Executive Director

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Subject: Your letter dated 13 July 2023, titled '*EFSA main findings on glyphosate*'

Dear Dr. Lysimachou and Dr. Dermine,

I refer to your letter received on 13 July 2023, of which EFSA acknowledged receipt on the same day.

In your letter, you raised several concerns regarding the content of EFSA's press release of 6 July 2023 ('EFSA's Press Release')[1] and of the factsheet published on the same day ('EFSA's Factsheet')[2], summarising the main findings of EFSA's Conclusion on the peer review of the pesticide risk assessment of the active substance *glyphosate* ('EFSA's Conclusion'). I write to address the points that you raised in that regard.

Please note that EFSA made its Conclusion[3], the Peer Review Report[4] and the final renewal assessment report (RAR) publicly available on 26 July 2023, 25 August 2023, and 13 September 2023[5] respectively.

I. On your claim that EFSA would not have acted in compliance with EU law and EU case-law

Preliminary considerations regarding the template used for EFSA's Conclusion on Pesticides Peer review:

Before entering into the specific points that you raised, I would like to provide some preliminary considerations regarding the template that is used for EFSA's Conclusion, and the wording used therein.

The wordings '*Critical areas of concern'*, '*Issues that could not be finalised'* and '*Outstanding issues'* refer to sections of the Conclusions that EFSA publishes at the end of the peer review of pesticide risk assessments (sections 9.2, 9.1 and 10 respectively).

Each section has a specific meaning in a regulatory context. They are intended to provide the European Commission and the Member States with an indication of the nature of the risks that may have been identified during the risk assessment, as an outcome of the peer-review. The definition of these sections and the structure of the template of the Conclusions is the result of a continuous dialogue between EFSA, the European Commission and the Member States, to allow for a better understanding of the weight of the data gaps and overall to make it more fit for purpose for risk managers. The present

[1] Publicly available on EFSA's website at https://www.efsa.europa.eu/en/news/glyphosate-no-critical-areas-concern-data-gaps-identified
[2] Publicly available on EFSA's website at https://www.efsa.europa.eu/en/factsheets/efsa-explains-scientific-assessment-glyphosate
[3] Publicly available on EFSA's website at https://doi.org/10.2903/j.efsa.2023.8164
[4] Publicly available on EFSA's website at https://open.efsa.europa.eu/study-inventory/EFSA-Q-2020-00140.
[5] Publicly available on EFSA's website at https://open.efsa.europa.eu/study-inventory/EFSA-Q-2020-00140.

template used for EFSA's Conclusions has been in place since early 2021[6] and EFSA is committed to applying it uniformly for all substances.

An issue is listed as a *Critical area of concern* if:

- there is enough information available to perform an assessment for the representative uses[7] but this assessment does not permit the conclusion that, for at least one of the representative uses, it may be expected that a plant protection product containing the active substance will not have any harmful effect on human or animal health or on groundwater, or any unacceptable influence on the environment; or,
- the assessment at a higher tier level could not be finalised due to lack of information, and the assessment performed at the lower tier level does not permit the conclusion that, for at least one of the representative uses, it may be expected that a plant protection product containing the active substance will not have any harmful effect on human or animal health or on groundwater, or any unacceptable influence on the environment; or,
- in the light of current scientific and technical knowledge using guidance documents available at the time of application, the active substance is not expected to meet the approval criteria provided for in Article 4 of Regulation (EC) No 1107/2009[8] regarding the hazard cut-off criteria.

Therefore, in line with the above and as discussed with the European Commission and Member States, a critical area of concern is indicated in cases where the identified concern is relevant for **all** representative uses proposed by the applicants. Consequently, the absence of critical areas of concern indicates that there are uses of the pesticide under evaluation, among those proposed by the applicant, that are not expected to pose safety concerns, i.e., that on the basis of available data it is not expected to have harmful effects on human or animal health or on groundwater, or any unacceptable influence on the environment. This does not exclude the possibility that there may be an impact on the current conclusions once the identified data gaps will be resolved.

1. <u>On your first concern regarding the absence of information on short and long-term toxicity on one of the co-formulants:</u>

In your letter, you refer to the judgment of the Court of Justice in the *Blaise* case[9]. You indicate that EFSA noted the absence of information on short and long-term toxicity of one of the co-formulants, but also considered that there were no indications of acute toxicity or carcinogenicity. You argue that such a toxicity cannot be excluded in the absence of a study on carcinogenicity or long-term toxicity on the formulation and you refer to published studies, which would indicate that exposure to *glyphosate*-based products would have been linked to carcinogenicity and neurotoxicity. As a result, you disagree with EFSA's reporting of its assessment and claim that this data gap should have been reported as a critical area of concern in Section 9.2 of EFSA's Conclusion.

EFSA's Factsheet indicated that '*information on the short- and long-term toxicity of one of the components present in the formulation evaluated for representative uses was not available and is needed to conclude the risk assessment of the formulated product for representative use. For this formulation there were no indications of acute toxicity and genotoxicity*.' In that regard, please note that EFSA's consideration in the last sentence concerns genotoxicity, not carcinogenicity, contrary to what you indicate. In the EFSA Conclusion, it is indeed reported that studies were performed on acute toxicity and genotoxicity endpoints, with the representative formulation '*MON 52276'*.

With regard to the co-formulants contained in the formulation '*MON 52276'*, toxicological studies were available for all components but one. During the peer review meeting, the Member State experts

[6] Refer to the publicly available minutes of the Pesticide Steering Network meeting (cf agenda item 6) on EFSA's website at https://www.efsa.europa.eu/sites/default/files/2021-04/27th-meeting-efsa-pesticide-steering-network-minutes.pdf.
[7] In line with the uniform principles in accordance with Article 29(6) of Regulation (EC) No 1107/2009 and as set out in Commission Regulation (EU) No 546/2011.
[8] Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC (2009), *OJ* L 309, p. 1.
[9] Judgment of 1 October 2019, *Blaise*, C-616/17, EU:C:2019:800.

considered that the available toxicological information was sufficient to conclude on the safety of the formulation '*MON 52276*'. From an overall assessment of the available data, the Member State experts considered that additional toxicity data on the co-formulant was not expected to impact the conclusion on the carcinogenicity or toxicity of the formulation. However, EFSA still considered that repeated-dose toxicity data for this component should be assessed to reach a final conclusion on the risk assessment of the formulation '*MON 52276'*. This issue resulted in a data gap for repeated-dose toxicity data on this component, which was reported with other outstanding issues in Section 10 of EFSA's Conclusion.

However, there was no positive indication that the formulation 'MON 52276' would exhibit long-term toxicity nor that this data gap would make it impossible to identify a formulation of the active substance without harmful effects.

In these conditions, in line with the definition set in the Conclusions' template, EFSA considered it appropriate to report the data gap as an outstanding issue without qualifying it as a critical area of concern. As such, EFSA's Conclusion is compliant with the applicable legal framework, relevant case-law and the definitions set in the Conclusions' template.

2. On your second concern regarding one of the impurities in the technical material for *glyphosate*:

In your letter, you claim that the fact that EFSA could not conclude on genotoxicity for one of the impurities in the technical material for *glyphosate* should have been reported in EFSA's Conclusion as a critical area of concern.

EFSA's Factsheet indicated that the '*assessment of one of the impurities in glyphosate could not be finalised without further information about its clastogenic potential [i.e. potential to cause DNA breakages]*'.

A data gap was indeed reported in relation to the toxicological potential of one impurity that is present in the technical material. This impurity was present in some of the batches used in toxicity studies at levels representative to, and above, the level of this impurity in the reference specification proposed by the applicants. An *in vitro* chromosome aberration test showed potential for clastogenicity, although this was not concluded (e.g. with an *in vivo* follow up).

Therefore, this was reported as an issue that could not be finalised, i.e. under section 9.1 of EFSA's Conclusion, in line with the categorisation followed for all conclusions. It was not considered as a critical area of concern since EFSA considered there were insufficient elements to conclude on the toxicological relevance of this impurity.

3. On your third concern regarding dietary risk assessment to consumers:

In your letter, you claim that the fact that EFSA could not finalise the dietary risk assessment for consumers should have been reported in EFSA's Conclusion as a critical area of concern because, in the absence of this (i) EFSA could not disregard harmful effects on human health and (ii) an Acceptable Daily Intake needs to be established.

EFSA's Factsheet indicated that the '*consumer dietary risk assessment could not be finalised due to incomplete data about the amount of glyphosate residues in rotational crops such as carrots, lettuce and wheat. However, this is not expected to lead to an exceedance of toxicological safety levels and so no critical concern was identified*.'

Firstly, please note that toxicological reference values (TRVs) have been derived for *glyphosate* (e.g. the acceptable daily intake (ADI) is 0.5 mg/kg bw per day).

Secondly, it is correct that a data gap was identified[10] in relation to rotational crop field trials, as they were insufficient to address all possible relevant scenarios. Therefore, a higher consumer exposure to

[10] See Experts' consultation 3.9 of the Pesticides Peer Review Experts' TC 83 on Residues in the Peer Review Report (refer to Part 3).

residues of glyphosate than the one considered in the current risk assessment could not be excluded. However, as it was expected that this potentially higher exposure would not lead to an exceedance of the toxicological reference values, EFSA decided to report this as an issue that could not be finalised rather than as a critical area of concern. This decision was further supported by the fact that this issue does not impact all representative uses, as safe uses could be indicated e.g. for the uses on orchards, vines and railway tracks, where no rotational crops are expected to be grown.

4. On your fourth concern regarding public literature on neurotoxicity:

In your letter, you also argue that (i) in the absence of a developmental neurotoxicity ('DNT') study for *glyphosate* and of long-term health toxicity studies for the formulation in the applicant's dossier and (ii) considering the case-law defining the precautionary principle and the *Blaise* judgment, the outstanding issue regarding developmental neurotoxicity should have been reported as a critical area of concern.

EFSA's Factsheet indicated that there '*is no indication that glyphosate as an active substance has neurotoxic potential. However, data from the public literature on glyphosate-based formulations and a study with a glyphosate salt (not approved in the EU) show effects of developmental neurotoxicity. A recommendation is made in the conclusions for the applicant to provide clarifications on this issue*.'

EFSA confirms that no DNT study was available in the dossier and that it was considered not needed based on the lack of neurotoxicity effects in the regulatory dataset on glyphosate active substance. During the risk assessment process, new evidence was brought forward. On the one hand, certain data showed no concern regarding *glyphosate*, in (i) a DNT *in vivo* study in rats and (ii) in *in vitro* data analysed by the ToxCast/Tox 21 program[11]. On the other hand, additional data, including public literature studies on *glyphosate*-based herbicides ('GBHs') and a study on *glyphosate-trimesium*, showed some DNT effects. Note that glyphosate-trimesium is an active substance not approved in the EU.

Applying a weight-of-evidence approach on the overall body of evidence, EFSA assessed that there was no clear pattern of effects suggesting a DNT effect for *glyphosate* and the current toxicological reference values were considered as sufficiently protective. However, EFSA still considered that there was a data gap related to the cause of the DNT effects seen in the public literature studies with GBHs and in the study with *glyphosate-trimesium*. The identification of this data gap is ultimately aimed at supporting Member States in their national assessments should the renewal be granted.

This data gap was reported as an outstanding issue in EFSA's Conclusion but is not considered as critical in view of the overall available data based on weight-of-evidence.

5. On your fifth concern regarding effect on microbiome:

In your letter, you indicate that EFSA would have taken no action regarding effects on microbiome as no internationally agreed guidelines are available and further research is needed to develop methodologies. You state that (i) the link between alterations in human microbiome and disease is well established, and therefore these publications indicate a potential harm to human health and non-target species, and (ii) the absence of internationally agreed guidelines is not a valid argument to not conclude on the wide range of available information. You further refer to the *Blaise* judgment to imply that EFSA should have given a more important weight to published scientific literature than it did. On this basis, you claim that EFSA's findings should have been reported as a critical area of concern.

EFSA's Factsheet indicated that '*studies reporting effects on microbiome were taken into account. Currently, no internationally agreed guidelines for the risk assessment of microbiome are in place in the pesticide area. Further research is needed to identify dedicated methodologies to better integrate microbiome into chemical risk assessment*.'

[11] The Toxicity ForeCaster program is a chemical screening program that identifies *in vitro* assays that can be relevant for *in vivo* toxicity. This program is led by the Center for Computational Toxicology and Exposure of the United States Environmental Protection Agency.

Several studies from the published literature investigated the potential effects of *glyphosate* on the human and animal gut microbiome, and possible consequent effects on health. Based on the current state of knowledge, considering that standardised regulatory guidance and/or established harmonised criteria are currently not available for the assessment of microbiome[12], EFSA assessed all available data and determined that no definitive conclusion establishing a correlation between the impact on microbiome and the occurrence of disease could be drawn from these studies. Although it is recognised that further developments are needed in this area to integrate such studies in the regulatory context and that this is a challenging task, no data gap was identified for the microbiota issue, neither for mammalian toxicology nor for ecotoxicology (currently they are not part of the data requirements).

However, EFSA considered that, based on the mammalian toxicity dataset that it assessed, the established toxicological reference values were sufficiently protective to reasonably exclude health impacts possibly mediated by the microbiome on humans, livestock and pet animals. Therefore, the Member States and EFSA were able to conclude, based on the available data, that EFSA's previous Conclusion[13] on the lack of impact of glyphosate on animal gut microbiome and health remains valid.

6. On your sixth concern regarding impact on biodiversity and the high long-term risk to mammals identified in 12 out of 23 proposed uses of *glyphosate*:

In your letter, you indicate that considering the number of scientific studies highlighting the negative impact of *glyphosate* and GBHs at field-realistic concentrations, EFSA's findings regarding biodiversity and the high long-term risk to mammals identified in 12 out of 23 proposed uses of *glyphosate* should have been reported as critical areas of concern. You indicate that the most recent studies of international research should be taken into account. You further argue that the absence of information provided by the applicants on the representative formulation for key environmental toxicity endpoints should also have been reported as a critical area of concern. Finally, you claim that scientific evidence points to a high risk to biodiversity and that EFSA's findings would not allow risk managers to implement the precautionary principle.

Regarding biodiversity and ecotoxicology, EFSA's Factsheet indicated that 'e*xperts recognised that the risks for biodiversity associated with the representative uses of glyphosate are complex and depend on multiple factors. They also noted a lack of harmonized methodologies and agreed specific protection goals. Overall, the available information does not allow firm conclusions to be drawn on this aspect of the risk assessment and risk managers can consider mitigation measures*' and that '*the data package allowed a conservative risk assessment approach, which identified a high long-term risk to mammals in 12 out of 23 proposed uses of glyphosate*'.

The assessment of the impact of *glyphosate* on biodiversity via indirect effects and trophic interactions was extensively discussed by the peer review experts[14]. Currently, there is no harmonised approach to assess biodiversity within the risk assessment and EFSA and Member States applied a weight-of-evidence approach, including all the information provided, and highlighted a lack of specific protection goals for non-target organisms. EFSA and Member States also looked at the proposed mitigation measures and assessed them to support the risk managers who will need to further consider this issue at a national level.

With regard to the effect on wild mammals, a data gap was identified in relation to 12 out of the 23 proposed uses of *glyphosate* (i.e. no concerns were identified regarding 11 of the uses), based on a tier 1 assumption. A tier 1 assumption represents a conservative approach, i.e. considering a worst-case scenario. In the absence of a higher-tier study, it was not possible to further refine the risk assessment to more realistic scenarios.

[12] Merten C, Schoonjans R, Di Gioia D, Pelaez C, Sanz Y, Maurici D and Robinson T, 2020. Editorial: exploring the need to include microbiomes into EFSA's scientific assessments. EFSA Journal 2020;18(6):e18061, 7 pp. https://doi.org/10.2903/j.efsa.2020.e18061.
[13] EFSA (European Food Safety Authority), 2018. Scientific Report on evaluation of the impact of glyphosate and its residues in feed on animal health. EFSA Journal 2018;16(5):5283, 22 pp. https://doi.org/10.2903/j.efsa.2018.5283.
[14] See Experts' consultation 5.25 of the Pesticides Peer Review Experts' TC 82 on Ecotoxicology and its Annex in the Peer Review Report (refer to Part 3).

Therefore, this resulted in a data gap, which was reported with other outstanding issues in Section 10 of EFSA's Conclusion. EFSA considered that it was not a critical area of concern as it did not cover all proposed uses. However, EFSA still reported it as a data gap to bring it to the attention of the Member States at the stage of the authorisation process for plant protection products, should the approval of *glyphosate* be renewed.

II. On your claim that EFSA would not have acted transparently

In the second part of your letter, you indicate that the fact that EFSA published a summary of the risk assessment of *glyphosate* before the publication of EFSA's Conclusion and of the background documents would prevent public scrutiny and result in a lack of transparency.

In order to address your concern, the publication of EFSA's Press Release must be put into context. EFSA's Conclusion was adopted on 6 July 2023 and shared on the same day, together with the background documents, with the European Commission and the Member States. Therefore, the renewal procedure for *glyphosate* was at the stage described in Article 13(2) of Regulation (EC) No 844/2012[15], i.e., EFSA communicated its conclusions to the applicants, giving them two weeks to potentially request confidential treatment of certain information (personal data or commercially sensitive information) under Article 63 of Regulation (EC) No 1107/2009. Please note that, at this stage of the procedure, applicants' input is limited to confidentiality matters; they may not request changes in the assessment or submit additional information. It is only following this step that EFSA can make publicly available the conclusions, except items that are successfully claimed confidential by the applicants.

Therefore, to respect the right of applicants to claim certain data as confidential, EFSA could not proceed with the publication of the full EFSA Conclusion on the day of its adoption, i.e., before having given to the applicants two weeks to submit potential confidentiality requests.

While there was no obligation on EFSA to inform the public that it had concluded its peer-review, EFSA decided to publish a summary of the conclusions on the day of its adoption, being mindful of the public interest in this substance and considering EFSA's commitment to transparency. This summary did not contain any element that could be deemed subject to confidentiality. Therefore, EFSA's Press Release corresponds to an additional transparency step proactively undertaken by EFSA, striking the balance between the right of applicants to submit requests for confidential treatment, and the public interest to be promptly informed.

EFSA allocated additional resources to reduce to a minimum the time interval between the adoption of EFSA's Conclusion and the publication of the full set of documents. This allowed the publication of EFSA's Conclusion as soon as 26 July 2023, as indicated above. As the applicant did not claim as confidential any element in EFSA's Conclusion, the latter was made publicly available without any redactions.

Moreover, as already indicated, the Peer Review Report was published on 25 August 2023 and the assessment report of the Rapporteur Member States on 13 September 2023.

III. On your claim that EFSA tried to influence risk management

In the third part of your letter, you claim that the concerns that you raised under the first part of your letter show an attempt by EFSA to influence risk managers to renew *glyphosate's* approval. You also claim that EFSA automatically dismissed thousands of peer reviewed scientific papers.

[15] Commission Implementing Regulation (EU) No 844/2012 of 18 September 2012 setting out the provisions necessary for the implementation of the renewal procedure for active substances, as provided for in Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market (2012), *OJ* L 252, p.26.

Firstly, I strongly object to the notion that EFSA automatically dismissed thousands of papers. Rapporteur Member States and EFSA followed the procedure for identifying and assessing the relevance of public literature, which is an iterative process. As stated in the EC regulation 1107/2009, a literature search shall be added by the applicant to the dossier on the active substance and its relevant metabolites dealing with side-effects on health, the environment and non-target species and published within the last 10 years before the date of submission of the dossier. It is verified by the Rapporteur Member State(s), who may ask for further information. EFSA is then in charge of the peer-review. In the specific case of glyphosate, the applicants screened more than 16000 published studies, of which about 2000 were considered as potentially relevant and further assessed for their relevance, resulting in about 780 relevant publications after full text screening. During public consultation, 300 additional studies were brought to the attention of the peer reviewers. Subsequently, the applicant(s) were requested to complement the available evidence, subject then to further assessment by the Rapporteur Member States. Therefore, all submitted studies from public literature were assessed based on their relevance and reliability for the risk assessment procedure.

In addition to this, about 200 newly available publications on glyphosate brought to EFSA's attention after the public consultation phase until the time point of drafting the EFSA Conclusion were screened by EFSA for their potential impact on the risk assessment to make sure that no relevant information was missed. In the interests of transparency, this list of additional publications has also been made publicly available as part of the background documentation to the Conclusion.

Secondly, I would like to remind you of the general principle of separation between risk assessment and risk management, which is strictly respected by EFSA. As a general rule, EFSA, as risk assessor undertakes risk assessment, defined as '*a scientifically based process consisting of four steps: hazard identification, hazard characterisation, exposure assessment and risk characterisation*'[16]. In the specific case of the pesticide risk assessment, the scientific evaluation is a shared task between EFSA[17] and the Rapporteur Member State as defined in Article 3(22) of Regulation (EC) No 1107/2009. The European Commission and the Member States are instead in charge of risk management, i.e. '*the process, distinct from risk assessment, of weighing policy alternatives in consultation with interested parties, considering risk assessment and other legitimate factors, and, if need be, selecting appropriate prevention and control options*'[18]. As in the case of all active substances, the next steps of the procedure for the renewal of glyphosate fall under the responsibility of the risk managers (the European Commission and the Member States) which will take a decision on the basis of the EFSA's Conclusion, the RAR and the comments received. In so doing, as appropriate, they might address issues which could not be finalised (Section 9.1.) and other outstanding issues (Section 10) with specific risk management measures.

EFSA is a scientific organisation, undertaking its risk assessment as an independent assessor. EFSA acts under the highest degree of transparency, allowing researchers and interested citizens to scrutinise its work and participate in public consultations. While EFSA welcomes discussion on the development of science and potential divergences in scientific assessment, EFSA strongly refutes any notion that it would not be undertaking an objective risk assessment and would be instead attempting to influence risk managers.

IV. Final remarks

As indicated above, the next steps with regards to the authorisation of *glyphosate* are now under the responsibility of the European Commission and the Member States.

[16] See Article 3(11) of Regulation (EC) No 178/2002 of the European Parliament and of the Council of 28 January 2002 laying down the general principles and requirements of food law, establishing the European Food Safety Authority and laying down procedures in matters of food safety (2002), *OJ* L 031, p. 1.

[17] Note that, where available, EFSA uses the hazard assessment carried out by the European Chemicals Agency, as this was the case for *glyphosate*.

[18] See Article 3(12) of Regulation (EC) No 178/2002.

If you believe that maladministration was committed by EFSA in dealing with the matter addressed by this letter, you may submit a complaint about it to the European Ombudsman pursuant to Article 228 of the Treaty on the Functioning of the European Union and within two years of receiving EFSA's final position on the matter. The Ombudsman's online complaint form and further indications on how to file a complaint are available at: http://www.ombudsman.europa.eu.

Yours sincerely,

Bernhard Url Date: 2023.09.13 18:20:22 +02'00'

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CC: Guilhem de Seze, Manuela Tiramani, Dirk Detken