Procedure for renewal of the approval of active substance glyphosate in accordance with Commission Implementing Regulation (EU) No. 844/2012

Glyphosate Renewal Group

Regulation (EC) No 1107 /2009, Commission's request on EFSA Conclusions

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Section I: Mammalian Toxicity

Key aspects

- **The salivary gland endpoint considered a rodent specific local effect and not relevant to human health risk assessment.**
    - **Proposed overall endpoint selection results in no change to ADI, and AOEL**
        - **Endpoint now NOAEL for 90-day dietary in dog, not rabbit developmental toxicity.**
    - **Proposed increase for ARfD from 0.5 to 1.5 mg/kg bw/day**
        - **Endpoint from a different rabbit developmental toxicity study**
    - **New proposed AAOEL**
        - **Same endpoint as proposed ARfD adjusted for GI absorption (additional 5-fold)**
- **New *in vitro* HPRT according to OECD TG 476 (2016) and *in vitro* micronucleus according to OECD TG 487 (2016) studies were performed with glyphosate and submitted in the AIR5 dossier. The conclusion is that glyphosate is devoid of genotoxic potential.**
- **Lack of carcinogenic effects attributable to glyphosate in animal studies**
    - **Reliable epidemiological studies are supportive of lack of carcinogenicity demonstrated in animal studies.**
    - **Acquavella (2023) paper valuable quality review of epidemiological studies vs NHL**
- **No endocrine or effect on reproductive and developmental toxicity; no classifications warranted.**
- **Lack of neurotoxic and DNT effects attributable to glyphosate**
- **Genotoxic assays ongoing for N-acetyl glyphosate, N-glyceryl AMPA, and completed for N-malonyl AMPA (both Ames test and *in vitro* micronucleus negative)**
- **Increased levels of oxidative stress were not demonstrated in the available literature studies**

Contents

Summary

The following document summarises points related to the mammalian toxicology of glyphosate in the environment within the Annex I renewal dossier submitted by the Glyphosate Renewal Group (GRG, applicant). The dossier was evaluated by the Assessment Group for Glyphosate (AGG) acting as RMS consisting of the corresponding competent authorities of France, Hungary, The Netherlands and Sweden.

The following provides targeted summaries of relevant topics for the ongoing EU Review process regarding mammalian toxicity.

Salivary Gland Endpoint

List of endpoints: effects on salivary glands were considered a local effect in rats. Not relevant to humans. Based on pathology peer review of existing rat salivary gland microscope slides following current International Harmonisation of Nomenclature and Diagnostic Criteria (INHAND) confirm the non-relevance to human.

Genotoxicity

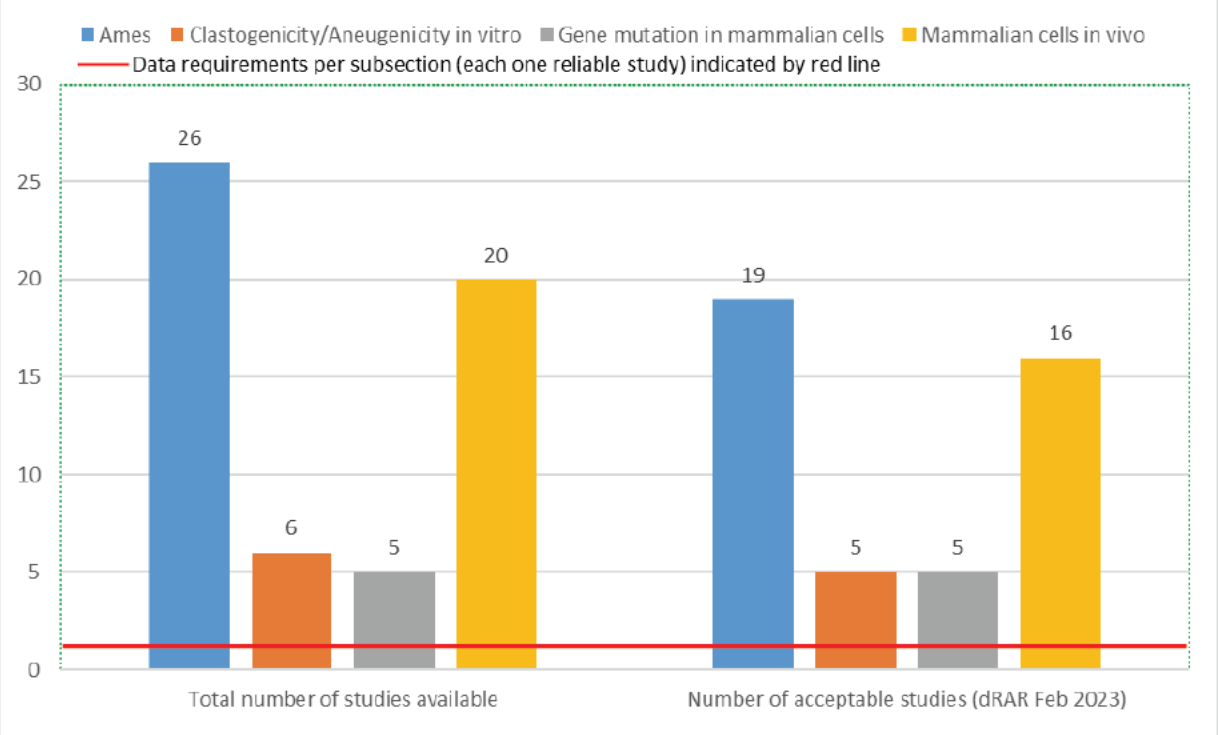
Many of the OECD testing guidelines for genotoxicity were updated and new requirements adopted in 2016. Therefore, the applicant has carried out new studies to fill the potential data gap for gene mutation in mammalian cells and aneugenicity. **New *in vitro* gene mutation in mammalian cell (HPRT) according to OECD TG 476 (2016) and new *in vitro* micronucleus (MN) according to OECD TG 487 (2016) studies were performed with glyphosate and submitted in the AIR5 dossier. These studies have been assessed by the Assessment Group on Glyphosate (AGG) and the evaluation of these good quality studies is available in the dRAR under points B.6.4.1.40 and B.6.4.1.41.**

These new studies (fully reliable to current guidelines) complete the requirement for genotoxicity evaluation under EC 1107/2009:

- Bacterial assay for gene mutation (Ames test)
- One test on clastogenicity/aneugenicity in mammalian cells (e.g. Micronucleus test *in vitro*)
- One mutagenicity test in mammalian cells (HPRT or MLA)
- One *in vivo* test (e.g., Micronucleus test *in vivo)*

Overall, more than one acceptable and supportive study is available for each of the different endpoints for genotoxicity assessment, as indicated in the Figure below.

As no indication of mutagenic properties was observed in any of the *in vitro* studies or in the *in vivo* micronucleus test, no further *in vivo* testing is triggered.



Overview on the total number of available genotoxicity studies as well as the number of studies assessed as acceptable in the dRAR 2023 by RMS. The minimum number of studies, which is ***one per subsection (red line)****, required by Commission Reg. (EU) No 283/2013 is indicated as red line. For all subsections studies are available that comply with the current OECD TG requirements. The numbers above the bars indicate the number of respective studies.*

During Public Consultation it was claimed that the studies submitted by the applicant do not assess fully the genotoxic potential of glyphosate and that in terms of regulatory requirements, two studies are missing, i.e., the transgenic rodent (TGR) somatic and germ cell gene mutation assays, (OECD 488, they report 2013, but there is an update version dated (2020) and a comet assay (OECD TG 489, 2016).
However, in terms of the regulatory requirement and taking into account the EFSA Scientific Opinion on genotoxicity testing strategies applicable to food and feed safety assessment (2011) and clarification of some aspects related to genotoxicity assessment (2017), the TGR or the comet test are follow-up studies to be carried out for substances positive in the *in vitro* tests. As glyphosate *in vitro* reliable genotoxicity studies were clearly negative, further *in vivo* studies are not triggered.

Overall, all the data available on glyphosate genotoxicity, including old and new studies submitted by the applicant and those found in public literature have been considered using a weight of evidence approach to draw the conclusion that glyphosate is devoid of genotoxic potential.

Conclusion on the genotoxic potential of glyphosate

The genotoxic potential of glyphosate has been assessed in the dRAR based on all the available information submitted by the applicant and published in the peer-reviewed scientific literature.

Oxidative stress

New studies identified after the public consultation period were requested to be considered by Expert Consultation (see point 2.17). Four publications were assessed. Both, applicant and RMS, were in agreement and concluded that the additional literature has no impact on the assessment.

Long-term toxicity and carcinogenicity

Summaries of six epidemiology meta-analyses, three epidemiology review papers, one exposure assessment, and one animal paper were prepared. Overall, these papers do not add significant information to the weight of evidence evaluation due to either their low relevance or low to moderate reliability for human health risk assessment. In addition, an independent expert in epidemiology recently evaluated the group of cancer types known as non-Hodgkin's lymphoma (NHL), (Acquavella, 2022), which is consistent with a more detailed peer reviewed publication (Acquavella, 2023[1]) that can be made available upon request. The overall conclusions below, align with the draft Renewal Assessment Report, which together with the May 30, 2022, ECHA CLH conclusion, clearly demonstrates a lack of carcinogenic effects attributable to glyphosate.

Summary & Assessment – from Acquavella (2022) State of the Science expert paper
With reference to established quality criteria only one epidemiologic study – Andreotti et al. *(2018) – is judged to be high quality on all counts. NHL cases were histologically confirmed, the prospective design obviated recall bias with respect to self-reported pesticide exposures, lost-to follow-up was minimal obviating concern about selection bias, the numbers of subjects were ample for analyses of NHL by quartiles of exposure, and control for confounding factors was comprehensive. In addition, the frequency of exposure for Agricultural Health Study (AHS) study participants (median 48 lifetime days and a highest exposure quartile of ≥ 109 days) far exceeded that of any of the other studies, most of which defined exposure as 1 day or more in a lifetime. This study is clearly on a much higher quality level than the other studies in the glyphosate NHL literature.*

Reproductive toxicity

During the stop-the-clock period, applicant was asked to provide additional information to support the assessment of the potential of glyphosate on reproductive and developmental toxicity. Overall, the requests considered 4 main areas:

1. Clarification of the approach followed for the literature review.
2. Setting the appropriate NOAELs in the reproductive toxicity studies.
3. Provision of historical control data to assess the relevance of certain findings in the developmental toxicity studies.
4. Assessment of the observed incidence of retro-oesophageal right subclavian artery in the rabbit developmental toxicity study in the context of a non-monotonic dose response (NMDR) effect.

[1] Acquavella J, Epidemiologic studies of glyphosate and non-Hodgkin's lymphoma: A review with consideration of exposure frequency, systemic dose, and study quality. Global Epidemiology 5 (2023) 100101. https://doi.org/10.1016/j.gloepi.2023.100101

General considerations on the approach followed for the literature review

The applicant has detailed the approach used for the literature review as also explained under the "literature data paragraph" of this section with respect to the relevance and reliability criteria applied for reproductive and developmental toxicity endpoints as well as further justification why some studies were not considered.

Very few of the publications analysed, fulfilled many of the reproductive criteria. For this reason, a large number of publications were not suitable for assessing effects of glyphosate on reproductive and developmental toxicity.

Assessment of reproductive toxicity studies to set the appropriate NOAELs

The effects of glyphosate on reproductive toxicity have been investigated in a large number of two-generation studies in the rat which were submitted by the applicant. Six of the submitted studies were considered to be either fully valid or supplementary according to the current OECD criteria for this type of study. Many publications on glyphosate reproductive and developmental effects retrieved from the literature search have been also considered depending on their relevance and reliability.

During the stop-the-clock period the applicant addressed additional endpoints to support setting the overall NOAELs by considering all the reproductive toxicity studies relevant for glyphosate assessment (those concluded to be reliable).The advantage of having multiple studies assessing the same endpoints allows a better understanding of the relevance of the findings based on the consistency of the effects when deriving the overall NOAELs for parental and offspring toxicity as well as for reproductive toxicity.

Following re-analysis of the submitted data, and by taking into account the effects observed in multiple studies, the following are considered to be appropriate values (expressed in mg/kg bw/day) to set the NOAELs for:

1. Parental toxicity overall NOAEL is 417 mg/kg bw per day, based on increased liver and kidney weights at 2151 mg/kg bw per day. The effect on salivary gland is considered to be adaptive and not adverse.
2. Offspring toxicity overall NOAEL is 293 mg/kg bw/day based on reduced body weight from doses equivalent to 985 mg/kg bw/day.
3. Reproductive toxicity overall NOAEL is 351 mg/kg bw per day, based on decrease in homogenisation resistant spermatid count in F0 males observed at limit dose.

Assessment of developmental toxicity studies

To better understand the relevance of the effects observed in the developmental toxicity studies in the rats and in the rabbit, the applicant was asked to provide appropriate historical control data (HCD) on developmental toxicity parameters, including the incidences of malformations, variations and implantation losses for the developmental toxicity studies as considered necessary based on all comments made in the dRAR.

For the rat, all studies together with the supplementary HCD demonstrate that glyphosate does not induce foetal malformation. The majority of studies demonstrate that foetal development is not impaired at the limit dose of 1000 mg/kg bw/day. The overall NOAEL for both maternal and developmental toxicity is 300 mg/kg bw/day in the rat.

In the rabbit, all studies together with the supplementary HCD demonstrate that glyphosate does not adversely affect foetal viability or induce foetal malformation. Some minor perturbations of skeletal ossification, considered to be a consequence of the slightly reduced foetal body weight at 300 mg/kg/day were observed but these did not include lumbar ribs. In the rabbit, the overall NOAEL for maternal toxicity is 50 mg/kg bw/day and for developmental toxicity is 150 mg/kg bw/day.

Non-monotonic dose response (NMDR) of retro-oesophageal right subclavian artery in the rabbit developmental toxicity study

EFSA expert meeting agreed that the retro-oesophageal right subclavian artery finding in the rabbit developmental toxicity study is not treatment-related and not consequent to a non-monotonic dose-response (NMDR).

Neurotoxicity

A number of scientific literature papers identified in the public commenting period were reviewed by the applicant. Summaries were prepared and submitted during stop-the-clock in April 2022 for additional consideration by the RMS and EFSA. The applicant's assessment of these papers agreed with those of both ECHA and of the RMS expressed in the draft RAR in correctly concluding glyphosate as not neurotoxic.

Two new papers providing a systematic review of public literature on glyphosate and neurotoxicity were published in 2022 and are publicly available. Chang *et al*., 2022[2], addressing epidemiology studies, and Moser *et al*., 2022[3] (study summary was included and evaluated in RAR Vol 3 CA B6.7.3.27), addressing animal literature, were published after stop-the-clock. Overviews and conclusions of these expert review papers were presented during a symposium at the recent International Congress of Toxicology on 19 September 2022, in Maastricht, NL.

Taken together, neither the epidemiological, nor toxicity studies demonstrate a consistent impact of glyphosate on the structure or function of the mammalian nervous system.

Overall, the additional studies do not give consistent results indicating (developmental) neurotoxicity.
RMS considers that these additional studies do not provide sufficient indication of a (developmental) neurotoxic potential of the active substance glyphosate acid. The RMS still considers that there is not a data gap for a developmental neurotoxicity study.

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[2] Chang *et al*, 2022. Systematic literature review of the epidemiology of glyphosate and neurological outcomes. Int Arch Occup Environ Health. 2023 Jan;96(1):1-26. doi: 10.1007/s00420-022-01878-0.
[3] Moser *et al*., 2022. Glyphosate and neurological outcomes: A systematic literature review of animal studies. Journal of Toxicology and Environmental Health, Part B, 25:4, 162-209. DOI: 10.1080/10937404.2022.2083739

All the information concerning DNT potential has been submitted, including a developmental neurotoxicity study conducted with glyphosate trimesium (a substance not registered in Europe for the past two decades and with a completely different toxicological profile). EFSA evaluated the study and concluded that it is not relevant for the risk assessment of glyphosate acid.

The draft OECD DNT *in vitro* battery (IVB) guidance provides a List of all Chemicals Tested in the DNT IVB Assays. For **glyphosate, 7 out of the 17 DNT IVB assays were conducted within the US EPA ToxCast/Tox21 program**. All the assays were found to be negative and the information has been included into Vol.3 CA B.6.7.3.26.

Additional new literature on developmental neurotoxicity (DNT) has emerged in 2022/2023 supporting the unlikelihood of DNT effect and can be made available upon request.

Metabolite data

Literature review on metabolites

The literature reviews submitted (see literature review reports KCA 9/001 and 9/002; one for the search period January 2010 – December 2019 and one for the search period January 2020 – June 2020), covers glyphosate and likewise its metabolites. Articles retrieved on metabolites, were assessed for relevance/reliability and summaries were submitted as appropriate.

Assessment of genotoxicity of metabolites

The QSAR report was updated with the corresponding new experimental data on metabolites (please see below table). Based on QSAR and/or subsequent read-across analysis on genotoxicity endpoints on mutagenicity, clastogenicity and aneugenicity were concluded negative for all metabolites of glyphosate where no (or incomplete) experimental data was available (N-acetyl-glyphosate, N-glyceryl-AMPA, N-malonyl AMPA, Methylphosphonic acid).

Apart from already submitted genotoxicity studies presented in RAR Volume 3 B6.8.1, the following studies were recently conducted or are planned (see overview Table 1).

Table 1: Overview on additional genotoxicity studies planned/submitted for metabolites

Metabolite	Study type	Status	Result
N-methyl glyphosate	Ames	Final; summary and report submitted herewith	Negative
	In vitro MN*	Final; summary and report submitted herewith	Negative
N-methyl AMPA	*In vitro* MN	Final; summary and report submitted herewith	Negative
N-acetyl glyphosate	*In vitro* MN	Ongoing	N/A

N-acetyl AMPA	*In vitro* MN	Final; summary and report available. Results: non-genotoxic. Not available by stop the clock deadline. Available on www.glyphosate.eu	Negative
N-malonyl AMPA	Ames	Final, study reports available	Negative
	In vitro MN		Negative
N-glyceryl AMPA	Ames	Ongoing	Negative
	In vitro MN		N/A

*MN = micronucleus

Considering the newly provided experimental data, a set of guideline compliant *in vitro* genotoxicity studies assessing potential mutagenicity (Ames), clastogenicity and aneugenicity (*in vitro* MN) is now available for metabolites AMPA, N-acetyl AMPA, N-methyl AMPA, and N-methyl glyphosate, from which all metabolites are concluded to be non-genotoxic.

In addition, genotoxicity studies for N-acetyl glyphosate (*in vitro* MN, N-glyceryl AMPA and N-malonyl AMPA (AMES and *in vitro* MN) have been initiated. Studies performed with N-malonyl AMPA have been completed and show no genotoxic concern.

Furthermore, the read-across analysis indicates that all three metabolites are non-genotoxic.
It is emphasised that the potential study requirement on genotoxicity for certain metabolites (N-acetyl glyphosate, N-acetyl AMPA, N-glyceryl AMPA and N-malonyl AMPA) are not considered relevant for the defended uses on non-GMO crops. However, genotoxicity studies have been carried out and showed no genotoxic potential.

Regarding methylphosphonic acid (M08), the experts unanimously concluded that the available QSAR analysis does not raise concern for genotoxicity. However, in the Expert Meeting Minutes from end 2022, it was concluded that an *in vitro* MN test would be needed to address the metabolite's clastogenic/aneugenic potential (data gap). According to REACH dossier[4], studies addressing clastogenicity and aneugenicity are already available and showed negative results. Applicant is waiting for acceptance of data sharing from the owner; no further data are deemed necessary.

General toxicity

For metabolites AMPA, N-acetyl glyphosate and N-acetyl AMPA acute and subacute toxicity data are available in rats. Moreover, AMPA was extensively investigated for metabolism/excretion, subacute toxicity, for skin sensitisation and developmental toxicity.

Overall, it can be concluded that AMPA, N-acetyl glyphosate and N-acetyl AMPA are of similar toxicity to glyphosate and the same reference values can be applied.

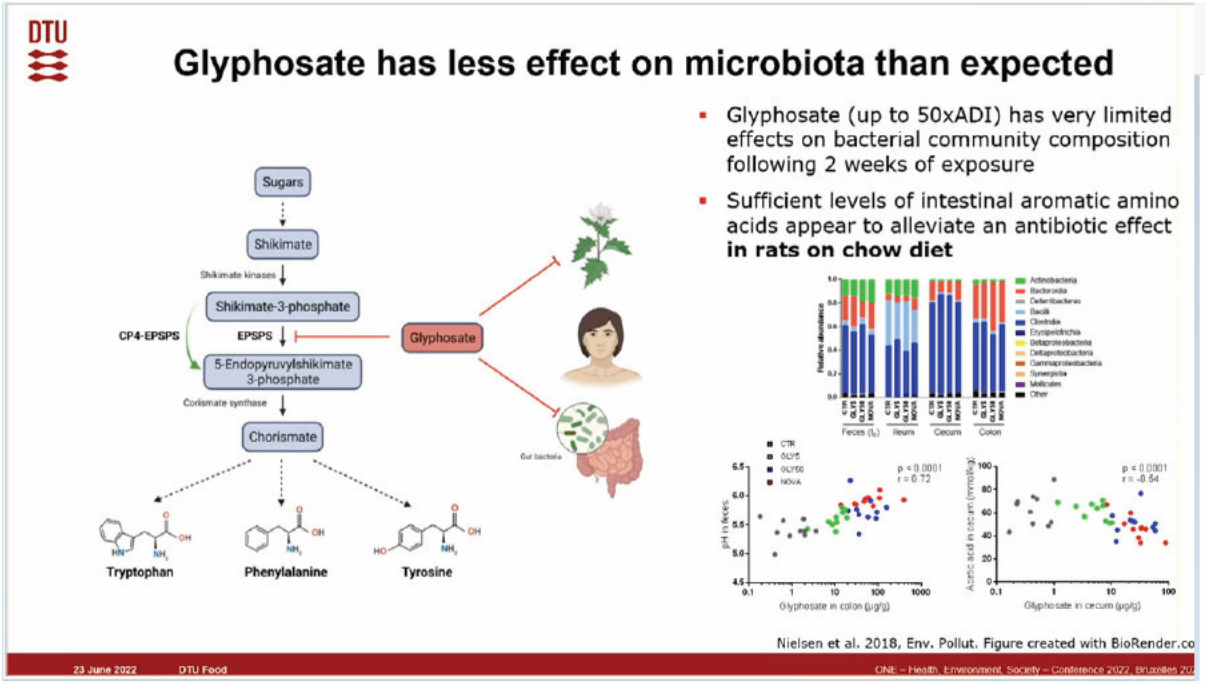
[4] https://echa.europa.eu/fr/registration-dossier/-/registered-dossier/10587/7/7/2

Gut microbiota

Glyphosate and its alleged microbial impacts, including on the gut microbiota.

In the absence of standardised, validated test and analytic methods, and a lack of consensus definitions of healthy microbiome states, consensus toxicity endpoints, or quantifiable endpoints that exhibit dose-dependent properties of adverse health outcomes mediated by the gut microbiota, a typical toxicology reliability and relevance assessment of the literature is challenging and fraught with ambiguities and caveats. It is critical that the focus of safety assessment for a substance remain on quantifiable endpoints that exhibit dose-dependent properties adverse health outcomes, which are detected by current animal safety studies.

Shikimate pathway (EFSA microbiota Workshop)



According to Nielsen *et al*. 2018[5], glyphosate has very limited effects on bacterial community composition following 2 weeks of exposure (included into Vol.3 CA B.6.8.2.43).

Endocrine Disruptor endpoint

The ED data package for glyphosate is compliant with the data requirements according to ECHA/EFSA ED guidance from 2018.

[5] Nielsen *et al*., 2018. Glyphosate has limited short-term effects on commensal bacterial community composition in the gut environment due to sufficient aromatic amino acid levels. Environmental Pollution 233 (2018) 364e376. DOI: 10.1016/j.envpol.2017.10.016.

It was confirmed in the last updated dRAR from February 2023, 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. Both the RMS and the EFSA ED WG concluded that the ED criteria are not met, and this was agreed upon by the experts during the expert consultation meeting.

Literature data

A position paper describing in more detail a specific part of the approach of the applicant to provide a comprehensive dossier for the renewal evaluation of the active substance glyphosate in the European Union (EU) was submitted. To ensure that all relevant research and scientific information regarding the effects of glyphosate and its metabolites on human health and the environment are included in the dossier, the applicant performed a systematic review of scientific peer-reviewed open literature, following the instructions in the established EFSA guidance. The approach followed is described in detail in this document and additional specific requests received from EFSA and other stakeholders during the public consultation are also addressed.

Section II: Residues

Key Aspects

- **Storage stability of AMPA in plant matrices**
  - **A weight of evidence approach supports a storage stability period of 12 months.**
  - **However, a new study will provide additional data.**
- **The submitted residue data package for primary crops may be considered complete:**
  - **Based on a storage stability period of 12 months for AMPA in plant matrices.**
  - **Based on the extrapolation rules applied in the context of the MRL review.**
  - **However, supplementary data will be submitted under Article 43.**
- **Completeness of the submitted field residue data for rotational crops**
  - **The final results of the limited field rotational crop study show a low uptake of residues, if any, and are in line with the preliminary results.**
  - **Therefore, at this stage, the dietary risk assessment based on the preliminary results does not need to be updated.**
  - **A full package of extended field rotational crop trials will be submitted under Article 43.**
- **Consumer risk assessment**
  - **The preliminary risk assessment shows a very wide margin of safety.**
  - **Therefore, it is possible to conclude that the representative uses do not cause unacceptable risks to consumers.**
  - **This conclusion will not be affected by the supplementary residue data that will be submitted under Article 43.**

Contents

Summary

In accordance with Regulation (EC) No 1107/2009, a dossier for the renewal of the approval of glyphosate was submitted by the Glyphosate Renewal Group (GRG, the applicant) to the Assessment Group for Glyphosate (AGG) on 8 June 2020. AGG consists of the competent authorities of France, Hungary, The Netherlands and Sweden that jointly act as the Rapporteur Member State (RMS) for Glyphosate. After a thorough evaluation of the dossier, AGG released a draft Renewal Assessment Report (dRAR) on 15 June 2021.
Comments on the dRAR were collected from other Member States, EFSA, GRG and other interested parties through a public consultation from 23 September 2021 to 22 November 2021. Based on the dRAR and the received comments, EFSA identified the need for additional information in various technical areas, including residues. The applicant was given the opportunity to address this EFSA request during a one month "stop-the-clock" period (which ended on 14 April 2022). The information that was provided by the applicant during the stop-the-clock was evaluated by the AGG and included, as appropriate, in an updated version of the dRAR.

The pending issues in the area of residues were further discussed during a peer review expert meeting on 2 December 2022, the minutes of which are available on the EFSA website[6]. Ultimately, on 06 July 2023, EFSA published their "Conclusions on the peer review of the pesticide risk assessment of the active substance glyphosate". In these Conclusions EFSA identifies a couple of issues and data gaps in the area of residues, none of which, however, are considered to be of critical concern as shown by the following statement: "The consumer risk assessment could not be finalised. […] A higher consumer exposure to residues of glyphosate than the one considered in the current risk assessment cannot be excluded. However, it is not expected that this might lead to an exceedance of the toxicological reference values. Therefore, no critical concern was identified."

The purpose of this document is to provide the perspective of the applicant on the residue-related issues and data gaps raised in the EFSA Conclusions, more specifically:

- The storage stability of AMPA in plant matrices.
- The completeness of the submitted residue data package for primary crops.
- The adequacy and completeness of the submitted field residue data for rotational crops.

The applicant believes that some of these data gaps are not justified while others are triggered by new guidelines or new results that were not available at the time of dossier preparation. Nevertheless, these issues will be addressed by submitting supplementary data at a later stage in the context of the evaluation of the glyphosate-containing products at zonal level. Appropriate studies are on-going, and some data are already available.

In line with EFSA, GRG is convinced that despite some missing data, especially on residues in rotational crops, and since the provisional risk assessment performed by EFSA shows a very wide margin of safety, enough information is already available to show that the representative uses are unlikely to cause unacceptable risks to consumers. This conclusion will not be affected by the provision of further residue data.

[6] For residues, refer to the Pesticide Peer Review TC 83 under : https://www.efsa.europa.eu/sites/default/files/2021-10/pesticides-residues-minutes.pdf

Storage stability of AMPA in plant matrices

Based on the submitted plant metabolism studies (both in primary and rotational crops) and with regard to the supported representative uses in conventional crops, the residue definition for risk assessment was established as the sum of parent glyphosate and its metabolite AMPA. Therefore, these two compounds were analysed in all the submitted residue studies (except for some obsolete studies where only the parent compound was measured, and which were only included in the dossier for the sake of transparency).

A total of 13 storage stability studies are available to assess the stability of glyphosate and/or AMPA in the respective samples during deep frozen storage between collection in the field and analysis.

Based on the results obtained and **according to the EFSA list of endpoints, parent glyphosate is considered stable in plant commodities for up to 12 months under frozen storage while the metabolite AMPA is considered stable in plant commodities for up to 6 months under frozen storage.** It is important to note that these storage stability periods only apply if no suitable data are available to demonstrate longer storage stability periods for the respective commodity (or category of commodities). Indeed, longer storage stability periods were established for glyphosate and/or AMPA in individual plant commodities or categories of plant commodities:

- Glyphosate was found to be stable for at least 18 months in high protein commodities and at least 24 months in oranges, high water commodities and high starch commodities). In case a significant decline of residues was observed, this decline only occurred after more than 24 months of storage.
- AMPA was shown to be stable under frozen storage for at least 12 months in soybean seed, maize forage, high protein commodities and high starch commodities, at least 18 months in sugar beet leaves, at least 24 months in oranges and soybean forage, and at least 31 months in tomatoes. An overview of the various study results is given in Table 1.

The fact that (with the above exceptions) AMPA is not considered to be stable in plant commodities for more than 6 months implies that some of the residue trials submitted to support the representative uses are not considered valid since the samples were stored for more than 6 months (with a maximum of 12 months) prior to analysis.

GRG believes that it is not justified to consider that (in the absence of specific data) AMPA is not stable for more than 6 months in plant commodities. It would be more appropriate to consider that AMPA is stable for up to 12 months. The standard storage stability period of 6 months for AMPA in frozen plant samples arises solely from the results of a single storage stability study in clover. In this study, degradation of AMPA (> 30% of the initial concentration) was found at storage intervals longer than 6 months (i.e. between 9 and 31 months). Noticeably, from 9 months onwards the levels of AMPA did not further decrease and remained at about 50-55% of the fortification level and about 60-70% of the initial level measured on day 0. GRG agrees that in this study a degradation of AMPA was observed after 6 months of storage. However, this finding must be put in perspective as it was not confirmed by other studies conducted in similar commodities. Clover belongs to the category of commodities with a high-water content and to the sub-category of forage crops. As shown in Table 1, five other tests demonstrate that AMPA is stable for at least 12 months in commodities of this sub-category. Two further tests demonstrate stability of AMPA under frozen conditions for at least 12 months in commodities with a high-water content, namely tomatoes (fruiting vegetables) and sugar beet leaves (leaves of root and tuber vegetables). Although the exact reasons for the degradation observed in clover could not be identified, GRG believes that this is an isolated, study-specific finding and that there is a sufficient weight of evidence showing that AMPA is stable for at least 12 months in forage crops and more generally in commodities with a high-water content. By virtue of the extrapolation

rules provided for in the OECD Guideline 506, it may be concluded that AMPA is generally stable under frozen conditions for at least 12 months in all five categories of plant commodities. This storage stability period of 12 months for AMPA properly supports all the residue trials in primary and rotational crops submitted for the representative uses.

Notwithstanding the above and to provide further experimental evidence, GRG has initiated a new storage stability study for AMPA in clover, grapes and walnuts. This study will cover storage intervals up to 24 months and is expected to be completed in Q3-Q4 2025.

Table 1: Overview of storage stability data for AMPA in plant commodities

Category (OECD 506)	Subcategory (OECD 506)	Matrix	Study (dRAR)	Stable for (dRAR) [months]	Comment
High acid content	Citrus fruit	Orange fruit	Study 1	**24***	-
High oil content	Oilseed	Soybean seed	Study 4	**12***	-
			Study 7	**6***	Storage at -10°C
High protein content	-	Dry beans	Study 13	**12***	Based on interim report (stable for 24 months according to final report)
High starch content	Cereal grain	Barley grain	Study 2	**12**	Degradation observed at the 18 months interval (linked to low procedural recoveries)
		Maize grain	Study 5	**12***	-
			Study 11	**31***	-
			Study 2	**18***	-
			Study 3	**12***	-
		Rye grain	Study 10	**10**	Degradation observed from 21 months onwards - the sample material was not homogenised prior to spiking
		Wheat grain	Study 10	**10**	Degradation observed from 21 months onwards - the sample material was not homogenised prior to spiking
	Root & tuber vegetable	Sugar beet root	Study 2	**12**	Degradation observed at the 18-month interval (linked to low procedural recoveries)

Category (OECD 506)	Subcategory (OECD 506)	Matrix	Study (dRAR)	Stable for (dRAR) [months]	Comment
High water content	Forage crop	Clover	Study 11	**6**	Degradation observed from 9 months onwards
		Maize forage	Study 5	**12***	-
			Study 3	**12***	-
		Maize green plant	Study 3	**12***	-
		Soybean forage	Study 11	**24**	Degradation observed at the 31-month interval
			Study 4	**12***	-
	Fruiting vegetables	Tomatoes	Study 11	**31***	-
	Leaves of root and tuber vegetables	Sugar beet leaf	Study 2	**18***	-
Other	-	Maize stover	Study 5	**6**	Degradation observed at the 12-month interval
			Study 3	**23***	-
		Rye straw	Study 10	**6**	Degradation observed from 10 months onwards - the sample material was not homogenised prior to spiking
		Sorghum stover	Study 11	**9**	Degradation observed from 12 months onwards partly due to low procedural recoveries
		Soybean hay	Study 4	**9**	Degradation observed at the 12-month interval
		Soybean straw	Study 7	**6***	Storage at -10°C
		Wheat straw	Study 10	**6**	Degradation observed from 10 months onwards - the sample material was not homogenised prior to spiking

* Corresponds to the longest storage interval investigated in the study

Completeness of the submitted residue data package for primary crops

According to the EFSA Conclusions, data gaps pertaining to residues in primary crops have been identified for nearly all the representative uses.

Some data-gaps are set by EFSA because samples were stored for more than 6 months before analysis. Therefore, the corresponding analytical results for AMPA are not considered to be sufficiently supported by the available storage stability data. **As explained in the previous section, GRG believes that, based on a weight of evidence approach, it should be concluded that AMPA is stable for at least 12 months under frozen conditions in all five categories of plant commodities and that because of this the submitted residue trials are indeed valid (since all samples were analysed within 12 months of storage).** This is especially true for the residue trials in grape. Based on a storage stability of 12 months for AMPA in plant commodities, enough valid residue trials are available to support the representative use of glyphosate in grapes (9 and 8 trials from the northern and southern residue zones, respectively). According to EFSA, and in line with the approach proposed by the RMS, these data may be extrapolated to cover the representative uses in citrus, tree nuts, pome fruit, stone fruit and kiwi. Based on a storage stability of 12 months for AMPA in plant commodities, enough valid residue trials are also available to support the representative uses of glyphosate in banana (3 trials) and in table olives in the southern part of the EU (4 trials). In the context of the active substance renewal, GRG only supports the use of glyphosate in olive plantations in the southern residue zone since this zone represents more than 99% of the total production of table olives in the EU. In summary, **based on a storage stability period of 12 months for AMPA in plant commodities, enough valid trials are available to support all representative uses for post-emergence of weeds in orchard crops and grape.**

Other data-gaps are set by EFSA because of an over-strict application of the extrapolation guidance. The technical guidelines SANTE/2019/12752 have been very strictly applied by EFSA **for all pre-sowing / pre-planting / pre-emergence representative uses as well as for all inter-row representative uses.** However, it is important to note that, **during the peer review expert meeting, a majority of Member State experts disagreed with this approach** and were of the opinion that with this type of use it is possible to extrapolate more broadly between crops and residue zones than provided for in the technical guidelines SANTE/2019/12752. This is because the herbicide is not applied to the crop itself and since based on information available from metabolism studies, residues were expected to be < LOQ for all these uses, irrespective of the crop type. Hence, all represented Member State experts considered the submitted residue data for the pre-sowing / pre-planting / pre-emergence uses to be sufficient, while for the inter-row uses all but one Member State considered the submitted residue data to be sufficient. In summary, **based on pragmatic extrapolation of the available data, enough valid trials are available to support all representative pre-planting, pre-sowing or pre-emergence uses as well as all inter-row representative uses.**

GRG notes that the technical guidelines SANTE/2019/12752 were issued in December 2020, which was about 6 months after submission of the glyphosate renewal dossier. Therefore, GRG could not refer to these guidelines during the preparation of the dossier. At the time of dossier preparation and submission, the applicable version of the respective guideline was SANCO 7525/VI/95 Rev. 10.3, which is nearly identical to SANCO 7525/VI/95 Rev. 10.2 since the only difference between the two revisions relates to extrapolation from apples and/or pears to kakis (Japanese persimmons). SANCO 7525/VI/95 Rev. 10.2 was the applicable guideline for the evaluation of the existing EU MRLs of glyphosate according to Article 12 of Regulation 396/2005. In this context two residue trials per crop, zone, and type of use (pre-sowing / pre-planting / pre-

emergence or interrow) were deemed both necessary and sufficient to confirm the no residue situation [7]. **Therefore, for the preparation of the glyphosate renewal dossier and based on the then available and applicable guideline SANCO 7525/VI/95 Rev. 10.3, the same requirements as for the Article 12 review were considered to apply and the number of trials submitted in the renewal dossier is in line with these considerations.** While the new guidelines SANTE/2019/12752 introduce more stringent requirements, with an increased number of trials to support a no-residue situation (at least 4 trials per zone for major crops and 3 trials per zone for minor crops), they also provide some room for interpretation and some flexibility since according to the introduction "In practice, special cases may be identified which are not fully described in these guidelines, as they would require ad-hoc approaches that cannot be described in a general document." GRG considers that the representative uses of glyphosate are such a special case and the ad-hoc approach to number of trials and extrapolations adopted is therefore compliant with current EU guidelines (SANTE/2019/12752). This also may be the reason why during the peer review expert meeting the majority of Member States considered the submitted residue data to be sufficient.

Notwithstanding the above, GRG has initiated a number of additional residue trials to comply with the new requirements of SANTE/2019/12752. Some of these trials were already submitted to AGG in the context of the stop-the-clock but, as they were not considered necessary by AGG, they were not evaluated by AGG and are not considered in the EFSA Conclusions. These trials, as well as trials that were completed additionally, will be submitted in the context of the renewal of the authorisation for the glyphosate-containing plant protection products according to Article 43 of Regulation 1107/2009.

Completeness of the submitted field residue data for rotational crops

Based on the available confined rotational crop studies, the presence of residues of glyphosate and/or AMPA > LOQ in rotational crops cannot be excluded. Therefore, a limited field rotational crop study is triggered.

In the context of the stop-the-clock, the applicant submitted the interim report for a limited field rotational crop study conducted at two sites (one in Germany and one in Spain). At each site, bare soil was treated at the nominal rates of 3.18 kg ae/ha glyphosate and 2.86 kg/ha AMPA. These application rates were selected to cover the possible plateau levels of glyphosate and AMPA residues in soil after repeated use of glyphosate at the maximum yearly rate for many years. Carrots, lettuce and wheat were sown after nominal plant-back intervals of 27±2 days, 135±10 days and 332±10 days.

The interim report provides the results for the two first plant-back intervals except for the wheat samples of the second plant-back interval in the Spanish trial. In the treated plots :

- No residues of glyphosate or AMPA above the LOQ of 0.025 mg/kg were found in carrots (root and leaves)
- Lettuce head showed residues of glyphosate < 0.025 mg/kg while in one trial AMPA was present at up to 0.049 mg/kg.
- Wheat forage showed residues of glyphosate < 0.025 mg/kg while in one trial AMPA was present at up to 0.039 mg/kg.

[7] European Food Safety Authority (EFSA), 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, 211 pp. https://doi.org/10.2903/j.efsa.2019.5862

- Wheat grain showed residues of glyphosate < 0.025 mg/kg while AMPA was present at levels up to 0.18 mg/kg.
- No residues of glyphosate or AMPA above the LOQ of 0.025 mg/kg were found in wheat straw.

Two control samples were found to contain residues above the LOQ (0.029 mg/kg of glyphosate in a carrot root sample and 0.041 mg/kg of AMPA in a wheat forage sample). The reason for these findings was not apparent, especially since the corresponding treated samples showed residues below the LOQ.

The above results from the interim report were included in the revised dRAR and, although the study now has been completed and the final report has been issued, they form the basis for the conclusions of the peer review.

Therefore, **a data gap was identified for the complete results of the limited field rotational crop study**. As already mentioned, **this study now has been completed and the final report with all the study results (including those missing in the interim report) can be provided upon request at any time. It is important to note that the new results do not impact the evaluation performed based on the interim report** since in general the uptake of residues from soil was found to decrease with increasing plant-back intervals. The only exception pertains to the residues of parent glyphosate in wheat forage which were found at a level of 0.029 mg/kg at the one-year plant-back interval in one of the trials (while these residues were so far found at levels < LOQ). However, since this finding does not impact the HR for the total residues of glyphosate and AMPA in wheat forage, the consumer risk assessment presented in the EFSA Conclusions does not need to be updated. In this assessment the potential residues of parent glyphosate and AMPA in rotational crops were taken into account based on the (then available) results of the limited field rotational crop study. The chronic and acute exposures were estimated to represent no more than 3% of ADI and 2% of ARfD, respectively. These estimates are provisional since they only take into account the results of the limited field rotational crop study. More accurate estimates can be derived once an extended residue data package for field rotational crops is available (see below). However, due to the wide margin of safety demonstrated by the preliminary estimates it is already possible to conclude that the supported representative uses (including the uses in annual crops) present no unacceptable risk to consumers.

In line with both Regulation 283/2013 and the OECD Guidance Document on residues in rotational crops ENV/JM/MONO(2018)9, the fact that residues ≥ LOQ were found in the limited field rotational crop study triggers the conduct of an extended set of field rotational crop trials. Hence the EFSA Conclusions call for "sufficient [supplementary] studies investigating the magnitude of residues in rotational crops (i.e., carrot, lettuce, wheat) including additional crops (as appropriate)". **As the need for an extended set of field rotational crop trials is a consequence of the limited field rotational crop study, these supplementary trials could only be initiated in 2022, once the first results of the limited field rotational crop study were known. Therefore, the trials are still on-going and could not be submitted during the peer review.** An overview of the extended set of field rotational crop trials is given in Table 2.

Table 2: Overview of ongoing field rotational crop trials

Category (OECD 506)	Matrix	Study (dRAR)	Stable for (dRAR) [months]	Comment
E22RC006	EUN/EUS	Maize	8	31/05/2024
E22RC012	EUN/EUS	Strawberry	4	31/05/2024
E22RC008	EUN/EUS	Cabbage	4	30/06/2024
E22RC010	EUN/EUS	Soybean	8	31/05/2024
E22RC009	EUN/EUS	Cauliflower	4	30/06/2024
E22RC001	EUN/EUS	Carrot*	2	31/05/2024
E22RC005	EUS	Wheat*	3	31/01/2025
E22RC007	EUN/EUS	Lettuce*	2	30/04/2024
E22RC004	EUN	Wheat*	3	31/05/2024
E22RC003	EUN/EUS	Leek	4	30/06/2024
E22RC002	EUN/EUS	Potato	4	30/04/2024
E22RC011	EUN/EUS	Pea	4	31/05/2024
E22RC013	EUN/EUS	Cucumber	4	31/05/2024

* Crops for which data are already available from the limited field rotational crop study

It is intended to submit the above studies in the context of the renewal of the authorisation for the glyphosate-containing plant protection products according to Article 43 of Regulation 1107/2009. While most of the studies are expected to be completed by the end of Q2 2024, the winter wheat study conducted in the southern residue zone won't be completed before the end of January 2025. This is because the studies were initiated at the beginning of 2022. At that time, it was still possible to grow most of the investigated crops in 2022 (first plant-back interval). However, the earliest opportunity to sow winter wheat was in autumn 2022 with a harvest in summer 2023. Therefore, the winter wheat study is delayed by about half a year compared to the other studies.

As already mentioned, the results of the extended set of field rotational crop trials are unlikely to change the conclusions of the consumer risk assessment. Since the provisional risk assessment showed a large margin of safety, it is already possible to conclude that the supported representative uses do not cause an unacceptable risk to consumers.

Conclusion

EFSA recently published its "Conclusions on the peer review of the pesticide risk assessment of the active substance glyphosate". GRG would like to provide the following comments on the residue-related issues raised in this document:

- According to the conclusions of the peer review, the metabolite AMPA is considered to be generally stable in plant commodities for 6 months under frozen storage. This is due to tests with clover in which AMPA was found to be stable for no more than 6 months. However, five other tests demonstrate that AMPA is stable for at least 12 months in commodities of the same sub-category as clover (i.e. forages). Based on this, and also considering the results available for the other plant commodities, GRG believes that the degradation observed in clover is an isolated, study-specific finding and that there is a sufficient weight of evidence showing that AMPA is stable in the five major categories of plant commodities for at least 12 months. To provide further experimental

evidence, GRG has initiated a new storage stability study for AMPA in clover, grapes and walnuts, which is expected to be completed in Q3-Q4 2025.

- According to the EFSA Conclusions, data gaps pertaining to residues in primary crops have been identified for nearly all representative uses. One of the reasons for this is because some samples were stored for more than 6 months before analysis. Therefore, the corresponding analytical results for AMPA are not considered to be sufficiently supported by the available storage stability data. As explained in the previous paragraph, GRG believes that AMPA is stable for at least 12 months under frozen conditions in all five categories of plant commodities and that because of this the submitted residue trials are indeed valid (since all samples were analysed within 12 months of storage). With a storage stability period of 12 months for AMPA in plant commodities, enough valid trials are available to support all the representative uses for post-emergence of weeds in orchard crops and grape. Another reason for the data gaps identified by EFSA is an over-strict application of the technical guidelines SANTE/2019/12752 for all pre-sowing / pre-planting / pre-emergence representative uses as well as for all inter-row representative uses. It is important to note that during the peer review expert meeting, a majority of Member State experts disagreed with this approach. All represented Member States considered the submitted residue data for the pre-sowing / pre-planting / pre-emergence uses to be sufficient while for the interrow uses all but one Member States considered the submitted residue data to be sufficient. GRG notes that the technical guidelines SANTE/2019/12752 were issued in December 2020, which was about 6 months after submission of the glyphosate renewal dossier. Therefore, GRG could not refer to these guidelines during the preparation of the dossier. Based on the guideline SANCO 7525/VI/95 Rev. 10.3 applicable at the time of dossier preparation and submission, a similar approach to extrapolation was to be expected to that applied during the evaluation of the existing EU MRLs of glyphosate according to Article 12 of Regulation 396/2005. In this context two residue trials per crop, zone, and type of use (pre-sowing / pre-planting / pre-emergence or interrow) were deemed both necessary and sufficient to confirm the no residue situation. The number of trials submitted in the renewal dossier is in line with these considerations. However, to comply with the new requirements of SANTE/2019/12752, GRG has initiated a number of additional residue trials that will be submitted in the context of the renewal of the authorisation for the glyphosate-containing plant protection products according to Article 43 of Regulation 1107/2009. Some of these trials were already submitted to AGG in the context of the stop-the-clock but, as they were not considered necessary, they were not evaluated by AGG and are not included in the EFSA Conclusions.
- In the EFSA conclusions a data gap was set for the complete results of the limited field rotational crop study for which an interim report was submitted during the stop-the-clock. This study now has been completed and the final report can be provided upon request at any time. The new results do not impact the conclusions drawn based on the interim report since, in general, the uptake of residues from soil was low and decreased with increasing plant-back intervals. Since some samples from the limited field rotational crop study showed residues ≥ LOQ, and in line with both Regulation 283/2013 and the OECD Guidance Document on residues in rotational crops ENV/JM/MONO(2018)9, a further data gap was set for "sufficient [supplementary] studies investigating the magnitude of residues in rotational crops (i.e. carrot, lettuce, wheat) including additional crops (as appropriate)". An extended set of field rotational crop trials is currently being performed in order to address this data gap. As the need for supplementary trials is a consequence

of the limited field rotational crop study, these supplementary trials could only be initiated in 2022, once the first results of the limited field rotational crop study were known. Therefore, the trials are still on-going and could not be submitted during the peer review. It is intended to submit them in the context of the renewal of the authorisation for the glyphosate-containing plant protection products according to Article 43 of Regulation 1107/2009.

- Despite the data gaps, EFSA did not identify any critical concern in the area of residues and concluded that, once the requested supplementary data are available, "A higher consumer exposure to residues of glyphosate than the one considered in the current risk assessment cannot be excluded. However, it is not expected that this might lead to an exceedance of the toxicological reference values." While GRG does not consider all data gaps identified in the area of residues to be fully justified, GRG shares EFSA's opinion on the dietary safety assessment. Since the preliminary risk assessment shows a very wide margin of safety (with chronic and acute exposures not exceeding 3% of ADI and 2% of ARfD, respectively) it is already possible to conclude that the representative uses are unlikely to cause unacceptable risks to consumers. This conclusion will not be affected by the supplementary residue data that will be submitted in the context of the renewal of the authorisation for the glyphosate-containing plant protection products according to Article 43 of Regulation 1107/2009.

Section III: Environmental fate and behavior

Key aspects

- **Endpoint selection for modelling**
- **Assessment of HMPA in sediment**
- **Assessment of AMPA degradation in field dissipation studies**
- **Monitoring data**

Contents

Summary

The following section summarises points relating to the fate of glyphosate in the environment within the Annex I renewal dossier submitted by the Glyphosate Renewal Group (GRG, applicant). The dossier was evaluated by the Assessment Group for Glyphosate (AGG) acting as RMS consisting of the corresponding competent authorities of France, Hungary, The Netherlands and Sweden.

This part of the document provides targeted summaries of relevant topics for the ongoing EU Review process regarding environmental fate.

Endpoint selection for modelling

In Appendix B, draft List of end points as of July 2023, two sets of modelling endpoints are given for Tier 2 groundwater and surface water PEC calculations for the active substance glyphosate:

i) Geometric mean DT_{50} values for acidic and alkaline soils covering a fast or a slow phase of degradation of glyphosate based on pathway fits. This applies for simulations when metabolite AMPA is simulated along with parent.
ii) Geometric mean DT_{50} values for acidic and alkaline soils assuming a slow degradation phase of glyphosate based on parent-only fits. This applies for simulations when glyphosate is modelled alone.

This approach is not typical for consideration of pH dependency of degradation in soil and it results in a total of six DT_{50} values for glyphosate to be tested when also considering metabolite AMPA in modelling. It is the opinion of the applicant that four geometric mean DT_{50} values derived from acceptable pathway fits would be adequate to estimate Tier 2 PEC values for glyphosate and AMPA in groundwater and surface water.

Assessment of HMPA in sediment

The metabolite hydroxymethylenephosphonic acid (HMPA) was not observed in sediments following application of the active substance glyphosate to water-sediment systems. Nevertheless, the draft List of endpoints (Appendix B of EFSA conclusion) sates that HMPA should be included in the residue definition for sediment. This is in strong contradiction to the observations made in the study indicating that no such transfer to the sediment occurred. Moreover, a very conservative default K_{foc} value of 10000 mL/g for HMPA should be used for estimation of PEC_{sed}. Updated PEC_{sed} values from the RMS are included in the draft LoE.

For application of glyphosate to railways, the PEC_{sed} of HMPA was calculated conservatively based on the parent maximum PEC_{sed}, taking into account the molar mass ratio and the maximum occurrence in water (10 %). This is in contrast to the more standard approach, whereby the PEC_{sed} of metabolite is calculated based on the parent maximum PEC_{sw} taking into account the molar mass ratio, the maximum occurrence in sediment and a conversion factor for concentration per unit mass of sediment.

Although these assumptions are not in line with experimental observations from the scientific perspective, no unacceptable risks for aquatic or sediment-dwelling organisms are indicated.

Assessment of AMPA degradation in field dissipation studies

Regarding metabolite AMPA, the exposure assessment presented in the draft LoE is based on the most conservative kinetic endpoint derived from laboratory aerobic soil degradation studies. This is a consequence of the absence of reliable field degradation rates, though a large range of field studies was available. The absence of evaluable field kinetics data thus resulted in the identification of a data gap. Nevertheless, the risk assessment could be finalised with a conservative approach in all environmental compartments and no critical issues were identified.

Monitoring data

An assessment of publicly available monitoring data is currently not a routine practise in regulation. There is no guidance on how the data should be generated, nor on how to assess the data. There exists, for example, no 'best monitoring practise' that would allow for an evaluation of data according to consistent criteria. Furthermore, such data are collected for a variety of different purposes (e.g., to assess compliance with other existing regulations, or to identify emerging issues) in the context of various protection goals.
While a large number of results are documented in various formats (e.g., electronic data bases or summarizing documents), very little is known about the context on procedures followed for selection of sampling sites, or details on how samples were taken. Therefore, the data must be regarded generally as of unknown quality and reliability in the context of evaluation. Although this lack of detail means that the demanding requirements of regulatory risk assessment for the use of such data directly in the risk assessment process are not fulfilled, at least it is possible to get information with respect to the chemical status of the environment at a local or regional scale.

Within the ongoing EU review process, the monitoring data for GLY and AMPA were compared to regulatory triggers available to put the findings into context. Public monitoring data should not be regarded as higher tier in risk assessment. They can be regarded as supportive information to confirm that safety as indicated by risk assessments is given. For the particular case of GLY and AMPA it is important to note that safety in accordance with risk assessment frameworks was and is demonstrated at the conservative lower tier levels.
Public monitoring data may also identify whether local issues could exist that would require further investigation through stewardship action or local mitigation measures; a process to which the applicant is committed. For example and following the analyses of Spanish regional monitoring data, stewardship measures (including farmer seminars) have been recently successfully initiated in Spain.

In the particular case of GLY and AMPA, though, the analyses are likely to provide a comprehensive picture of the chemical state of the environment, given that the assembled EU data set is large and captures a range of agronomic, geographical, pedoclimatic and hydrogeological contexts, as well as providing a good temporal coverage allowing assessment of the state of a compartment in different seasons and hydrological regimes; and, overall, the data do provide a high level of reassurance.

All accessible public monitoring data for glyphosate (GLY), its primary metabolite amino methyl phosphonic acid (AMPA) and for hydroxy methyl phosphonic acid (HMPA) were collected from public monitoring databases in the EU (including UK, Switzerland, Norway and Iceland). No data for HMPA was identified for any country or compartment, and very little data was available for GLY or AMPA in sediment and soil, but what was available didn't indicate levels are of concern. The monitoring data obtained was subjected to detailed and comprehensive analysis as reported in KCA 7.5-002 and updated in document KCA 7.5_[redacted]_2022_CEA.2365_GRG.pdf. Further detailed analysis included, particularly, investigations of consecutive detections, especially undertaken for consecutive trigger exceedances. It also

included a 'vulnerability of the sites analysis' for both groundwater and surface water as performed in Appendix 1 of document KCA 7.5_[redacted]_2022_CEA.2365_GRG.pdf. For a case study focussing on France, regression tree and random forest statistical models were developed and applied to predict total and consecutive rates of detection (%) for values above 0.1 µg/L in surface waters. Predictor variables were used describing potential sources of GLY/AMPA and factors affecting emission and detection. This is reported in Chapter 10 of document KCA 7.5_[redacted]_2022_CEA.2365_GRG.pdf. A potential influence of the sources of drinking water (SW vs GW, and 'small water supply' vs 'large water supply') was also investigated and reported in Section 5.8 of document KCA 7.5_[redacted]_2022_CEA.2365_GRG.pdf.

The following more general principles were applied for data evaluation:

- The approaches taken for any data processing were precautionary in that they preserved data-points in the analysis though there was doubt regarding their reliability.
- Outlier analysis[8] was performed on the combined EU datasets, and to ensure complete transparency, statistics were presented (i) with all of the data and (ii) with outliers excluded.
- Analyses of the datasets sought to assess the chemical state of the given environmental compartment and also to consider potential impacts on biota, ecosystems and human health. This was accomplished by using regulatory endpoints and thresholds from a range of European (EU) Directives like the Water Framework Directive (Directive 2000/60/EC) and associated ones like the Groundwater (2006/118/EC), Drinking Water (1998/83/EC) and Priority Substances (2008/105/EC28) Directives, in addition to the Plant Protection Products Directive (1107/2009/EC).

Groundwater

For groundwater (GW), monitoring data from 21 countries were analysed for compliance against non-scientific thresholds of 0.1 µg/L[9] for GLY and 10 µg/L[10] for AMPA.

- The GLY public monitoring dataset was large (> 251 700 samples collected from > 40 000 sampling sites). Detection of GLY in GW samples was ~2 % and compliance with the 0.1 µg/L threshold was very high (99.4 % samples from 97 % of sites). The maximum concentration (excluding 10 outliers[11]) was 39.2 µg/L. This value is well below the SW RAC[12] for groundwater fed ecosystems and it is also clearly below the life-time health-based ADI[13] concentration of 1500 µg/L.
- The AMPA public monitoring dataset was also large (> 228 400 samples collected from > 35 900 sampling sites). Detection of AMPA in GW samples was ~2.9 % and compliance with the arbitrary 10 µg/L regulatory threshold was very high (99.998 % of samples from 99.994 % of sites). The maximum concentration of 16 µg/L was well below the SW RAC (for groundwater fed ecosystems) and the lifetime health-based ADI concentration of 3960 µg/L.
- For GLY, only 0.21 % of samples were consecutively above the threshold of 0.1 µg/L allowing the conclusion that exceedances were rare and not caused by systematic factors. Analysis indicated that these sites are likely anomalous, sampling karstic terrain or alluvial gravels which were in direct contact

[8] The Inter-Quartile-Range approach was used, such that an upper fence limit is defined by Q75 + K * (Q75 – Q25), where Q75 is the upper quartile, Q25 the lower quartile and K typically has a value of 1.5. In order to ensure that a precautionary approach was taken, a K value of 1000 was used to define the upper fence limit

[9] From Drinking Water Directive (Directive 98/83/EC)

[10] Arbitrary threshold in drinking water for non-relevant metabolite in SANCO/221/2000-rev.10 (25 Feb 2003)

[11] Given the conservative nature of the procedure for identifying outliers, and the small number identified, it is believed that this should be regarded as a reasonable process.

[12] RAC – Regulatory Acceptable Concentration; 400 µg/L for GLY, and 1200 µg/L for AMPA

[13] ADI – Acceptable Daily Intake

with surface water or, in some cases, incorrectly assigned to groundwater when in fact they were surface water monitoring sites. Similar observations were noted for outliers with sites influenced by surface water and/or the data was historic (i.e., from the early 2000s, hence of less relevance to a current assessment of the state of the environment).

- Case studies were carried out to explore potential reasons for locally elevated rates of groundwater detection in ES, IT and the UK. Several dozen monitoring sites were elucidated predominately by a desk-based approach (45 sites in ES, 13 in IT, and 5 in UK) while this was followed up for Spain for 16 sites with field visits. The investigations suggest the reasons for the findings at these sites are most likely due to deteriorated monitoring locations, poor or specific local agronomic practice, and pollution events. The applicant has initiated the implementation of further stewardship measures to improve compliance in the future.
- Given the extent of use of GLY, the EFSA conclusion highlights possible groundwater exposure from riverbank infiltration and connectivity with surface water bodies in some susceptible locations. It should be noted that this is a new potential concern within the registration review procedure of plant protection products. This specific request was identified during a late-stage expert meeting during the renewal process is not covered by any existing pesticide-related regulation or water-related directives and regulations, nor by any EC- or OECD-Guidance. On the other hand, it is clear that new fields of evaluation in review processes need to be addressed in some form as the issue has been raised. Surface water does infiltrate riverbanks, particularly during periods of high streamflow. When stream levels recede, the stored water can flow back into the stream as bank return flow, which is an important source of water during both low-flow conditions[14] and following storm events[15]. In some locations surface water infiltrating riverbeds and riverbanks may contribute sufficiently to groundwater recharge that for some MS there may be uncertainty as to the degree of movement of GLY and AMPA residues from surface waters to groundwater via this recharge pathway. Raw drinking water may be abstracted from surface water via bank filtration. It has been established that where bank filtration of surface water is knowingly exploited for the derivation of drinking water (e.g., in France, the Netherlands and Germany), the residues of GLY and AMPA are such that the resulting drinking water complies with the 0.1 µg/L threshold. Infiltrating stream water will be subject to the same kinds of fate processes as for bank filtration used to "treat" surface water abstracted for drinking water. This attenuation of residues infiltrating into riverbank deposits can be significant (20 – >95% removal; through both high adsorption and degradation) over short travel distances. The monitoring data supports this observation indicating that groundwater recharge from surface water bodies is not a significant exposure pathway. Proximity to surface water analysis suggests that groundwater monitoring sites where occasional non-systematic exceedance of the regulatory threshold of 0.1 µg/L for glyphosate occurs, are statistically similar to all other sites where groundwater monitoring takes place. If recharge from surface water bodies was a significant exposure pathway monitoring sites with rare exceedances would be expected closer to surface water, but this is not observed. Furthermore, the lack of AMPA exceedances in groundwater, and especially accompanying the rare glyphosate exceedances, strongly suggests bank infiltration is not impacting groundwater quality. The GRG does, however, recognise that this is still a matter of concern for some MS, and further investigations have been initiated. It should be noted that bank filtration must be considered as one out of many steps in drinking water processing each contributing effectively to the elimination of glyphosate residues from the raw drinking water. This has been demonstrated by various investigations available as published literature, as well as submitted as particular information in the dossier. Anyway, the aspect of bank filtration will be subject to further review and to also put into context of overall processing of raw to drinking water.

[14] Cartwright, I., B. Gilfedder, and H. Hofmann. 2014. "Contrasts between estimates of baseflow help discern multiple sources of water contributing to rivers." *Hydrol. Earth Syst. Sci.* 18 (1): 15-30.

[15] McCallum, James L., Peter G. Cook, Philip Brunner, and Dawit Berhane. 2010. "Solute dynamics during bank storage flows and implications for chemical base flow separation." *Water Resources Research* 46 (7).

- For the representative use on railways, the EFSA conclusion presents a targeted monitoring study conducted in Sweden and peer reviewed in a scientific literature article (Cederlund, H., 2022[16]), groundwater sampling wells were installed at 12 sites associated with railways. Useful results were derived for wells adjacent to the railway down gradient to the groundwater flow direction. It was concluded that this information supported the exposure assessment for the single use pattern (1 x 1.8 kg a.s./ha) regarding the representative use on railways and the Swedish conditions. The results provide reassurance that groundwater exposure to glyphosate and AMPA above the parametric drinking water value of 0.1 µg/L generally did not occur in the monitored situations.

Surface water

For surface water (SW), data from 22 countries were analysed for compliance against RAC[17]. Additional analyses against country specific annual average (AA) and Maximum Allowable Concentration (MAC) EQS[18] values were also undertaken.

- The GLY public monitoring dataset was large (> 308 000 samples collected from > 15 000 sampling sites) and detection of GLY above the limit of quantification (> LOQ; average 0.43 µg/L, 0.0.1 – 1000 µg/L) in SW samples was ~37 %. Compliance with the GLY RAC of 400 µg/L was extremely high (99.994 % of samples; 99.90 % of sites) and the very occasional exceedances (0.006 % of samples; 0.10 % of sites) were largely on separate non-consecutive occasions (only 0.003 % of samples being consecutive). The maximum concentration of 77.2 µg/L (excluding outliers), was well below the RAC (mean measured concentration 0.06 µg/L (0.000 – 77.2 µg/L)).
- Distribution of locations that exceed the GLY RAC did not indicate any specific pattern or bias. Consideration of the country GLY data against country EQS values indicated a near total compliance (~99.96 % of samples) across the large EQS-MAC dataset. Similarly, compliance for the large EQS-AA dataset (~13 000 site-years from ~2 500 sites) was very high (99.96 % site-years at 99.98 % of sites).
- The AMPA public monitoring dataset (> 270 000 samples collected from > 12 600 sampling sites) was large and detection of AMPA > LOQ (average 0.07 µg/L, 0.01 – 10 µg/L) in SW samples was ~62 %, however, compliance with the AMPA RAC of 1200 µg/L was very high (99.999 % of samples; 99.98 % of sites) with infrequent exceedances (0.001 % of samples from 0.02 % of sites) occurring on 3 separate non-consecutive occasions. A small number of high maximum concentrations were confirmed to be outliers and once excluded the maximum concentration was 224.4 µg/L, which is well below the RAC (mean measured concentration 0.10 µg/L (0.000 – 224.4 µg/L)).
- Distribution of locations that exceed the AMPA RAC did not indicate any specific pattern or bias. Consideration of the country AMPA surface water data against country EQS values indicated that the presence of AMPA, from GLY or other sources (e.g., detergents, fire retardants or textile industry chemicals) is not expected to have any impacts with 100 % compliance for the large EQS-MAC (~218 000 samples from ~9 100 sites) and EQS-AA (~10 900 site-years from ~1 600 sites) datasets.
- For surface water destined to be drinking water, it is a routine of water works to apply **Water Treatment Processes** to remove bacteria and viruses and other organic micro-pollutants. In the EU, 88 % of raw water sources for drinking water production are subject to disinfection. Raw drinking water taken from surface water is practically quantitatively disinfected (99.9 % by volume). For disinfected surface water, chlorine disinfection is applied to a minimum of 62 % of the raw water. GLY and AMPA

[16] Cederlund, H., 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, 152361, 9pp. https://doi.org/10.1016/j.scitotenv.2021.152361

[17] 400 µg/L for GLY and 1200 µg/L for AMPA

[18] EQS – Environmental Quality Standard; this has not yet been set for GLY at the EU-level, although there are ongoing considerations in that direction.

are known to be very readily transformed by the most common disinfection methods, ranging from 60 to 99 % for GLY and from 25 to 95 % for AMPA. Chlorination results in small molecules as transformation products, often similar or identical to those found from natural sources. Drinking water treatment processes are carefully controlled and the water treatment process train at any given abstraction site is optimised to ensure that quality standards are met at the tap of consumers (e.g., GLY < 0.1 µg/L).

- It should be noted that the EU parametric trigger of 0.1 µg/L refers to drinking water at the tap of consumers. Any application of this trigger can be felt as an extremely high conservative approach ignoring additional steps of water processing (for example, treatment to ensure microbial safety) that are readily, effectively and quantitatively able to remove micro-residues like those of GLY and AMPA from raw drinking water. This applies in particular when surface water is abstracted as raw drinking water. Apart from this, only a science-based ecologically relevant threshold is required to be applied. Given that surface water abstracted for use as drinking water is always treated to ensure microbial safety, and that GLY and AMPA are known to be significantly removed by such treatments, the GRG are convinced that a threshold taking into account treatment processes is appropriate for GLY/AMPA for raw surface waters abstracted for use as drinking water. The exact appropriate value for this threshold should depend on the local circumstances (e.g., on the efficiency of the local water treatment train in place). The currently available public monitoring data for residues in drinking water (see below) strongly suggests that water treatment processes currently in place are sufficient.

Drinking water

For drinking water (DrW), monitoring data were identified and evaluated for the four countries DE, IE (GLY only), SK and SE.

- Compared to groundwater and surface water, the GLY dataset was comparatively small (~9 500 samples collected from ~3 700 sampling sites). Compliance with the DrW threshold of 0.1 µg/L was very high (99.90 % of samples). All of the exceedances reported are old (2007 and earlier).
- The AMPA monitoring dataset was similarly small (~7 250 samples collected from ~2 650 sampling sites). Compliance with the threshold of 10 µg/L was absolute at 100 %. Compliance with the DrW threshold of 0.1 µg/L was very high (99.90 % of samples).
- Approximately 75 % of EU inhabitants rely on drinking water from groundwater, 25 % on surface water. The high compliance rates in drinking water somewhat confirm that the treatment methods in place (e.g., for SW as drinking water) are effective at removing GLY and AMPA.

Air

For **air**, a small number of GLY and AMPA monitoring results (381 each from 8 sites) were collected from FR and analysed. The maximum measured concentration of 1.225 ng/m^3 for GLY and 0.015 ng/m^3 for AMPA are extremely low[19]. The EFSA conclusion states that despite the limited monitoring information available, and considering the intrinsic properties of glyphosate defined according to FOCUS Guidance Air (FOCUS, 2008), long range transport is not expected while particulate-bound concentration as a result of wind-eroded particle transport at the short and medium range is expected to occur. Surprisingly, the conclusion also suggests that medium range transport during periods of spraying, due to the formation of aerosols, is also expected to occur – however, the GRG regards transport following spray drift as likely to

[19] Considering the health-based reference values ADI, AOEL and AAOEL covering exposures from acute to lifetime duration, inhalation exposures at these combined maximum concentrations are several orders of magnitude lower even for the most sensitive group (children). Therefore, preliminary and very conservative calculations strongly suggest that air-borne exposure to GLY and AMPA would not result in adverse health effects.

result in only short-range transport. With respect to the other air monitoring results presented during the public consultation, the results from air samplers were considered not to contribute significant information.

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Section IV: Ecotoxicology

Key aspects

- **Long-term mammal dietary exposure risk assessment and residue decline.**
- **Direct contact exposure risk of aquatic macrophytes from glyphosate via the 'spray drift' exposure route.**
- **Dietary exposure risk of bees to AMPA from pollen and nectar.**
- **Biodiversity**

Contents

Summary

The following document summarises points relating to the ecotoxicology sections of the EFSA draft conclusion report (2023) 'Peer review of the pesticide risk assessment of the active substance glyphosate.'

The following provides further information relating to proposed data gaps identified in the draft EFSA conclusion report regarding relevant ecotoxicological topics for the ongoing EU Review process regarding ecotoxicology.

Long-term mammal dietary exposure risk assessment and residue decline

The tier I long-term mammal risk assessment in the draft EFSA conclusion report (EFSA, 2023) suggests a risk to small herbivorous mammals for some of the proposed Annex I GAP table uses.

A tier II refined long-term mammal risk assessment was **not** included in the risk assessment presented in the conclusion report, as grass residue decline data for glyphosate, previously submitted to support the 2017 Annex I renewal, were – after further evaluation by the RMS and EFSA, not considered 'sufficient' to refine the residue exposure estimates used in the long-term mammal risk calculations for the current Annex I evaluation. EFSA do however state in the conclusion report, that the previously submitted grass residue decline data suggest that glyphosate residue decline (DT_{50} / half-lives) in/on plants is shorter than 10 days (default plant decline DT_{50} applied by EFSA) and that *qualitatively*, these data may be used to support the long-term mammal risk assessment.

To further support the long-term mammal dietary exposure risk assessment and in direct response to comments received from the RMS and EFSA during the Annex I evaluation on the grass residue decline dataset, the applicant conducted new plant residue decline trials with glyphosate in 2022. The data generated in these trials are considered **'sufficient'** to support **quantitative refinement of** the dietary residue exposure estimates **in a refined tier II long-term mammal risk assessments, that demonstrates that a low long-term exposure risk to small herbivorous mammals**[20] can be achieved for **all** of the proposed Annex I GAP table uses.

In the additional plant residue trials conducted in 2022, nine separate glyphosate plant residue decline trials were conducted across eight European countries (Denmark, Poland, the Netherlands, Germany, France, Spain, Italy and Bulgaria) spanning the northern and southern EU residue zones. Early growth stage winter wheat and winter oilseed rape plants (that are representative of dietary items expected in herbivorous and omnivorous bird and mammal diets) were sprayed with the Annex I representative formulation. Glyphosate concentrations in plant material were measured in plant tissue samples collected from all trial plots on at least nine sampling occasions over 14 days following application, that included multiple sampling occasions on the day of application.

A kinetics residue decline data analysis was performed and plant specific residue decline half-life DT_{50} values were determined, which can be used to adapt the default time weighted average residues factor (fTWA) used in the residue exposure estimate calculations – see table below.

[20] the generic focal mammal species that drives the long-term risk to mammals in the EFSA risk assessment.

Decline DT_{50} values for glyphosate residues in Winter Wheat and Winter Oilseed rape with refined fTWA for use in a Tier II refined long-term mammal dietary exposure risk assessment

Plant type	Residue decline half-life DT_{50} (days)	Time weighted average residues factor (*fTWA)
Values used in EFSA conclusion - Tier I long-term mammal risk assessment	10	0.53
EU – Winter wheat	1.62	0.11
EU – Winter oilseed rape	3.2	0.22
EU- Plants combined	2.29	0.16

*fTWA – time weighted average residues factor accounts for decline of residues on dietary food items over time.

The **tier I** long-term mammal risk assessment in the EFSA conclusion, uses a **worst-case risk envelope approach**, that covers all proposed Annex I uses. Of the crop scenarios presented in the EFSA conclusion, the **highest dietary exposure residues** are encountered by a 'small herbivorous mammal' consuming 100% grasses and cereals following application of 1.8 kg glyphosate a.e./ha, (max single rate on GAP). This achieves glyphosate dietary residues of 69 mg glyphosate/kg bw/day, referred to as the 'daily dietary dose' (DDD) in the risk assessment table. That in turn achieves the lowest tier I **TER (toxicity exposure ratio)** i.e., the ratio between the long-term mammal endpoint (150 mg/kg bw/day) and the DDD of **2.2,** which is below the regulatory trigger value of 5, indicating a long-term mammal dietary exposure risk.

Residue exposure estimates may be refined in **a tier II long-term mammal risk assessment**, using substance specific DT_{50} values based on experimental data (such as those determined in the new decline trials - see table above). Using the re-calculated time weighted average residues factor (fTWA) to **refine the DDD values**, results in TER value that **exceeds** the trigger value, demonstrating that a **low long-term dietary exposure risk to mammals can be achieved** for all uses on the Annex I uses table.

Using the residue decline DT_{50} value of 1.62 days, achieved for 'EU - Winter wheat' gives a refined **fTWA value of 0.11**, which when applied to the crop scenario that achieved the lowest TER value in the draft EFSA conclusion, achieves a refined DDD value of 14.3 mg/kg bw/day, that results in a refined TER of 10.5, that exceeds the TER trigger value of 5. Indicating a low and acceptable long-term exposure risk to mammals for all uses on the proposed Annex I GAP table.

Report summaries for the new residue decline trials and for the kinetics evaluation can be made available upon request.

Direct contact exposure risk of aquatic macrophytes from glyphosate via the 'spray drift' exposure route

The applicant disagrees with the need to conduct an overspray exposure study and risk assessment with an emergent aquatic macrophyte species to address the drift route of exposure, as validated test guidelines and risk assessment approach that considers the direct overspray route of aquatic emergent vegetation exposure is not currently available in the EU.

In the EFSA conclusion, reference is made to aquatic macrophyte exposure studies conducted by Sesin et al., (2020), where exposure of an aquatic plant species via overspray resulted in larger effects when compared to other routes of exposure. The study was not considered relevant to the EU risk assessment as

the formulation used contained POEA (polyethoxylated tallowamine) which is a surfactant banned from use in the EU, as it is toxic to aquatic organisms and is known to enhance the aquatic toxicity of products in which it is used. In addition, in the overspray study **'methylated seed oil'** was added to the spray application solution, to 'increase the foliar surface wetting and facilitate better penetration into plant tissues.' The presence of both POEA and **methylated seed oil** in the spray solution **may account for the 'larger effects' observed in the overspray experiment compared to the other exposure routes in this work**. Therefore, conclusions based on the work by Sesin et al., (2020) should be considered with caution, as they do not reflect how a glyphosate containing product would be applied in the EU.

The existing non-target terrestrial plant vegetative vigour studies are considered protective of emergent aquatic vegetation the amount of glyphosate that could potentially reach an adjacent surface water body would be much lower than the lowest no observed effect rate (NOER) achieved in the submitted non-target terrestrial plant vegetative vigor study. To further support this statement, the applicant highlights that mitigation measures proposed in the Annex I uses table will significantly reduce the exposure risk from spray drift. The Annex I table proposes the use of at least 75% drift reducing nozzles, and a reduced standard drift value is required to achieve an acceptable non-target terrestrial plant risk assessment, where at least a 5 m in-field no spray buffer is required. This reduces the standard (off-target) drift value of 2.77% by a factor of 5, to 0.57%. When both spray drift mitigations are considered, the amount of glyphosate potentially reaching emergent aquatic vegetation via the drift exposure route is 2.57 g a.e./ha (based on a 1.8 kg a.e./ha application rate) which is six times lower than the lowest NOER value (15.7 g a.e./ha) achieved in the non-target terrestrial plant 'vegetative vigor' study (15.7 g a.e./ha).

Dietary exposure risk of bees to AMPA from pollen and nectar

The applicant submitted a honey-bee colony feeding study to support the Annex I submission, where the feeding concentrations were selected based on measured residue concentrations determined in samples of pollen and nectar after applying 2.88 kg a.e./ha to a crop of flowering *Phacelia tenacetafolia*. The application rate used exceeds the highest single Annex I proposed use rate. The glyphosate concentrations fed to the colonies exceeded those observed in the exposure study and exceed what would be expected to be found in pollen and nectar after an application of glyphosate at the maximum use rate.

In the applicants submitted risk assessment for exposure of bees to AMPA via pollen and nectar, a low exposure risk was concluded based on AMPA residue levels reported in an interim rotational crop study report submitted in the residues section.

Finally, in the conclusion, EFSA concludes a low exposure risk to honey-bees according to the 2013 bee guidance document and that higher tier data are not required to conclude on the honey-bee risk assessment.

Biodiversity

The applicant appreciates that EFSA Experts acknowledge **the lack of a harmonized approach to assess biodiversity within the prospective risk assessment**. The applicant also agrees with the EFSA experts that any risk associated with the representative uses of glyphosate on biodiversity are complex and depend on multiple factors, and that in-direct effects following removal of the target weeds are likely to be similar for any broad-spectrum herbicide used in the same manner.

It should be acknowledged that all efforts to reduce off-target movement of herbicides when applied to control unwanted vegetation is key to reducing the impacts on non-target organisms, either through direct contact, or through indirect effects via trophic interaction. A low direct exposure risk to non-target organisms

is demonstrated in the glyphosate ecotoxicological risk assessments, supported by an extensive set of toxicological, environmental fate and ecotoxicological regulatory study data. Whilst direct effects on target species and indirect effects on organisms that depend on targeted plant species in-field may not be avoidable, off-target areas must be protected from both direct and in-direct effects. As there is no regulatory guidance on how indirect effects on non-target species (both in and off-field) should be quantified within the context of an Annex I renewal, the applicant is committed to working with regulators towards an acceptable range of mitigation measures that protect and enhance biodiversity within agricultural landscapes. Decisions on how biodiversity should be supported at the landscape level should - more appropriately be made by risk managers, at national and/or European level, using achievable and appropriate tools, supported by agricultural policy, directives and regulations to drive a common approach. The approach submitted by the applicant was considered reasonable to address concerns highlighted in the 2017 Annex I Implementing Regulation relating to 'indirect effects through trophic interaction,' but accepts the limitations in the approach, that was conceived without adopted guidance being in place at EU level. The applicant does however disagree with EFSA's statement that the data presented were of questionable scientific quality and of limited use to address the topic.