Dear Honorable Members of the European Parliament,

Thank you for your letter of 10 November 2022 in which you raised several questions on the renewal of the approval of glyphosate as an active substance for use in plant protection products (PPP) under Regulation (EC) No 1107/2009.

ECHA and EFSA are conscious of the considerable public interest among EU citizens on this substance and we appreciate your desire to fully explore the process. Some of the questions included in your letter have already been addressed publicly, including during an exchange of views on glyphosate held by the ENVI Committee of the European Parliament on 11 July 2022.[1]

We welcome this opportunity to reiterate and further clarify the scope and status of our respective work on this dossier. Both ECHA and EFSA are committed to transparency and wish to reassure you and the public that due process has been followed and appropriate scientific rigour applied in the classification conclusions (ECHA) and the ongoing peer review (EFSA). Therefore, we welcome your questions, and with this letter wish to address the concerns you have raised regarding the opinion of the ECHA Committee for Risk Assessment (RAC) on the classification conclusions (on the carcinogenicity and germ cell mutagenicity of glyphosate) and also regarding some areas of the EFSA ongoing peer review.

Please do not hesitate to get back to us in case you need further clarifications.

Yours sincerely,

Sharon McGuinness

EUROPEAN CHEMICALS AGENCY * HELSINKI - FINLAND *
Dr Sharon MCGUINNESS
Executive Director
ECHA
12. 12. 2022

Bernhard Url

European Food Safety Authority
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Date: 2022.12.06 15:21:45 +01'00'

[1] Recording available at https://multimedia.europarl.europa.eu/en/webstreaming/envi-committee-meeting_20220711-1500-COMMITTEE-ENVI

Annex

ECHA Responses to technical questions in your letter

ECHA has already published a response to the report by HEAL referred to in your letter and has also published its reply to MEP Bas Eickhout who raised similar issues to those in your letter in the exchange of views between the European Parliament's Committee on the Environment, Public Health and Food Safety (ENVI), ECHA and the European Food Safety Authority (EFSA) on 11 July. ECHA has a dedicated glyphosate page on its website[2] where you can find these responses together with other relevant information.

Please note also that the RAC opinion[3] along with its supporting documentation was published on the ECHA website on 5 July this year. Given the vast amount of information covered by the opinion and interest in the process, ECHA also published an "Explanatory note"[4] to accompany the opinion on glyphosate.

The issues raised under question number 2 in the annex of your letter are addressed below in the order in which they appear in your letter.

Divergence with IARC

Regarding the reference to the conclusions in the IARC monograph from 2015 on the classification of glyphosate, ECHA points out that the genotoxicity and carcinogenicity evaluations conducted by IARC have been addressed in detail in the RAC opinion. The same also applies to the "*meta-analysis of 2019*", the "*comprehensive analysis published in 2020*" as well as the "*major review published in 2021*", which were referred to in your letter; also these papers have all been considered in detail in the RAC opinion.

The CLP Regulation requires the evaluation of all the available information, regardless of whether published in peer reviewed journals or elsewhere, the focus being on information obtained on the basis of internationally standardised test protocols and good laboratory practice.

Consequently, the database of information evaluated by RAC in both 2017 and 2022 was considerably larger than that assessed by IARC in 2015.

Claimed scientific shortcomings with reference to HEAL report

Concerning the statement in the letter that "*serious scientific shortcomings about the work of RAC with regard to the classification of glyphosate have been raised in a recent report of the Health and Environment Alliance*", ECHA notes that publication of this document by HEAL on 8 June 2022 actually preceded publication of the RAC opinion.

Additionally, ECHA's detailed response to the issues raised in this document has already been published on ECHA's website[5]. In our response we note the following "*The main claim in the HEAL report is that tumours in 10 out of 11 carcinogenicity studies were dismissed from the assessment. However, this allegation is unfounded - the tumours in the carcinogenicity studies were not dismissed from the assessment, as incorrectly claimed in*

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[2] Glyphosate - ECHA (europa.eu)
[3] Registry of CLH intentions until outcome - ECHA (europa.eu)
[4] 9a6bdbf8-0d3c-c029-8256-2112189a6f85 (europa.eu)
[5] 40ee075a-8b57-f524-9a82-b492a77a53f1 (europa.eu), 5 July 2022

the HEAL report. These tumour incidences (as well as other findings not mentioned in the HEAL report) observed in the carcinogenicity studies were in fact central to the assessment and hence they were analysed in detail by France, Hungary, The Netherlands and Sweden in preparing the classification proposal as well as by RAC in evaluating it."

While we welcome the opportunity to reiterate the reasoning in the RAC opinion on certain issues, we do not agree with the conclusions of the HEAL report and consider the criticisms unfounded for the reasons explained in our response. To summarise, RAC experts, in accordance with their mandate, applied the CLP Regulation's criteria to toxicological and epidemiological findings and weighed all the evidence in arriving at their conclusions on classification. They considered the strength of the statistical evidence, dose-response relationships, concurrent and historical control data and the biological relevance of the findings.

Therefore, the main claim in the HEAL report, that findings on tumours in carcinogenicity studies were dismissed from the assessment, is incorrect.

Genotoxicity and Carcinogenicity

As mentioned in your letter, this concerns text from pages 57 and 48 of the RAC opinion. You refer to RAC's statement that the biological relevance of an increased tumour incidence for the assessment of carcinogenicity is critical. Indeed, RAC considered biological relevance as key in its assessment and carefully deliberated on the tumour incidences as explained above. The outcome of these deliberations was that the tumour incidences were not biologically relevant and therefore of low weight in the assessment.

As regards your concern that key tests were not conducted due to a statement in the RAC opinion referring to the absence of specific assays in relevant target organs (OECD TG 489 "the comet assay" and OECD TG 488 "TGR"), firstly, it should be noted that the CLH process assesses available data – there is no mechanism to generate additional information. Secondly, please note that ECHA has addressed these particular issues in a letter[6] to Mr Bas Eickhout MEP, who raised this in the Exchange of views on 11 July, 2022. Briefly, the conclusion set out in our letter was that:

"The statement quoted from the opinion related to the Comet assay and Transgenic rodent (TGR) somatic and germ cell gene mutation assays which are two particular assays among many other lines of evidence potentially informing a classification. The opinion noted the absence of these assays/studies in relevant tissues, but also noted that the biological importance of such DNA lesions (i.e., as identified from these assays) in relation to mutagenicity is equivocal, therefore the fact that some studies of this type were not included is not crucial for the conclusion"

And

"the data available for evaluation of germ cell mutagenicity is extensive and includes studies covering bacterial and mammalian cell in vitro mutagenicity assays as well as in vivo mammalian mutagenicity assays and even some human data. Furthermore, according to the opinion, the data includes studies of sufficient reliability and relevance to allow a robust evaluation, especially in the perspective of the requirements of the CLP Regulation. In RAC's view, the data were sufficient to arrive at a robust conclusion without these assays/studies."

[6] Microsoft Word - D(2022)0887_MR2109.docx (europa.eu), 21 September, 2022

Therefore, ECHA considers these concerns to be addressed.

ECHA conclusions

We trust that the above information helps to reassure you that the latest assessment of glyphosate by RAC was complete and robust. The Committee has a long history of rigorous assessments against the criteria set out under the CLP Regulation and the integrity of RAC as the competent body to opine on such matters is well established with 500+ opinions adopted to date. Having published the opinion of RAC on the classification of glyphosate, ECHA sees no need to reopen matters at this time. ECHA remains committed to open, transparent discussion and resolution of any lingering concerns.

EFSA Responses to technical questions in your letter

As you know the peer review process is ongoing and for this reason EFSA is not in a position to anticipate the outcome of the scientific process, which is due to be completed in July 2023. However all aspects highlighted in your letter will be thoroughly considered by the experts who are working according to the applicable EU legislation. All available data will be duly scrutinised, considering all lines of evidence - including comments received from the public consultation - their reliability and relative weight.

Assessment of the impacts on the microbiome and on biodiversity and ecosystems carry several challenges due to the absence of established criteria and harmonised methodologies. This has been already identified by the Assessment Group on Glyphosate (AGG) in its draft renewal assessment report (RAR), which is being peer-reviewed.
To strengthen the scientific assessment of these specific and complex scientific areas, the peer review is supported by a dedicated Working Group established by EFSA with specialised experts in the relevant fields.

With no prejudice to the ongoing scientific work, you can find below some observations we can provide in relation to the specific points raised in your letter.

Microbiome

Currently, effects of pesticides on the microbiome are not part of the regulatory data requirements for plant protection products. Nevertheless, as a result of the high number of comments and concerns raised during the public consultation, EFSA did ask the applicant to submit additional information. Following up on this specific point, a dedicated expert consultation was set up in the context of the ongoing peer review. During this consultation the available data regarding the potential effects of glyphosate on the gut microbiota (in animals and humans) as well as their possible consequences were discussed using a weight of evidence approach.

To support the peer review process EFSA, with the support of experts, scrutinised the available public literature on impacts of glyphosate on the microbiome, evaluating its reliability and relevance for the glyphosate risk assessment.

Biodiversity

A similar approach was applied regarding the biodiversity assessment. The relevance of the indirect impact on non-target species for the overall risk regulation of glyphosate has already been acknowledged in the previous scientific assessment and the resulting renewal decision.

Commission Implementing Regulation (EU) 2017/2324 for glyphosate clearly states that *'Member States shall pay particular attention to the risk to diversity and abundance of non-target terrestrial arthropods and vertebrates via trophic interaction'.*

In response to the high number of comments received in the context of the public consultation and from Member States, EFSA requested additional information from the applicants, demanding a revised, more structured biodiversity assessment, which was further considered in the expert meeting.

Neurotoxicity

Likewise, EFSA and Member States' experts discussed the neurotoxic potential of glyphosate to consider in detail all available evidence from applicants, literature and epidemiological studies, following a weight of evidence approach.
Particular consideration was given to discussing the neurotoxicity studies available in the RAR, the possible effect of glyphosate on the concentrations of several neurotransmitters in the brain in rodents, and the relevance of the findings. Taking into consideration all available information received during the public consultation, experts also discussed the possible relationship between exposure to glyphosate and the development of chronic and/or neurodegenerative diseases, such as Parkinson's disease, autism spectrum disorder (ASD) and amyotrophic lateral sclerosis (ALS).

Formulations

Formulations are also part of the ongoing assessment. The EU pesticides legislation sets out that, based on an initial evaluation by the Rapporteur Member State, EFSA carries out the risk assessment for an active substance to be used in plant protection products. As part of this process, information related to at least one formulation for representative uses is evaluated.

The hazard properties of each co-formulant in the formulation for representative uses were considered in the glyphosate peer review. Based on the available data, the peer review will either conclude on the safety of the co-formulant or, if the data available are considered insufficient, identify respective data gaps in the EFSA conclusion.
In the case of glyphosate, EFSA has requested data on the formulation type and composition of formulations, other than the one for representative uses, tested in the available toxicological studies, to allow considerations on the possible impact of such studies for the current assessment, as appropriate.

A dedicated expert consultation of the ongoing peer review specifically discussed the toxicological profile of the co-formulants in the formulation for representative uses.

Studies

As regards literature studies, it is important to note that the body of evidence that EFSA (and ECHA, as explained further above) have at their disposal is always composed of both

regulatory studies and studies from publicly accessible literature, as required by the applicable legislation. All such studies are assessed according to their scientific relevance and reliability. In other words, to be relevant for the assessment a study needs to be designed, carried out and reported well. This applies to every substance, including glyphosate.

In the case of glyphosate, the search of the scientific peer-reviewed open literature conducted by the applicants, as required by Art 8(5) of Regulation (EC) No 1107/2009, was complemented by a large number of additional publications that were highlighted during the public consultation on the draft RAR. Based on the comments received, EFSA requested the applicants to submit additional studies so they can be formally considered during the ongoing peer review. In addition, since closing the public consultation EFSA remains attentive to new information that could be relevant for the on-going assessment.