

Appendix 2 – Significant New Information on the Environmental and Health Effects of Glyphosate and Glyphosate-based Herbicides

Introduction

Currently, there are well over 50,000 peer-reviewed articles evaluating the effects of glyphosate on both the environment and human health. To curate the wealth of available scientific evidence into a manageable submission, we searched the Google Scholar database using the search terms: glyphosate, toxicity, risk assessment, and systematic review. Next, we used the systematic reviews to identify additional articles across a range of topics. We then distilled the search results to key representative studies which demonstrate the current state of knowledge in the academic literature on the effects of glyphosate and glyphosate-based herbicides (GBHs). In doing so, we prioritised:

- Independent science
- Systematic reviews and meta-analysis studies. Articles that use the PRISMA methodology were preferred.
- Peer-reviewed academic papers from journals ranked in the top quartile of their field based on their impact score. Journals in the top 5% of their field were preferred.
- More recent articles and articles from the last 5 years where possible.

Where possible, we have also focussed on including scientific studies of the real-world impacts of glyphosate and GBHs. Such studies share a number of characteristics. Inter alia, they examine:

- The role of co-formulants
- Real world conditions, including interaction with existing environmental stressors
- Lethal and sub-lethal effects
- Community as well as individual impacts
- Long-term as well as short-term impacts

These independent scientific studies typically found strong negative impacts of GBH formulations in real-world conditions. This stands in contrast to non-independent lab focussed studies of the lethal effects of single doses of glyphosate on representative species. Furthermore, an independent expert assessment of the genetic toxicology studies submitted to the EU regulators found that only a small percentage of studies were reliable from a methodological standpoint (Nersesyan and Knasmueller 2021).¹

The independent scientific studies we present here have been organised into a number of categories:

- Exposure pathways
- Terrestrial ecotoxicity
- Aquatic ecotoxicity
- Co-formulants
- Human health impacts

¹ Nersesyan & Knasmueller. 2021. Evaluation of the scientific quality of studies concerning genotoxic properties of glyphosate. Available at https://usrtk.org/wp-content/uploads/2021/06/Comments-concerning-GLY_25.03.21-with-signatures-1.pdf.

Pathways to exposure

Initial risk assessments in the 1970s assumed glyphosate would be applied before crop germination or post-harvest so the residues in food would be low; however, current use includes pre-harvest desiccant on grains and certain vegetables, which changes the dietary exposure (Myers et al. 2016). Early studies also indicated that glyphosate had no impact on vertebrates; however, in the past 20 years, several vertebrate pathways have been identified, including hepatorenal damage and endocrine disruption (Myers et al. 2016). Finally, until recently, the persistence of glyphosate in the environment was considered low; however, recent studies have found that its persistence is dependent on soil type (Battisti et al. 2021; Myers et al. 2016). The following studies document how glyphosate persists in non-negligible amounts in the environment and in combination with other herbicides, pesticides, antibiotics, and fertilisers. These articles stress that toxicology studies need to be done in real-world conditions due to the synergistic effect of multiple chemicals found in soils.

1- Summary of the state of knowledge

Myers, John Peterson, et al. "Concerns over Use of Glyphosate-Based Herbicides and Risks Associated with Exposures: a Consensus Statement." *Environmental Health*, vol. 15, no. 19, 2016, p. 19–, <https://doi.org/10.1186/s12940-016-0117-0>.

Significance

- This article is a broad summary of the current knowledge on application, accumulation, exposure, and impacts as of 2016. Below are only a few of its many important results and conclusions:

Results

- Residual glyphosate and its metabolite AMPA have been found in crops at harvest and in food being sold.
- There is surface runoff and groundwater infiltration of GBHs, which contaminate drinking water and washing water.
- The half-life of glyphosate in soil and water is longer than previously known, depending on soil composition. This has led to long-term incremental build-up of contamination of surface water, ground water, and soil.
- Glyphosate and GBHs disrupt endocrine-signalling systems in vitro, including multiple steroid hormones, which play vital roles in the biology of vertebrates.
- The increase in glyphosate-resistant weeds has led to a combination of herbicides being used, which increases contamination and environmental interactions.

Conclusions

- Toxicology studies need to use up-to-date science and examine chronic environmentally relevant doses of glyphosate in conjunction with other insecticides, fungicides, and adjuvants as found in the environment.
- A fresh and independent examination of GBH toxicity should be undertaken, and that this re-examination be accompanied by systematic efforts by relevant agencies to monitor GBH levels in people and in the food supply, none of which are occurring today.

2- Pesticide mobility and accumulation

Maggi, Federico, et al. "Agricultural Pesticide Land Budget and River Discharge to Oceans." *Nature (London)*, 2023, <https://doi.org/10.1038/s41586-023-06296-x>.

Significance

- *Nature* is the top scientific journal in the world. This is a 2023 article.
- Investigated how pesticides move and accumulate in the environment.

Results

- It found that 82% of all pesticide active substances are biologically degraded, 10% remain as a residue in the soil and 7.2% leach below the root zone.
- Glyphosate was the primary pesticide found on land and was the second most common pesticide in rivers and river outlets.

Conclusion

- Non-negligible quantities of glyphosate remain in soils and surface waters.
- Glyphosate exists in the environment with numerous other pesticides and herbicides.

3- Mixtures of pesticide residues

Silva, Vera, et al. "Pesticide Residues in European Agricultural Soils – A Hidden Reality Unfolded." *The Science of the Total Environment*, vol. 653, 2019, pp. 1532–45, <https://doi.org/10.1016/j.scitotenv.2018.10.441>.

Significance

- This review article documents the agricultural soil contamination by pesticide residues throughout Europe.

Results

- Glyphosate is present in >10% of soil samples.
- Mixtures of pesticides in the soil were typical.

Conclusions

- It is critical to do toxicity assessments for glyphosate with a mixture of pesticide residuals that are found in soil.

Terrestrial ecosystems

Toxicology studies are typically completed in the lab using the glyphosate in isolation and a focus on lethal effects. However, there is strong evidence that GBH formulations in the actual environment have a negative impact on terrestrial organisms due to the complexities of real-world systems that include other pesticides and agricultural products, and they have important sub-lethal effects on both individuals and community structure.

1- Terrestrial ecotoxicity

Klátyik, Szandra, et al. "Terrestrial Ecotoxicity of Glyphosate, Its Formulations, and Co-Formulants: Evidence from 2010–2023." *Environmental Sciences Europe*, vol. 35, no. 1, 2023, pp. 1–29, <https://doi.org/10.1186/s12302-023-00758-9>.

Significance

- This article is an expansive review of the 19,500 scientific articles from 2010 - June 2023 concerning terrestrial organisms.

Results

- There is evidence that glyphosate has a negative impact on soil microbiota, non-target plants, terrestrial invertebrates (including nematodes, springtails, spiders, bees, snails, earthworms), and terrestrial vertebrates (ground dwelling and birds).
- The evidence of negative effects is often conflicting because many studies ignore the complexity of real-world systems. Most studies consider only the short-term effects of a single application of glyphosate to a single 'representative' species, and many of these studies are done in the lab under controlled conditions.
- There are many knowledge gaps on the effects of glyphosate and GBHs on terrestrial non-target organisms and ecosystems.
- Real world circumstances that are often ignored include:
 - Interactions with supposedly "inert" co-formulants which often increase toxicity of glyphosate by increasing solubility, adsorption, and absorption.
 - Interactions with other pesticides and agrochemicals.
 - Changes in ecosystems and trophic interactions due to varying impact of glyphosate of different species.
 - Impact of changing soil microbiota compositions and its effect on plant health.
 - Chronic exposure to long-term use of glyphosate and how this varies by generation length of species.
 - Impact on the millions of species that are not classified as 'representative species'.
 - Indirect effects on invertebrate and vertebrates through the impact of glyphosate on bacterial and fungal species (e.g., gut bacteria).

Conclusions

- The authors argue that given these knowledge gaps, the precautionary principle should be invoked and glyphosate removed from the market.

2-Invertebrate and vertebrate animals

Gill, Jatinder Pal Kaur, et al. "Glyphosate Toxicity for Animals." *Environmental Chemistry Letters*, vol. 16, no. 2, 2018, pp. 401–26, <https://doi.org/10.1007/s10311-017-0689-0>.

Significance

- This is a summary article of the impact of glyphosate throughout the animal kingdom, from unicellular to multicellular organisms, including humans.

Results

- Glyphosate negatively impacts the animal kingdom, including bacteria, unicellular organisms, fungus, molluscs, crustaceans, insects, echinoderms, fish, amphibians, reptiles, birds, and humans. Glyphosate decreases the rate of reproduction of earthworms and causes DNA damage.

- Glyphosate reduces the egg laying capacity of snails and sea urchins and negatively impacts the hatching process.
- Glyphosate decreases the growth of mycorrhizal fungus and changes the community structure in rhizospheric microbial communities.

Conclusions

- Glyphosate has lethal and sub-lethal effects in almost all groups within the animal kingdom.

2- Bee meta-analysis

Battisti, Lucas, et al. "Is Glyphosate Toxic to Bees? A Meta-Analytical Review." *The Science of the Total Environment*, vol. 767, 2021, p. 145397–, <https://doi.org/10.1016/j.scitotenv.2021.145397>.

Significance

- Many studies report conflicting results regarding the effect of glyphosate and GBH formulations on bees. Thus, this meta-analysis of 34 experimental studies uses statistical methods to draw overarching conclusions.

Results

- Glyphosate is considered toxic to bees.
- Glyphosate and GBH formulations are lethal to bees when ingested or through contact at ecologically relevant doses (those found in the environment) or doses recommended by the manufacturers.
- Glyphosate has multiple sublethal effects that impact colony health– it reduces the biodiversity of microorganisms in the bee microbiota, makes them more susceptible to pathogens or malnutrition, impairs cognitive ability including memory, impairs development in the larval stage, and impacts gene expression and enzymatic alterations.

Conclusions

- Glyphosate is implicated in the worldwide population decline of bees and the phenomenon of colony collapse disorder.

3- Bee thermoregulation

Weidenmüller, Anja, et al. "Glyphosate Impairs Collective Thermoregulation in Bumblebees." *Science (American Association for the Advancement of Science)*, vol. 376, no. 6597, 2022, pp. 1122–26, <https://doi.org/10.1126/science.abf7482>.

Significance

- *Science* is one of the top science journals in the world. This is a 2022 study.
- Evaluated community effects in non-ideal real-world scenarios.

Results

- Glyphosate had strong sublethal effects on individual bees.
- When colonies were well-fed, no effects of glyphosate were seen.
- When colonies were resource stressed (underfed at a level often seen in wild colonies), glyphosate-treated colonies struggled to maintain brood temperatures high enough to allow proper brood incubation, lowering colony growth and colony fitness.

Conclusions

- Glyphosate threatens bumblebees not only indirectly by reducing the availability of wildflowers but also directly by impairing a key collective behaviour -- the colony's

ability to maintain its brood at beneficial temperatures during periods of limited resource availability.

- It is critical to identify appropriate metrics to evaluate impacts of glyphosate. Lethal effects may be easy to study but nonlethal alterations to behaviour are critical to understanding the true impact of glyphosate.
 - It is critical to evaluate glyphosate in a natural setting where other stressors are common. Standard testing procedures assess toxicity on well-fed, parasite-free individuals. In these ideal conditions, harmful but nonlethal effects can be easily overlooked.
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Aquatic Ecosystems

Glyphosate is transported into water ways through leaching, surface runoff, direct spray, or drift. Although the half-life in water can be short, it is also dependent on temperature, pH, solar radiation, and microbial activity (Brovini et al. 2021), and can exist in aquatic environments for 45-60 days (Lopes et al. 2022). In addition, AMPA, a metabolite of glyphosate can persist for much longer, up to 958 days (Lares et al. 2022) and has its own lethal and sublethal effects on aquatic organisms.

1- Concentration and impact

Brovini, Emilia Marques, et al. "Glyphosate Concentrations in Global Freshwaters: Are Aquatic Organisms at Risk?" *Environmental Science and Pollution Research International*, vol. 28, no. 43, 2021, pp. 60635–48, <https://doi.org/10.1007/s11356-021-14609-8>.

Significance

- This is a systematic review using the PRISMA methodology that summarised in situ concentrations of glyphosate in freshwater systems in 21 countries and the impact of these concentrations on aquatic life and ecosystems.

Results

- Glyphosate concentrations in freshwater pose a moderate to high risk in 95% of the countries in the study, reaching maximum concentrations far exceeding regulations – 100 to 1000 times levels that can cause adverse effects to aquatic organisms.
- The articles reviewed found that glyphosate concentrations below regulatory limits still pose a high risk to aquatic organisms.
- As the glyphosate molecule contains phosphorous, glyphosate use can lead to eutrophication.

Conclusions

- Even concentrations below legal limits are a risk to aquatic organisms.
- The authors strongly recommend regulatory changes to ensure maximum acceptable values are monitored, to protect non-target species, and to guarantee water quality.

2- Freshwater environments

Annett, Robert, et al. "Impact of Glyphosate and Glyphosate-Based Herbicides on the Freshwater Environment." *Journal of Applied Toxicology*, vol. 34, no. 5, 2014, pp. 458–79, <https://doi.org/10.1002/jat.2997>.

Significance

- This review article evaluates all components of risk of glyphosate, including exposure, cellular responses, and toxicity to aquatic organisms.

Results

- Bioaccumulation may be greater than predicted from the low log K_{ow} value because co-formulants can increase permeability into animal cells.
- Glyphosate can induce oxidative stress, genotoxicity, and acetylcholinesterase inhibition in certain species.
- There is evidence of acute and chronic toxicity in microorganisms, invertebrates, fish, and amphibians, and there is evidence that differences in individual susceptibility can lead to changes in ecosystems.

Conclusions

- Sensitivity to glyphosate and its formulations is highly species specific. Often there is a greater difference between the sensitivity of two related species than between species with vast taxonomic separation.
- Across most phyla, studies have shown that the surfactant portion of the glyphosate formulation is the primary source of toxicity.

3- Fish Behaviour

Lopes, Andressa Rubim, et al. "Effects of the Herbicide Glyphosate on Fish from Embryos to Adults: a Review Addressing Behavior Patterns and Mechanisms Behind Them." *Aquatic Toxicology*, vol. 251, 2022, pp. 106281–106281, <https://doi.org/10.1016/j.aquatox.2022.106281>.

Significance

- This is a broad review article summarising the impact of glyphosate at environmentally relevant levels on the behaviour of fish from embryonic to adult life stage, and its impact on the biochemical and physiological pathways.

Results

- Glyphosate and its formulations have a strong negative impact on behaviours of fish in different life stages, negatively impacting swimming, escaping, foraging, and mating.
- Glyphosate negatively impacts energy imbalance, stress responses, physiological function, and endocrine function in fish.

Conclusions

- Changes in fish behaviour caused by glyphosate reduce individual fitness and may lead to population decline.

4- Invertebrates

Lares, Betsabé Ailén, et al. "Effects of Glyphosate on Cladocera: A Synthetic Review." *Aquatic Toxicology*, vol. 249, 2022, pp. 106232–106232, <https://doi.org/10.1016/j.aquatox.2022.106232>.

Significance

- This is a synthetic review paper focusing on the impact of both glyphosate and its metabolite (AMPA) on the water flea, which is often used in standardised toxicity tests.

Results

- Commercial formulations were 77 times more lethal than glyphosate in isolation.
- Glyphosate caused decreased fecundity, increased number of aborted eggs, reduced hatch size, reduced size of hatchlings, delayed hatching, and delayed age of first reproduction.

Conclusion

- Water fleas exposed to glyphosate use their energy budget to survive at the expense of reproduction and growth.
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Co-formulants

Although glyphosate is typically studied in isolation, there is extremely strong evidence that its co-formulants and GBH formulations are more toxic than glyphosate alone. This is because the co-formulants can have their own toxicity, but also because they enhance the toxicity of glyphosate by facilitating the uptake of glyphosate into cells and increasing the uptake of environmental pollutants (Mesnage et al. 2015). The 'inactive' ingredients in the formulations are not inactive, but because they are considered 'commercial in confidence' ingredients are not typically listed and thus are difficult to study.

1 - Toxicity of formulations

Mesnage, R., et al. "Potential Toxic Effects of Glyphosate and Its Commercial Formulations Below Regulatory Limits." *Food and Chemical Toxicology*, vol. 84, 2015, pp. 133–53, <https://doi.org/10.1016/j.fct.2015.08.012>.

Significance

- This review article summarised what is known about the animal and human impacts of glyphosate formulations at toxicity levels below that permitted by regulators.

Results

- Liver and kidneys are clearly affected at doses lower than regulatory limits.
- Glyphosate formulations were found to be more toxic than glyphosate alone in in-vitro studies of various mammal species in almost all peer-reviewed literature.
- Most formulations have been incompletely tested and lack both chronic toxicity tests and information about reproductive, neurodevelopmental, and transgenerational effects.

Conclusion

- Co-formulant toxicity brings into question the use of glyphosate in isolation in chronic tests used for regulatory approval.

2- Toxicity of individual co-formulants

Defarge, N., et al. "Toxicity of Formulants and Heavy Metals in Glyphosate-Based Herbicides and Other Pesticides." *Toxicology Reports*, vol. 5, 2018, pp. 156–63, <https://doi.org/10.1016/j.toxrep.2017.12.025>.

Significance

- This study compared the cytotoxicity of GBH formulations, their individual co-formulants, heavy metal contaminants, and glyphosate alone.

Results

- GBH formulations contain 10-20% co-formulants, which are mostly petroleum-based oxidised molecules.
- GBH formulations were 3 to 358 times more toxic than glyphosate alone. Glyphosate alone is less toxic than any formulant or any formulation.
- 11 of the 14 tested commercially available GBH formulations were heavily contaminated with heavy metals, including arsenic, chromium, nickel, lead, and cobalt (5 to 62 times the permitted level), which accumulate in the environment because they do not break down.
- The authors state that heavy metals are either accidentally added due to the manufacturing process of the co-formulants or intentionally added as nanoparticles.

Conclusions

- It is only a regulatory directive that differentiates between "active ingredients" and "inert compounds". This distinction has no demonstrated toxicological basis.
- Toxicity assessments protocols need to be updated.

Human Health

There has been a lot of controversy over the effect of glyphosate on humans since the IARC 2015 report² that recognised glyphosate as a probable carcinogen.

In 2016, EPA commissioned a report by Dr Wayne Temple "Review of the Evidence Relating to Glyphosate and Carcinogenicity" in response to the IARC report. Contrary to the IARC, this sole author report concluded that "– based on a weight of evidence approach, taking into account the quality and reliability of the available data – glyphosate is unlikely to be genotoxic or carcinogenic to humans and does not require classification under HSNO as a carcinogen or mutagen." The report was criticised by a number of national and international experts following publication.³

Since the publication of the IARC report and the EPA response, unsealed litigation documents have revealed that a number of the studies purportedly demonstrating a lack of genotoxicity (and referred to in EPA's 2016 report) were substantially authored or co-

² International Agency for Research on Cancer (IARC), Volume 112: Some organophosphate insecticides and herbicides: tetrachlorvinphos, parathion, malathion, diazinon and glyphosate. IARC Working Group. Lyon; 3–10 March 2015. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans.

³https://d3n8a8pro7vhm.cloudfront.net/beachheroes/pages/11445/attachments/original/1582249187/NZ_Public_Health_-_Glyphosate_and_Cancer_2017.pdf?1582249187

authored by employees of Monsanto without transparent acknowledgment of that fact. There have been calls to retract these studies⁴, including from the journal's publisher Taylor and Francis on the basis of clear breaches of research integrity standards.⁵

Since 2016, there is also strengthened evidence that glyphosate is a probable human carcinogen. In 2021, the French Institute for Health and Medical Research (INSERM) determined that there was a link between glyphosate exposure and the risk of developing non-Hodgkin lymphoma.⁶ There is also significant emerging evidence of neurodevelopmental toxicity effects and endocrine disruption.

1- Nervous system

Costas-Ferreira, Carmen, et al. "Toxic Effects of Glyphosate on the Nervous System: A Systematic Review." *International Journal of Molecular Sciences*, vol. 23, no. 9, 2022, p. 4605–, <https://doi.org/10.3390/ijms23094605>.

Significance

- This is a systematic review using the PRISMA methodology of literature from 2013-2022. It evaluated the impacts of both pure glyphosate and GBH formulations at doses under the NOAEL level.

Results

- The doses of glyphosate that produce neurotoxic effects are lower than regulatory limits.
- "It is unequivocal" that glyphosate exposure alters the structure and function of nervous systems in humans, rodents, fish, and invertebrates.

Conclusions

- GBH formulations have greater toxicity than glyphosate alone.
- Neurological impacts found in this study could be due to other components or the synergy between the co-formulants and glyphosate.

2- Endocrine System

Muñoz, Juan P., et al. "Glyphosate and the Key Characteristics of an Endocrine Disruptor: A Review." *Chemosphere (Oxford)*, vol. 270, 2021, p. 128619–, <https://doi.org/10.1016/j.chemosphere.2020.128619>.

Significance

- This is a systematic review of the epidemiological literature up to 2020 that evaluated glyphosate as an endocrine disruptor on both human and animal models.

Results

- Glyphosate satisfies 8 of the 10 key characteristics of endocrine-disrupting chemicals, including favouring hormonal receptor activity and negatively impacting estrogen and testosterone production.

⁴ https://www.biologicaldiversity.org/news/press_releases/2017/pesticides-10-12-2017.php

⁵ <https://usrtk.org/monsanto-roundup-trial-tracker/emails-reveal-science-publisher-found-papers-on-herbicide-safety-should-be-retracted-due-to-monsanto-meddling/>

⁶ Inserm. 2021. Glyphosate and glyphosate-based herbicides. Extract from « Pesticides and health effects: New data ». Collection Expertise collective. Available at <https://www.inserm.fr/wp-content/uploads/inserm-expertiscollective-pesticides2021-glyphosate-en.pdf>

- In animal models, glyphosate is associated with embryo loss and birth defects such as retardation of the foetal skeleton and differentiation of the uterus.
- Women exposed to glyphosate have reduced fecundity and an increased risk of late miscarriage.

Conclusions

- There is strong evidence that glyphosate alters hormonal activity, inducing defects in both the reproductive process and offspring.

3- Carcinogenicity

Rana, Imaan, et al. "Mapping the Key Characteristics of Carcinogens for Glyphosate and Its Formulations: A Systematic Review." *Chemosphere (Oxford)*, 2023, pp. 139572–139572, <https://doi.org/10.1016/j.chemosphere.2023.139572>.

Significance

- This study used the most up to date literature (2023) and used the PRISMA methodology to avoid bias. It evaluated the impacts of both pure glyphosate and GBH formulations.

Results

- There is strong evidence that glyphosate is a probable human carcinogen, and that it is genotoxic, causes epigenetic alterations, induces oxidative stress, induces chronic inflammation, and modulates receptor-mediated effects.

Conclusions

- GBH formulations have a higher genotoxic effect compared to glyphosate alone.
- The evidence that glyphosate and GBH formulations are carcinogenic has become stronger since IARC's initial evaluation of cancer risk in 2015.

4- Non-Hodgkin lymphoma

Zhang, Luoping, et al. "Exposure to Glyphosate-Based Herbicides and Risk for Non-Hodgkin Lymphoma: A Meta-Analysis and Supporting Evidence." *Mutation Research. Reviews in Mutation Research*, vol. 781, 2019, pp. 186–206, <https://doi.org/10.1016/j.mrrev.2019.02.001>.

Significance

- This article is a meta-analysis using the PRISMA methodology that evaluates the carcinogenicity of GBHs. It evaluated all published human studies including the most recent data from the Agricultural Health Study of 89,000 farmers and their spouses in the USA.

Results

- The meta-analysis showed that individuals exposed to GBHs have a 41% increase in risk for non-Hodgkin lymphoma.
- The animal literature supports this finding – mice treated with pure glyphosate have an increased incidence of malignant lymphoma.
- The mechanisms linking non-Hodgkin lymphoma to GBHs include immunosuppression, endocrine disruption, and genetic alterations.

Conclusions

- There is a compelling link between non-Hodgkin lymphoma and GBHs following high cumulative GBH exposure.

Conclusion

This literature review has highlighted the need for glyphosate and GBHs to be reassessed. It has found strong scientific evidence that:

- Glyphosate, co-formulants, break-down products, and heavy metals contaminants exist in the environment in non-negligible quantities.
- GBH formulations are significantly more toxic than glyphosate alone.
- Environmental and human impacts are wide ranging and significant.

Many of the articles that were read for this literature review called for glyphosate products to be reassessed. However, rather than using legacy toxicology methodologies, glyphosate products need to be reassessed with protocols that evaluate:

- The actual formulation used in the environment, rather than glyphosate alone
- Real world conditions, including interaction with existing environmental stressors
- Lethal and sub-lethal effects
- Community as well as individual effects
- Long-term as well as short-term effects