3. Verification of test item in stock solutions and presence of dose-response. Reliable with restrictions. Can be used for endpoint setting (quantitative risk assessment). 4. No analytical verification at all. Supportive or Unreliable. Not to be used for quantitative risk assessment, but in principle usable in uncertainty analysis. **Open point** RMS to update the reliability assessment of the available studies in a revised RAR by following these recommendations, to be incorporated in the outcome of expert discussion point 5.12.
Experts' consultation 5.10 Pending on the comparison between different formulations used in literature studies and the representative formulation 'MON 52276' and the active substance, experts to consider whether the available ecotoxicological data should be considered for potential use of endpoints obtained with these formulations for the risk assessment.	The following conclusions were agreed in order to improve the readability and the consistency of the methodology used for classifying the relevance of literature studies concerning the formulation being tested in the reported experiments. 1. Application of the flow diagram presented by EFSA, based on the following steps: • Is there information on the formulation? • If NO: **Potentially relevant but insufficient information.** • If YES: Is there evidence of forbidden surfactants? • If YES: **Not relevant.** • If NO: Is the composition similar to 'MON 52276'? • If YES: **Relevant.** • If NO: **Less relevant but supplementary.** 2. Check that any of the trade names of the representative formulation included in Volume 4 (for all applicants) have been used in literature studies. If this is the case, extrapolation should be carried out according to point 3. 3. Extrapolation at all points throughout the flow diagram is possible if formulations have the same trade name, they are used in the same country within 4 years. These criteria should

Subject	Conclusions Pesticide Peer Review Meeting
	be applied in any case, irrespectively of the suspected presence of forbidden surfactants (e.g., polyoxyethylene tallow amine (POEA)). 4. To use the agreed Relevance vs. Reliability table in terms of usage of study data for the risk assessment. 5. In the last point of the workflow proposed at the meeting, the relevance has to be proven against the formulation for representative uses 'MON 52276'. 6. The endpoints categorised under relevant + reliable or reliable with restrictions should be included in the list of endpoints (LoEP). All experts agreed with the conclusions. **Open points:** 1. Application of the flow diagram should be captured in the RAR (point 1 of the overall conclusions above) and categorisation of the available studies should be harmonised. 2. Captured in point 2 of the overall conclusions above. 3. Captured under point 3 of the overall conclusions above. 4. After the RMS completed the update of points 1-3 in the RAR, it should be confirmed that the available assessments cover the formulation for the representative uses and the active substance (e.g., including co-formulants). 5. Captured under point 6 of the overall conclusions above.
Experts' consultation 5.11 Experts to consider the available data to conclude on whether the toxicity of glyphosate to fish covers toxicity to the aquatic stages of amphibians.	The following conclusions were achieved at the meeting: 1. All studies on the aquatic stages of amphibians need to be reviewed in terms of relevance and reliability criteria as agreed (see expert consultation points 5.10 and 5.12). It is key that these criteria are applied consistently. 2. Since relevant and reliable chronic endpoints for amphibians are not available, it is not possible to compare chronic hazard for fish and amphibians. A full comparability between fish and aquatic stages in amphibians would anyway be hampered by the different endpoints being measured for the two groups.

Subject	Conclusions Pesticide Peer Review Meeting
	3. The current comparison based on the lowest endpoint for fish and the geomean for amphibians was considered not appropriate in view of uncertainty in the geomean calculation for amphibians pooling data from different life stages of the same species and in view of such comparison not being balanced. Thus, it was agreed that the comparison between fish and amphibians should be based on the lowest endpoint from each group. On such basis, the acute hazard for glyphosate active substance to amphibians is covered by the one for fish. 4. There is a need to remove Moutinho et al. (2020) from the acute studies, since it presents results for a 23-day exposure duration. 5. As information was provided only on a limited number of studies and formulations, the RAR should reflect that the data requirement for providing details on formulation was not completely fulfilled by the applicants. 6. Following the discussion and the agreement achieved under expert consultation point 5.10, the relevance classification of the study from Wagner et al. (2017) might need to change from 'Relevant' to 'Less relevant but supplementary'. This would hamper its use for a quantitative comparison of the representative endpoint for fish and amphibians. 7. Some data with the formulations without POEA seem to indicate a higher toxicity than the active substance to amphibians. However, it is unknown how comparable these formulations are to the representative one. The inability to compare them was because such comparison was not provided by the applicants. Specifically for the literature study by Tartu et al. (2022) identified by EFSA as potentially relevant for the assessment: 8. Some of the key reliability points could not be fully addressed by looking at the information included in the paper, however it was agreed that the authors would not be contacted, since it is outside of the scope of the peer-review to further contact the authors at this point of the process. 9. A summary of Tartu et al. (2022) should be included in the RAR and evaluated for relevance and reliability. 10. It was agreed that the information available for analytical verification is insufficient to conclude that this was actually

Subject	Conclusions Pesticide Peer Review Meeting
	performed for the experiment reported in the paper. The reliability classification should follow what was agreed under expert consultation points 5.9 and 5.12. 11. The example set by Cheron et al. 2020, not captured in the literature review submitted by the applicants, will be considered in the discussion point related to the coverage of the literature review. **Open points:** RMS to update the RAR with the following conclusion: • Clarify that the acute hazard of glyphosate to amphibians is covered by the one for fish; • Update every comparison by taking the lowest endpoints amongst the relevant and reliable ones for both fish and amphibians; • Relevance and reliability of the amphibian studies should be revised according to what was agreed under expert consultation points 5.12 and 5.10; • To remove the endpoint from Moutinho et al. (2020) from the list of acute studies in the RAR; • To reflect that the data requirement for providing details on formulation was not completely fulfilled by the applicants; • To clarify that some data with the formulations without POEA seem to indicate a higher toxicity than the active substance to amphibian, and the implication of this. • RMS to include a summary of Tartu et al (2020) in the RAR and assess its relevance/reliability. **References cited from the open literature** Cheron M and Brischoux F, 2020. Aminomethylphosphonic acid alters amphibian embryonic development at environmental concentrations. Environ Res, 190:109944. doi: 10.1016/j.envres.2020.109944 Moutinho MF, de Almeida EA, Espindola ELG, Daam MA and Schiesari L, 2020. Herbicides employed in sugarcane plantations have lethal and sublethal effects to larval *Boana pardalis* (Amphibia, Hylidae). Ecotoxicology, 29:1043-1051. doi: 10.1007/s10646-020-02226-z Tartu S, Renoirt M, Cheron M, Gisselmann L-L, Catoire S and Brischoux F, 2022. Did decades of glyphosate use have selected for resistant amphibians in agricultural habitats? Environ Pollut, 310:119823. doi: 10.1016/j.envpol.2022.119823

Subject	Conclusions Pesticide Peer Review Meeting
	Wagner N, Muller H and Viertel B, 2017. Effects of a commonly used glyphosate-based herbicide formulation on early developmental stages of two anuran species. Environ Sci Pollut Res Int, 24:1495-1508. doi: 10.1007/s11356-016-7927-z
Experts' consultation 5.12 Experts to discuss the reliability criteria and classification system to be used for all studies.	The following conclusions were achieved at the meeting: To ensure the same levels of evaluation for both literature and dossier studies, the following reliability classification should be used (based on the agreed classification under expert consultation point 5.9), and to ensure that the categories are equivalent among dossier and literature studies: • Reliable: used for the quantitative risk assessment • Reliable with restrictions: used for the quantitative risk assessment • Supportive (to be used in assisting for uncertainty analysis in the risk assessment). • Unreliable: not to be used. It was agreed that in order to acknowledge situations which are deemed of concern for downgrading the studies, at the bare minimum, the following **key criteria** should be considered: 1. Test method: if the study is conducted according to OECD protocols, it has to meet the OECD validity criteria. 2. Analytical measurement: see expert consultation point 5.9. 3. pH measurement: see expert consultation point 5.8, even though it is a specific point for the glyphosate acid. 4. Performance of negative control is suitable. If control / information on the control is not available, or in case of very clear deviation (e.g. high mortality), the study shoud not be used for quantitative endpoint derivation. 5. Level of detail of results: Raw data are not required. Table or plots that are reporting data for each tested dose, and the associated variability among replicates. 6. Statistical methods: qualitative assessment of robustness of statistical methods (at the bare minimum, replication is present and statistical methods are reported). 7. General characteristics of the organisms: information on age/life stage, sex and/or size of organisms should be available, when appropriate.

Subject	Conclusions Pesticide Peer Review Meeting
	8. Reporting of test item: in case of formulation/product, the dosing can be expressed with sufficient level of certainty as concentration of glyphosate active substance. For all the criteria which are applicable: • If even one of the key criteria is not met, the study should be downgraded as Unreliable or Supportive. • If one to two of the key criteria is not met: Supportive. • If three or more of the key criteria are not met: Unreliable. **Open point** RMS to update the reliability evaluation of the studies in the RAR according to the abovementioned criteria.
Experts' consultation 5.13 Experts to assess whether any new literature study provided after the commenting phase has an impact on the aquatic risk assessment.	The following conclusions were achieved at the meeting: • There is a need to update the reliability and relevance classification for all studies in light of the agreement of expert consultation points 5.10 and 5.12. • For **acute fish**: Wan et. al, 1989 should be downgraded based on a lack of biological information. • For **chronic fish**: Abdulkareem et al, 2014 should also be downgraded due to multiple issues. Du-Carree et al, 2021: no relevant effect was seen at the only tested concentration. Therefore, no endpoint should be set based on this study. • For **acute invertebrates**: Bringolf et al, 2007 was considered to be not sufficiently reliable for endpoint derivation due to lack of detailed reporting of the results. In the Akcha (2012), no relevant adverse effect was seen at the highest tested concentration. • For **chronic invertebrates**: Bringolf et al, 2007 should be revised since it is potentially relevant and reliable and might have an impact on the selected endpoint for chronic invertebrates. It was agreed that the endpoints measured in the Janssens (2017) study are not relevant since emergence rate was not measured; growth rate was only measured at the final instar larvae. Baglan et al, 2018: there was also no impact in the highest tested concentration. • For **aquatic plant**/Glyphosate: Roshon, 1997: The study is not useable for endpoint derivation based on the lack of analytical verification. Avaliable data show that the ErC_{50} for shoot length

Subject	Conclusions Pesticide Peer Review Meeting
	should be higher than the highest tested concentration (2.987 mg/L). • For **aquatic plant**/AMPA: Tajnaiova et al, 2020, should be considered supportive only at best. This could feed into the uncertainty analysis to indicate that *Lemna* would be more sensitive than *Myriophyllum aquaticum*. • **General conclusion**: the data from literature are not impacting on the endpoints selection previously performed by the RMS with the only exception represented by Bringolf et al, 2007, which should be reconsidered for the derivation of the chronic endpoint for invertebrates. **Open points** • RMS to reconsider the study from Bringolf et al, 2007, that could impact the chronic risk assessment for invertebrates. • RMS to reconsider the reliability and the relevance classification of the literature studies presented at the meeting in line with the outcome of the expert consultation points 5.10 and 5.12. **References cited from the open literature** Abdulkareem SI, Lawal NO and Moyebi OD, 2014. Effect of lethal and sublethal concentrations of glyphosate on some biochemical parameters and growth responses of African catfish (Clarias gariepinus). Egyptian Academic Journal of Biological Sciences B Zoology, 6:47-54 Akcha F, Spagnol C and Rouxel J, 2012. Genotoxicity of diuron and glyphosate in oyster spermatozoa and embryos. Aquat Toxicol, 106-107:104-113. doi: 10.1016/j.aquatox.2011.10.018 Baglan H, Lazzari CR and Guerrieri FJ, 2018. Glyphosate impairs learning in Aedes aegypti mosquito larvae at field-realistic doses. J Exp Biol, 221. doi: 10.1242/jeb.187518 Bringolf RB, Cope WG, Mosher S, Barnhart MC and Shea D, 2007. Acute and chronic toxicity of glyphosate compounds to glochidia and juveniles of Lampsilis siliquoidea (Unionidae). Environ Toxicol Chem, 26:2094-2100. doi: 10.1897/06-519R1.1 Du-Carree JL, Morin T and Danion M, 2021. Impact of chronic exposure of rainbow trout, Oncorhynchus mykiss, to low doses of glyphosate or glyphosate-based herbicides. Aquat Toxicol, 230:105687. doi: 10.1016/j.aquatox.2020.105687 Janssens L and Stoks R, 2017. Stronger effects of Roundup than its active ingredient glyphosate in damselfly larvae. Aquat Toxicol, 193:210-216. doi: 10.1016/j.aquatox.2017.10.028

Subject	Conclusions Pesticide Peer Review Meeting
	Roshon RD, 1997. A toxicity test for the effects of chemicals on the non-target submersed aquatic macrophyte, Myriophyllum sibiricum Komarov. University of Guelph. 496 pp. Tajnaiova L, Vurm R, Kholomyeva M, Kobera M and Koci V, 2020. Determination of the Ecotoxicity of Herbicides Roundup((R)) Classic Pro and Garlon New in Aquatic and Terrestrial Environments. Plants (Basel), 9. doi: 10.3390/plants9091203 Wan MT, Watts RG and Moul DJ, 1989. Effects of different dilution water types on the acute toxicity to juvenile Pacific salmonids and rainbow trout of glyphosate and its formulated products. Bull Environ Contam Toxicol, 43:378-385. doi: 10.1007/BF01701872
Experts' consultation 5.14 Experts to agree on the relevance of the exposure via overspray for aquatic macrophytes in view of the intended uses of glyphosate. In case this is found to be relevant, the experts should discuss and agree on the outcome of the risk assessment in view of the additional information provided by the applicants.	The following conclusions were achieved at the meeting: 1. In light of the robustness of the study by Sesin et al. (2020) and in light of the mode or action of glyphosate, all the experts unanimously agreed on the relevance of the exposure route via overspray of the emerging part of the macrophyte. 2. In light of the test item (containing POEA) and the non-standard species used in the study, it was considered that no relevant endpoint could be derived from Sesin et al. (2020). 3. It was agreed not to carry out an illustrative risk assessment using endpoint from Sesin et al. (2020). The data gap identified by the RMS will remain and further information should be requested to assess this route of exposure. **References cited from the open literature** Sesin V, Davy CM, Stevens KJ, Hamp R and Freeland JR, 2021. Glyphosate Toxicity to Native Nontarget Macrophytes Following Three Different Routes of Incidental Exposure. Integr Environ Assess Manag, 17:597-613. doi: 10.1002/ieam.4350
Experts' consultation 5.15 Experts to agree on the relevant chronic endpoint for fish.	The following conclusions were achieved at the meeting: 1. Study CA 8.2.2.1/002: It was agreed that the more appropriate endpoint from this study is the NOEC (1 mg/L) in order to cover the lethargy effect. However, the study can only be retained for

Subject	Conclusions Pesticide Peer Review Meeting
The discussion should consider: - That the endpoint currently set by the RMS (NOEC = 1 mg/L) is based on lethargy/mortality observed in the study (2000, CA 8.2.2.1/002); - That the reliability of any endpoint obtained from study (2000, CA 8.2.2.1/002) has been questioned; - That it is theoretically possibile to replace the NOEC with an EC_{10} for the same parameters, in consideration of the additional information provided by the applicants and of the estimation provided by DE (i.e. mortality EC_{10} = 4.6 mg/L [2.45 – 6.75]); - The reliability and the outcome of the available early life stage (ELS) study CA 8.2.2.1/001 (2010) on rainbow trout also in light of the additional information provided by the applicants; - The reliability and the outcome of the available fish full life cycle (FFLC) study (CA 8.2.2.2/001), also in light of the additional information provided by the applicants;	endpoint derivation if the analytical methods used are considered fit for purpose (see open point below). 2. Early life stage (ELS) study CA 8.2.2.1/001: All experts agreed with the approach proposed by the RMS and to set the NOEC at 2.804 mg a.e./L. It was decided not to retain any value from the EC_{10} parameter for hatching because, particularly the lower limit of the EC_{10}, it was considered to be poorly representative of the experimental results (below the NOEC where no effects were recorded). 3. Fish full life cycle (FFLC) study CA 8.2.2.2/001: All experts agreed with the approach proposed by the RMS to consider the study uniquely as supportive, mainly due to the analytical methods not being considered fit for purpose. 4. Other literature studies: After considering the available data from literature, the experts at the meeting did not identify reason to lower the chronic endpoint for fish. Rather, they considered that literature data could support the currently selected endpoint. **Open point** RMS to check if the analytical methods are available and fit for purpose for the study CA 8.2.2.1/002. If yes, the study could be used for endpoint derivation and in this case, the more appropriate endpoint agreed is the NOEC (1 mg/L) in order to cover the lethargy effect. If not, the study should be downgraded in terms of reliability classification.

Subject	Conclusions Pesticide Peer Review Meeting
- All other available information, including literature data (e.g. Uren Webster et al., 2014)[6].	
Experts' consultation 5.16 Experts to discuss the reliability and the potential use of any endpoint from the study by Dai, P. et al., 2018 in the risk assessment for bees.	The test design of the study by Dai et al., 2018 is very similar to OECD 239 guidance. However, several key aspects of the design are missing or not reported. Furthermore, the statistical trend observed on the larval survival is not supported by the other biological observations. The experts agreed that the reliability of the study needs to be reclassified according to the criteria agreed under expert consultation point 5.12. In addition, the experts agreed that the reliability and the relevance of all the studies on bees from the literature should be reclassified according to the criteria agreed under expert consultation points 5.10 and 5.12. **Open point** RMS to further evaluate Dai et al. (2018) using the reliability criteria agreed under expert consultation point 5.12, except for the reliability criterion addressing pH. RMS to reflect the potential changes in a revised RAR. **Open point** RMS to evaluate all the other available bee studies from literature included in the RAR using the reliability criteria agreed under expert consultation point 5.12, except for the reliability criterion addressing pH. RMS to evaluate all available bee studies from literature using the relevance criteria agreed under expert consultation point 5.10. RMS to reflect the potential changes in the revised RAR after consulting the table under expert consultation point 5.10. **References cited from the open literature** Dai, P., Yan, Z., Ma, S., Yang, Y., Wang, Q., Hou, C., Wu, Y., Liu, Y., Diao, Q., 2018. The herbicide glyphosate negatively affects midgut bacterial

[6] Uren Webster TM, Laing LV, Florance H and Santos EM, 2014. Effects of glyphosate and its formulation, roundup, on reproduction in zebrafish (Danio rerio). Environ Sci Technol, 48:1271-1279. doi: 10.1021/es404258h

Subject	Conclusions Pesticide Peer Review Meeting
	communities and survival of honey bee during larvae reared in vitro. J. Agric. Food Chem. 66, 7786–7793. https://doi.org/10.1021/acs.jafc.8b02212
Additional point on (re)classification of the studies from the literature; follow up exercise in view of the open point identified in experts' consultation 5.16, above.	Details of two selected bee studies from the literature (Tome et al., 2020 and Herbert et al., 2014) were discussed in order to check whether the relevance and reliability criteria as agreed under experts' discussion points 5.10 and 5.12 are applicable. The experts considered that those criteria (except the one on the pH) are applicable for these types of studies as well. As regards the classification of the two studies, some key information on the methodology is missing. Therefore, they should be considered as supporting information. **Open point** RMS to revise the study classification of Tome et al. (2020) and Herbert et al. (2014) to "relevant, supportive", reflecting the meeting discussions. See also open point above: "RMS to evaluate all the other available bee studies from literature included in the RAR using the reliability criteria agreed under expert consultation point 5.12, except for the reliability criterion addressing pH. RMS to evaluate all available bee studies from literature using the relevance criteria agreed under expert consultation point 5.10. RMS to reflect the potential changes in the revised RAR after consulting the table under expert consultation point 5.10". **References cited from the open literature** Herbert, L.T., Vázquez, D.E., Arenas, A., Farina, W.M., 2014. Effects of field-realistic doses of glyphosate on honeybee appetitive behaviour. J. Exp. Biol. 217, 3457–3464. https://doi.org/10.1242/jeb.109520 Tomé, H.V.V., Schmehl, D.R., Wedde, A.E., Godoy, R.S.M., Ravaiano, S.V., Guedes, R.N.C., Martins, G.F., Ellis, J.D., 2020. Frequently encountered pesticides can cause multiple disorders in developing worker honey bees. Environ. Pollut. 256. https://doi.org/ 10.1016/j.envpol.2019.113420
Experts' consultation 5.17	No valid tier 1 (glass plate) studies are available with any of the two indicator species (*Aphidius rhopalosiphi* and *Typhlodromus pyri*). Therefore, the risk assessment for non-target arthropods (NTAs) other than bees is mainly based on higher tier studies: (i) extended

Subject	Conclusions Pesticide Peer Review Meeting
Experts to discuss whether the overall data set of toxicity studies (i.e. extended studies with the standard species *Aphidius rhopalosiphi* and *Typhlodromus pyri*, and studies with additional species, *Poecilus cupreus*, *Pardosa* sp. and *Aleochara bilineata)* is sufficient to perform a risk assessment for non-target arthropods other than bees according to ESCORT 2[7] and the SANCO Guidance Document on Terrestrial Ecotoxicology (EC, 2002)[8].	laboratory studies with the indicator species, and (ii) laboratory studies with the ground-dwelling spider *Pardosa* sp. and the ground beetle *Poecilus cupreus*. The available data set suggests a rather low toxicity of glyphosate to NTAs. All experts agreed that the data set available is sufficient to perform the risk assessment according to ESCORT 2. **Open point** RMS to reclassify the relevance of the available two NTA studies from the peer reviewed open literature (Mirande et al., 2010; Siddhapara et al., 2012) according to the classification system agreed under expert consultation point 5.10. **References cited from the open literature** Mirande et al., 2010. Side-effects of glyphosate on the life parameters of *Eriopis connexa* (Coleoptera: Coccinelidae) in Argentina. Communications in Agricultural and Applied Biological Sciences, 75: 367-72 Siddhapara et al., 2012. Toxicity of some commonly used insecticides / herbicides on Zygogramma bicolorata Pallister (Coleoptera: Chrysomelidae). Biological Control, 26: 251-254
Experts' consultation 5.18 Experts to discuss the reliability of the extended laboratory study on *Aleochara bilineata* (CP 10.3.2.2/007). The outcome of the discussion should be taken into account when discussing the overall dataset for non-target arthropods.	An extended laboratory study with the rove beetle *Aleochara bilineata* was submitted to support the risk assessment for non-target arthropods (NTAs) other than bees. One of the validity criteria indicated in the test guideline (Grimm et al., 2000), is that a minimum reduction of 50% reproductive capacity relative to the control treatment is achieved in the reference item treatment. However, the toxic reference used in the study (chlorpyrifos) led to 100% mortality so that the minimum reproductive capacity relative to the control of the reference toxic could not be estimated.

[7] SETAC (Society of Environmental Toxicology and Chemistry), Candolfi MP, Barrett KL, Campbell PJ, Forster R, Grandy N, Huet MC, Lewis G, Oomen PA, Schmuck R and Vogt H (eds), 2001. Guidance document on regulatory testing and risk assessment procedures for plant protection products with non-target arthropods. ESCORT 2 workshop.
[8] European Commission, 2002. Guidance Document on Terrestrial Ecotoxicology Under Council Directive 91/414/EEC. SANCO/10329/2002-rev. 2 final, 17 October 2002.

Subject	Conclusions Pesticide Peer Review Meeting
	In addition, the compound used as the toxic reference (chlorpyrifos) was different than that recommended in Grimm et al. (2000). Besides, the use of chlorpyrifos was not justified and the concentration used in the study was not validated, as required by the test guideline. All experts at the meeting agreed that the study should be considered as supportive. **Reference** Grimm C, Reber B, Barth M, Candolfi MP, Drexler A, Maus C, moreth L, Ufer A and Waltersdorfer A, 2000. A test for evaluating the chronic effects of plant protection products on the rove beetle *Aleochara bilineata* (Coleoptera: *Staphylinidae*) under laboratory and extended laboratory conditions. In book: Guidelines to evaluate side effects of plant protection products to non-target arthropods. Editors: IOBC / OILB
Experts' consultation 5.19 Experts to discuss the appropriateness of the toxic reference concentrations used in the laboratory studies with non-target arthropods. The outcome of the discussion should be taken into account when discussing the overall dataset for non-target arthropods.	The toxic reference (positive control) used in the extended laboratory studies with non-target arthropods (NTAs) (specifically, studies CP 10.3.2.2/007, CP 10.3.2.2/001, CP 10.3.2.2/002, CP 10.3.2.2/003, CP 10.3.2.2/005, CP 10.3.2.2/008) was not in line with the relevant test guidelines because, either a different compound was used, or it was used at a higher concentration than that recommended in the applicable guideline. Other drawbacks and limitations were also identified in all those studies. The RMS evaluation of such deviations including the overall validity of the studies was presented by the RMS. All experts at the meeting agreed with the RMS evaluation and with the final conclusions for each NTA laboratory study (unanimous agreement). No open point was set for the RMS.
Experts' consultation 5.20 Experts to discuss the endpoints (NOER, LR_{50} and ER_{50}) derived from the extended laboratory study on *Typhlodromus pyri* (Report No.: MON-09-3).	A dose-response for mortality (Abbott corrected) was observed at the extended laboratory study with *Typhlodromus pyri* (Report No.: MON-09-3). At the highest concentration (16 L/ha) there was 40% mortality which was statistically significant compared to the control group. Therefore, a 50% lethal rate (LR_{50}) > 16 L/ha was agreed by all experts. As regards the reproductive endpoint, a no observed effect rate (NOER) = 8 L/ha had been initially proposed based on statistical

Subject	Conclusions Pesticide Peer Review Meeting
	significance. However, at that concentration, there was a 14% decrease in reproduction compared to the control group, which could be considered as biologically relevant. Therefore, all experts agreed with setting the NOER for reproduction at 3 L/ha. Also, for reproduction, all experts agreed with setting an ER_{50} > 12L/ha based on a dose-response that was observed at the highest three concentrations and a 56.5% reduction in reproduction at 16 L/ha. **Open point** RMS to update the RAR and the list of endpoints with the agreed NOER value of 3 L/ha for the extended laboratory study with *T. pyri*.
Experts' consultation 5.21 Experts to agree on the endpoints to be used for risk assessment for soil organisms.	<u>Endpoints used for the soil risk assessment</u> From the available regulatory studies with soil organisms, EC_{10} values could only be estimated from the earthworm chronic study with the soil metabolite AMPA. The no observed effect concentration (NOEC) derived from that study was used for the risk assessment since it is lower than the EC_{10}. The experts agreed with the endpoints that were already present in the list of endpoints for all groups of soil organisms (unanimous agreement). <u>Peer reviewed publication by Correia and Moreira (2010)[9]</u> The relevance and reliability of the peer-reviewed publication by Correia and Moreira (2010) were discussed. Several limitations pertaining to the study design and results of the study were identified by the experts. The experts agreed that the reliability assessment of the publication Correia and Moreira (2010) should be revised in light of the concerns raised at the meeting. The reliability key criteria agreed upon under expert consultation point 5.12 should be used (when applicable) (unanimous agreement). **Open point** RMS to update the study evaluation of the peer reviewed study by Correia and Moreira (2010) and to revise the reliability assessment accordingly, acknowledging the concerns raised at the meeting.

[9] Correia FV and Moreira JC. 2010. Effects of Glyphosate and 2,4-D on Earthworms *(Eisenia foetida)* in Laboratory Tests. Bulleting of Environmental Contamination and Toxicology, 85: 264–268. https://doi.org/10.1007/s00128-010-0089-7

Subject	Conclusions Pesticide Peer Review Meeting
Experts' consultation 5.22 Experts to discuss the issues raised for the two vegetative vigour studies (CP 10.6.2/002 (2014) and CP 10.6.2/005 (2021)) and the updated risk assessment for non-target terrestrial plants.	The available two vegetative vigour studies were compared and discussed. Due to some issues, mainly due to the considerably lower light intensity, the CP 10.6.2/002 study was agreed to be labelled as reliable with restrictions, while the CP 10.6.2/005 study was considered as reliable. This resulted in that the lowest endpoint from the two studies should be considered in the updated deterministic risk assessment. The available probabilistic risk assessment was not considered protective by the experts at the meeting (therefore not to be considered) since reliable endpoints from the available studies indicate higher sensitivity. **Open point** RMS to re-evaluate the literature studies available in the revised RAR based on the criteria agreed upon under expert consultation points 5.10 and 5.12 (except the criterion on pH). **Open point** RMS to reflect the results of the discussion in the risk assessment for non-target terrestrial plants and update the RAR.
Experts' consultation 5.23 Experts to discuss the risks to reptiles and terrestrial phases of amphibians.	The experts discussed the available information to assess risks to reptiles and terrestrial phases of amphibians. This consisted of several literature studies (see references below) and a risk assessment included in the RAR which followed the proposal made in EFSA PPR Panel (2018). <u>Conclusion for the literature studies:</u> Overall, considering all literature information, none of the studies were considered fully relevant considering the tested material. Of those that were "less relevant but supplementary", only some of the assessment endpoints (i.e., growth and length) were considered potentially relevant. Reliability issues were noted, with none of the studies being completely reliable. The only observed effect on a potentially relevant endpoint was from Poletta et al. (2011). However, the biological relevance of these effects may need to be further considered acknowledging the low effect levels, some of which were only observed at one growth stage (i.e., 2-4% change at birth and 3 months, but not at 12 months).

Subject	Conclusions Pesticide Peer Review Meeting
	Conclusion for the risk assessment: Overall, the experts agreed that the illustrative risk assessment provided by the applicants is not acceptable and cannot be relied upon to address the risks to terrestrial phases of amphibians. Additionally, a number of additional uncertainties and incorrect assumptions were identified. The experts noted that a similar illustrative risk assessment was not presented for reptiles. **Open points** - RMS to update the study summaries for reptiles and terrestrial phases of amphibians based on the criteria agreed upon under expert consultation points 5.10 and 5.12. The RMS should also reflect the relevance of the endpoints relating to size, such as growth and size (e.g., snout-to-vent length). - RMS to reflect in the RAR the additional uncertainties and incorrect assumptions which were not already captured concerning the illustrative risk assessment for terrestrial phases of amphibians, as discussed in the experts' meeting. - The illustrative oral risk assessment provided by the RMS should be revised by modifying the crop interception, the correct residue per unit dose (RUD) values and by acknowledging the additional uncertainties related the assumptions on drift. **References** EFSA PPR Panel (EFSA Panel on Plant Protection Products and their Residues), Ockleford C, Adriaanse P, Berny P, Brock T, Duquesne S, Grilli S, Hernandez-Jerez AF, Bennekou SH,Klein M, Kuhl T, Laskowski R, Machera K, Pelkonen O, Pieper S, Stemmer M, Sundh I, Teodorovic I,Tiktak A, Topping CJ, Wolterink G, Aldrich A, Berg C, Ortiz-Santaliestra M, Weir S, Streissl F and Smith RH,2018. Scientific Opinion on the state of the science on pesticide risk assessment for amphibians and reptiles. EFSA Journal 2018;16(2):5125, 301 pp. Poletta GL, Kleinsorge E, Paonessa A, Mudry MD, Larriera A, Siroski PA, Genetic, enzymatic and developmental alterations observed in Caiman latirostris exposed in ovo to pesticide formulations and mixtures in an experiment simulating environmental exposure, Ecotoxicology and Environmental Safety, Volume 74, Issue 4, 2011, Pages 852-859.

Subject	Conclusions Pesticide Peer Review Meeting
Experts' consultation 5.24 Experts to discuss: • the relevance and reliability of the available studies (both regulatory and from literature) and assessed parameters for their use in the weight of evidence for endocrine disruption (ED) assessment; • the information that can be derived from the available studies based on: tested item, test system (including species, where necessary) study design and parameters assessed; • the weight of evidence for ED leading to the overall conclusion on whether the criteria as laid down in point 3.8.2 of Annex II to Regulation 1107/2009 are met. Please note that EFSA is of the opinion that the maximum tolerated concentration (MTC) should not be used to consider a paper as not relevant/reliable and this is in line with the assessment done for humans.	*Please refer to the Pesticide Peer Review TC 84 Mammalian toxicology – Ecotoxicology joint ED session (1-2 December 2022)*
Experts' consultation 5.25	Applicant's approach

Subject	Conclusions Pesticide Peer Review Meeting
The experts should discuss the applicants updated biodiversity assessment. The exact points and structure of discussion will be decided in discussion with the RMS following their assessment of the submitted additional information.	Overall, the experts considered that the applicant's approach followed to assess the risk to biodiversity was inadequate and that the applicants could have: i) Performed an unbiased systematic data collection; ii) Considered higher tier studies to cover the links between the non-target organisms; iii) Attempted to perform an assessment using the proposed (by the applicants) operationalised specific protection goals for biodiversity; iv) Addressed the points of the additional data requested to the applicants after the public consultation. All experts agreed that a data gap will need to be identified in the EFSA conclusions to address the above points and therefore to address the data requested after the public consultation i.e. • The data collection should be done in a systematic manner and the information structured appropriately. This should be done considering the proceeding bullet points; • The direct effects on the target weeds (including the impact on the seed bank), non-target plants, non-target arthropods and bees should be quantified. Such quantification should consider the magnitude and duration of the impact in a spatial and temporal context. The quantification of the direct effects should then inform the extent of potential indirect effects via trophic interactions; • The assessment of biodiversity should be done to address all representative uses. Nevertheless, it may be more practical to focus the biodiversity assessment for a few representative scenarios (defined considering the GAP); • If proposed, specific mitigation should be linked to the representative uses. It is also suggested that the applicants demonstrate how both specific and general mitigation addresses the identified risks. Please note that only mitigation proposed by the applicants or the RMS can be considered as part of the assessment. <u>Relevance of peer-reviewed open literature to inform the biodiversity risk assessment</u> The experts agreed that: i) The relevance of the formulation is not critical for studies considering the indirect effects of weed removal (i.e., those studies where there is evidence that the indirect effect is driven by weed

Subject	Conclusions Pesticide Peer Review Meeting
	removal which will depend on the test system). In this case all formulations are relevant; ii) For other studies (where weed removal is not the primary direct effect), relevance of the formulation should be aligned to the already agreed flow-chart, meaning that studies done with glyphosate, the formulation for representative uses or equivalent are considered relevant. Those done with polyoxyethylene tallow amine (POEA) are not relevant. Those with unknown formulation details are 'potentially relevant but insufficient information'. Those with known formulation details are 'less relevant but supplementary'; iii) Refer to expert consultation point 5.10 for the general discussion on the relevance of the formulations. Overall, the experts agreed that the relevance of the studies should be assessed relative to the uses under assessment (i.e., the Good Agricultural Practice (GAP)). It was agreed that the use in the study should resemble those in the GAP and those studies which were not performed in accordance, should be down-weighted in terms of relevance. It was suggested that the most appropriate manner would be to perform a structured weight of evidence (WoE) approach covering all the available information, and the data which are of low relevance would be weighted appropriately. <u>Risk mitigation measures (RMM)</u> The experts considered: i) The proposed RMM is likely to be beneficial. Whether it is sufficient on its own, however, will be context and landscape dependent; ii) The adequacy of the size limitation of the field (>15 ha) and threshold for 100% of the treated area has not been demonstrated; iii) The applicants did not specify the quality of the multi-functional field margin (MFFM) and the experts considered that it is likely to have an impact on its effectiveness; iv) The extent to which the MFFM, and its quality, mitigates the effects has not been quantified by the applicants; v) It is suggested that the above points are reflected in the data gap identified.

Subject	Conclusions Pesticide Peer Review Meeting
	The experts discussed various approaches that could be done in the future to further enhance the assessment of indirect effects to biodiversity. Overall, in general the experts agreed with the proposals made by the EFSA Working Group regarding future activities related to the assessment of biodiversity in the context of prospective environmental risk assessment. **Open point** RMS to update the study evaluations regarding the revised relevance criteria for formulations and study conditions relative to the GAPs. <u>Terrestrial vertebrates</u> Overall, the expert agreed that the two relevance criteria previously agreed (see points i) and ii) under *Relevance of peer-reviewed open literature to inform the biodiversity risk assessment* above) would be sufficient for discriminating studies conducted under conditions that are clearly departing from the representative uses of glyphosate included in the GAP. These studies would be considered of low relevance and, while the evidence they present will be transparently reported, it will also be made clear that such evidence would be of low relevance for the present assessment in the context of glyphosate re-approval. As regards how review and meta-analysis papers should be considered for the biodiversity risk assessment, the experts agreed that: i) Reviews should not be included in the WoE tables; ii) However, they may be discussed in the general consideration of what information is available. The RMS can reflect that the underlying studies mentioned in the review were not available to them which emphasises the need for a proper systematic search of the literature as requested in the additional data request made to the applicants. **Open points** RMS to update the study evaluation for the terrestrial vertebrate studies to reflect the relevance assessment. The RMS is also requested to ensure that it is clear how the glyphosate treatments were made in the studies; i) The RMS may also consider updating their assessment of reliability of the studies to ensure that there is harmonisation in the approach

Subject	Conclusions Pesticide Peer Review Meeting
	of the evaluation of the terrestrial vertebrates studies and the other groups of non-target organisms; ii) RMS to update their WoE assessment to incorporate the level of relevance for the information included; iii) All reviews should be removed from the WoE tables. The general reviews may be reflected in the general discussion or a second table. The reviews with glyphosate may also be acknowledged in the general discussion. <u>Aquatic organisms</u> Overall, the experts agreed with the RMS WoE assessment, however, the following additional points should be emphasised: i) No conclusion can be reached given the lack of systematic literature search; ii) Reviews should not be included in the WoE assessment; iii) The studies performed with formulations containing POEA should be reassessed for their relevance in line with the agreements made above; iv) In principle a Regulatory Acceptable Concentration based on Ecological Threshold Option (ETO RAC) covers indirect effects as indicated in the EFSA PPR Panel aquatic guidance[10] with exception of some aspects (e.g., disruption of the biofilm, community shifts in microbes, direct effects on macrophytes via spray-drift, indirect effects driven by direct effects occurring outside of the water system) which are not currently covered by the guidance document. **Open points** RMS to update the RAR with the followings: i) RMS to reflect the discussions with regard to: a. The impact on emerging aquatic macrophytes exposed via spray-drift and potential consequential indirect effects; b. The direct effects on emerging aquatic macrophytes; c. The additional points of consideration given in the additional data request for the applicants (e.g., considerations on impact on decomposition processes in aquatic systems and

[10] EFSA PPR Panel (EFSA Panel on Plant Protection Products and their Residues), 2013. Guidance on tiered risk assessment for plant protection products for aquatic organisms in edge-of-field surface waters. EFSA Journal 2013;11(7):3290, 268 pp. doi:10.2903/j.efsa.2013.3290

Subject	Conclusions Pesticide Peer Review Meeting
	fitness impairment, and thus reproduction impairment, due to lack of plant food (e.g. pollen and nectar) for many species of insects which have aquatic life stages as well); ii) No conclusion can be reached given the lack of systematic literature search; iii) Reviews should not be included in the WoE assessment; iv) The studies performed with formulations containing POEA should be reassessed for their relevance in line with the agreements made above; v) In principle an ETO RAC covers indirect effects as indicated in the EFSA PPR Panel aquatic guidance document (EFSA PPR Panel, 2013). For glyphosate, the risk assessment is based on Tier 1 which, by default, provides an ETO RAC. It was, however, questioned whether this is inclusive of all types of effects (e.g., disruption of the biofilm, community shifts in microbes, direct effects on macrophytes via spray-drift, indirect effects driven by direct effects occurring outside of the water system); vi) The RMS is also requested to consider the general open points made for the terrestrial vertebrates (where relevant). <u>Bees</u> **Open points** RMS to update the RAR: i) By considering the general open points made for the terrestrial vertebrates (where applicable); ii) By reflecting that the conclusions with respect to the field size and threshold for multifunctional field margins (MFFM) under 'risk mitigation measures', above, are also relevant for bee biodiversity; iii) To remove the data gap referred to the Laberge et al. (1995) publication.[11] <u>Non-target arthropods (NTAs)</u> The relevance status of the peer reviewed publications included in the biodiversity assessment should be revised based on the relevance criteria agreed upon for terrestrial vertebrates.

[11] Laberge L, Couture G, Legris J, Langevin R. 1995. Evaluation des impacts du glyphosate utilisé dans le milieu forestier. Ministère des Ressources naturelles Direction de l'environnement forestier Service du suivi environnemental.

Subject	Conclusions Pesticide Peer Review Meeting
	Although no relevant publications addressing indirect effects on NTAs were provided by the applicants in the biodiversity assessment, when considering the representative uses of glyphosate, the monitoring study of Pleasants and Oberhauser (2013)[12] might provide some insights on the potential indirect effects of NTAs populations due to the loss of their host plants. However, the study presents several limitations and uncertainties that should not be disregarded. **Open points** RMS to update the RAR: i) By considering the general open points made for the terrestrial vertebrates (where applicable); ii) By revising the relevance of the publications used for the biodiversity assessment and reporting all strengths and limitations of the study by Pleasants and Oberhauser (2013). <u>Soil organisms</u> The available evidence in Dennis et al. (2018)[13] would also be informative for soil microorganisms. Based on the agreed updated criteria (see '*Relevance of peer-reviewed open literature to inform the biodiversity risk assessment*', above), the relevance assessment should be revised accordingly (relevant for all studies considered). **Open points** RMS to update the RAR: i) The relevance classification of the studies should be revised according to the general agreement (see '*Relevance of peer-reviewed open literature to inform the biodiversity risk assessment*', above); ii) To reflect that Dennis et al. (2018) might also be considered relevant for soil microorganisms.

[12] Pleasants JM and Oberhauser KS, 2013. Milkweed loss in agricultural fields because of herbicide use: effect on the monarch butterfly population. Insect Conservation and Diversity, 6: 135-144. https://doi.org/10.1111/j.1752-4598.2012.00196.x
[13] Dennis PG, Kukulies T, Forstner C. et al., 2018. The effects of glyphosate, glufosinate, paraquat and paraquat-diquat on soil microbial activity and bacterial, archaeal and nematode diversity. Scientific Reports, 8: 2119. https://doi.org/10.1038/s41598-018-20589-6

Subject	Conclusions Pesticide Peer Review Meeting
	<u>Non-target terrestrial plants (NTTPs)</u> The experts agreed to revise the relevance of the studies considered for the biodiversity assessment of NTTPs (unanimous agreement). **Open points** i) RMS to update the RAR appendix on biodiversity (Vol. 3 B.9-CP) by including all relevant studies on NTTPs; ii) The relevance classification of the NTTP studies should be revised according to the general agreement (see '*Relevance of peer-reviewed open literature to inform the biodiversity risk assessment*', above); iii) RMS to better clarify the classification of Boutin et al. (2014)[14] in a revised RAR; iv) RMS to revise the study evaluation of Damgaard et al. (2014)[15] and its relevance assessment; v) RMS to revise the relevance assessment of Strandberg et al. (2012[16] and 2021[17]) considering that it was confirmed that they used the formulation for representative uses. <u>Uses where less than 50% of the surface is treated (i.e., including band and spot applications) and railway uses</u> The experts agreed that uses where less than 50% of the surface is treated (i.e., including band and spot applications) and railway uses might be needed for safety and phytosanitary reasons. For such uses, a risk-benefit analysis should be considered by risk managers. **Open points** RMS to ensure that the additional points on the biodiversity assessment for uses where the treated area is less than 50% and railway uses are reflected in the RAR, e.g.: i) The effectiveness in terms of exposure reduction of the uses, such as spot treatments or strip applications, where the treated area is

[14] Boutin C. et al., 2014. Herbicide impact on non-target plant reproduction: What are thetoxicological and ecological implications? Environmental Pollution, 185: 295-306.
[15] Damgaard C, Strandberg B, Mathiassen SK and Kudsk P, 2014. The effect of glyphosate on the growth and competitive effect of perennial grass species in semi-natural grasslands. Journal of Environmental Science and Health, Part B, 49(12): 897-908. DOI: 10.1080/03601234.2014.951571
[16] Strandberg, B. et al., 2012. Effects of herbicides on non-target plants: How do effects in standard plant test relate to effects in natural habitats? Danish EPA, Pesticide Research, 137: 1-115.
[17] Strandberg B. et al., 2021. Effects of glyphosate spray-drift on plant flowering. Environmental Pollution, 280: 116953

Subject	Conclusions Pesticide Peer Review Meeting
	less than 50%, was not demonstrated (see discussion point on birds & mammals under 5.7); ii) The effectiveness of unsprayed strips to reduce potential risk to biodiversity in band application situations is questionable and would depend on the quality of those strips. Considering that the strips are managed, they cannot be considered equivalent to MFFM; The treatment of less than 50% of the area (i.e., including band and spot applications) and railway uses was not considered *per se* sufficient to exclude effects on biodiversity.
New experts' consultation point 5.26 proposed by EFSA for completeness of discussion (October 2022): Experts to consider some potentially relevant newly available publications arisen after the public consultation/reporting table stage. EFSA identified a number of publications that might be considered potentially relevant and therefore it was agreed to share these selected studies with MSs to allow a peer review and further consideration in the expert meetings. In particular, MS experts are asked to share their views whether these potentially relevant articles might be considered more critical or may alter the weight of evidence in the current assessment and to determine	<u>Systematic literature searches</u> The literature searches performed by the applicants were generally in line with the EFSA (2011) guidance (EFSA Journal 2011;9(2):2092). However, it was noted that several peer-reviewed publications identified after the public consultation, and which were seemingly published within the timeframe covered by the literature search (January 2010 - June 2020), were not originally captured by the applicant's literature searches. Therefore, there were some concerns about the sensitivity of the searches. These concerns had not been addressed by the applicants following a data requirement after the public consultation. During the discussions on the individual topics (individual non-target organisms, ED assessment), it was discussed and agreed that the RMS will reassess the relevance and reliability of all the available studies from the scientific literature considering the agreement reached under experts' consultation points 5.10 and 5.12. For the assessment on biodiversity and the assessment on microbiome, some specific considerations were agreed; those agreements are included under experts' consultation point 5.25 and expert consultation point 5.1 identified following comments by public. These agreements and considerations are equally relevant for studies captured by the literature search conducted by the applicants, studies highlighted during the public consultation on the RAR and for newly available papers identified subsequently. **Open point** RMS to further reflect on the sensitivity of the literature search performed by the applicants for the EU assessment, in light of the

Subject	Conclusions Pesticide Peer Review Meeting
if any eventual follow up would be needed.	presence of relevant studies not having been captured by the literature searches. <u>Newly available publications identified up to the expert consultations</u> Formally, in line with the legislation, there is no legal obligation to consider newly available data submitted outside of the dedicated public and targeted consultations or after the deadline of the window for providing the additional information within the clock stop period, unless they constitute adverse data (cf Article 56 of Regulation (EC) No 1107/2009 regarding information on potentially harmful or unacceptable effects). For this reason, although a systematic review of the literature has not been carried out by EFSA or the RMS, EFSA has identified newly available papers on glyphosate even outside of the legal requirements and collected a list of studies as a result. For the discussion related to the only study found as potentially relevant for the risk assessment for aquatic organisms (Tartu et al. 2022), please refer to expert consultation point 5.11. For the discussion related to the studies identified as potentially relevant for the assessment on the potential effect on microbiome/microbiota in relation to non-target organisms (Ruuskanen et al. 2022; Almasri et al. 2022; Motta and Moran, 2022), please refer to expert consultation point 5.1 identified following comments by public. For the ED assessment for non-target organisms, the only relevant study identified in the above exercise for the assessment of the endocrine disrupting properties of glyphosate is Verderame *et al.,* (2022). See open point under expert consultation point 5.24 It was acknowledged that there were publications identified at a later timepoint which were not discussed by the experts. The following publications were brought to the attention of the experts for further consideration: Ames et al. (2022) and Wathsala et al. (2022). **Open points** - RMS to ensure that all relevant publications identified up to the expert consultations are included in the RAR.

Subject	Conclusions Pesticide Peer Review Meeting
	- RMS to consider and, if needed, to include in the RAR the publications by Ames et al. (2022) and Wathsala et al. (2022) identified additionally. **Cited references** Almasri et al., 2022. Mild chronic exposure to pesticides alters physiological markers of honey bee health without perturbing the core gut microbiota. Scientific Reports, 12(1):4281; Ames J, Miragem AA, Cordeiro MF, Cerezer FO, Loro VL, 2022 Effects of glyphosate on zebrafish: a systematic review and meta-analysis. Ecotoxicology, 31(8):1189-1204. doi: 10.1007/s10646-022-02581-z Motta EVS, Powell JE and Moran NA, 2022. Glyphosate induces immune dysregulation in honey bees. *anim microbiome* 4: 16. https://doi.org/10.1186/s42523-022-00165-0 Ruuskanen S, Fuchs B, Nissinen R, Puigbò P, Rainio M, Saikkonen K, Helander M, 2022. Ecosystem consequences of herbicides: the role of microbiome. Trends Ecol Evol., 13:S0169-5347(22)00229-4. doi: 10.1016/j.tree.2022.09.009. Epub ahead of print. PMID: 36243622; Tartu S, Renoirt M, Cheron M, Gisselmann L-L, Catoire S and Brischoux F, 2022. Did decades of glyphosate use have selected for resistant amphibians in agricultural habitats? Environ Pollut, 310:119823. doi: 10.1016/j.envpol.2022.119823 Verderame M, Chianese T, Rosati, L, Scudiero R, 2022. Molecular and Histological Effects of Glyphosate on Testicular Tissue of the Lizard *Podarcis siculus*. International Journal of Molecular Sciences, 23(9), 4850 Wathsala RHGR, Folgueras EC, Iuffrida L, Candela M, Gotti R, Fiori J, et al., 2022. Glyphosate and its breakdown product AMPA elicit cytoprotective responses in haemocytes of the Mediterranean mussel (*Mytilus galloprovincialis*). Environmental Toxicology and Pharmacology 2022 Vol. 96 Pages 103997. DOI: https://doi.org/10.1016/j.etap.2022.103997
Experts' consultation 5.1 identified following comments by public Experts to consider the evidence provided on effects on microbiota and microbiomes in relation to non-target organisms.	For the current peer review process, studies were identified (both submitted via literature search and during the consultation phases) on the potential effects of glyphosate, and its formulation, on the microbiome of non-target organisms. Studies on microbial communities were provided for animals, plants and soil. The relevance and reliability criteria used for assessing the literature provided during the consultation phase were discussed in the context of the current assessment for glyphosate. It was agreed that the relevance evaluation should be consistent with the scheme used for other areas of the current assessment (see expert consultation point 5.10). Specific

Subject	Conclusions Pesticide Peer Review Meeting
See also expert consultation identified in the mammalian toxicology section for effect on microbiota and impact on animal health (mainly livestock).	reliability criteria to address the unstandardised methodologies across the provided literature studies were identified and agreed. It was recognised that no regulatory endpoint could be derived from any of the microbiome studies identified for the current glyphosate assessment, and no known link is possible between the potential effects on microbiome and the protection goals for non-target organisms. The impact of glyphosate on the microbiome was also discussed in the mammalian toxicology expert meeting TC 80 (expert consultation point 2.30). **Open points** - RMS to revise in the updated RAR the relevance and reliability status of studies on microbiome considering the agreed criteria; - RMS to include in the assessment the three publications on microbiome identified by EFSA additionally: • Ruuskanen S, Fuchs B, Nissinen R, Puigbò P, Rainio M, Saikkonen K, Helander M. Ecosystem consequences of herbicides: the role of microbiome. Trends Ecol Evol. 2022 Oct 13:S0169-5347(22)00229-4. doi: 10.1016/j.tree.2022.09.009. Epub ahead of print. PMID: 36243622 • Almasri, H., Liberti, J., Brunet, JL. et al. Mild chronic exposure to pesticides alters physiological markers of honey bee health without perturbing the core gut microbiota. Sci Rep 12, 4281 (2022). https://doi.org/10.1038/s41598-022-08009-2 • Motta, E.V.S., Powell, J.E. & Moran, N.A. Glyphosate induces immune dysregulation in honey bees. Animal microbiome 4, 16 (2022). https://doi.org/10.1186/s42523-022-00165-0 - EFSA to report in the EFSA Conclusion for glyphosate in a narrative way the outcome of those studies categorised as relevant and reliable/reliable with restrictions.
Experts' consultation 5.2 identified following comments by public	'MON 0139' is the actual salt form that is present in the formulation for representative uses. This salt form was used for the chronic studies on honey bees (adult and larva) and for the available non-*Apis* studies (only acute), therefore those studies are representative for the active substance. All available dossier studies with the active substance and

Subject	Conclusions Pesticide Peer Review Meeting
Experts to discuss and agree on the use of the studies for bees where the test item was neither the active substance nor the formulation for representative uses 'MON 52276'.	the formulation for representative uses indicate low toxicity towards bees with no indication of higher toxicity of the formulation for representative uses. Moreover, chronic exposure to the formulation as such is unlikely. The experts at the meeting agreed that no further data are needed; the effects are well represented by the existing data. Nevertheless, during the discussions some information in the RAR was identified as potentially erroneous; therefore, the following open point for corrections was identified: **Open point** RMS to correct the reference for the EFSA Technical Report[18] and reflect in the revised RAR that the conclusion in this report for bumble bees and solitary bees is in relation to the tier-1 risk assessment of EFSA, 2013[19].

[18] DOI: https://doi.org/10.2903/sp.efsa.2015.EN-924
[19] EFSA (European Food Safety Authority), 2013. EFSA Guidance Document on the risk assessment of plant protection products on bees (Apis mellifera, Bombus spp. and solitary bees). EFSA Journal 2013;11(7):3295, 268 pp., doi:10.2903/j.efsa.2013.3295

REPORT OF PESTICIDE PEER REVIEW TC 84

GLYPHOSATE – AIR V

Rapporteur Member State: Assessment Group on Glyphosate (AGG) consisting of FR, HU, NL, SE

5. Ecotoxicology (endocrine disruption (ED) properties)

Date: 02 December 2022

List of participants:

Institute	**Member States Country code**
Austrian Agency for Health and Food Safety (AGES)	AT
Federal Public Service Health	BE
Federal Institute for Risk Assessment (BfR)	DE
Federal Environmental Agency (UBA)	DE
Ministry of Environment and Food of Denmark, Environmental Protection Agency	DK
TRAGSATEC	ES
Finnish Safety and Chemicals Agency (Tukes)	FI
Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail (ANSES)	FR
National Food Chain Safety Office (NEBIH)	HU
Board for the Authorisation of Plant Protection Products and Biocides (Ctgb)	NL
Swedish Chemicals Agency (KemI)	SE
National Institute of Public Health	SI
External experts (2)	EFSA

Pesticide Peer Review TC 84 (01– 02 December 2022)
Glyphosate

In accordance with EFSA's Policy on Independence[1] and the Decision of the Executive Director on Competing Interest Management[2,] EFSA screened the Annual Declarations of Interest filled out by the participants invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process, and no interests were declared orally by the members at the beginning of this meeting.

[1] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf
[2] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf

Discussion points/Outcome

5. Ecotoxicology

Please note that information part of this report may have been masked by EFSA in accordance with Article 63 of Regulation (EC) No 1107/2009 as well as EFSA's Practical Arrangements concerning confidentiality in accordance with Articles 7 and 16 of Regulation (EC) No 1107/2009, or EFSA's Practical Arrangements concerning transparency and confidentiality as a consequence of confidentiality requests submitted by the applicant on application dossiers for pesticides active substances or Maximum Residue Levels, respectively. Please note that information disclosed in this report is without prejudice to pre-existing intellectual property rights and data exclusivity clauses set out in Union law, and particularly in Article 62 of Regulation (EC) No 1107/2009.
Minutes might be revised due to pending data gaps at the time of the meeting and /or eventual need for further follow up consultation after the meeting. If needed, the final agreement will be made available in the meeting report published at the end of the peer review process.

Subject	Conclusions Pesticide Peer Review Meeting
Experts' consultation 5.24 Experts to discuss: 1. the relevance and reliability of the available studies (both regulatory and from literature) and assessed parameters for their use in the weight of evidence for ED assessment; 2. the information that can be derived from the available studies based on: tested item, test system (including species, where necessary) study design and parameters assessed; 3. the weight of evidence for ED leading to the overall conclusion on whether the criteria as laid down in point 3.8.2 of Annex II	1. Relevance and reliability of the studies considered for the assessment of the endocrine disrupting (ED) properties of glyphosate were discussed. It was agreed that for the studies considered for the ED assessment there is no reason to deviate from the criteria discussed and agreed during the Pesticide Peer Review Experts' TC 82. It was also agreed that the choice of the tested concentrations and related Maximum Tolerated Concentration (MTC)) should not be considered as a criterion for relevance. **Open point** RMS to reconsider the relevance and reliability based on the agreement at the Pesticide Peer Review Experts' TC 82, see open point related to experts' consultation point 5.4 (bird studies), 5.10 and 5.12 (aquatic organisms). RMS to revise the relevance of the available studies in line with the criteria agreed, e.g., choice of tested concentrations and related MTC should not be considered a criterion for relevance. Moreover, the assessment of the studies should be reconsidered based on the specific comments given for each individual study as discussed during the meeting. 2. The experts discussed the studies considered in the ED assessment, with a particular focus on those that were captured by the literature search, even outside the timeframe considered for conducting the search.

Subject	Conclusions Pesticide Peer Review Meeting
to Regulation 1107/2009 are met. Please note that EFSA is of the opinion that the maximum tolerated concentration (MTC) should not be used to consider a paper as not relevant/reliable, and this is in line with the ED assessment done for humans.	**Open point** RMS to cross-check which studies evaluated in 2017[3] (Annex of RAR addendum of 2017) were captured by the systematic literature review conducted for the current evaluation. Studies that have not been re-assessed and are outside the timeframe considered for the current renewal need special attention, to try to better understand why some have been captured and some others not. If a plausible explanation cannot be given after this cross-check, all the studies previously evaluated might need to be considered in the current evaluation. Formally, in line with the legislation, there is no legal obligation to consider newly available data submitted outside of the dedicated public and targeted consultations or after the deadline of the window for providing the additional information within the clock stop period, unless they constitute adverse data (cf Article 56 of Regulation (EC) No 1107/2009 regarding information on potentially harmful or unacceptable effects). For this reason, although a systematic review of the literature has not been carried out by EFSA or the RMS, EFSA identified newly available papers on glyphosate even outside of the legal requirements and collected a list of studies as a result. **Open point** RMS to include the RMS evaluation of the study by Verderame et al., 2022 in the revised RAR: Verderame M, Chianese T, Rosati, L, Scudiero R, 2022. Molecular and Histological Effects of Glyphosate on Testicular Tissue of the Lizard *Podarcis siculus*. International Journal of Molecular Sciences, 23(9), 4850. It was noted that inclusion of studies considered for the ED assessment was not always consistent, e.g., in some cases studies with the formulations were mentioned, and in some other cases not.

[3] EFSA (European Food Safety Authority), 2017. Conclusion on the peer review of the pesticide risk assessment of the potential endocrine disrupting properties of glyphosate. EFSA Journal 2017;15(9):4979, 23 pp. doi:10.2903/j.efsa.2017.4979

Subject	Conclusions Pesticide Peer Review Meeting
	Open point RMS to amend the ED assessment in the RAR by clarifying and consistently reporting what studies are used for the ED assessment for the different taxa. RMS to revise the Appendix E as needed in line with the discussion. 3. The RMS presented the ED assessment. EFSA with the support of the EFSA ED Working Group (WG) also conducted an assessment of the available information. Overall, the conclusion of the ED assessment of both the RMS and EFSA was aligned, although the dataset considered was not fully congruent. All MSs agreed that based on the available evidence, glyphosate does not meet the ED criteria according to point 3.8.2 of Annex II to Regulation (EC) No 1107/2009, as amended by Commission Regulation (EU) 2018/605. **Open points** 1. RMS to revise the ED assessment and include the missing studies. a. RMS to conduct the reliability and relevance and uncertainty analysis of the endpoints measured in the studies. 2. RMS to make a reference to the EFSA ED WG WoE report. RMS to revise the WoE by clarifying the studies that were considered in the ED assessment and how they were weighted, and by clarifying which studies were not considered (not relevant, reliable). The newly added studies should also be included, e.g., Verderame et al., 2022.
New experts' consultation point proposed by EFSA for completeness of discussion (October 2022): Experts to consider some potentially relevant newly available publications arisen	Formally, in line with the legislation, there is no legal obligation to consider newly available data submitted outside of the dedicated public and targeted consultations or after the deadline of the window for providing the additional information within the clock stop period, unless they constitute adverse data (cf Article 56 of Regulation (EC) No 1107/2009 regarding information on potentially harmful or unacceptable effects). For this reason, although a systematic review of the literature has not been carried out by EFSA or the RMS, EFSA has identified newly

Subject	Conclusions Pesticide Peer Review Meeting
after the public consultation/reporting table stage. EFSA identified a number of publications that might be considered potentially relevant and therefore it was agreed to share these selected studies with MSs to allow a peer review and further consideration in the expert meetings. In particular, MS experts are asked to share their views whether these potentially relevant articles might be considered more critical or may alter the weight of evidence in the current assessment and to determine if any eventual follow up would be needed.	available papers on glyphosate even outside of the legal requirements and collected a list of studies as a result. For non-target organisms, the only relevant study identified in the above exercise for the assessment of the endocrine disrupting properties of glyphosate is Verderame *et al.,* (2022). See open point under expert consultation point 5.24 EFSA noted that for mammalian toxicology all the relevant studies identified were included, assessed for reliability and weighted in the EFSA ED WG WoE Report (see open point on this item under experts' consultation point 2.29).