EFSA's glyphosate "transparency", from a toxicologists' perspective

Briefing on the lack of full disclosure of Glyphosate studies by EFSA

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Background: In March 2016, 4 Members of the European Parliament filed an access to documents request to EFSA seeking access to the complete studies that were used by the EU's Food Safety Agency to determine - in contradiction to the findings of the World Health Organisation - that glyphosate was not a carcinogenic. In April 2017, after an initial answer from EFSA and an administrative appeal ("confirmatory application") from the requestors, EFSA's final decision was that it would release parts of the studies requested, but it would withhold entire sections of all the reports in order to protect the commercial interests of the companies that funded the research.

This briefing, prepared by toxicologists from the Pesticide Action Network, seeks to answer the following question: **Is the information that has so far been supplied by EFSA enough to permit independent scientific scrutiny on glyphosate?**

Potential conflicts of interest

There is an inherent risk of conflicts of interest in having industry doing safety testing on their own product. The enormous cases of fraud in the past with laboratory testing[1], also for Glyphosate, have demonstrated the extent of this historical mistake.

Despite this, governments still failed to impose independent testing, instead considering that an administrative certification system (GLP, Good laboratory Practice) would be sufficient to prevent fraud. GLP, however, is an administrative system that is still vulnerable to selective data registering. Also, GLP aims at controlling the generation of data, not their interpretation.

Perhaps most importantly, the results and discussion narrative sections of the companies' reports, which have been withheld by EFSA, are not subject to GLP. This leaves room for manipulation, for example, by not mentioning important things and emphasising unimportant ones. This is one of the reasons why the full reports need to be disclosed.

Independent scrutiny is currently still not possible

Details for verifying the outcome of animal studies are still not accessible. For instance, in the "materials and methods" sections of their assessment report, EFSA blacked out information or provided incomplete information on:

- the origin of the test animals,
- the recording of clinical signs,
- pre-terminal deaths,
- palpation of tumours,
- pathology and
- statistical analysis.

[1] https://en.wikipedia.org/wiki/Industrial_Bio-Test_Laboratories

In addition, the sections on results and discussion, which presumably contain elements like clinical signs, pre-terminal deaths, clinical investigations, pathology, and possible deviations from the study plan have been denied to us by EFSA.

The "materials and methods" and the "results and discussion" are precisely the sections that any independent scientist or peer-reviewer will insist on reading in order to verify that the verbal description of the results and their discussion appropriately reflect the data contained in the tables and figures which have been made public in a limited way by EFSA. Without this information, it is not possible to verify that the data was not presented in a certain way in order to get a desired outcome.

As toxicologists, our number one priority is to scrutinise if the very basis of the study result, which is based on the methods and materials, is in fact solid; and if the way of arguing and interpreting the findings in the results and discussion section is based on sound science.

Our second priority is to scrutinise the data found in the tables and figures, but this can only be done once it has been established that the data are in fact the genuine outcome of the animal testing in the labs.

EFSA misleads

EFSA, throughout their decisions to provide only some parts of the industry documents requested[2], argues that the release of "raw data and finding, (aggregated in tables and figures)", can be put together with the information or summaries that are already public, and that this would allow others "to redo the assessment and scrutinise the EFSA peer review". Unfortunately, this is not true.

First, the authorities' publicly available documents (i.e. BfR's (that is: the Bundesinstitut für Risikobewertung, the scientific authority of the Rapporteur Member State for glyphosate, Germany) Renewal Assessment Report[3], EFSA's conclusion[4]) do not contain crucial information on statistical assessment methods applied in the studies. This is most likely contained in the confidential parts of the industry study reports. For instance, for eight of the twelve carcinogenicity studies presented in the authorities' documents, information is lacking on whether one-tailed or two-tailed test statistics were used. This is of great importance, because the applicable OECD Guidance (Guidance No. 116, 2012) recommends the use of one-tailed tests which could render even more tumor incidences statistically significant.

Second, BfR and EFSA claim there is an "inconsistency" of tumor incidences between different studies by comparing "apples and pears". Caution is needed when directly comparing results of different sub-strains of mice, but detailed information on the animals used - which would allow us to scrutinize the alleged inconsistencies – is not included by the authorities in their public documents.

Third, the authorities, EFSA and BfR, accepted or rejected entire studies based on unknown information. This information could be found in part of the full study reports that we do not have access to. The exclusion of a particular study is one of the pillars behind EFSA's claim that

[2] Initial decision, dated 7 October 2016 here:
https://www.asktheeu.org/en/request/is_glyphosate_safe_we_have_the_r#incoming-11429
Final EFSA decision, dated 19 April 2017, here:
https://www.asktheeu.org/en/request/is_glyphosate_safe_we_have_the_r#incoming-13141

[3] Rapporteur Member State Germany's health institute "Bundesinstitut für Risikoberwertung" (German Federal Institute for Risk Assessment) or BfR, drafted the assessment report that can be retrieved here: http://dar.efsa.europa.eu/dar-web/provision/request/subid/562

[4] EFSA's opinion of the Glyphosate assessment report can be found here:
https://www.efsa.europa.eu/en/efsajournal/pub/4302

glyphosate is not carcinogenic. But, in case the study report were to reveal that the exclusion of this report was unjustified, the entire assessment made by EFSA could change.

In addition, in the dispute over whether trend tests are appropriate for the statistical analysis of carcinogenicity studies, EFSA's Executive Director, Bernhard Url, contended in an open letter[5] that the "studies under consideration were designed for pair-wise comparisons". From a scientific perspective it can be excluded that such a design exists in any of these studies, because all these studies consist of one control and three glyphosate-treated groups (a pair-wise design would be having just one treated group and one control group in the study). Scrutinising the paragraph on statistical methods contained in the study reports would be essential in order to clarify Mr. Url's claim which otherwise is difficult to understand.

The continuing reference of EFSA to the already public "summary dossier and background information" (RAR) documents on which EFSA based its opinion, is also misleading. In the case of glyphosate, summary dossiers and background information were actually drafted by industry; thus there is a huge potential for a conflict of interest. The summary dossier is based on the original animal studies, but without access to the materials & methods and results & discussion parts of the studies it is not possible to judge whether the description of the results of the animal studies might have been framed a particular the direction - for example, in industry's interest of getting the pesticide approved.

The Rapporteur Member State, Germany, has the official role of evaluating the outcome of animal studies and raw data. But given the quantity of study data (EFSA estimates the volume of the research for Glyphosate 700.000 - 1.000.000 pages), it is practically impossible for them to do so given the limited resources and experts member states have. There is an added scientific benefit therefore to allowing public access to the parts of the studies that are needed for an independent scientific assessment. Specific research teams would then have the possibility to uncover possible errors, be part of the scientific debate, and contribute to the decision-making process.

Indeed, the very reason for asking for the narrative part of the study reports is to be able to reconstruct how EFSA came to the conclusions summarised in their assessment report and to scrutinise whether or not they reflect the reality of the raw data. As the industry has a specific interest in the outcome of the studies on glyphosate the whole studies should be available for public scrutiny to ensure that the safety claims with regard to this substance are well-founded.

Séralini standards: It is also noteworthy that EFSA itself asked Prof. Séralini in a letter of October 12, 2012[6] to disclose all raw data on his Glyphosate study that demonstrated carcinogenic effects. EFSA stated they needed this data to be able to scrutinise his study, including the biological relevance of the strain used, the sample size calculations, measures taken to reduce the risk of bias, information on diets, contamination of diets, appropriate statistic analysis, etc.

However, by denying access to the materials and methods descriptions, and the results and discussion parts of the industry study reports, EFSA is in fact violating their own standards for the scientific assessment of studies.

[5] https://www.efsa.europa.eu/sites/default/files/EFSA_response_Prof_Portier.pdf
[6] https://www.efsa.europa.eu/en/press/news/121004a

Are the emissions levels used in these tests realistic or hypothetical?

Data on hypothetical emissions are not to be considered information on emissions that should always be disclosed, as follows from an EU Court of Justice Judgement of November 2016.

It is clear that the emissions in the non-disclosed studies used by EFSA are realistic: When applying Glyphosate to the field, the emission of Glyphosate into the environment is 360 gram/Liter[7] (360.000 ppm) according to the Good Agricultural Practices described in the EU's decision to approve its use.

Workers (highest dosage case) can be exposed to glyphosate-based formulations at this concentration as well as the environment, including organisms living in that environment. Bystanders and residents can also be exposed to high levels of Glyphosate, although these probably will be lower, due to the distance to the place of application. The maximum allowed residue level in food is 50 ppm in wild fungi[8].

The studies requested for disclosure actually used dietary concentrations between 30 and 40.000 ppm[9] for animal exposure in carcinogenicity studies, which is much lower than the current levels of emissions. It is therefore clear that the levels used in safety testing are not hypothetical at all but realistic for people and the environment under normal conditions of use.

In any case, higher concentrations in experiments are often needed to compensate for uncertainty with regard to inter-individual and inter-species differences in their susceptibility when extrapolating results from laboratory studies to the real world. The levels used in regulatory studies are meant to guarantee that medium to long-term consequences of emissions are excluded, without having to test thousands of animals during very long periods, which would make it very expensive and, from a practical point of view, very difficult to carry out the necessary tests. The results of the tests and studies thus are about realistic, not hypothetical emissions and its effects on the environment, specifically on human health. Disclosure of the requested studies thus would be in line with the verdict of EU Court of Justice on the disclosure of "information on emissions to the environment[10],[11].

CONCLUSION

Making the data of the industry studies accessible in tables and figures is a necessary, but not sufficient step to allow for an independent scrutiny of the science behind the studies and the decisions of EFSA and the regulators.

For a proper verification that the data generated were not influenced by flawed study designs, questionable methods and unscientific discussion outcomes, full access to the parts of the material and methods section described above is necessary.

To verify that the verbal description did not distract from important study results hidden in the (accessible) study data or mislead the authorities by making wrong conclusions, full access to the results and discussion section is essential.

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[7] http://onlinelibrary.wiley.com/doi/10.2903/j.efsa.2015.4302/pdf
[8] http://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event=activesubstance.detail&language=EN&selectedID=1438
[9] RAR, Renewal Assessment Report, Volume 1, Report and Proposed decision, December 18, 2013.
[10] http://curia.europa.eu/juris/liste.jsf?num=C-442/14
[11] The court ruled: "The public interest in accessing information on emissions into the environment is specifically to know not only what is, or foreseeable will be, released into the environment, but also, as the Advocate General stated in point 86 of her Opinion, to understand the way in which the environment could be affected by the emissions in question"