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THE IMPACTS OF GLYPHOSATE ON HUMAN AND ENVIRONMENTAL HEALTH

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1.0 INTRODUCTION

Glyphosate is the most used herbicide in human history. Glyphosate-based herbicides (GBHs) are broad-spectrum herbicides that act on the shikimate pathway in bacteria, fungi, and plants. A common GBH is Roundup, developed by Monsanto. The possible effects of GBHs on human health are the subject of an intense public debate for both its potential carcinogenic and non-carcinogenic effects, including potential effects on the endocrine system.[1]

Glyphosate is considered a 'Highly Hazardous Pesticide'(HHP) by Pesticide Action Network International because of its acute toxicity, long-term toxic effects, and other adverse effects on human health and the environment.[2]

Some 8.6 billion kilograms of GBHs have been sprayed worldwide since 1974.[3] Glyphosate use has increased 15-fold since genetically engineered (GE) crops were introduced in 1996, the majority of which are glyphosate-tolerant (GT) GE plants.[4]

This paper discusses the impacts of glyphosate on human and environmental health by highlighting some selected recent scientific studies on these.

2.0 IMPACTS OF GLYPHOSATE ON HUMAN AND ANIMAL HEALTH

There have been many studies showing significant adverse impacts of glyphosate and GBHs on human and animal health. Concerns over the health impacts of glyphosate came to a head with the World Health Organization's (WHO) International Agency for Research on Cancer's (IARC) categorisation of the herbicide as a probable carcinogen to humans in 2015 and have been growing since with increasing evidence of harm to humans, culminating in legal suits against its producer, Monsanto.

2.1 Genotoxicity of Glyphosate-based Herbicides

Genotoxicity refers to a substance's destructive effect on a cell's genetic material. Genotoxins can cause mutations in cells that can lead to cancer. The WHO's IARC, as of March 2015, considers glyphosate as genotoxic and "probably carcinogenic to humans (Group 2A)".[5]

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[1] Fabiana Manservisi, Corina Lesseur†, Simona Panzacchi, et al. The Ramazzini Institute 13-week pilot study glyphosate-based herbicides administered at human-equivalent dose to Sprague Dawley rats: Effects on development and endocrine system. 2019. Environmental Health 2019, 18:15. https://doi.org/10.1186/s12940-019-0453-y. https://ehjournal.biomedcentral.com/articles/10.1186/s12940-019-0453-y

[2] PAN International. 2018. PAN International List of Highly Hazardous Pesticides. http://www.panna.org/sites/default/files/PAN_HHP_List%202018.pdf

[3] CM Benbrook. 2016. Trends in glyphosate herbicide use in the United States and globally. Environ Sci Eur. 28:3. https://enveurope.springeropen.com/articles/10.1186/s12302-016-0070-0

[4] CM Benbrook. 2016. Trends in glyphosate herbicide use in the United States and globally. Environ Sci Eur. 28:3. https://enveurope.springeropen.com/articles/10.1186/s12302-016-0070-0

[5] IARC (International Agency for Research on Cancer). 2017. Some Organophosphate Insecticides and Herbicides. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Volume 112.

A 2019 peer-reviewed analysis[6]confirms the robustness of the IARC's conclusions, stating that the IARC review is grounded on more recent, more sensitive, and more sophisticated genotoxic studies, and more accurately reflects real-world exposures. The IARC relied on peer-reviewed published studies and public literature reports, 70% of which found that glyphosate was genotoxic. It considered a total of 118 genotoxicity assays on glyphosate, GBHs, and aminomethylphosphonic acid (AMPA), glyphosate's primary metabolite. The IARC further analyzed another 81 assays exploring other possible genotoxic mechanisms, of which 62 (77%) reported positive results. The IARC's assessment also encompassed data from typical dietary, occupational, and elevated exposure scenarios.

2.2 Glyphosate-based Herbicides and Non-Hodgkin Lymphoma

A meta-analysis has found compelling evidence that people with high exposures to GBHs had a 41% increased risk of developing non-Hodgkin lymphoma (NHL), concluding that there is "a compelling link" between the two factors.[7]

The researchers say their meta-analysis evaluated all published human studies, including a 2018 updated U.S. government-funded study known as the Agricultural Health Study (AHS). They focused on the highest exposed group in each study because those individuals would be most likely to have an elevated risk if in fact GBHs did cause NHL. This made it less likely that confounding factors would skew the results. In addition to human studies, the researchers also looked at many animal studies involving glyphosate.

The study's findings contradict the US Environmental Protection Agency's (EPA) assurances of safety over the weed killer and come as regulators in several countries consider limiting the use of glyphosate-based products in farming.

Monsanto and its German-owner, Bayer AG, face more than 9,000 lawsuits in the US brought by people suffering from NHL who blame Monsanto's GBH for their disease.[8] In August 2018, the first plaintiff to go to trial won a unanimous jury verdict against Monsanto with damages amounting to $289 million.[9]

In March 2019, a federal jury ruled that Monsanto was liable for a California man's cancer and ordered the company to pay $80 million in damages. The ruling is the first of its kind in US federal court. The jury ruled that Roundup's design was "defective", that the product lacked sufficient cancer warnings, and that Monsanto was negligent in its failure to warn the plaintiff of the NHL risk.[10]

2.3 Glyphosate Causes Reproductive and Developmental Effects in Rats

[6] CM Benbrook. 2019 (Jan). How did the U.S. EPA and IARC reach diametrically opposed conclusions on the genotoxicity of glyphosate-based herbicides? Environmental Sciences Europe 31:2. DOI: 10.1186/s12302-018-0184-7. https://link.springer.com/article/10.1186/s12302-018-0184-7. https://hygeia-analytics.com/wp-content/uploads/2019/01/FINAL_Published_1-14-19.pdf

[7] Luoping Zhang, Iemaan Rana, Rachel M. Shaffer, Emanuela Taioli, and Lianne Sheppard. 2019. Exposure to glyphosate-based herbicides and risk for non-hodgkin lymphoma: a meta-analysis and supporting evidence. Science Direct. https://doi.org/10.1016/j.mrrev.2019.02.001. https://www.sciencedirect.com/science/article/pii/S1383574218300887

[8] Carey Gillam. 2019 (14 Feb). Weedkiller 'raises risk of Non-Hodgkin Lymphoma by 41%. The Guardian. https://www.theguardian.com/business/2019/feb/14/weed-killing-products-increase-cancer-risk-of-cancer

[9] Sam Levin. 2019 (27 Mar). Monsanto found liable for California man's cancer and ordered to pay $80m in damages. The Guardian. https://www.theguardian.com/business/2019/mar/27/monsanto-trial-verdict-cancer-jury.

[10] Sam Levin. 2019 (27 Mar). Monsanto found liable for California man's cancer and ordered to pay $80m in damages. The Guardian. https://www.theguardian.com/business/2019/mar/27/monsanto-trial-verdict-cancer-jury.

A global pilot study on the health effects of GBHs has shown disrupting effects on sexual development, genes and beneficial gut bacteriaat doses considered safe by the US Environmental Protection Agency (EPA), leading its researchers to conclude that glyphosate poses "a significant public health concern".[11]

This was the Global Glyphosate Study which was launched as a pilot study in 2016. It was conducted by the Ramazzini Institute with Bologna University, the Italian National Health Institute, George Washington State University and the Icahn School of Medicine. It was a single-dose study on the health effects of GBHs on Sprague Dawley rats, focusing on the newborn, infancy and adolescence phases of life.

The study exposed Sprague Dawley rats, starting from prenatal life until 13 weeks after weaning, to doses of glyphosate and Roundup in drinking water corresponding to the US EPA's acceptable daily dietary exposure of 1.75 mg/kg bw/day.

The study found that such exposure caused reproductive and developmental effects in both male and female rats, at a dose level currently considered safe in the US. Exposure to GBHs was associated with androgen-like effects, including a statistically significant increase of anogenital distance (AGD) in males and females, delay of first estrous, and increased testosterone in females. AGD, the distance between the anus and the genitals, is a sensitive marker of prenatal endocrine disruption affecting the genital tract development.

The results show that GBHs – even at doses deemed safe and over a relatively short exposure time (which in human-equivalent terms correspond from embryo life to 18 years of age) – are able to alter certain important biological parameters, markers chiefly relating to sexual development, genotoxicity and alteration of the intestinal microbiome.[12] Significant and potentially detrimental effects from glyphosate were detected in the gut bacteria of rat pups born to mothers, who appeared to have been unaffected themselves. Disruption of the microbiome has been associated with a number of negative health outcomes, such as obesity, diabetes and immunological problems.[13]

2.4 Glyphosate Disrupts Gut Bacteria and Causes Liver and Kidney Damage in Rats

The primary mechanism by which glyphosate herbicides kill plants is by inhibiting an enzyme called 5-enolpyruvylshikimate-3-phosphate synthase (EPSPS), which is part of a biochemical pathway known as the shikimate pathway. When the synthesis of aromatic amino acids is blocked by glyphosate inhibition of EPSPS, the plant dies.[14]

Humans and animals do not have the shikimate pathway, so industry and regulators have claimed that glyphosate is non-toxic to humans. However, some strains of gut bacteria do

[11] The Ramazzini Institute. 2018 (16 May). Press release: Global glyphosate study pilot phase shows adverse health effects at 'safe' doses. https://glyphosatestudy.org/press-release/global-glyphosate-study-pilot-phase-shows-adverse-health-effects-at-safe-doses/

[12] The Ramazzini Institute. 2018 (16 May). Press release: Global glyphosate study pilot phase shows adverse health effects at 'safe' doses. https://glyphosatestudy.org/press-release/global-glyphosate-study-pilot-phase-shows-adverse-health-effects-at-safe-doses/

[13] The Guardian. 2018 (16 May). Glyphosate shown to disrupt microbiome 'at safe levels', study claims. https://www.theguardian.com/environment/2018/may/16/glyphosate-shown-to-disrupt-microbiome-at-safe-levels-study-claims

[14] GM Watch. 11 Dec 2019. Glyphosate and roundup proven to disrupt gut microbiome by inhibiting shikimate pathway. https://www.gmwatch.org/en/news/latest-news/19261-glyphosate-and-roundup-proven-to-disrupt-gut-microbiome-by-inhibiting-shikimate-pathway

have the shikimate pathway, leading to much debate about whether Roundup and glyphosate could affect the gut microbiome (bacterial populations). Imbalances in gut bacteria have been found to be linked to many diseases, including cancer, type 2 diabetes, obesity, and depression.

A study by an international team of scientists found that the herbicide, Roundup, and its active ingredient, glyphosate, caused a dramatic increase in the levels of shikimic acid and 3-dehydroshikimic acid in the gut.[15] This is a clear indication that the EPSPS enzyme of the shikimate acid pathway was inhibited by glyphosate and Roundup, since if it were active, it would rapidly convert the shikimic acid to the next substance in the pathway, which did not happen. In addition, the researchers found that both Roundup and glyphosate affected the microbiome at all dose levels tested, causing shifts in bacterial populations.

The researchers also saw other changes in the rats' gut metabolome that were indicative of oxidative stress, a type of imbalance that can lead to mutations in DNA, damage to cells and tissues, and diseases such as cancer. This introduces a new mechanism through which exposure to GBHs may cause cancer. The study also revealed that Roundup, and to a lesser extent glyphosate, damaged the liver and kidneys of the rats, even over the relatively short study period of 90 days.

The researchers applied a metagenomics analysis, which looked at the totality of DNA in the gut and thus identified all organisms present; and a metabolomics analysis, which looked at alterations in biochemistry of the gut microbiome environment.

2.5 Toxic Formulants and Heavy Metals in Glyphosate-based Herbicides

The toxicity of GBHs is highly debated. GBHs are mixtures of water, with commonly 36–48% glyphosate claimed as the active principle. As with other pesticides, 10–20% of GBHs consist of chemical formulants. They are mainly families of petroleum-based oxidized molecules, such as polyoxyethylenamines (POEA) and other contaminants. However, their composition is considered confidential business information which does not allow scientists to describe their mechanism of action either on non-target organisms or even on plants. They are declared as inert by manufacturers.

A study found that the formulants used in GBHs are much more toxic on both plants and human cells than glyphosate alone. It also found toxic heavy metals like arsenic in these herbicides.[16] Researchers studied the comparative herbicidal and toxicological effects of glyphosate alone and 14 of its formulations on plants and human cells. Glyphosate was found to be only slightly toxic on plants at the recommended dilutions in agriculture, in contrast with the general belief. In the short term, the strong herbicidal and toxic properties of its formulations were exerted by the POEA formulant family alone.

Tested on human cells, the formulations were found to have a more endocrine disruptive effect and were even highly more toxic than glyphosate. The study also identified the presence of the heavy metals, arsenic, chromium, cobalt, lead and nickel, which are known to

[15]Robin Mesnage et al., BioRxiv. 2019. Shotgun metagenomics and metabolomics reveal glyphosate alters the gut microbiome of Sprague-Dawley rats by inhibiting the shikimate pathway. https://doi.org/10.1101/870105. https://www.biorxiv.org/content/10.1101/870105v1.full

[16]N. Defarge, J. Spiroux de Vendômois, G.E. Séralini. 2018.Toxicity of formulants and heavy metals in glyphosate-based herbicides and other pesticides. Toxicology Reports. Volume 5, Pages 156-163. https://doi.org/10.1016/j.toxrep.2017.12.025 https://www.sciencedirect.com/science/article/pii/S221475001730149X

be toxic and endocrine disruptors, as contaminants in 22 pesticides, including 11 glyphosate-based ones. This could also explain some of the adverse effects of the pesticides.

In *in vivo* chronic regulatory experiments that are used to establish the acceptable daily intakes of pesticides, glyphosate or other declared active ingredients in pesticides are assessed alone, without the formulants. Considering these new data, this assessment method appears insufficient to ensure safety. These results thus also shed new light on the toxicity assessment of GE plants tolerant to Roundup because they could contain high residues of toxic formulants.

3.0 GLYPHOSATE RESIDUES IN THE FOOD CHAIN

Exposure to glyphosate is real threat to human and environmental health. Besides direct exposure from the spraying of glyphosate, glyphosate residues in or on crops, particularly GE crops, enter the food (and feed) chain while current risk assessments are inadequate to fully determine their true levels of concentration.

3.1 Thousands of Tonnes of Glyphosate Enter the Food Chain

About 77% of the global soybean production comes from glyphosate-tolerant (GT) soybean and the dominant soy producing countries of Brazil, USA and Argentina have a 94%–100% adoption rate of GE crops, mostly GT. Research has shown that an estimated 2,500–10,000 metric tonnes of glyphosate enter global food chains per year from commercial farms in these three countries.[17]

GT soybeans have been found to accumulate herbicides and contain altered nutritional composition. In addition, feeding studies on *Daphnia magna* have shown dose-related adverse effects (mortality, reduced fecundity and delayed reproduction) of glyphosate residues in soybeans, even at glyphosate concentrations below allowed residue levels.

Scientific data[18] shows that glyphosate residues are substantially increased when herbicides are applied late in the growing season, and commercial farm samples of GT soybeans contain far higher concentrations of glyphosate compared to GT soybeans from corporate field trials which are used for safety assessments.

The implications of such high residues of glyphosate constitute knowledge gaps from incomplete evaluations of potential interactions between glyphosate residues and plant composition, and potential negative effects on consumers. The current GE crop risk assessment system has only required and received data from field trials with beans that were sprayed with much lower doses of glyphosate as compared to contemporary commercial farms. GT soybeans, as well as other herbicide-tolerant GE crops, therefore need to be tested in fully representative and realistic contexts.

3.2 Evidence of the Health Impacts of Glyphosate Residues

[17] Bøhn, T., & Millstone, E. 2019. The introduction of thousands of tonnes of glyphosate in the food chain—an evaluation of glyphosate tolerant soybeans. *Foods* 2019, *8*(12), 669. https://doi.org/10.3390/foods8120669. https://www.mdpi.com/2304-8158/8/12/669

[18] Bøhn, T., & Millstone, E. 2019. The introduction of thousands of tonnes of glyphosate in the food chain—an evaluation of glyphosate tolerant soybeans. *Foods* 2019, *8*(12), 669. https://doi.org/10.3390/foods8120669. https://www.mdpi.com/2304-8158/8/12/669

Non-alcoholic fatty liver disease (NAFLD) is currently the most common chronic liver disease in developed countries. Non-alcoholic steatohepatitis (NASH) is a type of NAFLD. Patients with NASH are considered to be at high risk of developing even more serious diseases, such as cirrhosis and liver cancer. Among potential environmental contributors to the pathophysiology of NAFLD are exposure to pesticides, which could be found as residues in or on crops.

In a study involving 93 people, researchers examined glyphosate excretion in the urine samples of two patient groups — those with a diagnosis of NASH and those without.[19] The results were significant: Regardless of age, race, body mass index (BMI), ethnicity or diabetes status, glyphosate excretion was significantly higher in patients with NASH than it was in patients with a healthier liver. Glyphosate excretion was elevated in women, which presumably reflected an increased exposure to glyphosate.

The findings, coupled with prior animal studies, suggest a link between the use of commercial glyphosate in our food supply, which has increased significantly over the past 25 years, and the prevalence of NAFLD in the United States, which too has been on the rise for two decades. The study suggests that people should minimise their exposure to glyphosate and other pesticides by seeking out organically grown food.

3.3 Glyphosate Levels Higher in Children

Diet is a primary source of glyphosate exposure. A 2020 study[20] investigated levels of glyphosate and its main metabolite, aminomethyl phosphonic acid (AMPA), in the urine of adults and children. Glyphosate was detected in 93.7% of urine samples tested, and AMPA was detected in 96.9% of samples.Of special concern is that children had significantly higher levels of glyphosate and AMPA in their urine than adults during the study.

The researchers tested the participants' urine for glyphosate and AMPA over six days on a conventional diet, followed by six days on an all-organic diet, and found average reductions of more than 70% in both the adults and children after just days on the organic diet.

However, even with an organic diet, there is so much glyphosate in the ambient environment, soil and water, as well as in grain bins, trucks and food production lines.[21] The exposure of children to glyphosate from food as well as the environment all through their growing years remains a serious threat to their health.

3.4 Health Risks from Herbicide Residues Underestimated

Consumers cannot assume that approval of herbicide-tolerant (HT) GE food or feed products by regulatory bodies is tantamount to a clean bill of health. Even in the European Union (EU), such risk assessments have been shown to be inadequate.

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[19] Paul J Mills, Cyrielle Caussy, and Rohit Loomba. 2019. Glyphosate excretion is associated with steatohepatitis and advanced liver fibrosis in patients with fatty liver disease. Clinical Gastroenterology and Hepatology, Science Direct. https://doi.org/10.1016/j.cgh.2019.03.045https://www.sciencedirect.com/science/article/pii/S1542356519303611

[20] John Fagan,Larry Bohlen,Sharyle Patton, Kendra Klein. 2020. Organic diet intervention significantly reduces urinary glyphosate levels in U.S. children and adults. https://www.sciencedirect.com/science/article/pii/S0013935120307933?via%3Dihub

[21] Meg Wilcox. 11 August 2020. Environmental Health News. Organic diets quickly reduce the amount of glyphosate in people's bodies. https://www.ehn.org/glyphosate-organic-food-2646939278.html

A 2019 study[22] found that current risk assessment practice for HT GE plants could not be considered to fulfil EU regulatory standards for food and feed safety. The GMO and pesticide regulation provisions of the EU both request for the conditions of agricultural production to be taken into account and for the evaluation of combinatorial effects. Implementing regulations explicitly require field trials with and without the application of the complementary herbicide. However, the study found that the dossiers currently submitted for market approval were seriously flawed.

Herbicide applications in studies for risk assessment did not correspond with real-life farming practice. Crucial information was missing such as on the safety testing of the residues from spraying, cumulative and combinatorial effects related to the application of the complementary herbicides, and herbicide–plant (constituent) interactions and long-term effects.

The researchers considered it highly likely that concerns about the health risks of HT GE plant material used for food and feed have been underestimated. They recommended the following requirements for the risk assessment of HT GE plants: (i) All residues of active substances must be assessed, including taking various practical conditions into consideration; (ii) All applied additives/adjuvants and their residues must be assessed; (iii) Combinatorial effects of the applied herbicides must be investigated, i.e. both herbicide–herbicide interactions, but also herbicide–plant (constituent) interactions; (iv) Potential changes in plant composition due to various herbicide applications must be investigated; and (v) Long-term effects of consumption of HT GE soybeans must be investigated, also including potential effects on the endocrine system, reproduction and the intestinal microbiome.

The findings of the above study were confirmed by the RAGES(Risk Assessment of Genetically Engineered Organisms in the EU and Switzerland) Project that was carried out between 2016 and 2019.[23] Its purpose was to critically evaluate the risk assessment of GE food plants as performed by the European Food Safety Authority (EFSA) and its Swiss counterpart. In respect of HT GE crops, the researchers confirmed that EFSA has only accepted and relied on data from field trials with GE plants not treated with high and repeated doses of glyphosate, which is the current practice in many countries where GE crops are being cultivated. Consequently, the Project researchers concluded that the approval process was completely inadequate to deal realistically with the risks posed by consuming products derived from these plants. Furthermore, several potential health impacts on the immune system, and especially potential combinatorial effects, were discounted and ignored.

4.0 IMPACTS OF GLYPHOSATE ON THE ENVIRONMENT

Glyphosate and GBHs have also had detrimental effects on the environment. Their use is closely linked with GT GE crops such as Roundup Ready soy. Glyphosate has been found to harm soil, bees, and amphibians among others, as well as increase antibiotic resistance in bacteria.

4.1 Glyphosate Harms Soil Health

[22]Miyazaki, J., Bauer-Panskus, A., Bøhn, T., Reichenbecher, W., & Then, C. 2019. Insufficient risk assessment of herbicide-tolerant genetically engineered soybeans intended for import into the EU.Environmental Sciences Europe, 31(1), 92. https://doi.org/10.1186/s12302-019-0274-1. https://link.springer.com/article/10.1186/s12302-019-0274-1

[23]ENSSER (European Network of Scientists for Social and Environmental Responsibility), CSS (Critical Scientists Switzerland), GeneWatch UK and Testbiotech, 2020. Overview: The RAGES Project. https://www.testbiotech.org/sites/default/files/RAGES_%20Factsheet_Overview_0.pdf

Over the last decade, about 6.1 billion kilograms of glyphosate have been sprayed on the world's farms, gardens and public spaces.The Soil Association reviewed the scientific evidence on the impact of glyphosate on soils and soil life, finding harm to beneficial soil fauna such as microbes, fungi and earthworms along with risks of pollution of water bodies from glyphosate use.[24] The key findings are as follows:

a) *Leaching into water:*Glyphosate can leach into the deeper soil layers and end up in groundwater, rivers or lakes. In particular types of soil or weather conditions, glyphosate can leach out and pose a potential pollution threat to water courses.
b) *Impact on soil micro-organisms that are vital to soil health*: Glyphosate has been shown to negatively affect the abundance of the culturable bacterial community, and the total bacterial composition. For e.g. a study found that the relative abundance of *Acidobacteria* decreased in response to glyphosate exposure. Decreases in the abundance of these bacteria over the long-term could impair the ability of soil to perform certain biogeochemical reactions.
c) *Impact on fungi:* Beneficial fungi that live near plant roots have been found to be harmed by glyphosate. For example, studies found 40% reduction of mycorrhization after the application of glyphosate in soils.
d) *Severity and occurrence of crop diseases:* Using glyphosate has increased the severity or the re-emergence of crop diseases, potentially by changing the balance between beneficial and harmful microbes in the soil. Increased frequency of soil-borne pathogens and reduced ability of crops to defend against them, are both reported to result from glyphosate use. In one study, the colonisation of roots by *Fusarium* fungi increased steadily as soybean growth progressed and as the rate of glyphosate increased.
e) *Impact on earthworms:* Glyphosate showed a negative impact on the reproduction, growth, movement or activity of different species of earthworms. A study also found that earthworms avoided soil treated with the herbicide.

4.2 Harm to Honeybees and Stingless Bees

Bees rely on a specialized gut microbiota that benefits growth and provides defence against pathogens. A study[25] demonstrated that the relative and absolute abundances of dominant gut microbiota species decreased in bees exposed to glyphosate at concentrations documented in the environment. This increased the insects' susceptibility to deadly infections by pathogens. This is because some of the key beneficial bacteria in bees' guts have a particular enzyme that is targeted by glyphosate.

The researchers found that young worker bees exposed to glyphosate died more often when later exposed to a common bacterium, *Serratia marcescens*. Thus, exposure of bees to glyphosate can perturb their beneficial gut microbiota, potentially affecting their health and effectiveness as pollinators.

Other research from China showed that honeybee larvae grew more slowly and died more often when exposed to glyphosate.[26] An earlier study, in 2015, showed that exposure of adult

[24]Soil Association. 2016. The impact of glyphosate on soil health - The evidence to date. https://www.soilassociation.org/media/7202/glyphosate-and-soil-health-full-report.pdf
[25]Erick V. S. Motta, Kasie Raymann, and Nancy A. Moran. 2018. Glyphosate perturbs the gut microbiota of honey bees. The Proceedings of the National Academy of Sciences (PNAS). https://doi.org/10.1073/pnas.1803880115. http://www.pnas.org/content/early/2018/09/18/1803880115
[26] Pingli Di et al. 2018. The herbicide glyphosate negatively affects midgut bacterial communities and survival of honey bee during larvae reared in vitro. J. Agric. Food Chem. 66, 29, 7786-7793. https://doi.org/10.1021/acs.jafc.8b02212. https://pubs.acs.org/doi/abs/10.1021/acs.jafc.8b02212

bees to the herbicide at levels found in fields "impairs the cognitive capacities needed for a successful return to the hive".[27] Glyphosate may thus be contributing to the global decline in bees, along with the loss of habitat.[28]

Brazil is the second largest producer of GE crops in the world. As a result, native bees are being exposed to various herbicides applied to such crops, including glyphosate. A study in the country found that glyphosate was highly toxic to the stingless bee *M. quadrifasciata*, causing lethal or sublethal effects which can severely impair colony growth and viability, and reduce pollination ability.[29] Glyphosate was very toxic to the bee larvae, killing all of them within only a few days of exposure.

4.3 Adverse Impacts of GBHs on Amphibians

Several studies on the impacts of GBH exposure on amphibians have found evidence of harm. The results of four such studies are summarised below.

- Frog embryos of *Xenopus laevis* showed inhibition on growth of the embryo larva as well as teratogenicity.[30] Characteristic malformations induced by GBHs included generalized edema, cardiac and abdominal edema, improper gut formation and axial malformations.
- Glyphosate had lethal effects on tadpoles from two South American native species, *Physalaemus cuvieri* and *P. gracilis*.[31] Tadpoles showed shorter lengths and lower masses; that is, those that survived suffered the chronic effects on growth and weight. The GBH maximum acceptable toxicant concentration for mortality and malformation was lower than the allowed level for Brazilian waters.
- Tadpoles of *Dendropsophus molitor*, an endemic tropical frog of South America, exhibited histological alterations in the liver.[32]
- The exposure of four common amphibian species from South America across 91 ponds in Argentina to cypermethrin, chlorpyrifos, endosulfan, glyphosate, and 2,4-Dichlorophenoxyacetic acid was evaluated.[33] Tadpole survival dramatically decreased after pesticides reached the ponds. Glyphosate exposure caused sublethal effects, reducing tadpole mobility in 79%.

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[27] María Sol Balbuena et al. 2015. Effects of sublethal doses of glyphosate on honeybee navigation. Journal of Experimental Biology. 218: 2799-2805.Doi: 10.1242/jeb.117291.

[28] Damian Carrington. 2018 (24 Sept). Monsanto's global weedkiller harms honeybees, research finds. The Guardian. https://www.theguardian.com/environment/2018/sep/24/monsanto-weedkiller-harms-bees-research-finds

[29] VE Seide, RC Bernardes, EJG Pereira, & MAP Lima. 2018. Glyphosate is lethal and Cry toxins alter the development of the stingless bee *Melipona Quadrifasciata.* Environmental Pollution. 243,1854-1860. https://doi.org/10.1016/j.envpol.2018.10.020. https://www.sciencedirect.com/science/article/pii/S0269749118325478.

[30] Babalola, O. O., Truter, J. C., & van Wyk, J. H. 2019. Mortality, teratogenicity and growth inhibition of three glyphosate formulations using Frog Embryo Teratogenesis Assay□Xenopus. Journal of Applied Toxicology. https://onlinelibrary.wiley.com/doi/abs/10.1002/jat.3811

[31] Herek, J. S., Vargas, L., Trindade, S. A. R., Rutkoski, C. F., Macagnan, N., Hartmann, P. A., & Hartmann, M. T. 2020. Can environmental concentrations of glyphosate affect survival and cause malformation in amphibians? Effects from a glyphosate-based herbicide on Physalaemus cuvieri and P. gracilis (Anura: Leptodactylidae). Environmental Science and Pollution Research, 1-12. https://link.springer.com/article/10.1007%2Fs11356-020-08869-z

[32] Riaño, C., Ortiz-Ruiz, M., & Gómez-Ramírez, E. 2020. Effect of glyphosate (Roundup Activo®) on liver of tadpoles of the Colombian endemic frog Dendropsophus molitor (Amphibia: Anura). Chemosphere, 126287. https://www.sciencedirect.com/science/article/pii/S004565352030480X

[33] MG Agostini, I Roesler, C Bonetto, AE Ronco, & D Bilenca. 2020. Pesticides in the real world: the consequences of GMO-based intensive agriculture on native amphibians. Biological Conservation. 241, 108355. https://doi.org/10.1016/j.biocon.2019.108355. https://www.sciencedirect.com/science/article/pii/S0006320719309905

4.4 Herbicides Increase Antibiotic Resistance in Bacteria

A study found that herbicides like Roundup and Kamba (dicamba) can increase the rate of antibiotic resistance development in bacteria by a factor of up to 100,000 times faster than occurs without the herbicide.[34,35] Both herbicides are used on crops genetically engineered to tolerate them.

The researchers studied multiple bacteria including *Salmonella* and *E. coli*. *E. coli* accounts for 17.3% of clinical infections requiring hospitalization.[36] The study found that even when herbicides made the bacteria weaker or stronger, it still developed resistance, and when the chemicals in herbicides were combined with antibiotics, the rate of antibiotic resistance increased because the genetic makeup in the bacteria had changed. The research demonstrates that bacteria may acquire antibiotic resistance in the environment at rates substantially faster than predicted from laboratory conditions. The researchers predict that antibiotic resistance may increase even if total antibiotic use is reduced, and new ones are invented, unless other environmental exposures are also controlled.

5.0 GLYPHOSATE USE AND GLYPHOSATE-TOLERANT GE CROPS IN MALAYSIA

Districts/Cities/Towns/Municipalities/Organizations as well as national governments in about 40 countries have issued outright bans on glyphosate, imposed restrictions or have issued statements of intention to ban or restrict glyphosate-based herbicides, including Roundup, over health concerns and the ongoing Roundup cancer litigation.[37]

The Consumers' Association of Penang reported in January 2020 that there were more than 200 herbicides with glyphosate, which were used for a variety of crops and in oil palm plantations in Malaysia.[38]

Given the scientific evidence of the harm that glyphosate and GBHs pose to human and environmental health, Malaysia should seriously consider banning GBHs and any food and feed produced using glyphosate, including GE glyphosate-tolerant food and feed.

According to the Malaysian Department of Biosafety, 40 genetically engineered crops have been approved for food, feed and processing of which 11 are glyphosate-tolerant. The Department of Biosafety of Malaysia should review and revoke these approvals in light of the increasing evidence of harm from glyphosate and GBHs.

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Table 1. Glyphosate-tolerant Genetically Engineered Crops Approved for Food, Feed and Processing in Malaysia

Event	Applicant	Ref. No.	Date of Decision
MON 87427 corn	Monsanto Malaysia Sdn. Bhd.	JBK(S) 602-1/1/43	22 May 2018
DP73496 canola	Du Pont (Malaysia) Sdn. Bhd.	JBK(S) 602-1/1/41	22 May 2018
DAS-44406-6 soybean	Dow Agrosciences (Malaysia) Sdn. Bhd.	JBK(S) 602-1/1/37	19 October 2017
MZHG0JG corn	Syngenta Crop Protection Sdn. Bhd.	JBK(S) 602-1/1/35	01 August 2017
GHB614 cotton	Bayer Co. (Malaysia) Sdn. Bhd.	JBK(S) 602-1/1/29	17 January 2017
Glyphosate tolerant GA21 corn	Syngenta Crop Protection Sdn. Bhd.	JBK(S) 602-1/1/24	10 March 2016
Corn Rootworm-Protected and Glyphosate-Tolerant Corn MON88017	Monsanto Malaysia Sdn. Bhd.	JBK(S) 602-1/1/19	30 April 2015
Glyphosate and Isoxaflutole Tolerant FG72 Soybean	Bayer Co. (Malaysia) Sdn. Bhd.	JBK(S) 602-1/1/16	19 December 2014
MON 89788 Glyphosate Tolerant Soybean (RoundupReady2Yield™)	Monsanto Malaysia Sdn. Bhd.	JBK(S) 602-1/1/9	27 November 2012
MON 603 Roundup Ready™ Maize	Monsanto Malaysia Sdn. Bhd.	JBK(S) 602-1/1	25 May 2010
MON 4032 Roundup Ready™ Soybean	Monsanto Malaysia Sdn. Bhd.	JBK(S) 602-1/1	25 May 2010

Source: http://www.biosafety.gov.my/en-my/nbb-decision/Pages/NBB-Decision-Food-Feed-Processing.aspx (Updated: 29 August 2020)