Secrets Toxiques
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Mr. Pascal Canfin,
Chair of ENVI Committee of the European Parliament
Mr. Adrián Vázquez Lázara
Chair of JURI Committee of the European Parliament
Members of the JURI and ENVI Committees in the European Parliament

Dear Mr. Canfin,
Dear Mr. Vázquez Lázara,
Dear Members of ENVI and JURI Committees,

Since more than two years, our organization is working on pesticides' assessment, trying to understand how pesticides can be identified as a major factor of human health issues and biodiversity destruction, while EU regulation requires to ensure that such adverse effects shall not occur. **We have highlighted a major flaw leading to a significant underestimation of the toxicity of authorized pesticides, which is the absence of a proper assessment of long-term effects of formulated products** – i.e. pesticides as they will be used – whether at the level of EU institutions or Member States.

The decision upon glyphosate reapproval is imminent. In its peer review's conclusions, EFSA has pointed a major data gap: **the acute toxicity and genotoxicity data on one co-formulant of the representative formulation in glyphosate's reapproval dossier are absent**. In such case, data must be produced on the whole formulation, as Health Commissioner Stella Kyriakides admitted in a letter to Mr. Canfin on October 20th, 2022. While such supplementary analysis has not been required from manufacturers by regulatory agencies, recent scientific knowledge produced on the representative formulation do show adverse effects. **In such case, the absence of adverse effects in normal conditions of use cannot be guaranteed, leading to consider that regulation requirements for glyphosate's reapproval are not met**. This last development comes on top of the elements that we have gathered in the last two years, showing the absence of a sound methodology for formulation assessment, as admitted by EFSA's director Bernhard Url in front he the ENVI Committee in November 2022.

You will find attached to this introduction an extended letter exposing all the reasons for which we consider that a renewal of glyphosate's approval as an active substance in pesticides would constitute, under the current conditions, an infringement of Regulation 1107/2009 that would put at risk the health of European citizens and European biodiversity. Should glyphosate's reapproval be enacted nevertheless**, the European Parliament can act on the matter** in order to protect both, as well as the rule of law in the European Union, by **filing an action in annulment of glyphosate's reapproval which is guaranteed to be received by the European Court of Justice.**

Such action would be undertaken by JURI and ENVI committees. **We are willing to meet you in person in the following weeks in order to bring further details on the matter**.

Sincerely yours

Secrets Toxiques

Extended Letter

Dear Mr. Canfin,
Dear Mr. Vázquez Lázara,
Dear Members of ENVI and JURI Committees,

As you know, the procedure renewal of the approval of the European Union on the use of glyphosate as an active substance in pesticides is currently ongoing, and a vote of the Member States is expected in the weeks to come.

We are in a position to assert that shall this renewal be voted in its current form, its legal validity would be under question. Indeed, a major flaw of both scientific and legal nature exists in the process, which shall currently lead to an important underestimation of the chronic toxicity of the molecule as it is used in pesticides in the European Union. Given the situation, **ENVI and JURI committees have a crucial role to play in order for lawful procedures to be respected in the glyphosate's approval procedure.**

As you know, **Article 4 of Regulation 1107/2009 requires, for the approval of a pesticide's active substance, the proof that products containing this substance have no adverse effect on human health or the environment in normal conditions of use, considering cumulative and synergistic effects**. Although the approval of commercial pesticide products is a competence of Member States, **this regulation requires the same proof to be brought for the approval of the active substance for "one or more representative uses of at least one plant protection product containing that active substance"** (Article 4(5), own emphasis added).

This requirement is the condition for cumulative and synergistic effects to be accounted for during the pesticides' active substances approval process. Indeed, pesticides contain more than their active substance, and some of these compounds have the effect to increase the toxicity of the product. It is the case of so-called "synergists", which can have for instance the effect to help the pesticides to stick to targeted organisms in order for the poison to effectively penetrate in it.

According to EFSA and the European Commission, which we had the opportunity to question repeatedly on this matter in the last two years, the assessment of this representative use is not realized by experimental studies on the formulations, but by an extrapolation based on the data available on individual compounds declared in the formulation by the manufacturer. The conditions necessary for a proper assessment via this extrapolation are threefold: completeness of declaration of the compounds in the formulation, availability of a reliable method, and availability of reliable data on all compounds in the formulation.

Two of those three conditions, the availability of reliable methodology and data, are clearly not met in the case of this year's glyphosate's approval renewal process, leading to major scientific and legal flaws in the assessment procedure.

Problems of method

About the methodology employed to assess long-term toxicology of formulations, two elements are very clear. The first one is the Blaise decision (C-616/17, October 1st 2019) of the Court of Justice of the European Union (CJEU). In its point 116, the Court answered the question of whether the tests currently demanded by EU regulation on formulations were sufficient to assess the toxicity of products in regard of the precautionary principle. The Court answered that **while the "cursory tests" demanded by EU regulation are not sufficient to perform the verification of absence of carcinogenicity or other type of long-term toxicity, it is the responsibility of the competent authorities to provide a proper analysis answering the requirements of regulation 1107/2009 and the precautionary principle**.

However, when asked by the European Parliament on November 8th 2022, **EFSA's director has admitted that the agency has currently no method to assess synergistic effects**, therefore including the long-term toxicology of formulations:

> *"**You could say : "are you looking at all the possible synergistic effects the active substance and the coformulants could have on each other? Could there be an increased toxicity because they would act together on the same organ?** Yes, we are developing this methodology. This is a very complex scientific endeavor. But EFSA has invested in the last ten years an enormous amount of workforce and also money to invest these, what we call, assessment of chemical mixtures, of cocktails, of combined exposure to multiple chemicals. We are making progress, together with member states. I want to mention here, also specifically the public health institute of the Netherlands, RIVM, one of our main partners here. But..**we are not yet there, because not everything has been solved yet.** We have a roadmap, a plan. How to move forward from one organ to the next organ. So that is still a multiannual endeavor in front of us."*[1]

This statement shows that EFSA cannot yet assess any representative formulation according to the requirements of regulation 1107/2009 requirements, with regard to the assessment of synergistic effects.

Between February 2021 and December 2021, we have repeatedly asked European and National food safety agencies about the methods used to assess co-formulants' long-term toxicity and synergistic effects in formulated products. We obtained very little answers, mentioning *Adverse outcome pathway* and threshold definitions following requirements of CLP regulation (EU 1272/2008), which cannot suffice to consider the long-term toxicology

[1] https://multimedia.europarl.europa.eu/fr/webstreaming/envi-committee-meeting_20221108-0900-COMMITTEE-ENVI
Minute : 09:52

assessment as fully performed – an opinion also shared by the French National Commission Alert and Deontology in Public Health and Environment[2].

Last spring, the EU Commission has started to address this problem in a series of workshop to which we were invited. Our proposal to perform an experimental assessment on the whole formulation was not really considered. We are waiting for the conclusions of this workshop, but its existence itself admits the lack of reliable method to assess the synergistic effects of representative formulations, and the impossibility to answer the requirements of regulation 1107/2009 in the case of glyphosate's approval renewal.

Problems of data:

Even if a sound method existed to assess the long-term toxicity assessment of a formulation, including synergistic effects, those methods would necessarily need very solid and exhaustive data to function.

Unfortunately, data gaps in the REACH chemical universe have been long highlighted, in particular by the German authorities[3]. More specifically**, EFSA's peer review of glyphosate published in July 2023 mentioned that "a lack of information about the toxicity of one of the components present in the glyphosate-based pesticide formulation submitted for evaluation, which is needed to conclude the risk assessment of the formulation for representative uses. For this formulation there were no indications of acute toxicity and genotoxicity"**. This co-formulant makes up 10% of the glyphosate based formulation. Nevertheless, EFSA decided to consider this merely as an "outsanding issue", leaving to the European Commission and the Member States the responsibility to consider the relevance of this data gap in the context of the approval of glyphosate.

However, in October 2022**, EU Commissioner Stella Kyriakides admitted** in a public letter to Pascal Canfin, chair of ENVI Committee, that

> "If the information is insufficient to conclude on the long-term toxicity, Member States are empowered to require applicants to submit the necessary additional information up to the same level as for active substances. […] [I]n the light of the judgement in Case C-616/17, I agree with you that in case insufficient information is provided by applicants, the Member States and EFSA have an obligation to request further information."

The Commission has visibly decided to act differently than what was stated in this letter, since it has submitted a draft renewal decision to the Standing Committee on Plants, Animal, Food

[2] https://www.alerte-sante-environnement-deontologie.fr/deontologie-et-alertes-en-sante-publique-et-environnement/actualites/article/avis-relatif-a-la-methode-d-evaluation-des-risques-des-pesticides-pour-la-sante

[3] https://www.bfr.bund.de/cm/349/data-quality-of-environmental-endpoints-in-registrations.pdf

and Feed (Scopaff) this summer, as revealed by the NGO PAN Europe[4]. In this draft report, the Commission eluded EFSA's concern about the co-formulant's data gap, stating that "*all Member State experts who took part in the expert discussions, as well as the AGG [Assessment Group on Glyphosate], agreed that the available toxicological information is sufficient to conclude on the safety of 'MON 52276' [the representative formulation in the dossier], for which acute toxicity and genotoxicity data exist and indicate no concern*".

The Commission visibly considers that Members States and AGG possess data on toxicological information of the representative formulation that EFSA does not have. However, **we can reasonably raise important concerns on the soundness and legal validity of these data**: why would EFSA claim a data gap that Member States and AGG can fill? Moreover, **data produced in the academic literature do indicate toxicological concerns regarding long-term toxicity of MON 52276.**

Studies on the formulation that is subject to the application for renewal decision

Scientific studies have been performed on the precise formulation that is mentioned in the current glyphosate's renewal dossier, named MON52276. Between 2019 and 2022, a research program led by Robin Mesnage has performed *in vitro* (using the mammalian stem cell-based ToxTracker system) several *in vivo* animal studies comparing the effects of glyphosate alone and MON52276 (90 days exposure studies). They have found that the formulation led to more biological changes linked with carcinogenesis than glyphosate alone, and that hepatic damage was provoked by the formulation – but not glyphosate alone[5].

> *"While the co-formulants contained in the representative EU commercial GBH formulation MON 52276 are known to have one of the best safety profiles among agricultural surfactants,* ***the results from the study presented here and in our previous investigation with the same animals (Mesnage et al. 2021) suggests that it is more toxic than previously claimed****. Previous studies on human cells found that MON 52276 was no more cytotoxic than glyphosate alone at equivalent concentrations (Mesnage et al. 2013), and that it was less toxic than glyphosate on rainbow trout and water fleas (Mesnage et al. 2019). However,* ***our study shows that exposure to MON 52276 causes liver steatosis and necrosis and supports the need for long-term toxicity evaluations of the toxicity of formulated products."***[6]

[4] https://www.pan-europe.info/press-releases/2023/07/leaked-eu-commission-plans-swiftly-reapprove-glyphosate-avoid-scientific-and

[5] Mesnage et al., 2021, Comparative toxicogenomics of glyphosate and Roundup herbicides by mammalian stem cell-based genotoxicity assays and molecular profiling in Sprague-Dawley rats

[6] Ibid.

Besides, they also found in another 90 days exposure study that MON52276, and not glyphosate alone, provoked alterations of the gut microbiome in rats[7]. The Ramazzini institute has also characterized, in the preliminary results of a study on the matter, the formulation MON52276 as a probable endocrine disruptor[8]. **The results of these scientific works directly contradict the conclusions of EFSA's peer review when it says that "There were no indications of acute toxicity or genotoxicity in studies performed with the formulation for representative uses 'MON 52276'".**

These works, focused on the specific formulation used for the current glyphosate's renewal procedure, are coming on top of a very large corpus of science that led **IARC to classify glyphosate as "probably carcinogenic" in its 2015's monography**[9], based both on studies on glyphosate itself and glyphosate-based formulations. In a very recent literature review, Rana et al. showed that IARC's monography was in fact conservative. Indeed, while it had brought evidence for genotoxicity and oxidative stress, **studies performed since have brought strong evidence for other carcinogenicity mechanisms, namely epigenetic alterations, chronic inflammation, and endocrine disruption**[10].

Problem of instable composition of pesticides products

Finally, if we would consider for a moment that both a method is available and data requirements fully complied with, a third concern would have to be underlined when it comes to the formulations' stability. This *per se* do not constitute a break from EU institutions in the legal requirements for glyphosate's assessment, but questions the idea that the studied formulation is actually representative and that manufacturers fully comply with their obligation to declare exhaustively the compounds present in their products.

Three studies[11] have performed a mass spectrometry of pesticides available on the market at the time of the studies. That is an analysis of their composition. **In most studied products,**

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[7] Mesnage et al., 2019, Shotgun metagenomics and metabolomics reveal glyphosate alters the gut microbiome of Sprague-Dawley rats by inhibiting the shikimate pathway

[8] Manservisi, Fabiana (2021) *Reproductive and developmental toxicity study using Sprague-Dawley rats exposed under various calendars to the weedkiller Glyphosate and commercial formulations Glyphosate-based*, [Dissertation thesis], Alma Mater Studiorum Università di Bologna. Dottorato di ricerca in Scienze veterinarie, 33 Ciclo. DOI 10.48676/unibo/amsdottorato/9579.

[9] https://www.iarc.who.int/featured-news/media-centre-iarc-news-glyphosate/

[10] Rana, I., Nguyen, P. K., Rigutto, G., Louie, A., Lee, J., Smith, M. T., & Zhang, L. (2023). Mapping the key characteristics of carcinogens for glyphosate and its formulations: A systematic review. *Chemosphere*, 139572.

[11] Defarge, N., De Vendômois, J. S., & Seralini, G. E. (2018). Toxicity of formulants and heavy metals in glyphosate-based herbicides and other pesticides. Toxicology reports, 5, 156-163. Seralini, G. E., & Jungers, G. (2020). Toxic compounds in herbicides without glyphosate. Food and Chemical Toxicology, 146, 111770.

they have outlined the presence of low concentrations of compounds that should have been declared to food safety authorities: arsenic, lead, several heavy metals and polycyclic aromatic hydrocarbons. Moreover, they have observed that **the amount of those compounds present in different samples of the same commercial product would significantly vary**, therefore leading to consider the idea that pesticides products authorized on the market are not stable in composition.

In such case, EFSA's guidelines[12] recommend to avoid using a component-based approach, and to rather process to a whole-mixture approach, using the whole formulation as a basis to assess various toxicity parameters, including long-term toxicity. We have produced a literature review on the potential effects of heavy metals and hydrocarbons in the concentrations detected by the three above-mentioned studies[13]. If the presence of those compounds is actually generalized, its potential harmful effects on human health and environment cannot be ignored. Studying the effect of pesticides products as a whole mixture would be a way to properly address risk assessment, on both a scientific and a legal level.

Conclusion

It is very clear, from Berhard Url's audition in front of the AGRI commission on August 30th, that despite numerous data gaps leading to uncertainties about whether glyphosate meets the approval criteria for active substances of pesticides, EFSA has put the responsibility to decide on glyphosate's reapproval in the hands of the Commission and the Member States. Indeed, Mr. Url gives a precise definition of what EFSA could consider as critical area of concern – leading to a rejection of the reapproval dossier – and explains why EFSA did not define one. He explains that defining a critical area of concern means that "none of the proposed uses by the applicant will meet the approval criteria". Considering this, he says that however, EFSA identified "issues that could not be finalized" which are "now something for the European Commission and Member States to consider within their role as risk managers in the next stages of approval process". The issue of lack of data on the short and long-term toxicity of one component in the representative formulation is mentioned among those outstanding issues, defined as "data gaps which are considered necessary to comply with the requirements" and "not critical but [which] may lead to uncertainties in the assessment, and thus are considered relevant".

However**, the Commission's draft renewal report decided to stay blind to the scientific and legal fallacies highlighted in this letter, as well as to EFSA's outstanding issues**. **In this situation, lacking of method and data, it is clear that an assessment that would meet the approval criteria – i.e. ensuring the absence of short and long-term adverse effects of the representative formulation on both human health and the environment – has not been performed, both from a legal and a scientific point of view. A proper assessment of the representative formulation in the glyphosate dossier is therefore needed**. Thus, we are facing a situation where the preservation of public health and the environment would not be

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Jungers, G., Portet-Koltalo, F., Cosme, J., & Seralini, G. E. (2022). Petroleum in Pesticides: A Need to Change Regulatory Toxicology. Toxics, 10(11), 670.

[12] *https://efsa.onlinelibrary.wiley.com/doi/pdf/10.2903/j.efsa.2019.5634*

[13] https://icedrive.net/s/tYNF78QgA4uBkXy5xvZTRW9hYBj9

ensured at the level required by the pesticides regulation. Beyond being a matter of public health and environmental protection, this situation carries issues related to the respect of the rule of law and democratic institutions.

Considering this, it appears crucial that the European Parliament takes action on the matter. ENVI and JURI commissions in the European Parliament have this power, since they can file a remedy in annulment in order to block illegal decisions from the Commission and the Member States. Unlike civil society organizations, the European Parliament is ensured to see his request taken in account by the Court of Justice of the European Union, since it is receivable by default**. Shall glyphosate be renewed in the current conditions, we ask the Members of ENVI and JURI commissions to file an action in annulment of this decision within the two months authorized by the procedure.**

We are here asking for a meeting with you and any MEP of your Committee concerned in the topic. We are ready to meet you in person in order to discuss this matter.

Sincerely yours

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