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Report on the use of glyphosate

Utah Physicians for a Healthy Environment (UPHE) is concerned that there are many state and federal agencies and other entities using insecticides and herbicides without understanding the public health and wildlife consequences of spreading those chemicals throughout our environment. UPHE has posted on our website an extensive report on the health hazards of insecticides used by mosquito abatement districts, it is available here:

<https://www.uphe.org/priority-issues/mosquito-pesticide-spraying/>

Below is a report on the consequences of the most commonly used herbicide, glyphosate (Roundup).

Overview

Strategies to achieve otherwise worthy environmental goals, should not include large-scale use of herbicides. Manufacturers of glyphosate and glyphosate-based herbicides (GBH) have carefully crafted a reputation for these products that is far different from the conclusions that should be drawn by public health experts. Independent research now thoroughly challenges, and in many cases outright contradicts claims of glyphosate's ecological, wildlife, and human safety. The medical research is very strong that, at real life environmental exposures, GBHs are hazardous to human health, including as carcinogens, reproductive toxins, and neurotoxins.

Glyphosate is so ubiquitous in our environment it is present in the air we breathe, water we drink and rain that falls from the sky. It should be no surprise then that the average human body in the developed world, and only to a slightly lesser extent the developing world, is contaminated with thousands of biologically toxic chemicals on a continuous basis, and pesticides as a group are one of the most prevalent. The result for humans is "impaired health (and sometimes death) by a thousand cuts."

Numerous environmental toxins affect residents of the West side of the Salt Lake Valley and the Northwest quadrant, and synergistic toxicity may be the end result. Air pollution from heavy freeway traffic, the airport, multiple industrial sources, such as the Rio Tinto mining operations, and the Beck St. gravel pit plague neighborhoods in the area. GBH use on invasive plants species in the wetlands at the south end of the Great Salt Lake adds to that toxic mix.

In a situation where many sources contribute to the contamination, we should not accept that no one is responsible, everyone should accept responsibility. Although for most of us our greatest exposure to glyphosate and GBHs is from our food supply, we should be looking at every opportunity to reduce our use of, and exposure to, all these environmental toxins. Furthermore, glyphosate is toxic to the entire Great Salt Lake ecosystem, including the birds that so many are trying to preserve.

UPHE encourages those individuals and agencies using herbicides to control invasive species on the Utah's two largest lakes, and those engaged in managing our forest ecosystems to use all available non-toxic means, rather than the herbicides that are currently being used.

1. Glyphosate Safety Claims Not Consistent With the Science

The safety of glyphosate, the “active ingredient” in Roundup and hundreds of other commercial herbicidal preparations (GBHs) has been historically taken as a given by the chemical industry and regulatory agencies. But the bulk of the research supporting this contention has been based on outdated, and even unpublished studies commissioned by the manufacturers to defend their application for regulatory authorization.^{72,73} Developments of the last 15 years have painted a much more worrisome picture of this herbicide, still the most commonly used pesticide in the world.

For years Monsanto has publicly claimed that their best-selling pesticide Roundup is safer than table salt⁹⁴ or caffeine, and more specifically, benign to humans because glyphosate inhibits an enzyme supposedly found only in plants and microbes, but not in people, EPSP synthase. The problem, or more accurately the deception, with that contention is five-fold.

1. The toxicity scale cited for that claim is based on the LD 50 value, which is the concentration of a substance required to kill 50% of the organisms given a short-term exposure, in other words, acute lethality. The type of exposure that most humans are subjected to is much different, i.e. cumulative, low dose, chronic exposure. Diseases like cancer and reproductive disorders are seldom caused by acute, one-time exposures. For example, you don't judge the health hazard of cigarettes by analyzing one day of heavy smoking.

2. Glyphosate is not the only potentially toxic ingredient in GBHs like Roundup. Numerous studies have shown much greater toxicity of commercial glyphosate formulations with additives and adjuvants that will be discussed in more detail later in this report.

3. Just because glyphosate targets that specific enzyme doesn't mean that other adverse effects are not triggered inadvertently as collateral damage. Similarly, just because alcohol targets the brain, doesn't mean it doesn't also affect the liver. Glyphosate also affects other biologic pathways such as the retinoic acid signaling pathway which can alter gene expression in animals and humans.⁸²

4. EPSP synthase is certainly found in the 100 trillion bacteria that constitute the bacterial flora of the human GI tract. A healthy intestinal bacterial flora is essential to good health for any human, and other animals.¹

5. The timing of exposure is paramount in its potential to cause human organ dysfunction and disease. Exposure during critical, early life developmental windows represents a completely different risk profile, than the same exposure to an adult. Furthermore, glyphosate behaves as an “endocrine disruptor” or hormone mimicker.² Endocrine disruptors (EDC) are chemicals implicated in insidious diseases like reproductive disorders, cancer, and birth defects at very low doses, either with long term exposure, or during critical developmental windows in early life stages. Perhaps the most distinctive characteristic of endocrine disruptors is that they do not function like other poisons, where the harm is linearly related to the dose. Often, endocrine disruption occurs at low doses but not at higher doses,^{84,85} and for many EDC there may be no safe level of exposure.⁹⁵ Some EDC may have transgenerational adverse impacts.⁹⁵ Typical industry studies are not designed to evaluate these outcomes.

Federal legislation passed in 1996 required the EPA to test all pesticides for endocrine disrupting activity. Twenty-seven years later that still has not happened. The Office of Chemical Safety and Pollution Prevention recommended in 2015 that 17 pesticides be tested for endocrine disruption. But that hasn’t happened either. The Office of Inspector General issued a scathing report in July 2021, stating that, “EPA’s Endocrine Disruptor Screening Program [EDSP] Has Made Limited Progress in Assessing Pesticides.”⁸⁹ That report stated, “some EPA staff indicated that they were instructed to function as if the EDSP was eliminated from the EPA’s budget.” Given the apparent unwillingness of the EPA to investigate this critical issue in any meaningful time frame, despite its legal mandate, we must act on what evidence is available. And that evidence is very disturbing.

In human cells, glyphosate causes DNA damage and antagonizes androgens at levels up to 800 times lower than glyphosate residue levels allowed by EPA in some GM crops used for animal feed in the US.⁹⁰ Roundup at environmentally realistic levels (down to 0.00023% glyphosate dilution of the commercial formulation) caused the dysregulation of over one third of genes in human breast cancer cells grown in the laboratory in vitro.⁹¹ Glyphosate increased the proliferation of breast cancer cells in vitro via interaction with estrogen receptors at the same level allowed in drinking water in the European Union.⁹² In vitro exposure of human cells to Roundup at levels lower than allowed in drinking water in Australia prevented the cell from producing progesterone.⁹³

As an endocrine disruptor, glyphosate has the potential to precipitate a wide variety of maladies including birth defects, hormone and reproductive disorders,^{3,4,5} cancer,^{6,7,8} fatty liver disease,⁹ and impaired brain development through inhibition of the thyroid gland and through other multiple pathways,¹⁰ all at very low doses of exposure. At the microscopic level the biologic common denominators behind glyphosate’s effects include alteration of energy metabolism, a reduction in oxygen consumption and mitochondrial respiration, and promotion of oxidative stress. As an EDC, glyphosate inhibits the production of estrogen in placental and embryonic cell lines and reduces testosterone production.^{11,12,13} Human pregnancy complications, miscarriages and pre-term births, correlate to GBH exposure.¹⁴ Commercial formulations at sub-agricultural

concentrations caused death of testicular somatic cells,¹⁵ while glyphosate alone demonstrated genotoxicity in red blood cells.¹⁶

Teratogenicity from GBH has been shown in fish, rats, mice, and chickens,^{17,18,19} and in humans, with multiple birth defects including cleft lip and Down's syndrome.²⁰ In rats, exposure to GBH causes heart arrhythmias and myocardial mechanical dysfunction.²¹

The nervous system is particularly vulnerable to glyphosate.²² Glyphosate enters the brain, and is associated with an increase in the chemical hallmarks of brain inflammation in both brain tissue and blood.²³ Production of dopamine and serotonin are decreased in exposed mice, leading to depressive type behavior²⁴ as well as decreases in locomotion, memory and learning capability.^{25,26} Exposure to pesticides, including glyphosate, is associated with neurodegenerative diseases like autism²⁷ and Parkinsonism,^{28,29,30,31,32,33} most of which is environmentally caused, and has become the fastest growing non-genetic neurologic disease.

One mechanism may be that pesticides can prevent the brain from disposing of its own "toxic waste." In vitro studies have revealed toxicity to genes from the primary metabolite of glyphosate.³⁴ Workers occupationally exposed to pesticides show increased DNA damage.^{35,36}

Glyphosate enhances the adverse effects of other food borne chemical residues and environmental toxins, increasing levels of systemic inflammation, the common denominator of many chronic diseases like gastrointestinal disorders, obesity, diabetes, heart disease, depression, autism, infertility, cancer and Alzheimer's disease.³⁷

Many of the now out of date studies that Monsanto claimed exonerated Roundup from causing any health effects, and that formed the basis of the EPA's approval, made the mistake of only testing the main active ingredient, glyphosate. But Roundup contains other chemicals as adjuvants and surfactants that facilitate binding to the plant. These chemicals were billed by the manufacturers as benign, and by and large regulators bought into the premise. But a 2014 study found that the toxicity of eight out of nine pesticide formulas was greater than the toxicity of their active ingredient alone.³⁸ Roundup was the most toxic of the pesticides studied, and the commercial formulas of the pesticides were as much as 1,000 times more toxic than the "active ingredient" by itself.

Glyphosate was originally patented as an antibiotic, (U.S. Patent number US7771736 B2), so it is not surprising that it might affect beneficial bacteria in the soil and in the human colon, the same site of concern as Bt toxin (a gram-positive, soil-dwelling bacterium, and the most commonly used biological pesticide worldwide). There is evidence that glyphosate destroys beneficial bacteria and allows harmful ones, such as salmonella, and clostridium, to flourish in the intestines of farm animals.^{39,40,41,42}

The neurotoxic effect of glyphosate formulations on the brain is likely both direct--by impairing neuronal growth and differentiation, impairing signaling pathways and neurotransmission--and indirect through its effect on the GI tract and the thyroid.

Inflammatory bowel disease (IBD) is a chronic inflammatory disorder that afflicts 1.4 million persons in the US and the incidence has been steadily rising worldwide in the last two decades.

In some countries the rate is five times greater than it was in the 1950s. Developing countries such as India, China and South Korea, where IBD was almost unheard of 30 years ago, have seen a dramatic increase that is now paralleling the incidence in the Western world.

IBD results from a loss of homeostasis, or balance, between the immune system and the microbes that inhabit the intestine. Not only is IBD a devastating and debilitating chronic illness, in and of itself, it is also one of the three highest risk factors for the development of colorectal cancer, and highly associated with neurological diseases. Fifty years ago, IBD was almost exclusively diagnosed in adults, today it is increasingly common in younger people, even teenagers and children. The rise in IBD parallels the rise in colorectal cancer, especially in young people. Colorectal cancer rates have been increasing in people ages 20 to 39 years since the mid-1980s, and in those 40 to 54 years since the mid-1990s, increasing 1.5% per year in those younger than 50.⁶¹ Even more disturbing, colorectal cancer, found to be metastatic at the time of diagnosis, is making up a rising proportion of cases in young patients. Exposure to pesticides is certainly one of the possible causes.⁶²

Recently the connection between the GI tract and the brain has been solidified by evidence that a wide range of neurologic disorders--like autism, depression, and Parkinson's--have been shown to be related to changes in the "trillions of bacteria, viruses, archaea, and eukaryotes that make up the gut microbiome."⁴²

The neonatal period is, simultaneously, a critical window of development for microbes to inhabit the infant gut as well as rapid brain growth and development. In the early 2000s animal studies showed that both beneficial and adverse manipulation of the bacterial content of the GI tract was associated with changes in neurological development of the animals.⁴³

Autism is well known to occur four to five times more often in boys than girls. Researchers found that manipulating the intestinal microbiome resulted in altered levels of the neurotransmitter serotonin in male mice but not in their female counterparts.⁴⁴

Several studies show that organophosphate chemicals (nerve agents and pesticides) cause greater neurotoxicity in male than female animals.^{45,46,47} Other studies show that altering the gut microbiome impaired a person's ability to excrete other known neurotoxicants like mercury, arsenic, and nicotine.

The gut microbiome is often abnormal in children with poor neurological development, and there is a wide range of abnormal GI symptoms among people with Autism Spectrum Disorder. Furthermore, changes in the gut bacterial flora are associated with changes in the symptoms of autism.^{48,49}

Strong circumstantial evidence suggests that by altering the microbiome of the gut, Bt-toxins from GMOs, and the pesticides used concomitantly with them, could be causing microscopic leaking in the intestinal walls of newborns, facilitating the absorption of incompletely digested foods and toxins into the blood. That, in turn, triggers systemic inflammation, precipitating autoimmune diseases and food allergies. Furthermore, since the blood-brain barrier is not developed in newborns, toxins in the blood may migrate into brain tissue itself interfering with

normal brain development. This is a very plausible biological pathway for autism. The brains and cerebrospinal fluid of autism patients consistently show a marked inflammatory process.⁵⁰

All environmental toxins, including glyphosate are more hazardous in children than adults because of the differences in their physiology and developmental life stage. Exposure during critical developmental windows, in utero and infancy, can have a greater and more persistent impact on organ function and disease vulnerability. Glyphosate can damage human placental embryonic, and umbilical cells, and cross the placenta directly reaching the fetus.¹⁰⁷

The clinical significance is apparent in the following study. In agricultural areas of Brazil, after Roundup was introduced for soybean production, populations at distance from the spraying, but living downstream, experienced significant deteriorations in birth outcomes, such as increases in infant mortality, pre-term births, and low birth weights compared to upstream areas.¹⁰⁸ This amounted to about 550 infant deaths in a population of about 500,000.

Children have a higher metabolic rate and therefore more rapid breathing, higher heart rate, and greater ingestion of food and water. Their smaller size means an exposure will deliver a proportionately a larger dose of ingested toxins per weight. They live and play in closer proximity to the ground, to dirt, and indoor dust, and have high hand to mouth activity. They have longer to live after exposure and therefore a greater chance of developing chronic diseases like cancer.

In June 2022, in a ruling on a lawsuit filed by the Natural Resources Defense Council and the Pesticide Network North America, a federal appeals court ordered the EPA to vacate their safety determination of glyphosate.¹⁰²

2. Many Pesticides Contaminated With Even More Toxic PFAS Compounds

Adding to the concern about glyphosate toxicity are recent studies that show many pesticides are contaminated with the highly toxic chemical group, known as the Teflon group, or “forever chemicals,” i.e. Per- and Polyfluoroalkyl Substances (PFAS and PFOS).¹⁰⁴ In June, the EPA set a safety limit for PFOS in drinking water at 0.02 parts per trillion (ppt), a level so low that means essentially there is no safe level of exposure. But PFOS was found in numerous pesticide concentrates at levels ranging from 3,920,000 to 19,200,000 ppt before dilutants were added. A former EPA scientist said, “If the intent was to spread PFAS contamination across the globe there would be few more effective methods than lacing pesticides with PFAS.”¹⁰⁵ Nearly 70% of all pesticides introduced for commercial sale between 2015 to 2020 were found to be contaminated with PFAS/PFOS compounds.¹⁰⁶

Illustrating both the extreme toxicity and wide spread environmental contamination of PFAS, a recent study that measured PFAS contamination in 500 freshwater fish caught from throughout the US, found significant contamination in the majority of samples, and only one fish did not contain detectable amounts of PFAS. Fish from every one of the 48 continental states showed contamination. The researchers concluded that “a single serving of freshwater fish per year with the median level of PFAS as detected by the U.S. EPA monitoring programs, translates into a significant increase of PFOS levels in blood serum.”¹⁰⁹ Most of the PFAS measured was PFOS,

one of the most toxic of this group that includes thousands of different compounds, because of its potency as a teratogen, carcinogen, and reproductive toxin. A pollution researcher at the UK's Liverpool John Moores University, Patrick Byrne, said PFAS are “probably the greatest chemical threat the human race is facing in the 21st century.”¹¹⁰

At the bare minimum all high volume herbicides and insecticides used in the state of Utah should be required to be tested for PFAS/PFOS contamination. Even this minimum amount of protection is not being pursued.

3. The Glyphosate Safety Narrative Has Been Manufactured by an Aggressive Industry PR Campaign, not Reputable Independent Science

The potential for glyphosate to behave as a carcinogen led to the most high-profile public drama about glyphosate controversy, and speaks volumes about why it is still on the market.

The International Agency for Research on Cancer (IARC), located in Lyon, France, is an arm of the World Health Organization and the UN. The IARC is responsible for creating a public inventory of cancer-causing substances in the interest of public health protection, and whose scientific conclusions have been regarded above reproach for 50 years. Their working groups are typically about 20 scientists selected from a world-wide pool, specifically for their expertise and lack of conflicts of interest on a specific issue. IARC conclusions are based on studies published in independent scientific journals and specifically exclude, confidential industry-funded research, in sharp contrast to the methods used by the EPA and other regulatory bodies that routinely use industry research.

After working on an evaluation of pesticides for over a year, on March 20, 2105, in a “shot heard round the world” the IARC working group announced their finding that several pesticides were probably human carcinogens. One of those so classified was glyphosate, the bed rock of Monsanto’s chemical empire. The famed French journal, *Le Monde*, won a prestigious international award, for their “Monsanto Papers” investigative report where they exposed the company’s response.⁵¹

First, Monsanto issued this defiant public statement: “All labeled uses of glyphosate are safe for human health.” Without even a pause for introspection, hesitation or the stirring of a corporate conscience, Monsanto demanded a retraction from the WHO.⁶³ Christopher Wild, IARC director, recently said, “We have been attacked in the past, we have faced smear campaigns, but this time we are the target of an orchestrated campaign of an unseen scale and duration.” He was talking about Monsanto’s response to the IARC declaring glyphosate genotoxic (it causes DNA damage), carcinogenic to animals, and a “probable carcinogen” to humans.

Using a no holds barred arsenal of public berating, false accusations, legal harassment and intimidation, intrusive demands, calls for Congressional investigations, spies posing as fake journalists, paid off academics and social media trolls, and arm twisting media outlets like Reuters, Monsanto essentially waged an unprecedented, all-out campaign to literally destroy the

IARC, its scientists, and even loosely affiliated public institutions like the highly respected National Institute of Environmental Health Sciences (NIEHS) in the US, and the 180 scientists that are members of the Ramazzini Institute of Italy.

Common sense and reality was turned on its head. Monsanto demanded that these highly respected international institutions, established for the protection of the public, must now be accountable to Monsanto. Monsanto-allied academicians and politicians jumped onto the international stage calling for the IARC to be abolished. The closest Monsanto came to actual scientific exoneration of glyphosate came in the form of six articles that appeared in the journal, *Critical Reviews in Toxicology*. But that journal is openly funded by Monsanto. The sixteen authors of those six articles had been recruited by a crisis management consulting group that specializes in ginning up scientific reports that defend companies whose profits are threatened by regulatory or legal action.⁶⁴

In 2017 the notorious lobbying organization, the American Chemistry Council overtly joined Monsanto's war in launching the "Campaign for Accuracy in Public Health Research," a vicious PR and legislative initiative to silence glyphosate's scientific critiques and attack their funding.

The IARC, NIEHS, and Ramazzini Institute are three pillars of independent science whose work is critical to public health protection from environmental contaminants. Their battle with Monsanto is a David vs. Goliath battle because these three institutions have no staff or money to defend themselves, only their integrity and their publicly funded research. Monsanto and the ACC freely spend millions on their weapons of war.

Among the many expose' on Monsanto behavior, "The Monsanto Papers," exposed the company as having interfered with much of the research that exposed glyphosate's toxicity, and even ghost wrote academic papers attempting to demonstrate its benignity.⁶⁵

In studies not tainted by influence from Monsanto, there is a modest correlation between GBH exposure and multiple cancers, including melanoma, as well as leukemia, colon, rectum, bladder, and kidney cancers⁵⁴ and a stronger correlation with non-Hodgkin's lymphoma⁵⁵ the malignancy at the center of the numerous cancer lawsuits against Monsanto. Numerous news stories have been written about the thousands of lawsuits that have been filed against Monsanto (now Bayer), for causing cancer, primarily lymphomas.

For more on the inappropriate relationship between pesticide manufacturers and regulatory agencies, and the failure to protect the public, see Appendix A.

4. Glyphosate is ubiquitous in our environment and in human bodies

Glyphosate use has increased 30-fold globally in the last four decades,⁹⁶ and one fifth of that use occurs in the United States. Glyphosate is so ubiquitous in our environment it is present in the air we breathe, water we drink and rain that falls from the sky. An extensive analysis by the US Geological Survey from 38 states sampling streams, groundwater, ditches and drains, rivers, soil

water, lakes, ponds, wetlands, precipitation, soil and sediment, and waste water treatment plants found glyphosate in 39.4% of samples (1470 out of 3732) and its metabolite AMPA (aminomethylphosphonic acid) in 55% of samples (2,052 out of 3732). It should be no surprise then that the average human body in the developed world, and only to a slightly lesser extent the developing world, is contaminated with thousands of biologically toxic chemicals on a continuous basis, and pesticides as a group are one of the most prevalent. Well over 2,200 environmental chemicals have been identified in urine of the average person.⁹⁹ Glyphosate specifically was detected in the urine of more than 80% of Americans of all ages.¹⁰⁰ Another study found the average concentration of glyphosate in urine of American subjects was greater than the European standard for drinking water.¹⁰¹ The result for humans is “impaired health (and sometimes death) by a thousand cuts.”

Exposure to multiple pesticides, multiple heavy metals, or combinations of pesticides and heavy metals can have synergistic neurotoxicity, all of which describe the situation on the Salt Lake Valley’s West side and in the Northwest Quadrant.^{56,57} In addition to the many sources of environmental contaminants that affect the residents of the Salt Lake Valley as a whole, the Northwest Quadrant and areas near the south shore of the Great Salt Lake are particularly exposed to the oil refineries, the airport, the nearby freeways, the Beck Street gravel pit, the Rio Tinto mining operations, the dust from the Great Salt Lake, and the soon to be inland port.

5. Glyphosate’s effect on the food web and wildlife

The wildlife and ecological impacts can be enhanced from repeated GBH applications, because they have been shown to slow its degradation in soil.^{70,71} Glyphosate’s reputation of breaking down quickly in soil defies numerous studies. Depending on conditions, glyphosate can persist in the environment for a long time. In Hawaii, in soils with pH<6, glyphosate half-life was found to be as high as 22 years.⁷⁵ Glyphosate’s toxic, major metabolite, AMPA, has a soil half-life of between 119 and 958 days.^{76,77} Glyphosate was found in pond sediments 400 days after direct application.⁷⁸

Roundup applied at a concentration equivalent to direct overspray on a wetland (3.8 mg glyphosate/L), resulted in a 22% reduction in species richness of all animal species in the exposed communities.⁷⁹ This study showed Roundup is particularly toxic to amphibians.

Chronic exposure to concentrations of Roundup and glyphosate well below the approved regulatory threshold causes multiple biologic harms to the keystone organism, *Daphnia*; including embryonic developmental failure, genotoxicity, epigenetic toxicity, immune dysfunction, oxidative stress, inflammation, cell death, hormone and cell division disruption, and alteration of metabolic pathways via direct effect on the host and indirect effect on the gut bacteria.¹²⁸ *Daphnia* are central to the food web of aquatic ecosystems and a broad indicator of ecosystem health. This means the biologic toxicity of glyphosate-based herbicides can reverberate throughout food webs. Indeed, similar harm has been found in multiple other key organisms including tadpoles, caimans, fish, lizards, shrimp, invertebrates, rats, and human cell lines.^{58,59,60}

Glyphosate can impair learning behaviors in honeybees and severely impair long-term colony performance when exposed to environmentally relevant doses.^{80,97} Just as in humans, honey bees require a healthy gut bacterial population, and glyphosate can damage the bees' microbiota.⁹⁸

Pesticides can penetrate the porous eggshells of birds increasing the mortality or developmental anomalies of bird embryos.⁶⁷ GBH compounds harm embryonic development of avian embryos,⁶⁶ including damage to lipid membranes of the embryonic brain. A chronic dietary exposure of hens to GBH at a concentration lower than NOAEL results in accumulation of glyphosate in the egg yolk and severe early embryonic mortality, and a delayed embryonic development in survivors.⁶⁸ GBH were found to be more toxic to avian embryonic development than glyphosate itself.⁶⁹ The significant loss of bird populations worldwide has been well documented. More than half of bird species populations are in decline.¹²⁹ Through direct and indirect effects (decreasing insect populations), insecticides and herbicides of various types are almost certainly contributors to the global bird loss.

Numerous studies on animals suggest a role for glyphosate and GBH as endocrine disruptors. Glyphosate interfered with puberty development, testosterone production, and testicular formation in rats,⁸³ harmed catfish reproduction by altering hormone levels in female catfish and decreased egg viability,⁸⁶ and disrupted production of progesterone in mouse cells.⁸⁷ Roundup added to drinking water for rats, diluted to 50ng/L glyphosate equivalence (half of the level permitted in drinking water in the EU and 14,000 times lower than that permitted in drinking water in the USA), caused severe organ damage and a trend of increased incidence of mammary tumors in female animals.⁸⁸

Mosquito abatement districts in the area are using large amounts of organophosphate and pyrethroid insecticides in much of the same area that GBH compounds are being used against phragmites. While as a group, insecticides are more toxic to birds than herbicides, that may not be true of GBH.

Conclusion

Public health protection should not be sacrificed by any public policy, even those that have other worthy environmental objectives. We must adopt a tenant that any practice that cannot be considered safe for the most vulnerable stage of human life, i.e. intrauterine stage, cannot be considered safe for society as a whole. We believe the scientific evidence is convincing that even low doses of herbicides are unsafe for human exposure, especially when the exposure is chronic and recurrent, and particularly so for fetal development.

This priority should apply to strategies to rid Utah's two largest lakes of invasive species. UPHE encourages those individuals and agencies using herbicides to control phragmites to use all available non-toxic means, rather than the herbicides that are currently being used.

Furthermore, such a shift in strategy would likely produce better results in the attempt to sustain bird and wildlife populations in these ecosystems, the primary purpose of suppressing the invasive species.

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References

1. Antoniou, M., Robinson, C., & Fagan, J. (2012). Teratogenic effects of glyphosate-based herbicides: Divergence of regulatory decisions from scientific evidence. *Journal of Environmental Analytical Toxicology* S4:006. <http://www.omicsonline.org/2161-0525/2161-0525-S4-006.php?aid=7453>
2. Gasnier, C. et al, Glyphosate-based herbicides are toxic and endocrine disruptors in human cell lines. *Toxicology* doi:10.1016/j.tox.2009.06.00688.
3. Clair, É., Mesnage, R., Travert, C., Séralini, G-É. A glyphosate-based herbicide induces necrosis and apoptosis in mature rat testicular cells in vitro, and testosterone decrease at lower levels. *Toxicology in Vitro* 26 (2) 269-279 2012.

4. de Liz Oliveira Cavalli VL et al. Roundup® Disrupted Male Reproductive Functions By Triggering Calcium-Mediated Cell Death In Rat Testis And Sertoli Cells104.
5. Yousef, M.I. et al. Toxic effects of carbofuran and glyphosate on semen characteristics in rabbits. *J Environ Sci Health B*. 1995 Jul; 30(4):513-34
6. Eriksson M, Hardell L, Carlberg M, Akerman M. Pesticide exposure as risk factor for non-Hodgkin lymphoma including histopathological subgroup analysis100. *Int J.Cancer*. 2008, 123:1657-1663
7. Thongprakaisang S, Thiantanawat A, Rangkadilok N, Suriyo T, Satayavivad J. Glyphosate induces human breast cancer cells growth via estrogen receptors. *Food Chem Toxicol*. 2013, 59C: 129-136. doi: 10.1016/j.fct.2013.05.057101
8. Alavanja, M.C.R., Ross, M.K., Bonner, M.R. Increased Cancer Burden Among Pesticide Applicators and Others Due to Pesticide Exposure. *CA Cancer J Clin* 2013 63 (2): 120– 142.
9. <https://www.nature.com/articles/srep39328>
10. Vandenberg LN, Blumberg B, Antoniou MN, Benbrook CM, Carroll L, Colborn T, Everett LG, Hansen M, Landrigan PJ, Lanphear BP, et al. 2017. Is it time to reassess current safety standards for glyphosate-based herbicides? *J Epidemiol Community Health*. 71(6):613–618.
11. Richard S, Moslemi S, Sipahutar H, Benachour N, Seralini G. 2005. Differential effects of glyphosate and Roundup on human placental cells and aromatase. *Environ Health Perspect*. 113(6):716–720.
12. Benachour N, Sipahutar H, Moslemi S, Gasnier C, Travert C, Seralini G. 2007. Time- and dose-dependent effects of Roundup on human embryonic and placental cells. *Arch Environ Contam Toxicol*. 53(1):126–133.
13. Romano M, Romano R, Santos L, Wisniewski P, Campos D, de Souza P, Viau P, Bernardi M, Nunes M, de Oliveira C. 2012. Glyphosate impairs male offspring reproductive development by disrupting gonadotropin expression. *Arch Toxicol*. 86(4):663–673.
14. Arbuckle T, Lin Z, Mery L. 2001. An exploratory analysis of the effect of pesticide exposure on the risk of spontaneous abortion in an Ontario farm population. *Environ Health Perspect*. 109(8):851–857.
15. Vanlaeys A, Dubuisson F, Seralini G, Travert C. 2018. Formulants of glyphosate-based herbicides have more deleterious impact than glyphosate on TM4 sertoli cells. *Toxicol in Vitro*. 52:14–22.
16. Alvarez-Moya C, Silva M, Ramírez C, Gallardo D, Sánchez R, Aguirre A, Velasco A. 2014. Comparison of the in vivo and in vitro genotoxicity of glyphosate isopropylamine salt in three different organisms. *Genet Mol Biol*. 37(1):105–110.

17. Dallegrave E, Mantese F, Coelho R, Pereira J, Dalsenter P, Langeloh A. 2003. The teratogenic potential of the herbicide glyphosate-Roundup in Wistar rats. *Toxicol Lett.* 142(1–2):45–52.
18. Fagan J, Antoniou M, Habib M, Howard C, Jennings R, Leifert C, Nodari R, Fagan J, Robinson C. 2012. Teratogenic effects of glyphosate-based herbicides: Divergence of regulatory decisions from scientific evidence. *J Environ Anal Toxicol.* S4:006.
19. Roy N, Ochs J, Zambrzycka E, Anderson A. 2016. Glyphosate induces cardiovascular toxicity in *Danio rerio*. *Environ Toxicol Pharmacol.* 46:292–300.
20. Campaña H, Pawluk M, López Camelo J, Grupo de Estudio del E. 2010. Births prevalence of 27 selected congenital anomalies in seven geographic regions of Argentina. *Arch Argent Pediatr.* 108:409–417.
21. Chan Y, Chang S, Hsuan S, Chien M, Lee W, Kang J, Wang S, Liao J. 2007. Cardiovascular effects of herbicides and formulated adjuvants on isolated rat aorta and heart. *Toxicol in Vitro.* 21(4):595–603.
22. Costas-Ferreira, C.; Durán, R.; Faro, L.R.F. Toxic Effects of Glyphosate on the Nervous System: A Systematic Review. *Int. J. Mol. Sci.* 2022,23,4605. <https://doi.org/10.3390/ijms23094605>
23. Winstone, J.K., Pathak, K.V., Winslow, W. et al. Glyphosate infiltrates the brain and increases pro-inflammatory cytokine TNF α : implications for neurodegenerative disorders. *J Neuroinflammation* 19, 193 (2022). <https://doi.org/10.1186/s12974-022-02544-5>
24. Ait Bali Y, Ba-Mhamed S, Bennis M. 2017. Behavioral and immunohistochemical study of the effects of subchronic and chronic exposure to glyphosate in mice. *Front Behav Neurosci.* 11:146.
25. Gallegos C, Bartos M, Bras C, Gumilar F, Antonelli M, Minetti A. 2016. Exposure to a glyphosate-based herbicide during pregnancy and lactation induces neurobehavioral alterations in rat offspring. *Neurotoxicology.* 53:20–28.
26. Ait Bali Y, Kaikai N-E, Ba-M'hamed S, Bennis M. 2019. Learning and memory impairments associated to acetylcholinesterase inhibition and oxidative stress following glyphosate based-herbicide exposure in mice. *Toxicology.* 415:18–25.
27. von Ehrenstein O S, Ling C, Cui X, Cockburn M, Park A S, Yu F et al. Prenatal and infant exposure to ambient pesticides and autism spectrum disorder in children: population based case-control study *BMJ* 2019; 364 :l962 doi:10.1136/bmj.l962
28. Ya-xing Gui et al. Glyphosate induced cell death through apoptotic and autophagic mechanisms. *Neurotoxicology and Teratology* 2012, 34 (3): 344–349
29. Pezzoli G, Cereda E "Exposure to pesticides or solvents and risk of Parkinson disease" *Neurology* 2013; 80: 2035-2041.

30. Ross S, McManus IC, Harrison V, Mason O. Neurobehavioral problems following low-level exposure to organophosphate pesticides: a systematic and meta-analytic review. *Critical Reviews in Toxicology*, Ahead of Print : Pages 1-24 (doi: 10.3109/10408444.2012.738645)
31. <https://www.sciencedirect.com/science/article/abs/pii/S135727252200070X#sec0010>
32. Caballero M, Amiri S, Denney JT, Monsivais P, Hystad P, Amram O. Estimated Residential Exposure to Agricultural Chemicals and Premature Mortality by Parkinson's Disease in Washington State. *Int J Environ Res Public Health*. 2018 Dec 16;15(12):2885. doi: 10.3390/ijerph15122885. PMID: 30558363; PMCID: PMC6313412.
33. Winstone, J.K., Pathak, K.V., Winslow, W. et al. Glyphosate infiltrates the brain and increases pro-inflammatory cytokine TNF α : implications for neurodegenerative disorders. *J Neuroinflammation* 19, 193 (2022). <https://doi.org/10.1186/s12974-022-02544-5>
34. Mañas F et al. Genotoxicity of AMPA, the environmental metabolite of glyphosate, assessed by the Comet assay and cytogenetic tests. *Ecotoxicol Environ Saf*. 2009 72 (3):834-7. doi: 10.1016/j.ecoenv.2008.09.01932
35. Simoniello, M.F. et al. DNA damage in workers occupationally exposed to pesticide mixtures. *J Appl Toxicol*. 2008, 28 (8): 957-65. doi: 10.1002/jat.1361
36. Benedetti D, et al. Genetic damage in soybean workers exposed to pesticides: Evaluation with the comet and buccal micronucleus cytome assays. *Mutation Research/Genetic Toxicology and Environmental Mutagenesis* 2013, 752 (1–2): 28–33
37. Samsel A, Seneff S. Review: Glyphosate's Suppression of Cytochrome P450 Enzymes and Amino Acid Biosynthesis by the Gut Microbiome: Pathways to Modern Diseases. *Entropy* 2013, 15(4), 1416-1463; doi:10.3390/e15041416
38. Mesnage, R.; Defarge, N.; Spiroux de Vendômois, J. and Séralini, G.-E. (2014, in press): Major pesticides are more toxic to human cells than their declared active principles.
39. Shehata, A.A. et al. The Effect of Glyphosate on Potential Pathogens and Beneficial Members of Poultry Microbiota In Vitro. *Current Microbiology* 2013, 66 (4): 350-358
40. Krüger, M. et al. Glyphosate suppresses the antagonistic effect of *Enterococcus* spp. on *Clostridium botulinum*. *Anaerobe* 2013, Feb 6
41. Clair, E. et al. Effects of Roundup® and Glyphosate on Three Food Microorganisms: *Geotrichum candidum*, *Lactococcus lactis* subsp. *cremoris* and *Lactobacillus delbrueckii* subsp. *bulgaricus*. *Curr Microbiol*. Epub 2012 Feb 24
42. <http://www.organic-systems.org/journal/81/8106.pdf>

43. Sudo N, Chida Y, Aiba Y, Sonoda J, Oyama N, Yu X-N, et al. 2004. Postnatal microbial colonization programs the hypothalamic-pituitary-adrenal system for stress response in mice. *J Physiol (Lond)* 558(Pt 1):263–275, PMID: 15133062, 10.1113/jphysiol.2004.063388.
44. Clarke G, Grenham S, Scully P, Fitzgerald P, Moloney RD, Shanahan F, et al. 2013. The microbiome-gut-brain axis during early life regulates the hippocampal serotonergic system in a sex-dependent manner. *Mol Psychiatry* 18(6):666–673, PMID: 22688187, 10.1038/mp.2012.77.
45. Roegge CS, Timofeeva OA, Seidler FJ, Slotkin TA, Levin ED. 2008. Developmental diazinon neurotoxicity in rats: later effects on emotional response. *Brain Res Bull* 75(1):166–172, PMID: 18158111, 10.1016/j.brainresbull.2007.08.008.
46. Slotkin TA, Ryde IT, Levin ED, Seidler FJ. 2008. Developmental neurotoxicity of low dose diazinon exposure of neonatal rats: effects on serotonin systems in adolescence and adulthood. *Brain Res Bull* 75(5):640–647, PMID: 18355640, 10.1016/j.brainresbull.2007.10.008.
47. Timofeeva OA, Roegge CS, Seidler F, Slotkin TA, Levin ED. 2008. Persistent cognitive alterations in rats after early postnatal exposure to low doses of the organophosphate pesticide, diazinon. *Neurotoxicol Teratol* 30(1):38–45, PMID: 18096363, 10.1016/j.ntt.2007.10.002.
48. Hsiao EY. 2014. Gastrointestinal issues in autism spectrum disorder. *Harv Rev Psychiatry* 22(2):104–111, PMID: 24614765, 10.1097/HRP.0000000000000029.
49. Kang DW, Adams JB, Gregory AC, Borody T, Chittick L, Fasano A, et al. 2017. Microbiota Transfer Therapy alters gut ecosystem and improves gastrointestinal autism symptoms: an open label study. *Microbiome* 5(1):10, PMID: 28122648, 10.1186/s40168-016-0225-7.
50. Pardo C, et al. Immunity, neuroglia and neuroinflammation in autism. *International Review of Psychiatry*, December 2005; 17(6): 485–495
51. <http://www.ehn.org/monsanto-glyphosate-cancer-smear-campaign-2509710888.html>
52. http://www.ehn.org/monsanto-takes-on-world-health-organization-2509721283.html?utm_source=EHN&utm_campaign=b5fcab2cab-EMAIL_CAMPAIGN_2017_11_25&utm_medium=email&utm_term=0_8573f35474-b5fcab2cab-99026613
53. McHenry L. 2018. The Monsanto Papers: Poisoning the scientific well. *Int J Risk Saf Med*. 29(3–4):193–205.
54. de Roos A, Blair A, Rusiecki J, Hoppin J, Svec M, Dosemeci M, Dale P, Sandler D, Alavanja M. 2005. Cancer incidence among glyphosate-exposed pesticide applicators in the Agricultural Health Study. *Environ Health Perspect*. 113(1):49–54.
55. Zhang L, Rana I, Shaffer R, Taioli E, Sheppard L. 2019. Exposure to glyphosate-based herbicides and risk for Non-Hodgkin Lymphoma: A meta-analysis and supporting evidence. *Mutat Res*. 781:186–206.

56. Singh N, Gupta VK, Kumar A, Sharma B. Synergistic Effects of Heavy Metals and Pesticides in Living Systems. *Front Chem*. 2017 Oct 11;5:70. doi: 10.3389/fchem.2017.00070. PMID: 29075624; PMCID: PMC5641569.
57. Laetz CA, Baldwin DH, Collier TK, Hebert V, Stark JD, Scholz NL. The synergistic toxicity of pesticide mixtures: implications for risk assessment and the conservation of endangered Pacific salmon. *Environ Health Perspect*. 2009 Mar;117(3):348-53. doi: 10.1289/ehp.0800096. Epub 2008 Nov 14. PMID: 19337507; PMCID: PMC2661902.
58. Suppa, A., Kvist, J., Li, X. et al. Roundup causes embryonic development failure and alters metabolic pathways and gut microbiota functionality in non-target species. *Microbiome* 8, 170 (2020). <https://doi.org/10.1186/s40168-020-00943-5>
59. Webster TMU, Santos EM. Global transcriptomic profiling demonstrates induction of oxidative stress and of compensatory cellular stress responses in brown trout exposed to glyphosate and Roundup. *Bmc Genomics*. 2015;16, doi: ARTN 32.
60. Mesnage, R. et al. Transcriptome profile analysis reflects rat liver and kidney damage following chronic ultra-low dose Roundup exposure. *Environ Health Glob* (14, pg 70, 2015).
61. <https://www.beaumont.org/health-wellness/blogs/colorectal-cancer-rates-increase-in-young-people>
62. <https://www.cancer.gov/news-events/cancer-currents-blog/2020/colorectal-cancer-rising-younger-adults>
63. <https://www.reuters.com/article/us-monsanto-herbicide/monsanto-seeks-retraction-for-report-linking-herbicide-to-cancer-idUSKBN0MK2GF20150324>
64. . http://www.ehn.org/monsanto-takes-on-world-health-organization-2509721283.html?utm_source=EHN&utm_campaign=b5fcab2cab-EMAIL_CAMPAIGN_2017_11_25&utm_medium=email&utm_term=0_8573f35474-b5fcab2cab-99026613
65. <https://www.usatoday.com/story/news/nation-now/2017/03/16/emails-show-monsanto-tried-ghostwrite-research/99248950/>
66. Ruuskanen, S., Rainio, M.J., Uusitalo, M. et al. Effects of parental exposure to glyphosate-based herbicides on embryonic development and oxidative status: a long-term experiment in a bird model. *Sci Rep* 10, 6349 (2020). <https://doi.org/10.1038/s41598-020-63365-1>
67. Köhler, H. R. and Triebskorn, R. (2013): Wildlife ecotoxicology of pesticides: can we track effects to the population level and beyond? *Science* 341 ,759–765.
68. Estienne A, et al. Chronic dietary exposure to a glyphosate-based herbicide results in reversible increase early embryo mortality in chicken, *Ecotoxicology and Environmental Safety*, Volume 241, 2022, 113741, ISSN 0147-6513
69. Winnick, Blake Edward. *The Effects of Glyphosate Based Herbicides on Chick Embryo Development*, thesis, August 2013; Denton, Texas.

70. De Andrea, M.M.; Peres, T.B.; Luchini, L.C.; Bazarin, S.; Papini, S.; Matallo, M.B.; Savoy, V.L.T. Influence of repeated applications of glyphosate on its persistence and soil bioactivity. *Pesqui. Agropecuária Bras.* 2003, 38, 1329–1335. [CrossRef]
71. Carretta, L.; Cardinali, A.; Onofri, A.; Masin, R.; Zanin, G. Dynamics of Glyphosate and Aminomethylphosphonic Acid in Soil Under Conventional and Conservation Tillage. *Int. J. Environ. Res.* 2021, 15, 1037–1055.
72. European Commission Health & Consumer Protection Directorate-General. “Review report for the active substance glyphosate.” 2002. Available at: <http://bit.ly/HQnkFj>
73. Fagan J PhD, Antoniou M PhD, Robinson C MPhil. “GMO Myths and Truths 2nd Edition. Earth Open Source.” 2014:4.1:205. Available at: <http://earthopensource.org/earth-open-source-reports/gmo-myths-and-truths-2nd-edition/>
74. Sirinathsinghji, E. Widespread Glyphosate Contamination in USA. ISIS Report August 2014. Institute of Science in Society. Available at: http://www.i-sis.org.uk/Widespread_Glyphosate_Contamination_in_US.php
75. Nomura, N.S., Hilton, H.W., The adsorption and degradation of glyphosate in five Hawaiian sugarcane soils. *Weed Res.* 1977. 17:113–121.
76. World Health Organization (WHO). Glyphosate. Environmental Health Criteria 159. The International Programme on Chemical Safety (IPCS). WHO, Geneva. 1994.
77. Buffin, D., Jewell, T. Health and Environmental Impacts of Glyhosate. Pesticide Action Network UK. 2001. Available at: http://www.foe.co.uk/sites/default/files/downloads/impacts_glyphosate.pdf
78. Buffin, D., Jewell, T. Health and Environmental Impacts of Glyhosate. Pesticide Action Network UK. 2001. Available at: http://www.foe.co.uk/sites/default/files/downloads/impacts_glyphosate.pdf
79. Relyea, R. 2005. The Impact of Insecticides and Herbicides on the Biodiversity and Productivity of Aquatic Communities. *Ecological Society of America.* 15(2):618-627. Available at: <http://why.org/91FM/ybyg/relyea2005.pdf>
80. Herbert LT, Vazquez DE, Arenas A, Farina WM. 2014. Effects of field-realistic doses of glyphosate on honeybee appetitive behavior. The Company of Biologists Ltd. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/25063858>
81. Fagan J PhD, Antoniou M PhD, Robinson C MPhil. GMO Myths and Truths 2nd Edition. Earth Open Source. 2014:4.1:205. Available at: <http://earthopensource.org/earth-open-source-reports/gmo-myths-and-truths-2nd-edition/>

82. Fagan J PhD, Antoniou M PhD, Robinson C MPhil. *GMO Myths and Truths 2nd Edition*. Earth Open Source. 2014;4.1:215. Available at: <http://earthopensource.org/earth-open-source-reports/gmo-myths-and-truths-2nd-edition/>
83. Romano RM, Romano MA, Bernardi MM, Furtado PV, Oliveira CA. Prepubertal exposure to commercial formulation of the herbicide glyphosate alters testosterone levels and testicular morphology. *Arch Toxicol*. 2010 Apr;84(4):309-17. doi: 10.1007/s00204-009-0494-z. Epub 2009 Dec 12. PMID: 20012598.
84. Vandenberg LN, Colborn T, Hayes TB, et al. Hormones and endocrine-disrupting chemicals: Low-dose effects and nonmonotonic dose responses. *Endocr Rev*. 2012;33(3):378-455. doi:10.1210/er.2011-1050.
85. Vom Saal FS, Akingbemi BT, Belcher SM, et al. Chapel Hill bisphenol A expert panel consensus statement: integration of mechanisms, effects in animals and potential to impact human health at current levels of exposure. *Reprod Toxicol*. 2007;24:131-138. doi:10.1016/j.reprotox.2007.07.005.
86. Soso AB, Barcellos LJG, Ranzani-Paiva MJ, et al. Chronic exposure to sub-lethal concentration of a glyphosate-based herbicide alters hormone profiles and affects reproduction of female Jundiá (*Rhamdia quelen*). *Environ Toxicol Pharmacol*. 2007;23:308-313.
87. Walsh LP, McCormick C, Martin C, Stocco DM. Roundup inhibits steroidogenesis by disrupting steroidogenic acute regulatory (StAR) protein expression. *Env Health Perspect*. 2000;108:769-776.
88. Séralini G-E, Clair E, Mesnage R, et al. Republished study: long-term toxicity of a Roundup herbicide and a Roundup-tolerant genetically modified maize. *Environ Sci Eur*. 2014;26(14). doi:10.1186/s12302-014-0014-5.
89. https://www.epa.gov/system/files/documents/2021-07/_epaoig_20210728-21-e-0186.pdf
90. Gasnier C, Dumont C, Benachour N, Clair E, Chagnon MC, Séralini GE. Glyphosate-based herbicides are toxic and endocrine disruptors in human cell lines. *Toxicology*. 2009;262:184-191. doi:10.1016/j.tox.2009.06.006.
91. Hokanson R, Fudge R, Chowdhary R, Busbee D. Alteration of estrogen-regulated gene expression in human cells induced by the agricultural and horticultural herbicide glyphosate. *Hum Exp Toxicol*. 2007;26:747-752. doi:10.1177/0960327107083453.
92. Thongprakaisang S, Thiantanawat A, Rangkadilok N, Suriyo T, Satayavivad J. Glyphosate induces human breast cancer cells growth via estrogen receptors. *Food Chem Toxicol*. 2013;59:129-136. doi:10.1016/j.fct.2013.05.057.
93. Young F, Ho D, Glynn D, Edwards V. Endocrine disruption and cytotoxicity of glyphosate and roundup in human JAr cells in vitro. *Integr Pharmacol Toxicol Genotoxicol*. 2015;1(1):12-19.

94. <https://apnews.com/article/d196b9a5bb54637a7b281760b0f7a966>
95. <https://www.endocrine.org/topics/edc/where-we-stand>
96. <https://enveurope.springeropen.com/articles/10.1186/s12302-016-0070-0>
97. Balbuena M, et al. Effects of sublethal doses of glyphosate on honeybee navigation. *J Exp Biol* (2015) 218 (17): 2799–2805.
98. Dai P, Yan Z, Ma S, Yang Y, Wang Q, Hou C, Wu Y, Liu Y, Diao Q. The Herbicide Glyphosate Negatively Affects Midgut Bacterial Communities and Survival of Honey Bee during Larvae Reared in Vitro. *J Agric Food Chem*. 2018 Jul 25;66(29):7786-7793. doi: 10.1021/acs.jafc.8b02212. Epub 2018 Jul 11. PMID: 29992812.
99. <https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0073076>
100. https://wwwn.cdc.gov/Nchs/Nhanes/2013-2014/SSGLYP_H.htm
101. Gillezeau C, van Gerwen M, Shaffer RM, Rana I, Zhang L, Sheppard L, Taioli E. The evidence of human exposure to glyphosate: a review. *Environ Health*. 2019 Jan 7;18(1):2. doi: 10.1186/s12940-018-0435-5. PMID: 30612564; PMCID: PMC6322310.
102. <https://www.thenewlede.org/wp-content/uploads/2022/06/9th-circuit-on-glyphosate.pdf>
103. <https://www.scientificamerican.com/article/pesticides-are-spreading-toxic-forever-chemicals-scientists-warn/>
104. Lasee S, et al. Targeted analysis and Total Oxidizable Precursor assay of several insecticides for PFAS, *Journal of Hazardous Materials Letters*, Volume 3, 2022, 100067, ISSN 2666-9110
105. <https://www.ecowatch.com/pfas-insecticides.html>
106. Alexandrino D, et al. Revisiting pesticide pollution: The case of fluorinated pesticides, *Environmental Pollution*, Volume 292, Part A, 2022, 118315, ISSN 0269-7491
107. Benachour, N. and Séralini, G. E. (2009). Glyphosate formulations induce apoptosis and necrosis in human umbilical, embryonic, and placental cells. *Chem. Res. Toxicol.*, 22(1):97–105
108. <https://docs.iza.org/dp12164.pdf>
109. Barbo N, et al. Locally caught freshwater fish across the United States are likely a significant source of exposure to PFOS and other perfluorinated compounds, *Environmental Research*, 2022, 115165, ISSN 0013-9351
110. <https://www.yahoo.com/news/eating-one-wild-fish-same-050328070.html>

111. <https://theintercept.com/2022/03/30/epa-new-chemicals-division-workplace/>
112. <https://theintercept.com/2019/08/23/monsanto-republicans-cancer-research/>
113. McHenry LB. *The Monsanto Papers: Poisoning the scientific well*. *Int J Risk Saf Med*. 2018;29(3-4):193-205. doi: 10.3233/JRS-180028. PMID: 29843257.
114. Schneider, Keith (Winter 1983). "IBT – Guilty". *Amicus Journal*. Archived from the original on 2012-07-19. Retrieved 2012-07-19.
115. Foster, Doug (1983-12-07). "Industrial Bio-Test Lab's Dirty Research" *Oakland Tribune*. Center for Investigative Reporting. Archived from the original on 2013-04-14. Retrieved 2012-07-11.
116. Shabecoff, Philip (1983-07-12). "E.P.A. Threatens to Suspend Approval of Pesticides over Test Flaws". *The New York Times*. Retrieved 2012-07-16.
117. Schneider, Keith (Winter 1983). "IBT – Guilty". *Amicus Journal*. Archived from the original on 2012-07-19. Retrieved 2012-07-19.
118. <https://truthout.org/articles/unsafe-at-any-dose-diagnosing-chemical-safety-failures-from-ddt-to-bpa/>
119. [http://precaution.org/lib/ruckelshaus_risk_in_a_free_society_\(risk_assessment\).1984.pdf](http://precaution.org/lib/ruckelshaus_risk_in_a_free_society_(risk_assessment).1984.pdf)
120. <https://www.nap.edu/read/1802/chapter/1>
121. Curtis L, et al. Potentiation of the hepatotoxicity of carbon tetrachloride following preexposure to chlordecone (Kepone) in the male rat, *Toxicology and Applied Pharmacology*, Volume 51, Issue 2, 1979, Pages 283-293
122. <https://theintercept.com/2021/06/30/epa-pesticides-exposure-opp/>
123. <https://www.nrdc.org/sites/default/files/flawed-epa-approval-process-IB.pdf>
124. <http://www.chicagotribune.com/news/watchdog/flames/ct-met-flames-regulators-20120510,0,6880244.full.story>
125. <http://www.truth-out.org/news/item/43517-the-precautionary-principle-asks-how-much-harm-is-avoidable-rather-than-how-much-harm-is-acceptable>
126. <http://www.businessinsider.com/epa-only-restricts-9-chemicals-2016-2>
127. <http://www.businessinsider.com/epa-only-restricts-9-chemicals-2016-2#nitrites-mixed-with-p6-mixed-mono-and-diamides-of-an-organic-acidpp7-triethanolamine-salts-of-a-substituted-organic-acidpp8-triethanolamine-salt-of-tricarboxylic-acidpp9-tricarboxylic-acidp6>
128. Cuhra M, Traavik T, Bøhn T. Clone- and age-dependent toxicity of a glyphosate commercial formulation and its active ingredient in *Daphnia magna*. *Ecotoxicology*. 2013 Mar;22(2):251-62. doi: 10.1007/s10646-012-1021-1. Epub 2012 Dec 6. PMID: 23224423; PMCID: PMC3572389.
129. <https://www.audubon.org/news/more-half-us-birds-are-decline-warns-new-report>

Appendix

EPA regulatory approval does not exonerate the pesticides it allows on the market

Problems with Toxicology Risk Assessments (TRAs) Acceptable Daily Intakes (ADIs), and No Observed Adverse Effects Levels (NOAELs)

“The ultimate effect of these institutional defects is that chemical risk assessments in the US and the EU have a safety bar for approval that is so low that regulators virtually never decline to approve a chemical. In contrast, the exact same institutions use standards for taking any chemical off the market that are so high that such an event nearly never happens. Yet if both standards were based purely on science, as they claim to be, both bars would be the same height... Chemical risk assessments themselves are the problem”

---Jonathan Latham, PhD, the Cornucopia Institute

Virtually all toxicity data used by the EPA comes from “toxicology risk assessments (TRAs),” the same approach that polluting industries, chemical manufacturers, and unfortunately regulatory bodies use to assess whether a certain project such as citing of a pollution source, like a refinery or incinerator, or a chemical spraying program will create a public health risk. It is an antiquated, inadequate and scientifically deeply flawed process.

How TRAs, ADIs, and NOAELs originated is instructive. TRAs were first used by the EPA in 1975 under pressure from industry to dismiss health risks of one of the earliest known toxins, vinyl chloride. The EPA felt like they could respond authoritatively if they could calculate the number of cancers that would be caused by exposing the population to vinyl chloride. Federal regulators then started adopting that technique with many other environmental controversies and disputes with industry, and that methodology continues today. The makers of toxic chemicals and industrial polluters are content to see it continue because with supposedly hard, mathematical data, the risks of chemicals and contaminants are easily obscured.

ADIs and NOAELs were developed for similar reasons in the 1980s, not as an organic outgrowth of the scientific evidence, but as a means of satisfying regulatory and political demands, primarily to provide justification for allowing pollution and contaminant exposures. These mathematical calculations were, and still are, based on two assumptions. 1. That there must exist a threshold below which no systemic effects occur, and 2. That the relationships between exposure and toxicity are linear, i.e. monotonic. We now know both of those assumptions are often not correct.

The science of toxicology is still tethered to a principle first advocated by the father of toxicology, Paracelsus (Theophrastus von Hohenheim), a 15th-16th Century Swiss physician, alchemist, and astrologer. His contribution to the Renaissance was the fundamental classic toxicology theory that “the dose makes the poison.” In other words, there is a threshold at which

low concentrations of toxic substances no longer present a threat to human health and above that threshold, the harm is proportional to the dose. That is still the basis of modern-day toxicology and government environmental regulations. But that assumption, and the methodology based upon that assumption, was flawed when it was adopted in the 1970s, and those flaws are all the more evident now.

Regulatory toxicology testing primarily has consisted of high dose testing on adult animals, usually mice or rats, and subsequent testing at progressively lower doses in an attempt to establish a dose response model from which a threshold can be derived below which effects, usually death or cancer, could no longer be identified. This methodology is deeply flawed for numerous reasons, and has contributed greatly to a barrage of unsafe and inadequately tested chemicals being unleashed upon the public and the environment.

Below are thirteen reasons why TRAs, ADIs, and NOAELs fail to identify many health risks, and usually underestimate the toxicity of chemicals.

1. Numerous books and investigative reports have documented corporate capture of government regulatory agencies, Congress, state legislators, free market think tanks, and even academia using a Big Tobacco type strategy. There are almost countless reports of EPA staffers being overruled by senior officials resulting in scientifically unwarranted favorable treatment for pesticides, corporate influence over research, chemical company lobbyists killing unfavorable legislation, and even collusion with EPA personnel to defend specific pesticide products. The nine-part investigative report by *The Intercept*¹¹¹ is just one of many alarming investigations. Contributing further to these highly compromised relationships is an ongoing revolving door of EPA scientists often moving on to work for industry and sometimes vice versa.

Monsanto's attack on the IARC, alluded to earlier is only one of numerous examples of individual scientists, journalists, and entire organizations drawing negative conclusions, or reporting unfavorable stories about their products, becoming victims of vicious attempts by pesticide corporations to silence, intimidate, smear, and punish them, including losing government and academic positions and funding. Corporate lobbyists have succeeded in enlisting members of Congress to help bully and defund their scientific detractors.¹¹²

University departments have become too dependent on donations from agribusiness such that research truly independent of industry has severely contracted and scientists have been pressured to conform to chemical corporation agendas. Court documents in the recent explosion of lawsuits against the manufacturers of pesticides like Roundup and chlorpyrifos add more proof to the case of corruption between industry, academia, and federal agencies, including the EPA. The previously referred to, *The Monsanto Papers*,¹¹³ is just one of many examples of investigations of this compromised relationship.

A foundational problem in this dynamic is the gross mismatch between a perennially underfunded government agency and the immense wealth of the corporations they are supposed to regulate. To the extent that public health protection is actually the EPA's priority, it is continually outfoxed, outmaneuvered, and far outspent by pesticide manufacturers to maintain their profitability.

2. Most of the data used in risk assessments is supplied by the chemical manufacturers themselves or from contract labs hired by the companies.¹⁰³ The potential for corruption of that system is obvious, but starkly illustrated by the history of Industrial Bio-Test Labs (IBT). For three decades IBT performed one third of all the toxicology testing in the United States. Several

of its executives were convicted in 1983 of extensive scientific misconduct for fraudulent research favoring industry.^{114,115}

IBT had performed over 2,000 key product safety tests resulting in the release of 212 pesticides. After an extensive review in 1983, EPA determined that only 16% of IBT's testing results were valid.¹¹⁶

Only a tiny number of the invalid studies have been replaced, the agency admits, and most of those pesticides continue to be marketed, sold, and used.¹¹⁷

As disturbing as this scandal is, the EPA process created in the wake of that scandal is even more so. EPA has established a research protocol called Mutual Acceptance of Data (MAD), whose effect is to exclude truly independent, peer-reviewed scientific research, like from academia, in favor of industry produced research.

Jonathan Latham, PhD, writes for the Cornucopia Institute, ...“no EPA employee ever sets eyes on the original experiments or the primary data, and only a handful can access even the summarised results. This system has the consequence of excluding any formal possibility that whistleblowing on the part of Federal employees or FOIA requests (from outsiders) might reveal fraudulent or otherwise problematic tests. EPA calculatedly turned a blind eye to any potential future wrongdoing in the full knowledge that the chemical regulatory system it oversaw was systemically corrupt.”¹¹⁸

3. The anachronistic premise that the “dose makes the poison,” established almost exclusively in lab animals, is still the basis of toxicology risk assessments. TRAs overlook the presence of non-monotonic dose-response curves, i.e. the relationship between dose and toxicity outcome is not necessarily linear. There are hundreds of studies that show non-linearity, which is also true for other thoroughly researched toxins like air pollution and lead. Non-linear dose response curves open the possibility that adverse health outcomes occur at concentrations below the classic toxicological no-observed-adverse-effect level (NOAEL). Indeed, numerous studies have shown that some toxins are actually more dangerous at lower concentrations than higher ones. Furthermore, these magical thresholds of safety don't really exist even in those cases where the relationship is linear.

4. There are obviously numerous health outcomes beyond death and cancer that are more difficult or impossible to identify in animals, like infertility, immunosuppression, endocrine disruption, neurodegenerative diseases, altered behavior and subtle, reduced intellectual capacity, which are exactly the health outcomes of greatest concern with pesticides in general, including glyphosate.

5. The impact of toxins on genetic and epigenetic integrity may show up in subsequent generations, even if they are not exposed. But examining subsequent generations are seldom part of the research on chemical toxins.

6. The “safety factors” introduced to buffer for sensitivity variability between humans and between humans and other species (inter and intra-species differences) were arbitrarily established as multiples of ten based loosely on research of the 1950s. Very little research since then supports those arbitrary numbers. Those safety factors, ADIs, TRAs, and NOAEL virtually ignore the most crucial aspect of developmental neurotoxicity, the timing of exposure, intrauterine stages in particular.

7. There is increasing evidence that neurotoxicity can be very sex specific, something that is increasingly apparent in human studies, but seldom part of the animal studies done for risk assessments. Males are usually more vulnerable to environmental neurotoxins than females.

8. TRAs virtually ignore critical differences in physiology, metabolism, microanatomy, hormones, liver function, and enzyme production between fetuses, infants, children and adults. Chemicals crossing the placenta and affecting fetal development has been an after-thought at best.

9. TRAs are essentially mathematical calculations. These calculations dramatically oversimplify very complex biologic, physiologic and molecular processes that don't lend themselves to mathematical equations.

10. TRAs do not pass the acid test of scientific reproducibility. Two different "assessors" can come up with widely disparate results given the same input data, especially if they have different motivations—subjectivity rather than objectivity. William Ruckelshaus the former EPA director wrote in 1984, "We should remember that risk assessment can be like the captured spy: If you torture it long enough, it will tell you anything you want to know."¹¹ In 1991, the National Academy of Sciences wrote, "Risk assessment techniques are highly speculative, and almost all rely on multiple assumptions of fact -- some of which are entirely untestable."¹²⁰

11. Through biological processes many toxic substances accumulate in organisms, concentrate in certain tissues of those organisms, and increase in concentration as they move up the food chain. Humans are at the top of the food chain and because our capacity to break down toxic chemicals is very limited, concentrations in our bodies usually increase over time. Lipophilic (fat-like) toxins will concentrate especially in human breast milk, increasing the risk to progeny, but that kind of exposure consequence is not addressed by EPA methodology.

12. Classical toxicology assessments almost never attempt to evaluate more than one toxin at a time, and the regulations derived from those risk assessments are similarly singularly focused. The default assumption is that the hazard posed by each individual compound, tested out of context and in isolation, can predict the hazard of the entire complex mixtures of chemicals. Obviously, no one in America or anywhere on earth is exposed to merely one toxic chemical. Furthermore, the potential for toxicity may be much greater than just the additive sum of all these chemicals individually. Specifically, synergistic effects from chemical interactions are quite possible, if not likely, which would significantly increase the potential for health hazards.¹²¹

In fact, in Salt Lake City and many other areas, mosquito abatement pesticides are often used with a synergistic agent, PBO, that may increase the lethality of the chemical mix to insects, and the toxicity to humans by a factor of ten.

Under the absurd methodology of only considering one toxin at a time, a safe dose of aspirin, combined with safe doses of ibuprofen, Oxycontin, Toradol, Celebrex, acetaminophen, three glasses of wine, and a pint of Jack Daniels would all be considered individually "safe," but in reality might very well add up to be lethal. When a supposedly tolerable exposure to diesel exhaust is combined with a tolerable exposure to cadmium, fluoride, lead, arsenic, permethrin and naled, the end result can be an intolerable health consequence. But the source of each of these toxins can claim to the community that their toxin is safe.

In 1978 Congress changed requirements for chemical manufacturers such that they would only be required to test "active ingredients." Since then it is routine for toxicology experiments to only test exposure to the "active ingredient" in a product. This leaves an important loop hole.

“Inactive” compounds, like adjuvants and surfactants, are often toxic as well, sometimes more so, and yet are exempt from testing, and the end product, the commercial mix of active and inactive ingredients, may not be tested at all.

Furthermore after 1978, pesticide manufacturers were given the option of registering their commercial products “conditionally,” which allows them to sell them without complete safety data and thousands of pesticides entered the market through that gaping loop hole.^{122,123}

13. Traditional toxicology assessments wrongly assume that we have a comprehensive understanding of the complexity of biological processes and chemical toxicity when in reality there are vast information gaps. Lack of knowledge cannot be equated with safety; it can only be equated with lack of knowledge. Much of that lack of knowledge is deliberately orchestrated by the manufacturers. The most basic information is not available on over 90 percent of the industry inventory of chemical products. The Government Accountability Office says that 95 percent of the information given to the EPA by companies on their new chemicals are wrapped up in confidentiality claims, which makes them unavailable to regulators. Almost all the data that is available is supplied by the manufacturer whose obvious self-interest obscures objectivity. And the cumulative health impact of exposure to all these chemicals is ignored.

Manufacturers don’t even have to reveal enough of the chemical mix of their products to allow government agencies to track their spread in the environment or to independently test for toxicity. The TSCA requires manufacturers to submit safety data only if they have it. Most don’t, so EPA is left with computer models to predict whether chemicals will pose health problems, and no one believes that is adequate. Because of chronic underfunding and understaffing they are usually left with contracting out their review of the available science. In the overwhelming majority of cases they merely accept the conclusions of the contract reviewers.

In those rare instances where evidence stacks up implicating a chemical as a serious hazard, industry response follows a well-worn path. “By the time the scientific community catches up to one chemical, industry moves on to another and they go back to their playbook of delay and denial,” said Deborah Rice, a former EPA toxicologist who now works for the Maine Center for Disease Control and Prevention.¹²⁴

Industry has followed this path consistently from the outset. When DDT and organochlorides were found to be unacceptably toxic, industry replaced them with malathion and chlorpyrifos. When they were found to also be toxic, they were largely replaced by other organophosphates (OP). When the OPs were also found to be toxic, they were replaced with neonicotinoids and pyrethroids. These chemical groups have also been found to be toxic. When glyphosate was found to be carcinogenic, paraquat was marketed as a safer alternative, but its connection to Parkinson’s was established 40 years ago. This ongoing merry-go-round of always replacing one toxic chemical with another that is also eventually found to be toxic verifies what is common sense: that chemicals toxic enough to be fatal to the microbiological world are inevitably found to be toxic to the macrobiological world. Virtually the only pesticide in this entire cascade that is no longer on the market is DDT. This cycle is a reflection of the power of the pesticide manufacturers to maintain their profitability, almost regardless of the human and environmental cost.

Because of the obvious shortcomings of risk assessments, countries in Europe began embracing a more protective approach to toxic chemical exposures guided by the “precautionary principle.” The principle can be expressed this way. When there is reasonable evidence of harm, society is compelled to act to protect the public, rather than wait for scientific proof. This adoption of the

precautionary principle was even written into the Maastricht Treaty that formed the European Union. Journalist Peter Montague describes this difference between European and American regulation of chemicals this way. The European model asks, “How much is avoidable?” The American model asks, “How much harm is acceptable?”¹²⁵

The United States’ approach prioritizes protection of corporations and chemicals rather than public health. The precautionary principle has not been allowed to enter the arena of government regulation under either Democratic or Republican Administrations because of corporate pressure.

The result has been wide spread, frank regulatory failures. And the failures started with original chemical safety law, the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) passed in 1947 which governs the registration, distribution, sale, and use of pesticides in the United States, and the Toxic Substances Control Act (TSCA), passed in 1976, both virtually written by the chemical industry. Both laws were designed to prioritize approving chemicals, not protecting public health or the environment. TSCA allowed all 62,000 chemicals that were on the market at the time to remain so, unless the EPA found at some later time that they represented unacceptable risk. FIFRA requires that the EPA take into account “economic and social costs” and benefits of a pesticide in granting approval, opening an enormous door for vague and often unsubstantiated economic benefits to take priority over public health protection.

Only undeniable health consequences and apparent toxicity after consumer use and wide spread environmental contamination of the products must be reported to the EPA. If this seems like closing the barn door after the horses have already escaped, bear in mind that before 1976, there was no barn door at all preventing or regulating chemicals that were unleashed upon the public.

Furthermore, the law only allowed testing if information from the chemical makers themselves suggested it was likely to be dangerous. Moreover, the law allowed chemical corporations to claim just about everything was a trade secret allowing them to hide critical information from the public, regulators, and even health care providers. As a result, EPA has only tested about 200 of all 140,000 industrial chemicals produced since WWII. For chemicals entering the market since 1976 they are also allowed unless EPA again determines they constitute unreasonable risk.¹²⁶

But they only have 90 days to make that determination and hardly ever do they have all the data they need. The end result is virtually all the chemicals made by corporations will make it into the bodies of consumers. For example, despite it being an undeniable killer of tens of thousands of people, it is still legal to manufacture and sell asbestos. EPA in its entire history has only succeeded in completely banning eight chemicals--PCBs, dioxins, fully halogenated chlorofluoroalkanes (ozone depleters), hexavalent chromium (the Erin Brockovich chemical), and four metal working chemicals. The last time the EPA banned anything completely was in 1984.¹²⁷

Regulatory impotence flows from the default assumption that industrial chemicals are safe, unless or until, unequivocally proven unsafe. Essentially human consumers are today’s guinea pigs of the chemical industry, just like the previous generation was for DDT, PCBs, asbestos, radiation and lead. Once a dangerous product is put on the market, it is only withdrawn after it has already caused large scale, undeniable damage and/or death.

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