Annex
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ECHA statement regarding the EU assessment of glyphosate and the so-called "Monsanto papers"

Background

On 29 May 2017, ECHA received a request from the European Commission to produce a statement concerning the EU assessment of glyphosate following allegations made in the so-called "Monsanto papers". The "Monsanto papers" are published articles referred to in documents ordered to be released by a US state court, that allegedly show that Monsanto planned to ghostwrite scientific review articles on the toxicity profile of glyphosate and to financially reward scientists for their authorship of these articles.

The Commission asked ECHA to provide responses to the following points:

- What impact the allegations about Monsanto ghostwriting scientific review articles would have, if they were confirmed, on the overall assessment and conclusions of glyphosate agreed by the Committee for Risk Assessment of the European Chemicals Agency (RAC), in the final Opinion proposing harmonised classification and labelling at EU level of glyphosate;
- The role of the scientific review articles in question, including the type of publication, amount of available information, transparency of industry support for some articles;
- The legal provisions on the assessment of scientific peer-reviewed literature in the EU legislation on classification and labelling and their implementation in the RAC assessment;
- A description of the concrete steps taken in the course of the EU assessment to ascertain the reliability of the information submitted, both for regulatory guideline studies and for scientific peer-reviewed open literature, to ensure the absence of undue influence on the sources of this information.

General

In evaluating the German Dossier Submitter's proposal on the classification of glyphosate, RAC relied mainly on the information provided in the harmonised classification and labelling (CLH) report and the information submitted during public consultation. This included published and unpublished carcinogenicity studies. They also had access to the original study reports. This allowed the Committee to come to their independent conclusion, based on the original data and not on someone else's interpretation.

Documents considered by RAC in preparing the CLH opinion on glyphosate

- The harmonised classification and labelling (CLH) report, which was developed and processed in accordance with Article 37 of the CLP Regulation (Regulation (EC) No. 1272/2008)[1]

[1] For further detail on the process set up by ECHA to manage the CLH process, please see

- "EFSA Conclusion 2015" and the "Renewal Assessment Report Addenda"[2] which provided background information, additional to that summarised in the CLH report.
- Comments (including attachments, references to study reports - published and unpublished - as well as confidential information) received during the public consultation (PC) on the CLH report
- The responses of the Dossier Submitter (DS) to the comments received during the PC
- Original study reports and published papers that had been summarised in the CLH report
- Relevant publicly available reports and review articles
- Information requested by RAC during the opinion forming process
- Unsolicited information submitted after the public consultation had ended

A similar set of documents is considered in developing the Opinion for any substance under CLP. However, the inclusion in the public consultation of the "EFSA Conclusion 2015" and what we have referred to as the "Renewal Assessment Report Addenda"[2] are not routinely done. Their inclusion on this occasion was to ensure that the information base available at public consultation was as comprehensive as possible.

ECHA understands that the articles referred to in the "Monsanto papers" are the following review articles, all of which considered by the RAC:

- Kier LD and Kirkland DJ (2013). Review of genotoxicity studies of Glyphosate and Glyphosate-based formulations. Crit Rev Toxicol; 43(4): 283–315
- Williams GM, Kroes R, Munro IC (2000). Safety evaluation and risk assessment of the herbicide Roundup and its active ingredient, glyphosate, for humans. Regulatory Toxicology and Pharmacology 31, 117-165
- Greim H, Saltmiras D, Mostert V, Strupp C (2015) Evaluation of carcinogenic potential of the herbicide glyphosate, drawing on tumor incidence data from fourteen chronic/ carcinogenicity rodent studies. Crit Rev Toxicol, 2015; 45(3): 185–208

The review papers in question represented only three of a large number of scientific references summarised in the CLH report and the "Renewal Assessment Report Addenda" in the area of mammalian toxicology. The three review articles were not referred to directly in the CLH report and, although they were brought to the attention of the rapporteurs during the public consultation, they are not referred to in the draft Opinion.

The interest and authorship of these studies was evident from the Declarations of Interest and Acknowledgements in the papers themselves. For example, the Kier and Kirkland (2013) paper states that the authors were paid by the Glyphosate Task Force to carry out the review and the Williams et al. (2000) paper acknowledges that Monsanto

https://echa.europa.eu/addressing-chemicals-of-concern/harmonised-classification-and-labelling

[2] The document includes summaries of the studies (level of detail generally equivalent to robust study summaries) and is a compilation of the following documents prepared by the CLH dossier submitter:

- Final addendum to the Renewal Assessment Report (RAR) (public version – dated October 2015), incorporating the public version of the RAR dated 18 December 2013 and revisions thereof dated 29 January 2015 and 31 March 2015;
- The document "Does glyphosate cause cancer? Preliminary assessment of the carcinogenic risk of glyphosate with regard to the recent IARC evaluation" (BfR Communication, 1st April 2015);
- Addendum1 to the RAR (August 2015) which was commissioned by EFSA to evaluate the IARC Monographs Volume 112 on glyphosate prepared by the Rapporteur Member State (RMS), Germany, for the European renewal of approval of glyphosate;
- A separate Addendum1 to the RAR (October 2015) addressing ecotoxicology issues arising from the IARC assessment of glyphosate.

facilitated the authors' work by providing them with original, unpublished studies.

As is usual practice regarding potentially relevant articles, RAC and the rapporteurs were made aware of all of them. However, the information they contained was not considered to add anything to the Opinion and was therefore not cited in the Opinion.

For the sake of completeness, other studies were also considered by RAC which, although not mentioned in the "Monsanto papers", had some level of involvement of companies who make glyphosate (the Glyphosate Task Force (GTF), which includes Monsanto):

- Kimmel GL, Kimmel CA, Williams AL, DeSesso JM (2013). Evaluation of developmental toxicity studies of glyphosate with attention to cardiovascular development. Critical Reviews in Toxicology, 43:2, 79-95 (referred to during public consultation)
- Williams GM, Berry C, Burns M, de Camargo JLV, Greim H (2016). Glyphosate rodent carcinogenicity bioassay expert panel review. Critical Reviews in Toxicology, 46:sup1, 44-55
- Williams GM, Aardema M, Acquavella J, Berry C, Brusick D, Burns MM, de Camargo JLV, Garabrant D, Greim HA, Kier LD, Kirkland DJ, Marsh G, Solomon KR, Sorahan T, Roberts A, Weed DL (2016). A review of the carcinogenic potential of glyphosate by four independent expert panels and comparison to the IARC assessment. Critical Reviews in Toxicology, 46:sup1, 3-20.
- Acquavella JF, Alexander BH, Mandel JS, Gustin C, Baker B, Chapman P, Bleeke M (2004). Glyphosate Biomonitoring for Farmers and Their Families: Results from the Farm Family Exposure Study. Environ Health Perspect 112:321–326. This paper was referred to in the "Renewal Assessment Report Addenda".

Legal provisions relating to the assessment of information for CLH by RAC

In addition to the legal obligations imposed by the plant protection products regulation (Regulation (EC) No. 1107/2009), the principles relating to study quality for any new studies are described in Article 8 of the CLP Regulation. Article 8 of the CLP Regulation refers to Article 13(4) of REACH (Regulation (EC) No. 1907/2006), which states that "*ecotoxicological and toxicological tests and analyses shall be carried out in compliance with the principles of good laboratory practice provided for in Directive 2004/10/EC or other international standards recognised as being equivalent by the Commission or the Agency and with the provisions of Directive 86/609/EEC, if applicable*". Furthermore, the carcinogenicity data should be from "*reliable and acceptable*" studies[3]. At the same time, where the criteria cannot be applied directly to available identified information, a weight of evidence determination using expert judgment shall be applied[4].

By law then, the factors which are taken into account when weighting the information

[3] CLP Regulation, Annex I, 3.6.2.2.1: "Classification as a carcinogen is made on the basis of evidence from reliable and acceptable studies and is intended to be used for substances which have an intrinsic property to cause cancer. The evaluations shall be based on all existing data, peer-reviewed published studies and additional acceptable data".

[4] CLP Regulation, Article 6(3): "Where the criteria cannot be applied directly to available identified information, manufacturers, importers and downstream users shall carry out an evaluation by applying a weight of evidence determination using expert judgement in accordance with section 1.1.1 of Annex I to this Regulation, weighing all available information having a bearing on the determination of the hazards of the substance or the mixture, and in accordance with section 1.2 of Annex XI to Regulation (EC) No 1907/2006".

include whether the studies have been performed in accordance with agreed (internationally standardised) methodology and quality requirements (OECD or equivalent technical guidelines and good laboratory practice (GLP)). Therefore in this process, the OECD and GLP compliant studies are given the greatest weight. In principle such studies are usually by themselves sufficient for classification. Studies - whether reported in published articles or not - which do not comply with the above principles are given less weight. Review articles, even where they provide relevant information, are given the lowest weight and would not normally on their own be sufficient for a conclusion to be made on the classification of a substance.

Impact of the "Monsanto papers" on the assessment conclusions of RAC

The impact of any piece of research on an Opinion is best seen by the extent to which it influenced the final opinion, and consequently the extent to which its findings are referred to in the Opinion and preparatory documentation. ECHA assessed the primary documents (CLH report, "EFSA Conclusion 2015" and the "Renewal Assessment Report Addenda" and the response to comments (RCOM) document, but not the RCOM attachments) for references to any of the named articles.

None of the articles are cited in the RAC opinion on glyphosate.

- There are no references to the paper by Kier and Kirkland (2013) in the (draft) opinion or in the CLH report. However, the paper is referred to in a comment received (from the Glyphosate Task Force) during the public consultation. The paper is also briefly summarised, quoted once and referred to in a few places in the "Renewal Assessment Report Addenda" provided by the German dossier submitter. A number of references to other publications relating to the genotoxicity of glyphosate (dating from 1992 onwards) which have the same author were also referred to in the addenda.
- There are no references to Williams et al (2000) in the RAC opinion. However, there is a single reference in the CLH report to the paper by Kimmel et al (2013), which includes the same author. The paper (and others with the same author, up to 2013) is mentioned a few times in the comments received from the Glyphosate Task Force during the public consultation as well as in a comment from an individual. It is also referred to in the "Renewal Assessment Report Addenda".
- There are no references to the article by Greim et al (2015) in the CLH report, the draft Opinion or the comments received during the public consultation, but it is referred to in the "Renewal Assessment Report Addenda", in the Addendum1 issued in August 2015, in relation to the IARC monograph that mentions this review.

Concrete steps taken to ascertain the reliability of the information submitted

1. Although the relevant studies were summarised in the CLH report, the original study reports were obtained by ECHA to enable RAC to verify the findings by looking at the source data.
2. The CLH report, along with the associated documentation (including the "Renewal Assessment Report Addenda") was subject to public consultation, enabling anyone with views or concerns about the data to speak out. A large number of comments were received, indicating that parties concerned with the proposal have taken the opportunity to comment.

3. A preliminary discussion of the issues with RAC was organised in December 2016, to which various stakeholders, including NGOs, Industry and IARC had an opportunity to express their views through invited presentations as well as interventions.
4. The same stakeholders were also present at the RAC meeting that resulted in the adoption of the opinion, and had the opportunity to contribute to the discussion.

Concrete steps taken to ensure the reliability of the opinion forming process

Although not requested, it could be helpful to recall that the Agency also takes a number of measures to protect the integrity of the opinion forming process itself.

1. All RAC members, their advisors and ECHA staff working on a substance need to sign a conflict of interest declaration.
2. RAC members from Germany (the dossier submitter) were not involved in the preparation of the draft opinion and did not contribute to the discussion on the opinion.
3. In addition to the 2 rapporteurs usually appointed to the case, an additional 6 RAC members were appointed to an *ad hoc* working group of the RAC, to assist with the opinion development. This increased the likelihood that any anomalies in the data would be picked up and minimised the influence any single person could exert on the conclusions.
4. Prior to the RAC meeting, RAC members had an opportunity to comment on the draft opinion, and the comments were taken into account in a revised draft opinion which was discussed at RAC.
5. The draft opinions were openly shared with the stakeholders, as is usual practice.

Conclusion

ECHA can confirm that there was no impact on the overall assessment of the classification of glyphosate that was discussed and adopted by the Committee for Risk Assessment on 15 March 2017.

Throughout the opinion forming process, RAC relied on the considerable number of OECD guideline and CLP–compliant studies summarised in the CLH report to form their own independent conclusion. Original study reports were made available to enable RAC to verify the findings reported. None of the "Monsanto papers" were deemed sufficiently influential to merit a reference in the opinion.