21 SEPTEMBER 2021

Glyphosate re-registration

academic studies largely ignored!

générations FUTURES

Background

Article 8.5 of EU Regulation 1107/2009 on the marketing of pesticides states that for each application dossier for the registration of a pesticide active substance:

« The applicant shall submit with the dossier the available scientific literature, as determined by the Authority, validated by the scientific community and published within the last ten years preceding the date of submission of the dossier, concerning the secondary effects on health, the environment and non-target species of the active substance and its relevant metabolites »

This requirement to take into account the scientific literature of the last 10 years in the dossier, introduced for the first time in Europe in this regulation in 2009, has not been systematically applied in the past. For example, **a previous publication (1) by Générations Futures and PAN Europe showed that, during the previous registration of glyphosate in Europe, the application for re-registration submitted by the industry in 2014** (RAR: Renewal assessment report) **contained barely more than half (52%) of the scientific studies on the effects of glyphosate** that were easiest to find and should have been included. **Of the 7 pesticides studied in this report, only 23% of the academic studies were included in the industry's files!**

This is why, **as the process of examining the new application for the re-registration of glyphosate in 2020 begins, we wanted to know if, this time, the academic scientific literature on the toxicity of glyphosate (including epidemiology) and its ecotoxicity would really be taken into account i**n the industry's application files. This is a good opportunity to check whether the assessment is based on all the available scientific data, and not just the studies provided by the industry itself, which are mostly not published in peer-reviewed scientific journals, i.e. not validated by peers.

New application for re-registration of glyphosate in Europe

The Glyphosate Renewal Group (GRG), which brings together the industrialists behind the new glyphosate re-registration application, claims that "*With over 180,000 pages and 1,500 scientific studies, the 2020 glyphosate renewal dossier is the most comprehensive ever submitted to the European authorities [...] more than 12,000 studies have been reviewed*."

Beyond these claims, we wanted to check whether the studies published in scientific journals and validated on the toxicity and ecotoxicity of glyphosate in the 10 years preceding the submission of the application file were indeed present in the manufacturers' re-registration application file, as required by Article 8.5 of Regulation 1107/2009.

11Pesticides: Incomplete European evaluations that go against the law! Générations Futures and PAN Europe, 2014. https://www.generations-futures.fr/wp-content/uploads/2014/09/Pesticides_Reglement_Etude_scientifique_080920141.pdf

Data search* and method

The same exclusion/inclusion criteria were used to determine the number of published toxicity/ecotoxicity studies in both lists: those from industry and from scientific studies found in PubMed. We excluded corrections, revisions (except meta-analysis), comments and letters to the editor from these lists (again, unless new data or recalculations were submitted). Studies on exposure, toxicokinetics and environmental fate were also excluded; analytical methods; and anything that was clearly not toxicity/ecotoxicity data or epidemiological findings.

INDUSTRY STUDIES.

With regard to glyphosate toxicity/ecotoxicity results alone, the GRG, in its application for the 2020 re-authorisation of glyphosate, submitted to the four Rapporteur Member States (RMS, who oversee the re-authorisations) two (published) lists totalling 486 studies published in scientific journals: one list of toxicity studies, the other of ecotoxicity studies.

In both of these industry lists, our determination of study type was largely based on reading the titles only, but, in case of doubt, at least the abstract (if not the full article) was checked additionally.

In these lists, we classified as studies on glyphosate toxicity/ecotoxicity, 250 studies as investigating exposure to the active substance (s.a); 145 as investigating exposure to the "glyphosate-based formulation" (GBH); and 91 as not being toxicity findings at all.
We then went through the other two lists of studies provided by the GRG ("Environmental fate and behaviour" and "Metabolism and residue data"). In the "Metabolism and residue data" list, we identified 10 studies as potential toxicity/ecotoxicity studies.

405 toxicity/ecotoxicity results for glyphosate were therefore submitted to fulfil the legal mandate under Article 8.5.

SCIENTIFIC STUDIES FOUND IN PUBMED.

We then undertook to quantify the number of results published in scientific journals on the toxicity of glyphosate in the 10 years preceding the submission of the re-registration application (March 2010 - March 2020); whether they were devoted to the declared active substance glyphosate or to glyphosate-based formulations (s.a or GBH).

*Research conducted by R.I.S.K. Consultancy, Brussels..

There are four main databases for finding toxicity studies; only PubMed is free, and it is this database that we have chosen to use for this report.

[The Web of Science (WoS) database - in particular its BIOSIS (formerly Biology Abstracts) component - is known to complement PubMed well, but we were unable to access it because of the high access costs. Based on experience of research with other chemicals, we estimate that WoS would have added 10-30% to the existing number of published results on glyphosate toxicity. Scopus and Scholar.google would add a negligible number of new studies, which we estimate at around 2%. **The result of our search for studies on glyphosate toxicity on PubMed therefore significantly underestimates the actual number of published studies.**]

In PubMed, we tried to find as many published studies on glyphosate side effects (toxicity/ecotoxicity) as possible with this search term: ("glyphos*" OR "Roundup") AND (caus* OR effect* OR hazard* OR risk* OR toxic* OR safet* OR danger* OR harm*) - scientific literature is published in English)

We then examined each study abstract to determine whether it was a toxicity/ecotoxicity or epidemiological finding. Where this was not clear enough, we reviewed the full paper, where available.

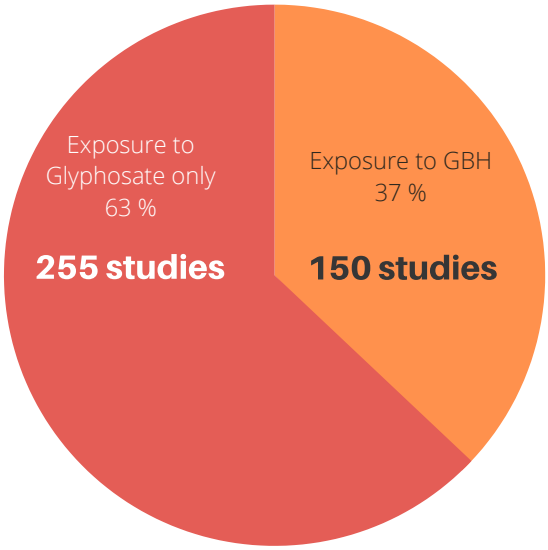
If a study tested both the active substance and the formulation, it was counted as testing the glyphosate molecule. Poisoning studies were counted as GBH exposures. All but a few of the epidemiological studies (of workers in glyphosate manufacturing plants) were also classified as GBH exposures, even though levels of the glyphosate molecule or the metabolite AMPA in the body were measured.

However, our estimate of the ratio of studies using the glyphosate molecule to those investigating a formulation should be considered indicative due to the large use of supplied titers only.

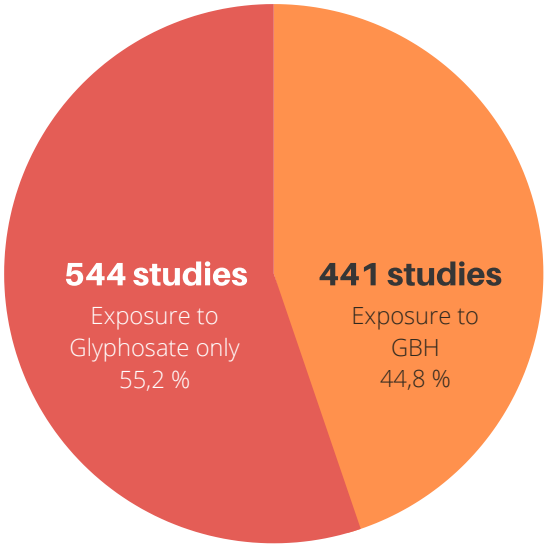
Results

58.88% of the glyphosate toxicity/ecotoxicity studies found in PubMed alone were ignored by the GRG industry

Toxicity/ecotoxicity studies submitted by Glyphosate Renewal Group (GRG) companies



Toxicity/ecotoxicity studies found in PubMed



	Tox/ecotox studies from GRG	Tox/ecotox studies from PubMed	% studies from GRG / % studies from Pubmed
Exposure to Glyphosate only	255	544	46,87%
Exposure to GBH	150	441	34,01%
Total: GBH + glyphosate	**405**	**985**	**41,12%**
Non tox/ecotox studies	91	0	-
Total	496	985	-

Our search therefore clearly shows **that industry provided only 41.12% of the glyphosate toxicity/ecotoxicity studies we identified on PubMed alone. This means that 58.88% of the glyphosate toxicity/ecotoxicity studies found in PubMed alone were ignored** by the GRG !

Note that this percentage of missing studies is probably still very underestimated because in our experience a search on Web of Science would have added between 10% and 30% more published studies and thus led to an even lower ratio of 'GRG-supplied studies to published studies in PubMed' !

How to explain such a low percentage of academic scientific studies provided?

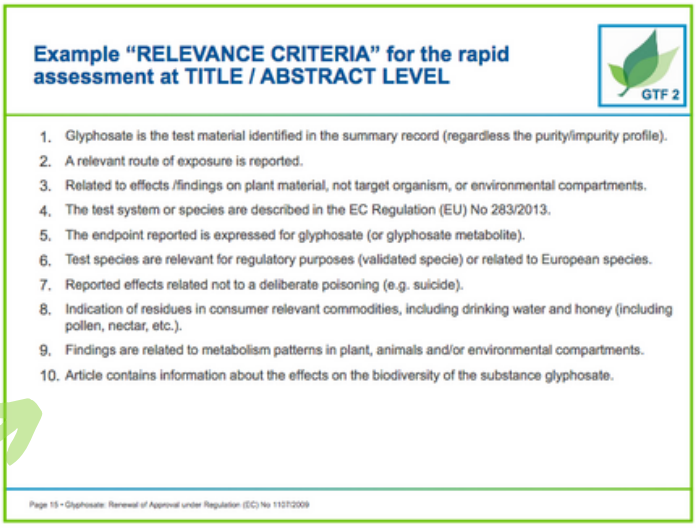
Efsa has published a guidance document (2) for the publication of scientific literature in the context of pesticides legislation. However, this guidance states that "*To avoid missing relevant studies, the relevance criteria should not be too restrictive. Only clearly irrelevant studies should be excluded from a dossier*".

In a meeting (3) with the rapporteur Member States (RMS) prior to submitting their application, **the industry gave their criteria for assessing the relevance of published scientific studies when examining the results of the literature review** (the RMS then made them public).

For Générations Futures, in view of Article 8.5 of Regulation 1107/2009 the main criterion when searching the scientific literature on glyphosate toxicity should clearly only be "is this a glyphosate toxicity result? - Reliability should be assessed later, during the evaluation; the crucial task at this stage is not to miss the relevant data. **However, slide 15 of this meeting (see below) shows that industry has taken several opportunities to dismiss toxicity results en masse without any assessment in the name of a supposed lack of relevance.** For example by introducing criteria such as. "must test a regulatory endpoint (EC 283/2013)" or: "glyphosate residues must be observed in consumer products"

At this meeting (minutes are public), the RMS asked the industry to submit all criteria, not just "examples". **So to this day we still don't know exactly how the industry conducted its literature search and assessment of the 'relevance' of glyphosate toxicity studies.**

The list of studies published by the GRG ignored hundreds of studies that do not fit the industry's criteria but which might be of interest to better assess the toxicity of glyphosate.



Example "RELEVANCE CRITERIA" for the rapid assessment at TITLE / ABSTRACT LEVEL

GTF 2

1. Glyphosate is the test material identified in the summary record (regardless the purity/impurity profile).
2. A relevant route of exposure is reported.
3. Related to effects /findings on plant material, not target organism, or environmental compartments.
4. The test system or species are described in the EC Regulation (EU) No 283/2013.
5. The endpoint reported is expressed for glyphosate (or glyphosate metabolite).
6. Test species are relevant for regulatory purposes (validated specie) or related to European species.
7. Reported effects related not to a deliberate poisoning (e.g. suicide).
8. Indication of residues in consumer relevant commodities, including drinking water and honey (including pollen, nectar, etc.).
9. Findings are related to metabolism patterns in plant, animals and/or environmental compartments.
10. Article contains information about the effects on the biodiversity of the substance glyphosate.

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Note that the industry's glyphosate task force later changed its name from GTF to GRG.

2. https://efsa.onlinelibrary.wiley.com/doi/pdf/10.2903/j.efsa.2011.2092
3. Teleconference of 11 December 2019, presentation 'General literature search and literature review report (LRR)' presentation downloadable from the European Commission website here: https://ec.europa.eu/food/system/files/2020-03/pesticides_glyphosate_asess-grp_20191211_pres.pdf

CONCLUSION & REQUESTS

This 2021 glyphosate re-authorisation process is far from being the most rigorous ever at this stage. It is just as incomplete as the previous one, and perhaps even worse, as it fails to find all the available scientific information on the toxicity of glyphosate that should be provided under Article 8.5 of Regulation 1107/2009.

This practice has the effect of removing from the glyphosate dossier a majority of the academic studies published during the 10 year period prior to the application and these studies will therefore not be taken into account for the scientific assessment during the formal evaluation/registration process.

As long as this initial step of research and production of all 'available scientific literature' is not carried out properly, **the assessment process cannot be conducted on a scientifically sound basis and real adverse effects can be completely ignored.**

We therefore call for all published academic literature to be included in the dossier and then assessed by the Agencies for relevance, reliability and scientific quality in a transparent manner independent of industry. It is not up to the industry, which is both judge and party, to make this selection!

As long as the dossier on glyphosate does not contain all the available data, the rapporteur Member States and the European Commission should not accept the GRG dossier as it stands and should reject it.

A worrying outlook for the future.

The reliability criteria for industry studies could still wipe out many academic studies during the evaluation process! Of course, when published findings of academic studies are not missed or rejected for supposed lack of relevance (in contradiction with Article 8.5) and well taken into account in the dossier, they can still be rejected during the assessment.

The RMS were also informed in the pre-application meetings with the industry GRG what their criteria would be for judging the reliability of the toxicity studies found that were being assessed (whether industry-specific or published in the industry list). Although the draft Revised Assessment Report (RAR) is not yet public, we do know the criteria that industry planned to apply to assess the reliability of toxicity studies. We also know that the RMS has already announced, in June 2021, that it has found no significant new toxicity results since the previous re-authorisation. The trick for industry here is to show a patina of scientific objectivity in their criteria, while ensuring that they produce the same result as the old system, where industry's insensitive studies (to find toxicity) were universally assumed to be the most reliable.

One of the main ways to achieve this is to select only studies that follow 'Good Laboratory Practice' (GLP) or OECD protocols. But, as a report by the Citizens for Science in Pesticide Regulation coalition pointed out in 2018: 'Compliance with OECD guidelines or GLP does not mean that the study is better than a study published in a peer-reviewed non-OECD/GLP journal, nor does it guarantee its correct interpretation' (4).

But, the industry could again throw away the hundreds of toxicity results it has found by this means...or others.

We will follow the process closely to check this in detail in due course and keep you informed.

4. See the French translation of this collective report by Générations Futures here: "Recasting Pesticide Risk Assessment, Ensuring a High Level of Protection from Pesticides in Europe" https://www.generations-futures.fr/wp-content/uploads/2018/10/working-document-reform-final-october-2018-en.pdf

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