EASTERN EUROPEAN JOURNAL OF TRANSNATIONAL RELATIONS

Approval procedure for active substances in plant protection products - doubts of scientific certainty as a source of controversy. Analysis of systemic imperfections on the example of glyphosate

Anna Gembicka
University of Białystok, Poland
gembicka.anna1@gmail.com
ORCID 0000-0003-1258-4181

Jakub Ali Farhan
University of Białystok, Poland
jakub.farhan@gmail.com
ORCID 0000-0002-3360-1553

Abstract. The purpose of this article is to examine the causes of recurring doubts regarding the safety of plant protection products used in the European Union. Plant protection products are a particular subject of regulation. All standards concerning them require prior in-depth scientific research in the field of exact sciences. Achieving adequate safety of humans, animals and the environment in connection to the use of plant protection products requires not only good law, but a law based on representative research and scientific certainty. Bearing in mind the above, the authors undertook an analysis of what seems to be the cause of significant social doubts as to the actual achievement of the purposes of Regulation 1107/2009, i.e. inclusion of scientific research in the procedure of approval of active substances in plant protection products. First, the approval procedure for the active substance of the plant protection product was presented, and then the main shortcoming of the procedure was analyzed on the example of the approval of glyphosate. In the authors' opinion, guidance documents on literature review should be revised to reflect the best scientific practice, and their standards should be enforced, in particular, to ensure that there is no doubt about the objectivity of the literature review.

Keywords: active substance approval, pesticides, glyphosate.

JEL Classification: K32, K39, Q18.

Citation: Gembicka, A., & Farhan, J.A. (2022). Approval procedure for active substances in plant protection products - doubts of scientific certainty as a source of controversy. Analysis of systemic imperfections on the example of glyphosate. *Eastern European Journal of Transnational Relations*, *6*(1), 49-57. https://doi.org/10.15290/eejtr.2022.06.01.04

Publisher's Note:

INTRODUCTION

Plant production plays a key role in the modern world. The increase in the efficiency of agriculture is one of the main factors that contributed to such a dynamic demographic development of the global community. This increase in efficiency was possible largely due to the chemical method of plant protection, i.e. chemical plant protection products. However, its use may adversely affect plant production and even pose a threat to humans, animals and the environment (Antoniou et al., 2011). Therefore, the role of legal regulations in ensuring a high level of protection of life and health is indispensable. The law sets the standards for placing on the market, use and control of plant protection products. The law in this respect was developed in particular at the European Union (EU) level, where the regulations in force are among the most stringent in the world. It seems, however, that extensive regulations do not guarantee the public's sense of security. In the public space, the issue of doubts related to the safety of certain plant protection products is constantly recurring, and non-compliance of the practice with established standards is detected.

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 (hereinafter: Regulation 1107/2009) is the framework legal act that regulates the placing of plant protection products on the market in the EU. According to its recital 9, harmonized rules for the approval of active substances and for the placing of plant protection products on the market, including rules on mutual recognition of authorizations and parallel trade have been established to increase the free movement and availability of pesticides in the EU. In its Art. 1(3) it is indicated that the purpose of the regulation is to ensure a high level of protection of both human and animal health and the environment and to improve the functioning of the internal market through the harmonisation of the rules on the placing on the market of plant protection products, while improving agricultural production. Moreover, according to the following paragraph of this article, the provisions of the regulation are based on the precautionary principle in order to ensure that active substances or products placed on the market do not adversely affect human or animal health or the environment. Plant protection products are a particular object of regulation. All standards concerning them require prior in-depth scientific research in the field of exact sciences. This is one of the reasons why it is so difficult to achieve the stated purpose of Regulation 1107/2009. It requires not only a good law, but a law that is based on representative research and scientific certainty. Bearing in mind the above, the authors undertook an analysis of what seems to be the cause of significant social doubts as to the actual achievement of the purposes of Regulation 1107/2009, i.e. inclusion of scientific research in the procedure of approval of active substances in plant protection products.

APPROVAL OF ACTIVE SUBSTANCES OF PLANT PROTECTION PRODUCTS

Regulation 1107/2009 foresees a partially decentralized risk assessment process for plant protection products. Placing a plant protection product on the market requires carrying out two procedures - first, it is necessary to approve the active substance of a plant protection product, i.e. substances, including microorganisms, having general or specific action against harmful organisms or on plants, parts of plants or plant products (Regulation 1107/2009, art. 2(2)). Each plant protection product containing an approved substance must then be authorized to each Member State where the plant protection product is intended to be placed on the market (Regulation 1107/2009, art. 33(1)). The European Commission, with the participation of the Member States, is responsible for the evaluation and approval of the active substances of plant protection products. Member States are responsible for the evaluation of plant protection products that are composed of active substances – their main ingredients – and components that are added for various purposes, such as stability and potency – to have them placed on the market in their territory. The active substance approval procedure is described in subsection 2 of Regulation 1107/2009 in art. 7–13. It begins at the application of the manufacturer of the active substance or the association of manufacturers of the active substance, submitted to a Member State (RMS – Rapporteur Member State), for the approval of an active substance

or for an amendment to the conditions of an approval conditions together with the summary and complete dossier or a scientifically reasoned justification for not providing certain parts of those dossiers, demonstrating that the active substance fulfils the approval criteria provided for in Art. 4 of Regulation 1107/2009 (Regulation 1107/2009, art. 7(1)). These criteria concern, inter alia, impact on human health and life, persistence, bioaccumulation, mobility in the environment, toxicity and ecotoxicity. It should be emphasized that the applicant has the right to demand, in accordance with Art. 63, to keep certain information, including certain parts of the dossier confidential, and physically separate that information (Regulation 1107/2009, art. 7(3)). The RMS carries out an independent, objective and transparent assessment of an active substance in the light of current scientific and technical knowledge, and if additional studies or information are needed, the applicant may be required to supply the dossier. The RMS prepares and submits to the Commission a report (draft assessment report), with a copy to the European Food Safety Authority (EFSA), in which it assesses whether an active substance can be expected to meet the approval criteria for active substances provided for in Art. 4 of Regulation 1107/2009 (Regulation 1107/2009, art. 11(2-3)). EFSA circulates to the applicant and the other Member States the draft assessment report it has received from RMS and adopts a conclusion on whether, in the light of current scientific and technical knowledge, an active substance can be expected to meet the approval criteria provided for in Art. 4, and informs the applicant, the Member States and the Commission thereof, and also makes this conclusion available to the public (Regulation 1107/2009, art. 12(1-2)). EFSA also may request additional information, as well as may ask the Commission to consult a Community reference laboratory, designated pursuant to Regulation (EC) No 882/2004 for the purposes of verifying whether the analytical method for the determination of the residues proposed by the applicant is satisfactory and meets the requirements in Art. 29 (1) (g) of this Regulation (Regulation 1107/2009, art. 12(3)). EFSA presents its conclusion to the Commission, which presents a review report and a draft Regulation to the representatives of the Member States within the Standing Committee on the Food Chain and Animal Health, whose members vote on the proposal. Qualified majority vote in favor has the effect of approving the active substance at EU level (Regulation 1107/2009, art. 13(1) and 79(3)). After an active substance has been approved at this level, the applicant may apply for the authorization of individual preparations based on the active substance at the level of the individual Member States where the products are intended to be used.

The complexity of the procedure outlined above is an area for a potential abuse. Moreover, a potential failure in the procedure is not easy to identify, prevent or eliminate. The possibility of concealing anomalies or particular interests in the complexity of the legal system is worrying as something that prima facie appears to be a technical or soft choice can significantly hinder the achievement of the purpose of the legislator – ensuring a high level of protection of human and animal health and the environment.

PRACTICAL PROBLEMS ON THE EXAMPLE OF GLYPHOSATE

To illustrate the key problems of the procedure above, the most appropriate case is glyphosate, which concentrates its imperfections like in a lens. It should be emphasized, however, that the problems described herein with glyphosate can be generalized – they may also emerge in the approval of other active substances.

Although glyphosate is the most widely used herbicide in the world, there is social and scientific uncertainty about the risks it may pose. Given the stringent EU legislation, it may be surprising that peer-reviewed scientific literature shows that plant protection products that have successfully passed the authorization process may have negative effects on humans, animals or the environment (see Bellanger et al., 2015; Stehle & Shulz, 2015; Woodcock & Isaac, 2016; EFSA, 2017; Mostafalou & Abdollahi, 2017; Pesticide Action Network Europe, 2017; Hallmann et al., 2017; Navarrete-Meneses & Perez-Vera, 2019). One of the contentious issues which became apparent during the assessment of the glyphosate was the source of the scientific research on which its assessment was based.

Regulation 1107/2009 places the burden of proof on the applicant. Consequently, the scientific research submitted by the applicants was largely financed by the chemicals industry or was classified as confidential in accordance with Art. 63 of Regulation 1107/2009.

Article 8 of Regulation 1107/2009 contains a catalog with the content of the dossier of the application for approval of an active substance. Although the catalog requires the submission of tests and studies on the active substance, it is not required to submit all test results. This gives an applicant some discretion and the possibility to selectively use publications, data and scientific evidence for risk assessment, which may be detrimental to the completeness of the evidence base on which the evaluation of the active substance is based. Pursuant to Art. 8(5) of Regulation 1107/2009, the applicant in the submitted documentation should include peer-reviewed, publicly available scientific publications, as determined by EFSA, 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. The EFSA guidance provides a definition of scientific peer-reviewed open literature and instructions on how to minimise bias in the identification, selection and inclusion of peer-reviewed open literature in dossiers, according to the principles of systematic review (i.e. methodological rigour, transparency, reproducibility). It states that research should be „as extensive as possible" and that research should be „systematic, transparent and reproducible" in order to „retrieve as many relevant studies as possible". The EFSA Guidance is compatible with existing OECD Guidance documents for the preparation of active substances dossiers (EFSA, 2011).

However, in practice it is noted that peer-reviewed studies in the published scientific literature indicated harmful effects of glyphosate and its commercial formulations, but were not considered in the evaluation of this active substance. For glyphosate, a draft assessment report by the German Federal Institute for Risk Assessment (BfR) was prepared on the basis of 52% (76) studies reported in the peer-reviewed scientific literature, in which authors reported adverse effects from glyphosate exposure. Of these, only 31% are covered in the draft assessment report. These studies often show negative effects of glyphosate use that are not shown in industry funded studies (Pesticide Action Network Europea and Générations Futures, 2014). When evaluating glyphosate, the BfR did not take into account scientific publications showing that glyphosate can cause oxidative stress in cells - a mechanism that can cause DNA damage and is therefore an important risk factor in cancer development. The presumed lack of explanation of this mechanism was presumably an important argument for BfR to conclude that glyphosate is not carcinogenic (Pesticide Action Network Europea and Générations Futures, 2014). Although EFSA identified in its assessment additional peer-reviewed studies that were not presented in the draft assessment report, it considered them to be of minor importance and did not affect the overall assessment (EFSA, 2015). Even if published studies not financed by industry are included in the assessment (in the draft assessment report or in the EFSA peer review process), the adverse effects identified in them may be rejected and excluded by reviewers for reasons that could not justify it upon closer examination (see International Agency for Research on Cancer, 2015) .

The way of selecting studies – establishing their comprehensiveness and representativeness for a given active substance – seems to raise some doubts. One of the criteria for assessing the quality of scientific research is its evaluation in terms of compliance with OECD protocols and the principles of GLP (Good Laboratory Practice). The vast majority of industry testing for registration purposes is carried out following OECD protocols and GLP principles, while independent university studies, conducted in line with the latest scientific knowledge, often do not follow these guidelines. The result is that when they are taken into account in the evaluation, the weight of their values is systematically lowered and they are effectively excluded from the group of independent scientific studies of pesticide risk assessment for reasons that are not relevant for assessing the reliability of such studies (see Krauth et al., 2013; Myers et al., 2009; Kase et al., 2016; Buonsante et al., 2014; Kaltenhäuser et al., 2017). On the other hand, industry research, due to its adherence to OECD protocols and GLP principles, is assessed as sufficiently „reliable" and „relevant" to be used in risk assessment (Ingre-Khans et al., 2019). This may distort the evaluation of the active substance, especially due to the adoption by EFSA of a weighted evidence system. At the same time, it

should be remembered that OECD protocols and GLP principles are not and have never been considered benchmarks of scientific excellence. They were developed following disclosures of widespread industry fraud in testing chemicals (including glyphosate) to provide greater credibility for industry research (Organisation for Economic Cooperation and Development, 2015).

An example of an important study that was rejected by experts during the evaluation of glyphosate by BfR experts due to inadequately applied study quality criteria was the epidemiological study by De Roos et al. (2003) among 3,417 farmers . Moreover, three case-control studies conducted in the 1980s by the National Cancer Institute (United States) showed a relationship between the use of, inter alia, glyphosate (as well as organophosphorus insecticides - coumaphos, diazinon and phonophos, insecticides - chlordane, dieldrin, copper acetoarsenite, and herbicides - atrazine and sodium chlorate) and an increased incidence of non-Hodgkin's lymphoma. The authors of the study confirmed that considering cumulative exposure is important for the precise estimation of specific effects and the assessment of realistic exposure scenarios. The BfR in its draft assessment report gave the study a low reliability score of 3 (i.e. "not reliable"), partly on the basis of alleged errors, the occurrence of which is contested by some scientists (Weber & Burtscher-Schaden, 2019). It is argued that the application of the criteria for assessing the quality of epidemiological studies according to the OECD protocol or GLP principles was not appropriate as these criteria were developed to evaluate data from experimental and ecological toxicological studies and not from epidemiological studies. These test quality criteria may influence the final grade as they are imprecisely defined and therefore difficult to implement in a transparent or consistent manner (Kase et al., 2016). This allows the assessing expert to subjectively overestimate or underestimate the value of the research while giving the impression that he or she is following a rigorous trial evaluation process. This approach results in deficiencies in the reliable and comprehensive evaluation of both industry regulatory tests and peer-reviewed studies from published literature. The EFSA guidelines state that the fact that the test is not conducted in accordance with GLP does not mean that the test is irrelevant, but the EFSA guidelines constitute the so-called soft law and are not mandatory regulations (see EFSA, 2011).

Failure to take into account qualitative studies not carried out according to the OECD protocol or GLP principles is for experts a matter of non-compliance with EFSA guidelines, not a violation of the law. On the other hand, if, for example, a toxicity study describes multiple works with extremely heterogeneous results, then it is common practice to reject studies showing toxicity in favor of finding no toxicity, without giving any reason other than that the results are inconsistent (Clausing, 2017). This is because the toxicity is „false positive" meaning that the toxic effect is being shown when it is not in fact occurring. However, assuming an adverse effect as a false positive and discarding it from the assessment without carefully examining all the evidence may lead to a misjudgment of no toxicity. It should be remembered that existing methodologies in environmental and health sciences to measure adverse effects are themselves provoking false negative results (Gee, 2006) – that is, neglecting the adverse effects even though they exist.

The history of regulatory risk assessment is full of examples of false negative outcomes where early warnings of adverse effects have been dismissed, leading to decades of harmful exposure. In contrast, false alarms, which are situations where regulators have acted with caution but were later found to be unnecessary, turn out to be infrequent. The practice of assuming that adverse reactions reported as false positives in studies without providing scientific justification are apparent in the BfR analyzes of glyphosate. The BfR argued that the findings of malignant lymphomas, kidney tumors, and angiosarcoma in male mice were not related to glyphosate due to inconsistent data (George et al., 2010; EFSA, 2015; RMS Germany, 2015)

However, the BfR did not provide any analysis to support this argument and ignored study differences such as exposure time and mouse strain, which would naturally lead to variability in the results. Rejecting adverse effects

because they are not consistent across many studies encourages industry to continue research until one shows any effect, falsifying the assessment result.

CONCLUSION

It is not the authors' intention to make lawyers enter the research area of representatives of exact sciences and explain how to conduct their research. However, good law requires to be based on scientific certainty, and the objectivity of the legislator's choices can not be apparent.

Various alternatives were considered during the glyphosate dispute. The most radical solution in assessing the safety of substances was to adopt as the basis for the assessment only published peer-reviewed literature and independent research entrusted to state entities, thus excluding, by default, studies generated by private entities (see European Citizens' Initiative, n.d.). A less radical approach was to strengthen public control over the design and conduct of laboratory tests (e.g. through audits and the establishment of a register of all commissioned tests) and to ensure a balance between the importance of private and public research in risk assessment (European Parliament, 2017).

This article shows the flaws in the approval procedure for active substances that may lead to the placing of hazardous plant protection products on the EU market. The assessment of the controversial glyphosate was used to illustrate the key concerns related to this procedure. The glyphosate case shows that the shortcomings in the placing of plant protection products on the market are systemic in nature and they are not individual errors or frauds. The high market value of this product, projected at $ 9.91 billion by 2022 (Marketsandmarkets, 2020), has undoubtedly contributed to exploitation of the existing loopholes in the system, but the same shortcomings could be replicated with other plant protection products. Guidance documents should be revised to reflect best scientific practice, and their standards should be enforced, in particular to ensure that there is no doubt about the objectivity of the literature review. Providing a methodology for a comprehensive research search strategy and clarifying the criteria for their eligibility can be a guarantee that all relevant studies will be taken into account when reviewing the evidence. Unclear criteria mean that some works may be omitted and thus distort the results of the assessment. The use of validated research critical appraisal tools will ensure that each test will be assessed against the same standard, regardless of its results. This will help prevent the audit's value from being deprecated on the basis of questionable criteria. Methods for critical evaluation of studies have developed in the 20 years since the publication of the Klimisch criteria, which are now at the core of the evaluation of the reliability of studies (Woodruff & Sutton, 2014).

Regulatory authorities should be required to ensure that all available and published studies are reviewed when assessing plant protection products. Assuming this approach would be in line with precautionary principle, that was expressed in Art. 1(4) of Regulation 1107/2009, according to which the provisions of the Regulation are underpinned by the precautionary principle in order to ensure that active substances or products placed on the market do not adversely affect human or animal health or the environment. Communication from the Commission on the precautionary principle assumes that potentially dangerous effects resulting from a phenomenon, product or process have been identified, and scientific assessment does not allow to determine the risk with sufficient certainty (European Commission, 2000, point 4). These conditions for the application of the precautionary principle are met in the context of placing plant protection products on the market. The implementation of the precautionary approach should start with a scientific assessment carried out as fully as possible, identifying as far as possible the degree of scientific uncertainty at each stage (European Commission, 2000, point 4). Assessors should conduct research as thoroughly as possible, using appropriate methodology, in relation to the considered risk (de Sadeleer, 2006, p. 156). Another element of the precautionary principle is, according to point 5.1 of Communication from the Commission on the precautionary principle, the emergence of a „potential risk" associated with a given phenomenon, product or process as a consequence of scientific assessment; this Communication defines potential risks as „legitimate cause for concern about potentially dangerous effects" (point 3). Risk management involves

reducing that risk to an acceptable level (de Sadeleer, 2006, p. 159), e.g. by approving active substances in plant protection products or granting authorizations for the use of plant protection products .

Finally, the authors would like to point out that the „quality" of studies should be assessed by the likelihood of systematic bias in the results („risk of bias") and the extent to which they provide a representative research model for the risks to human health or the environment from exposure ¬– rather than by assessing compliance with GLP principles or the OECD protocol.

ACKNOWLEDGEMENTS

The work was supported by the National Science Centre, Poland, under research project no. 2021/41/N/HS5/01316.

REFERENCES

Antoniou, M., Habib, M. E. E. M., Howard, C. V., Jennings, R. C., Leifert, C., Nodari, R. O., Robinson, C., & Fagan, J. (2011). *Roundup and Birth Defects: Is the Public Being Kept in the Dark?*. Earth Open Source. http://earthopensource.org/earth-open-source-reports/roundup-and-birth-defects-is-the-public-being-kept-in-the-dark/.

Bellanger, M., Demeneix, B., Grandjean, P., Zoeller, R. T., & Trasande, L. (2015). Neurobehavioral Deficits, Diseases, and Associated Costs of Exposure to Endocrine-Disrupting Chemicals in the European Union. *The Journal of Clinical Endocrinology & Metabolism, 100*(4), 1256–1266. https://doi.org/10.1210/jc.2014-4323.

Buonsante, V.A., Muilerman, H., Santos, T., Robinson, C., & Tweedale, A. C. (2014). Risk Assessment's Insensitive Toxicity Testing May Cause It to Fail. *Environmental Research, 135*, 139-47. https://doi:10.1016/j.envres.2014.07.016.

Clausing, P. (2017). *Glyphosate and Cancer: Authorities Systematically Breach Regulations*. GLOBAL 2000. Available at: http://www.gmwatch.org/files/GLO_02_Glyphosat_EN.pdf.

De Roos, A.J. et al. (2003). Integrative assessment of multiple pesticides as risk factors for non-Hodgkin's lymphoma among men. *Occupational and Environmental Medicine, 60*(9), 11e–111. https://doi.org/10.1136/oem.60.9.e11.

de Sadeleer, N. (2006). The Precautionary Principle in EC Health and Environmental Law. *European Law Journal 12*(2), 139-172. https://doi.org/10.1111/j.1468-0386.2006.00313.x.

European Chemicals Agency (ECHA). (2017). Opinion of the Committee for Risk Assessment proposing harmonised classification and labelling of glyphosate (ISO); N-(phosphonomethyl)glycine. (EC Number: 213-997-4; CAS Number: 1071-83-6). Available at: https://echa.europa.eu/documents/10162/2f8b5c7f-030f-5d3a-e87e-0262fb392f38.

European Citizens' Initiative (n.d.). Ban Glyphosate and Protect People and the Environment from Toxic Pesticides. Available at: http://ec.europa.eu/citizens-initiative/public/initiatives/successful/details/2017/000002.

European Commission. (2000). Communication from the Commission on the Precautionary Principle, COM/2000/0001 final, available at: https://eur-lex.europa.eu/legal-content/EN/TXT/HTML/?uri=CELEX:52000DC0001&from=EN.

European Commission. (2017). Communication from the Commission on the European Citi-zens' Initiative, Ban glyphosate and protect people and the environment from toxic pesticides, C(2017) 8414 final, Strasbourg, available at: https://ec.europa.eu/food/system/files/2017-12/pesticides_glyphosate_eci_final.pdf.

European Food Safety Authority (EFSA). (2011). Submission of scientific peer- reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009. EFSA Journal, 9(2). https://doi.org/10.2903/j.efsa.2011.2092.

European Food Safety Authority (EFSA). (2015). Conclusion on the peer review of the pesticide risk assessment of the active substance glyphosate. *EFSA Journal, 13*(11). https://doi.org/10.2903/j.efsa.2015.4302.

European Food Safety Authority (EFSA). (2017). Pesticide Residues in Food: Risk to Consumers Remains Low. Available at: http://www.efsa.europa.eu/en/press/news/170411.

European Parliament. (2017). Renewing the Approval of the Active Substance Glyphosate, European Parliament resolution of 24 October 2017 on the draft Commission implementing regulation renewing the approval of the active substance glyphosate in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market, and amending the Annex to Implementing

Regulation (EU) No 540/2011 (D053565-01 – 2017/2904(RSP)), P8_TA(2017)0395. Available at: https://www.europarl.europa.eu/doceo/document/TA-8-2017-0395_EN.html.

European Parliament. (2017). Sustainable Use of Pesticides, European Parliament resolution of 12 February 2019 on the implementation of Directive 2009/128/EC on the sustainable use of pesticides. (2017/2284(INI)), P8_TA-PROV(2019)0082. Available at: https://www.europarl.europa.eu/doceo/document/TA-8-2019-0082_EN.html.

Gee, D. (2006). Late Lessons from Early Warnings: Toward Realism and Precaution with Endocrine-Disrupting Substances. *Environmental Health Perspectives, 114*(Suppl 1), 152–160. https://doi.org/10.1289/ehp.8134.

George, J., Prasad, S., Mahmood, Z., & Shukla, Y. (2010). Studies on glyphosate-induced carcinogenicity in mouse skin: A proteomic approach. *Journal of Proteomics, 73*(5), 951–964. https://doi.org/10.1016/j.jprot.2009.12.008.

Hallmann, C.A., Sorg, M., Jongejans, E., Siepel, H., Hofland, N., Schwan, H., Stenmans, W., Müller, A., Sumser, H., Hörren, T., Goulson, D., & de Kroon, H. (2017). More than 75 percent decline over 27 years in total flying insect biomass in protected areas. *PLOS ONE, 12*(10), e0185809. https://doi.org/10.1371/journal.pone.0185809.

Ingre-Khans, E., Ågerstrand, M., Beronius, A., & Rudén, C. (2019). Reliability and relevance evaluations of REACH data. *Toxicology Research, 8*(1), 46–56. https://doi.org/10.1039/c8tx00216a.

International Agency for Research on Cancer. (2015). *IARC Monographs Volume 112: Evaluation of Five Organophosphate Insecticides and Herbicides*. World Health Organization. Available at: https://monographs.iarc.fr/iarc-monographs-on-the-evaluation-of-carcinogenic-risks-to-humans-4/.

Kaltenhäuser, J., Kneuer, C., Marx-Stoelting, P., Niemann, L., Schubert, J., Stein, B., & Solecki, R. (2017). Relevance and reliability of experimental data in human health risk assessment of pesticides. *Regulatory Toxicology and Pharmacology, 88*, 227–237. https://doi.org/10.1016/j.yrtph.2017.06.010.

Kase, R., Korkaric, M., Werner, I., & Ågerstrand, M. (2016). Criteria for Reporting and Evaluating ecotoxicity Data (CRED): comparison and perception of the Klimisch and CRED methods for evaluating reliability and relevance of ecotoxicity studies. *Environmental Sciences Europe, 28*(1). https://doi.org/10.1186/s12302-016-0073-x.

Krauth, D., Woodruff, T. J., & Bero, L. (2013e). Instruments for Assessing Risk of Bias and Other Methodological Criteria of Published Animal Studies: A Systematic Review. *Environmental Health Perspectives, 121*(9), 985–992. https://doi.org/10.1289/ehp.1206389.

MarketsandMarkets. (2020). Glyphosate Market – Global Forecast to 2022. Available at: https://www.marketsandmarkets.com/Market-Reports/glyphosate-market-8522593.html.

Mostafalou, S., & Abdollahi, M. (2016). Pesticides: an update of human exposure and toxicity. *Archives of Toxicology, 91*(2), 549–599. https://doi.org/10.1007/s00204-016-1849-x.

Myers, J.P., et. al. (2009). Why Public Health Agencies Cannot Depend on Good Laboratory Practices as a Criterion for Selecting Data: The Case of Bisphenol A. *Environmental Health Perspectives, 117*(3), 309–315. https://doi.org/10.1289/ehp.0800173.

Navarrete-Meneses, M.D.P., & Pérez-Vera, P. (2019). Pyrethroid pesticide exposure and hematological cancer: epidemiological, biological and molecular evidence. *Reviews on Environmental Health, 34*(2), 197–210. https://doi.org/10.1515/reveh-2018-0070.

Organisation for Economic Cooperation and Development (OECD). (2015). General Questions and Answers Concerning OECD Principles of Good Laboratory Practice (GLP) and Mutual Acceptance of Data (MAD). Available at: https://tinyurl.com/yy8czckz.

Pesticide Action Network Europe and Générations Futures. (2014). Missed and Dismissed. Available at: http://www.pan-europe.info/old/Resources/Reports/PANE%20-%202014%20-%20Missed%20and%20dismissed.pdf.

Pesticide Action Network Europe. (2017). How Many Pesticides Did You Eat Today? Plenty According to European Food Safety Authority. Available at: https://www.pan-europe.info/press-releases/2017/04/how-many-pesticides-did-you-eat-today-plenty-according-european-food-safety.

Pesticide Action Network Germany and Testbiotech. (2015). Does Glyphosate Cause Cancer? Important Gap in German Risk Assessment. Available at: https://tinyurl.com/y4wxl6dd.

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.

RMS Germany (German Federal Institute for Risk Assessment, BfR). (2015). Renewal Assessment Report: Glyphosate Addendum 1 to RAR: Assessment of IARC Monographs Volume 112 (2015): Glyphosate. Available at: http://www.gmwatch.org/files/Renewal_Assessment_Report_Glyphosate_Addendum1_RAR.pdf.

Stehle, S. & Schulz, R. (2015). Pesticide Authorisation in the EU – environment unprotected? *Environmental Science and Pollution Research International, (22)*24, 19632-47. https://doi.org/10.1007/s11356-015-5148-5.

Weber, S., & Burtscher-Schaden, H. (2019). *Detailed Expert Report on Plagiarism and Superordinated Copy Paste in the Renewal Assessment Report (RAR) on Glyphosat*. Available at: https://left.eu/content/uploads/2019/01/Expertise-RAR-Glyphosat-2018-01-11-1.pdf.

Woodcock, B.A., Isaac, N.J.B., Bullock, J.M., Roy, D.B., Garthwaite, D.G., Crowe, A., & Pywell, R.F. (2016). Impacts of neonicotinoid use on long-term population changes in wild bees in England. *Nature Communications, 7*(1). https://doi.org/10.1038/ncomms12459.

Woodruff, T.J., & Sutton, P. (2014). The Navigation Guide Systematic Review Methodology: A Rigorous and Transparent Method for Translating Environmental Health Science into Better Health Outcomes. *Environmental Health Perspectives, 122*(10), 1007–1014. https://doi.org/10.1289/ehp.1307175.