GLYPHOSATE - Understanding and Managing it in Massachusetts

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There is a multitude of documents and studies to justify total elimination of glyphosate-based herbicides (GBHs) in Massachusetts and elsewhere. However, there is resistance to such a ban and prominent among them (as given by some government agencies, towns, golf course personnel and pesticide technicians) are:

a. Classification of glyphosate as a human carcinogen (Group C, 2A) by WHO's International Agency for Research on Cancer is questioned.
b. It binds to soil, rapidly degrades and is not transported elsewhere.
c. There has not been significant research to justify reevaluation of its effects on public and environmental health.
d. Since the EPA registers it and FIFRA (Federal Insecticide, Fungicide, and Rodenticide Act) regulates it, it is legal to use and safe for applicators, consumers, and the environment.

Thus, let's look at significant facts provided by historical review, independent science and courtroom discovery:

In **1985**, toxicology staff of the US EPA Office of Pesticides and Toxic Substances concluded that glyphosate was a Class C oncogen; and clearly refuted challenges to the contrary from Monsanto (1).

After 1985, the EPA, at least at the administrative level, began to display behavior that was ill-suited to a government agency charged with protecting human and environmental health. Such behavior was challenged by some of its scientific staff in **2013** (2), but corruption and collusion persisted and intensified after WHO's International Agency for Research on Cancer concluded in **March 2015** that glyphosate is a human carcinogen (3,4). IARC noted that glyphosate also caused DNA and chromosomal damage in human cells. IARC's scientific rigor has been challenged, largely influenced by Monsanto, and such challenges have been successfully refuted by independent science (5,7).

March 15, 2017, U.S. Congressman Ted Lieu recommended that consumers stop using glyphosate because of the risks of non-Hodgkin's lymphoma (6). And, importantly, he called for an investigation by the Department of Justice to look into any potential misconduct by employees of the EPA.

Mostly post-2017 there have been many scientific studies related to morbidity and mortality in humans and other animals and to environmental degradation. Examples (details on p. 3) include: the link between glyphosate and non-Hodgkin's lymphoma (8); other disease relationships and finding glyphosate in childhood vaccines (9,10); pregnancy complications (11); breast cancer (12); inheritance of disease across generations and sperm mutations (13); increased development rate of antibiotic resistance (14); dire effects on honey bee gut microbiome and on sensory and cognitive abilities, and complications associated with GMO crops (15,16); negative effects below ground on microbes, earthworms and mycorrhizal fungi and interference with nutrient cycling (17,18); forestry spray drift with persistent contamination of edible plants (19); waterbody pollution from treatment of invasive species (20); glyphosate and breakdown products widespread transport off-site from agricultural and urban sources (21); atmospheric pollution and rainfall's contribution to the surface levels of glyphosate pollution (22); persistence in soil and leaching of glyphosate breakdown products through soil and transfer to waterways (23); glyphosate-derived phosphorous influences the cycling of phosphorus in soil, persists in the environment, and can influence soil phosphorus accumulation and losses to surrounding freshwater systems prone to nutrient pollution (24); research from the European Commission's Joint Research Centre and two Dutch laboratories shows glyphosate persists in soils affecting not only soil fertility and crop quality, but also human and environmental health. The concentrations of glyphosate and AMPA found in the

study have been shown to be toxic to soil organisms such as earthworms, beneficial bacteria and fungi, as glyphosate weakens down plants' natural defences making them susceptible to pathogens. These substances that get adsorbed by soil particles are not immobile, but can propagate through wind or rainfall, leading to air pollution and exposure through the atmosphere as well as contamination of surface and ground waters (25); GBHs have the potential to undermine crop health via: (i) impairment of the innate physiological defences by interruption of the shikimic acid pathway; (ii) impairment of physiological disease defences; (iii) interference with rhizosphere microbial ecology (in particular, GBHs have the potential to enhance the population and/or virulence of some phytopathogenic microbial species in the crop rhizosphere); and finally, (iv) the reduction in the uptake and utilisation of nutrient metals by crops (26).

Since March 2017, the Monsanto Papers have provided a treasure trove of internal documents slowly released as part of a US lawsuit by cancer victims against Monsanto over glyphosate (https://www.baumhedlundlaw.com/toxic-tort-law/monsanto-roundup-lawsuit/monsanto-secret-documents/). These documents show the company's real, and rather troubling, approach to science and evidence; and its unsavory alliances with government, universities, scientific journals, etc. to cover-up the harmful nature of glyphosate.

Conclusions:

a. Glyphosate is a carcinogen for humans and other mammals.
b. Glyphosate can be very persistent in soil and water, and moves both vertically and horizontally above and below ground including in groundwater, surface runoff and rainfall.
c. Abundant research shows a wide variety of morbidity and mortality in humans and other species, and ecosystem damage, attributable to glyphosate exposure.
d. The EPA cannot be considered a reliable source for information regarding this herbicide's impact on human and environmental health, and it's recent re-evaluation and registration approval of glyphosate-based herbicides should be considered invalid and subject to independent review. To justify glyphosate use on the basis of its "legal registration" by the EPA is specious at best; and following FIFRA regulations for glyphosate is scientifically irrelevant since it is based on incomplete or distorted science that fails to safely protect applicators, consumers, and the environment.

Recommendations:

Upon evaluating the information provided, it is scientifically and ethically illogical for MassDEP, MDAR and the Mass Pesticide Board to follow guidance of the EPA with regard to glyphosate. Further, MassDEP (https://www.mass.gov/files/documents/2019/09/30/mwcvrltr.pdf) appears to rely on MDAR for glyphosate guidance (https://www.mass.gov/files/documents/2016/08/xh/glyphosate-2011.pdf), and MDAR depends on USDA Forest Service for comprehensive glyphosate reviews and data (http://www.fs.fed.us/foresthealth/pesticide/risk.shtml). Unfortunately, the latter agencies are not scientifically current; that is, MDAR's data is basically pre-1989, and USDA mostly predates 2010. Glyphosate's effects on all life forms needs to be reevaluated with regard to available independent science, a sampling of which is provided herein. Note also that carbon storage/cycling (and soil fertility) depend on healthy plants and a healthy soil rhizosphere. Glyphosate interferes with RuBisCO's enzymatic function critical for plants' fixation of atmospheric CO_2 during photosynthesis; and it alters the rhizosphere microbial composition and disrupts microbial metabolism and nutrient cycling — resulting in reduced carbon sequestration. Overall, this can be called "The Glyphosate Complication" — as in an unfavorable evolution of a disease, health condition or medical treatment. I think "unfavorable" might be the kindest of adjectives that could be applied to the evolution of glyphosate, its series of patents, and its application history. It is obvious that the manner in which glyphosate policies and procedures are managed in the Commonwealth of Massachusetts are in critical need of revision. This document gives unambiguous reasons for such revision and for a Statewide ban on glyphosate that would maximize protection of public and environmental health, protect the food supply and water resources, and enhance carbon sequestration.

SUPPORTING DOCUMENTATION ——————————————————————————

—— CARCINOGEN ——

1)••March 4, 1985. **EPA Consensus review of glyphosate** signed by eight Toxicology Branch personnel and addressed to Robert Taylor, Product Manager, Herbicide-Fungicide Branch, US EPA Office of Pesticides and Toxic Substances. (https://archive.epa.gov/pesticides/chemicalsearch/chemical/foia/web/pdf/103601/103601-171.pdf)

Part E. Classification of Glyphosate

"In accordance with EPA proposed guidelines (FR of Nov. 23, 1984) the panel has classified Glyphosate as a Category C oncogen."

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2)••March 4, 2013 — Court Document - 2017. **March 4, 2013 Letter from Marion Copley to Jess Rowland.** *Monsanto Papers*: Case 3:16-md-02741-VC Document 141-1 Filed 02/10/17 Page 1 of 1.

Note: Marion Copley, EPA Senior Scientist re. glyphosate (retired and dying of breast cancer), writing to her former supervisor, Jess Rowland, EPA Administrator in charge of glyphosate.

Jess,

Since I left the Agency with cancer, I have studied the tumor process extensively and I have some mechanism comments which may be very valuable to CARC based on my decades of pathology experience. I'll pick one chemical to demonstrate my points.

Glyphosate was originally designed as a chelating agent and I strongly believe that is the identical process involved in its tumor formation, which is highly supported by the literature.

-Chelators inhibit apoptosis, the process by which our bodies kill tumor cells
-Chelators are endocrine disruptors, involved in tumorigenesis
-Glyphosate induces lymphocyte proliferation
-Glyphosate induces free radical formation
-Chelators inhibit free radical scavenging enzymes requiring Zn, Mn or Cu for activity (i.e. SODs)
-Chelators bind zinc, necessary for immune system function
-Glyphosate is genotoxic, a key cancer mechanism
-Chelators inhibit DNA repair enzymes requiring metal cofactors
-Chelators bind Ca, Zn, Mg, etc to make foods deficient for these essential nutrients
-Chelators bind calcium necessary for calcineurin-mediated immune response
-Chelators often damage the kidneys or pancreas, as glyphosate does, a mechanism to tumor formation
-Kidney/pancreas damage can lead to clinical chemistry changes to favor tumor growth
-Glyphosate kills bacteria in the gut and the gastrointestinal system is 80% of the immune system
-Chelators suppress the immune system making the body susceptible to tumors

Previously, CARC concluded that glyphosate was a " possible human carcinogen". The kidney pathology in the animal studies would lead to tumors with other mechanisms listed above. Any one of these mechanisms alone listed can cause tumors, but glyphosate causes all of them simultaneously. It is essentially certain that glyphosate causes cancer. With all of the evidence listed above, the CARC category should be changed to "probable human carcinogen". Blood cells are most exposed to chelators, if any study shows proliferation of lymphocytes, then that is confirmatory that glyphosate is a carcinogen.

Jess, you and I have argued many times on CARC. You often argued about topics outside of your knowledge, which is unethical. Your trivial MS degree from l971 Nebraska is far outdated, thus CARC science is 10 years behind the literature in mechanisms. For once in your life, listen to me and don't play your political conniving games with the science to favor the registrants. For once do the right thing and don't make decisions based on how it affects your bonus. You and Anna Lowit intimidated staff on CARC and changed HIARC and HASPOC final reports to favor industry. Chelators clearly disrupt calcium signaling, a key signaling pathway in all cells and mediates tumor progression. Greg Ackerman is supposed to be our expert on mechanisms, but he never mentioned any of these concepts at CARC and when I tried to discuss it with him he put me off. Is Greg playing your political games as well, incompetent or does he have some conflict of interest of some kind? Your Nebraska colleague took industry funding, he clearly has a conflict of interest. Just promise me not to ever let Anna on the CARC committee, her decisions don't make rational sense. If anyone in OPP is taking bribes, it is her.

I have cancer and I don't want these serious issues in HED to go unaddressed before I go to my grave. I have done my duty.
Marion Copley
March 4, 2013

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3)••IARC. 2015. **Some organophosphate insecticides and herbicides/ IARC Working Group on the Evaluation of Carcinogenic Risks to Humans.** *IARC monographs on the evaluation of carcinogenic risks to human*s: V.112. Lyon, France - 2017.
https://monographs.iarc.fr/wp-content/uploads/2018/07/mono112.pdf
Lyon, France, 20 March 2015 – The International Agency for Research on Cancer (IARC), the specialized cancer agency of the World Health Organization, has assessed the carcinogenicity of five organophosphate pesticides. The herbicide glyphosate and the insecticides malathion and diazinon were classified as probably carcinogenic to humans (Group 2A).
For the herbicide glyphosate, there was limited evidence of carcinogenicity in humans for non-Hodgkin lymphoma. The evidence in humans is from studies of exposures, mostly agricultural, in the USA, Canada, and Sweden published since 2001. In addition, there is convincing evidence that glyphosate also can cause cancer in laboratory animals. On the basis of tumours in mice, the United States Environmental Protection Agency (US EPA) originally classified glyphosate as possibly carcinogenic to humans (Group C) in 1985. After a re-evaluation of that mouse study, the US EPA changed its classification to evidence of non-carcinogenicity in humans (Group E) in 1991. The US EPA Scientific Advisory Panel noted that the re-evaluated glyphosate results were still significant using two statistical tests recommended in the IARC Preamble. The IARC Working Group that conducted the evaluation considered the significant findings from the US EPA report and several more recent positive results in concluding that there is sufficient evidence of carcinogenicity in experimental animals. Glyphosate also caused DNA and chromosomal damage in human cells, although it gave negative results in tests using bacteria. One study in community residents reported increases in blood markers of chromosomal damage.

What does Group 2A mean?
Group 2A means that the agent is probably carcinogenic to humans. This category is used when there is limited evidence of carcinogenicity in humans and sufficient evidence of carcinogenicity in experimental animals. Limited evidence means that a positive association has been observed between exposure to the agent and cancer but that other explanations for the observations (called chance, bias, or confounding) could not be ruled out. This category is also used when there is limited evidence of carcinogenicity in humans and strong data on how the agent causes cancer.(micronuclei) after glyphosate formulations were sprayed nearby.

4)••April 28, 2015 — Court Document - 2017. **April 28. 2015 Email from Daniel Jenkins (U.S. Agency Lead, Regulatory Affairs, Monsanto, AG/1920) to William Heydens (Monsanto, AG/1000) re. Glyphosate IARC Question.** *Monsanto Papers*: Case 3:16-md-02741-VC Document 189-4 Filed 03/14/17 Page 1 of 4
Referring to the same EPA's Jess Rowland as in the March 4, 2013 document cited earlier, Daniel Jenkins notes that Jess Rowland requested a contact at ASTDR (US DHHS, Agency for Toxic Substances and Disease Registry because it was considering a review of glyphosate), and is quoted as saying "**If I can kill this I should get a medal"**. Jenkins goes on to caution Heydens: "However, don't get your hopes up, I doubt EPA and jess can kill this; but it's good to know they are going to actually make the effort now to coordinate due to our pressing and their shared concern that ASTDR is consistent in its conclusions with EPA."
NOTE: Monsantos 2015 efforts did succeed in delaying the ASTDR report, Toxicological Profile for Glyphosate, that was published in **April 2019**. This report supports and strengthens the 2015 cancer assessment of the International Agency for Research on Cancer (IARC noted above),

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5)••Portier CJ, BK Armstrong, BC Baguley, et al. 2016. **Differences in the carcinogenic evaluation of glyphosate between the International Agency for Research on Cancer (IARC) and the European Food Safety Authority (EFSA)**. *J Epidem Commun Health:* 70 (8). https://jech.bmj.com/content/70/8/741.full
The International Agency for Research on Cancer (IARC) Monographs Programme identifies chemicals, drugs, mixtures, occupational exposures, lifestyles and personal habits, and physical and biological agents that cause cancer in humans and has evaluated about 1000 agents since 1971. For Monograph 112, 17 expert scientists evaluated the carcinogenic hazard for four insecticides and the herbicide glyphosate. The WG concluded that the data for glyphosate meet the criteria for classification as a probable human carcinogen. The European Food Safety Authority (EFSA) is the primary agency of the European Union for risk assessments regarding food safety. In October 2015, EFSA reported on their evaluation of the Renewal Assessment Report (RAR) for glyphosate that was prepared by the Rapporteur Member State, the German Federal Institute for Risk Assessment (BfR). EFSA concluded that 'glyphosate is unlikely to pose a carcinogenic hazard to humans and the evidence does not support classification with regard to its carcinogenic potential'. Serious flaws in the scientific evaluation in the RAR incorrectly characterize the potential for a carcinogenic hazard from exposure to glyphosate. Since the RAR is the basis for the European Food Safety Agency (EFSA) conclusion, it is critical that these shortcomings are corrected.

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6)••Lieu, TW. 2017. **Rep. Lieu Statement on new glyphosate safety concerns. March 15, 2017**/ Press Release
"…consumers should immediately stop using *Roundup*, whose core ingredient glyphosate has been labeled a likely carcinogen and has been linked to non-Hodgkin's lymphoma by the International Agency for Research on Cancer" He further stated, "We need to find out if Monsanto or the Environmental Protection Agency mislead the public. Reports suggest that a senior official at the EPA [undoubtedly re. Jess Rowland - see Apr. 28, 2015 above] worked to suppress a U.S. Department of Health and Human Services review of glyphosate [undoubtedly re. ASTDR -see Apr. 28, 2015 above], and may have leaked information to Monsanto." He also said, "I believe a Department of Justice Investigation is warranted to look into any potential misconduct by employees of the EPA. I also believe a congressional hearing in immediately warranted."

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7)••Benbrook CM. 2019. **How did the US EPA and IARC reach diametrically opposed conclusions on the genotoxicity of glyphosate-based herbicides?** *Environ Sci Eur* (2019) 31: 2. https://doi.org/10.1186/s12302-018-0184-7
EPA and IARC reached diametrically opposed conclusions on glyphosate genotoxicity for three primary reasons: (1) in the core tables compiled by EPA and IARC, the EPA relied mostly on registrant-commissioned, unpublished regulatory studies, 99% of which were negative, while IARC relied mostly on peer-reviewed studies of which 70% were positive (83 of 118); (2) EPA's evaluation was largely based on data from studies on technical glyphosate, whereas IARC's review placed heavy weight on the results of formulated GBH and AMPA assays; (3) EPA's evaluation was focused on typical, general population dietary exposures assuming legal, food-crop uses, and did not take into account, nor address generally higher occupational exposures and risks. IARC's assessment encompassed data from typical dietary, occupational, and elevated exposure scenarios. More research is needed on real-world exposures to the chemicals within formulated GBHs and the biological fate and consequences of such exposures.

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8)••L Zhang, I Rana, E Taioli, RM Shaffer & L Sheppard. 2019. **Exposure to glyphosate-based herbicides and risk for Non-Hodgkin Lymphoma: A meta-analysis and supporting evidence.** *Mutation Research/Rev in Mut Res:* (Available online 10 February 2019).
https://www.sciencedirect.com/science/article/pii/S1383574218300887?mc_cid=23c18e62e7&mc_eid=ff8c3a64ef
Glyphosate is the most widely used broad-spectrum systemic herbicide in the world. Recent evaluations of the carcinogenic potential of glyphosate-based herbicides (GBHs) by various regional, national, and international agencies have engendered controversy. We investigated whether there was an association between high cumulative exposures to GBHs and increased risk of non-Hodgkin lymphoma (NHL) in humans. We conducted a new meta-analysis that includes the most recent update of the Agricultural Health Study (AHS) cohort published in 2018 along with five case-control studies. Using the highest exposure groups when available in each study, we report the overall meta-relative risk (meta-RR) of NHL in GBH-exposed individuals was increased by 41% (meta-RR=1.41, 95% confidence interval, CI: 1.13–1.75). For comparison, we also performed a secondary meta-analysis using high-exposure groups with the earlier AHS (2005), and we calculated a meta-RR for NHL of 1.45 (95% CI: 1.11–1.91), which was higher than the meta-RRs reported previously. Multiple sensitivity tests conducted to assess the validity of our findings did not reveal meaningful differences from our primary estimated meta-RR. To contextualize our findings of an increased NHL risk in individuals with high GBH exposure, we reviewed publicly available animal and mechanistic studies related to lymphoma. We documented further support from studies of malignant lymphoma incidence in mice treated with pure glyphosate, as well as potential links between glyphosate / GBH exposure and immunosuppression, endocrine disruption, and genetic alterations that are commonly associated with NHL or lymphomagenesis. Overall, in accordance with findings from experimental animal and mechanistic studies, our current meta-analysis of human epidemiological studies suggests a compelling link between exposures to GBHs and increased risk for NHL.

—— CANCER AND OTHER HEALTH ISSUES ——

9)••Samsel A & S Seneff. 2014. **Glyphosate, pathways to modern diseases IV: cancer and related pathologies.** *J Biol Phys and Chem:* 15 (2015) 121–159.
doi: 10.4024/11SA15R.jbpc.15.03 https://www.drperlmutter.com/wp-content/uploads/2016/03/Glyphosate_pathways_to_modern_diseases_IV_cancer_and_related_pathologies.pdf
Glyphosate is the active ingredient in the pervasive herbicide, Roundup, and its usage, particularly in the United States, has increased dramatically in the last two decades, in step with the widespread adoption of Roundup®-Ready core crops. The World Health Organization

recently labelled glyphosate as “probably carcinogenic.” In this paper, we review the research literature, with the goal of evaluating the carcinogenic potential of glyphosate. Glyphosate has a large number of tumorigenic effects on biological systems, including direct damage to DNA in sensitive cells, disruption of glycine homeostasis, succinate dehydrogenase inhibition, chelation of manganese, modification to more carcinogenic molecules such as N-nitrosoglyphosate and glyoxylate, disruption of fructose metabolism, etc. Epidemiological evidence supports strong temporal correlations between glyphosate usage on crops and a multitude of cancers that are reaching epidemic proportions, including breast cancer, pancreatic cancer, kidney cancer, thyroid cancer, liver cancer, bladder cancer and myeloid leukaemia. Here, we support these correlations through an examination of Monsanto’s early studies on glyphosate, and explain how the biological effects of glyphosate could induce each of these cancers. We believe that the available evidence warrants a reconsideration of the risk/benefit trade-off with respect to glyphosate usage to control weeds, and we advocate much stricter regulation of glyphosate.

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10)••Samsel A & S Seneff. 2017. **Glyphosate pathways to modern diseases VI: Prions, amyloidoses and autoimmune neurological diseases.** *J Biol Phys and Chem:*17 (2017) 8–32. **https://www.researchgate.net/publication**
316601847_Glyphosate_pathways_to_modern_diseases_VI_Prions_amyloidoses_and_autoimmune_neurological_diseases
Usage of the herbicide glyphosate on core crops in the USA has increased exponentially over the past two decades, in step with the exponential increase in autoimmune diseases including autism, multiple sclerosis, inflammatory bowel disease, type 1 diabetes, coeliac disease, neuromyelitis optica and many others. In this paper we explain how glyphosate, acting as a non-coding amino acid analogue of glycine, could erroneously be integrated with or incorporated into protein synthesis in place of glycine, producing a defective product that resists proteolysis. Whether produced by a microbe or present in a food source, such a peptide could lead to autoimmune disease through molecular mimicry. We discuss similarities in other naturally produced disease-causing amino acid analogues, such as the herbicide glufosinate and the insecticide L-canavanine, and provide multiple examples of glycine-containing short peptides linked to autoimmune disease, particularly with respect to multiple sclerosis. Most disturbing is the presence of glyphosate in many popular vaccines including the measles, mumps and rubella (MMR) vaccine, which we have verified here for the first time. Contamination may come through bovine protein, bovine calf serum, bovine casein, egg protein and/or gelatin. Gelatin sourced from the skin and bones of pigs and cattle given glyphosate-contaminated feed contains the herbicide. Collagen, the principal component of gelatin, contains very high levels of glycine, as do the digestive enzymes: pepsin, trypsin and lipase. The live measles virus could produce glyphosate-containing haemagglutinin, which might induce an autoimmune attack on myelin basic protein, commonly observed in autism. Regulatory agencies urgently need to reconsider the risks associated with the indiscriminate use of glyphosate to control weeds.

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11)••Parvez S, RR Gerona, C Proctor, M Friesen, JL Ashby, JL Reiter, Z Lui & PD Winchester. 2018. **Environmental Health Glyphosate exposure in pregnancy and shortened gestational length: a prospective Indiana birth cohort study.** *Environmental Health*: 17, Article number: 23 (2018).
https://ehjournal.biomedcentral.com/articles/10.1186/s12940-018-0367-0
The mean age of participants was 29 years, and the majority were Caucasian. Ninety three percent of the pregnant women had GLY levels above the limit of detection (0.1 ng/mL). Mean urinary GLY was 3.40 ng/mL (range 0.5–7.20 ng/mL). Higher GLY levels were found in women who lived in rural areas (p =0.02), and in those who consumed >24 oz. of caffeinated beverages per day (p =0.004). None of the drinking water samples had detectable GLY levels. We observed no correlations with fetal growth indicators such as birth weight percentile and

head circumference. However, higher GLY urine levels were significantly correlated with shortened gestational lengths (r=−0.28, p=0.02). This is the first study of GLY exposure in US pregnant women using urine specimens as a direct measure of exposure. We found that >90% of pregnant women had detectable GLY levels and that these levels correlated significantly with shortened pregnancy lengths. Although our study cohort was small and regional and had limited racial/ethnic diversity, it provides direct evidence of maternal GLY exposure and a significant correlation with shortened pregnancy. Further investigations in a more geographically and racially diverse cohort would be necessary before these findings could be generalized.

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12)••Duforeste M, A Nadaradjane, G Bougras-Cartron, J Briand, C Olivier, Jean-Sébastien Frenel, F. M. Vallette, SA Lelièvre & Pierre-François Cartron. 2019. **Glyphosate Primes Mammary Cells for Tumorigenesis by Reprogramming the Epigenome in a TET3-Dependent Manner.** *Front Genet:* 27 September 2019.
https://doi.org/10.3389/fgene.2019.00885
https://www.frontiersin.org/articles/10.3389/fgene.2019.00885/full
The acknowledgment that pollutants might influence the epigenome raises serious concerns regarding their long-term impact on the development of chronic diseases. The herbicide glyphosate has been scrutinized for an impact on cancer incidence, but reports demonstrate the difficulty of linking estimates of exposure and response analysis. An approach to better apprehend a potential risk impact for cancer is to follow a synergistic approach, as cancer rarely occurs in response to one risk factor. The known influence of glyphosate on estrogen-regulated pathway makes it a logical target of investigation in breast cancer research. We have used nonneoplastic MCF10A cells in a repeated glyphosate exposure pattern over 21 days. Glyphosate triggered a significant reduction in DNA methylation, as shown by the level of 5-methylcytosine DNA; however, in contrast to strong demethylating agent and cancer promoter UP peptide, glyphosate-treated cells did not lead to tumor development. Whereas UP acts through a DNMT1/PCNA/UHRF1 pathway, glyphosate triggered increased activity of ten-eleven translocation (TET)3. Combining glyphosate with enhanced expression of microRNA (miR) 182-5p associated with breast cancer induced tumor development in 50% of mice. Culture of primary cells from resected tumors revealed a luminal B (ER+/PR-/HER2-) phenotype in response to glyphosate-miR182-5p exposure with sensitivity to tamoxifen and invasive and migratory potentials. Tumor development could be prevented either by specifically inhibiting miR 182-5p or by treating glyphosate-miR 182-5p-cells with dimethyloxallyl glycine, an inhibitor of TET pathway. Looking for potential epigenetic marks of TET-mediated gene regulation under glyphosate exposure, we identified MTRNR2L2 and DUX4 genes, the hypomethylation of which was sustained even after stopping glyphosate exposure for 6 weeks. Our findings reveal that low pressure but sustained DNA hypomethylation occurring via the TET pathway primes cells for oncogenic response in the presence of another potential risk factor. These results warrant further investigation of glyphosate-mediated breast cancer risk.

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13)••Kubsad D, E E Nilsson, S E King, I S-Riggleman, D Beck & M K Skinner. 2019. **Assessment of Glyphosate Induced epigenetic transgenerational Inheritance of pathologies and sperm epimutations: Generational toxicology. Scientific RepoRts |** (2019) 9:6372 | https://doi.org/10.1038/s41598-019-42860-0
https://skinner.wsu.edu/documents/2019/04/2019-kubsad-etal-glyphosate-scientificreports.pdf/
Ancestral environmental exposures to a variety of factors and toxicants have been shown to promote the epigenetic transgenerational inheritance of adult onset disease. one of the most widely used agricultural pesticides worldwide is the herbicide glyphosate (N-(phosphonomethyl)glycine), commonly known as Roundup. There are an increasing number of conflicting reports regarding the direct exposure toxicity (risk) of glyphosate, but no rigorous investigations on the generational actions. the current study using a transient exposure of gestating F0 generation female rats found negligible impacts of glyphosate on the directly exposed F0 generation, or F1 generation offspring pathology. In contrast, dramatic increases in

pathologies in the F2 generation grand-offspring, and F3 transgenerational great- grand-offspring were observed. The transgenerational pathologies observed include prostate disease, obesity, kidney disease, ovarian disease, and parturition (birth) abnormalities. epigenetic analysis of the F1, F2 and F3 generation sperm identified differential DNA methylation regions (DMRs). A number of DMR associated genes were identified and previously shown to be involved in pathologies. Therefore, we propose glyphosate can induce the transgenerational inheritance of disease and germline (e.g. sperm) epimutations. observations suggest the generational toxicology of glyphosate needs to be considered in the disease etiology of future generations. Glyphosate (N-(phosphonomethyl)glycine) was discovered in 1950 and was commercialized for its herbicidal activity as Roundup in the 1970s by Monsanto, St. Louis Missouri1. Glyphosate is the world's most commonly used herbicide accounting for nearly 72% of global pesticide usage1. It is the primary herbicide used in the agriculture of corn, soy, and canola, with extensive use in the USA, Supplemental Figure S1. The current "safe"

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14)••Kurenbach B, AM Hill, W Godsoe, S van Hamelsveld, JA Heinemann. 2018. **Agrichemicals and antibiotics in combination increase antibiotic resistance evolution.** *PeerJ* 6:e5801 https://doi.org/10.7717/peerj.5801

Antibiotic resistance in our pathogens is medicine's climate change: caused by human activity, and resulting in more extreme outcomes. Resistance emerges in microbial populations when antibiotics act on phenotypic variance within the population. This can arise from either genotypic diversity (resulting from a mutation or horizontal gene transfer), or from differences in gene expression due to environmental variation, referred to as adaptive resistance. Adaptive changes can increase fitness allowing bacteria to survive at higher concentrations of antibiotics. They can also decrease fitness, potentially leading to selection for antibiotic resistance at lower concentrations. There are opportunities for other environmental stressors to promote antibiotic resistance in ways that are hard to predict using conventional assays. Exploiting our previous observation that commonly used herbicides can increase or decrease the minimum inhibitory concentration (MIC) of different antibiotics, we provide the first comprehensive test of the hypothesis that the rate of antibiotic resistance evolution under specified conditions can increase, regardless of whether a herbicide increases or decreases the antibiotic MIC. Short term evolution experiments were used for various herbicide and antibiotic combinations. We found conditions where acquired resistance arises more frequently regardless of whether the exogenous non-antibiotic agent increased or decreased antibiotic effectiveness. This is attributed to the effect of the herbicide on either MIC or the minimum selective concentration (MSC) of a paired antibiotic. The MSC is the lowest concentration of antibiotic at which the fitness of individuals varies because of the antibiotic, and is lower than MIC. Our results suggest that additional environmental factors influencing competition between bacteria could enhance the ability of antibiotics to select antibiotic resistance. Our work demonstrates that bacteria may acquire antibiotic resistance in the environment at rates substantially faster than predicted from laboratory conditions.

—— ANIMALS, MICROBES and FUNGI ——

15)••Motta EVS, K Raymann, and NA Moran. 2018. **Glyphosate perturbs the gut microbiota of honey bees.** *Proc. Nat. Acad. Sci. (PNAS):* October 9, 2018 115 (41) 10305-10310. https://doi.org/10.1073/pnas.1803880115 https://www.pnas.org/content/115/41/10305

Glyphosate, the primary herbicide used globally for weed control, targets the 5-enolpyruvylshikimate-3-phosphate synthase (EPSPS) enzyme in the shikimate pathway found in plants and some microorganisms. Thus, glyphosate may affect bacterial symbionts of animals living near agricultural sites, including pollinators such as bees. The honey bee gut microbiota is dominated by eight bacterial species that promote weight gain and reduce pathogen susceptibility. The gene encoding EPSPS is present in almost all sequenced

genomes of bee gut bacteria, indicating that they are potentially susceptible to glyphosate. We demonstrated that the relative and absolute abundances of dominant gut microbiota species are decreased in bees exposed to glyphosate at concentrations documented in the environment. Glyphosate exposure of young workers increased mortality of bees subsequently exposed to the opportunistic pathogen *Serratia marcescens*. Members of the bee gut microbiota varied in susceptibility to glyphosate, largely corresponding to whether they possessed an EPSPS of class I (sensitive to glyphosate) or class II (insensitive to glyphosate). This basis for differences in sensitivity was confirmed using in vitro experiments in which the EPSPS gene from bee gut bacteria was cloned into *Escherichia coli*. All strains of the core bee gut species, *Snodgrassella alvi*, encode a sensitive class I EPSPS, and reduction in *S. alvi* levels was a consistent experimental result. However, some *S. alvi* strains appear to possess an alternative mechanism of glyphosate resistance. Thus, exposure of bees to glyphosate can perturb their beneficial gut microbiota, potentially affecting bee health and their effectiveness as pollinators.

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16)••Farina, W M, M. S Balbuena, L T Herbert, C Mengoni Goñalons and D E Vázquez. 2019. **Effects of the herbicide glyphosate on honey bee sensory and cognitive abilities: Individual impairments with implications for the hive.** *Insects* **2019, 10(10), 354**
https://doi.org/10.3390/insects10100354 (open access)
The honeybee Apis mellifera is an important pollinator in both undisturbed and agricultural ecosystems. Its great versatility as an experimental model makes it an excellent proxy to evaluate the environmental impact of agrochemicals using current methodologies and procedures in environmental toxicology. The increase in agrochemical use, including those that do not target insects directly, can have deleterious effects if carried out indiscriminately. This seems to be the case of the herbicide glyphosate (GLY), the most widely used agrochemical worldwide. Its presence in honey has been reported in samples obtained from different environments. Hence, to understand its current and potential risks for this pollinator it has become essential to not only study the effects on honeybee colonies located in agricultural settings, but also its effects under laboratory conditions. Subtle deleterious effects can be detected using experimental approaches. GLY negatively affects associative learning processes of foragers, cognitive and sensory abilities of young hive bees and promotes delays in brood development. An integrated approach that considers behavior, physiology, and development allows not only to determine the effects of this agrochemical on this eusocial insect from an experimental perspective, but also to infer putative effects in disturbed environments where it is omnipresent.
Key points include:
* In 2015, of the 179.9 million ha of global GMO crop area, about 84% contained crops that carried herbicide-resistant genes. Most GMO crops are engineered for tolerance to glyphosate herbicides.
* Glyphosate herbicides are also used on many non-GMO crops and in non-farm environments.
* Honeybees' ingestion of food containing high concentrations of glyphosate resulted in a higher proportion of disoriented foragers. Despite this, honeybees continued foraging from resources that contain glyphosate traces. These sublethal effects on their learning abilities could impact not only the foraging efficiency, but also the coordination of collective activities within the colony.
* Honeybees' ability to establish an association between an odour and a sucrose reward was impaired by an acute exposure to glyphosate.
* There is evidence that glyphosate diminishes short-term memory retention in honeybees.
* Honeybee colonies that are permanently exposed to glyphosate are likely to show a deficit in information propagation and nectar distribution.
* Glyphosate causes changes in gut microbiota and greater susceptibility to pathogens and malnutrition.
* Honeybee brood provided with food containing glyphosate traces were more likely to show delayed moulting and weighed less than control brood.

* Glyphosate acts as a stressor that affects larval development (manifested in in vitro exposure by a lower proportion of larvae achieving moulting success and reduced final weights), which could have implications for overall long-term colony survival.

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17)••Zaller JG, F Heigl, L Ruess & A Grabmaier. 2014. **Glyphosate herbicide affects belowground interactions between earthworms and symbiotic mycorrhizal fungi in a model ecosystem.** *Sci Rep*. 2014; 4: 5634. doi: 10.1038/srep05634
Herbicides containing glyphosate are widely used in agriculture and private gardens, however, surprisingly little is known on potential side effects on non-target soil organisms. In a greenhouse experiment with white clover we investigated, to what extent a globally-used glyphosate herbicide affects interactions between essential soil organisms such as earthworms and arbuscular mycorrhizal fungi (AMF). We found that herbicides significantly decreased root mycorrhization, soil AMF spore biomass, vesicles and propagules. Herbicide application and earthworms increased soil hyphal biomass and tended to reduce soil water infiltration after a simulated heavy rainfall. Herbicide application in interaction with AMF led to slightly heavier but less active earthworms. Leaching of glyphosate after a simulated rainfall was substantial and altered by earthworms and AMF. These sizeable changes provide impetus for more general attention to side-effects of glyphosate-based herbicides on key soil organisms and their associated ecosystem services.

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18)••Gaupp-Berghausen M, M Hofer, B Rewald, & J G Zaller. 2015. **Glyphosate-based herbicides reduce the activity and reproduction of earthworms and lead to increased soil nutrient concentrations.** *Sci Rep:* 2015; 5: 12886.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4542661/
Herbicide use is increasing worldwide both in agriculture and private gardens. However, our knowledge of potential side-effects on non-target soil organisms, even on such eminent ones as earthworms, is still very scarce. In a greenhouse experiment, we assessed the impact of the most widely used glyphosate-based herbicide Roundup on two earthworm species with different feeding strategies. We demonstrate, that the surface casting activity of vertically burrowing earthworms (*Lumbricus terrestris*) almost ceased three weeks after herbicide application, while the activity of soil dwelling earthworms (*Aporrectodea caliginosa*) was not affected. Reproduction of the soil dwellers was reduced by 56% within three months after herbicide application. Herbicide application led to increased soil concentrations of nitrate by 1592% and phosphate by 127%, pointing to potential risks for nutrient leaching into streams, lakes, or groundwater aquifers. These sizeable herbicide-induced impacts on agroecosystems are particularly worrisome because these herbicides have been globally used for decades.

—— CONTAMINATION of VEGETATION, AIR, WATER and SOIL ——

19)••Anon. 2019. **Glyphosate use in forestry drifts on wild, edible plants, leading to lasting contamination.** *Beyond Pesticides/Daily News Blog*: March 5, 2019.
Wild, edible plants subject to drift from the herbicide glyphosate during forestry operations can be contaminated with the chemical an entire year after an initial application, according to a **new study published in the Canadian Journal of Forest Research.** Glyphosate is often used in forestry to knock down unwanted trees, shrubs, and other plants after clear-cutting to provide room for the regrowth of trees deemed valuable. However, this new research shows that "non-target" species, such as raspberries and blueberries, eaten by wildlife and sometimes wild foraged by humans can retain significant levels of glyphosate contamination due to drift and overspray. Forester Lisa Wood, PhD, from the University of Northern British Columbia began this research based on input and requests from Canadian indigenous First Nations communities. Back in 2013, shrubs foraged by traditional berry-pickers in northeastern British

Columbia were sampled and found to contain glyphosate residues, leading to the need for a broader investigation. Dr. Wood sampled the roots and shoots of 10 plant species from an area that had been aerially sprayed with glyphosate a year prior as part of forestry operations to clear aspen and make room for coniferous re-plantings. The 10 plants, which included highbush cranberry, prickly rose, bunchberry, pink wintergreen, blueberries and red raspberries, among others, were compared against those chosen from a control region where glyphosate was not applied. Results show that 12 of 23 plant shoots (new growth) sampled contain detectable levels of glyphosate one year after application, with some levels ranging over 1 ppm. The roots of plants contain higher levels on average, ranging from .1 ppm to over 4 ppm. Researchers specifically analyzed the fruit of raspberries and blueberries, finding average glyphosate levels of roughly .14 ppm. "If a plant dies from an application it falls to the soil and there are microbes that gobble up the glyphosate," Dr. Wood told the **Vancouver Sun**. "When they don't die, they have interesting ways of coping, often by storing and isolating the glyphosate." In general, plants appear to store glyphosate in their roots during dormancy, but translocate the chemical to shoots during the growing season. Dr. Wood found that lower growing plants appear to contain higher levels of glyphosate contamination than those farther from the ground.

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20)••Anon. 2019. **Nutrient runoff, aquatic weed killers, and Florida's Red Tide collide in public debate.** *Beyond Pesticides/Daily News Blog*: March 6, 2019.

After a brief hiatus, Florida Fish and Wildlife Conservation Commission (FWC) is continuing use of aquatic herbicides, including glyphosate, for invasive species management. Public pressure and feedback caused FWC to take a **temporary pause** from spraying while the commission collected public comment through public hearings and emails from late January through February. FWC ultimately decided to resume spraying invasive species, and points to its improved integrated management system as reducing overall herbicide use. **Glyphosate**, one of the 17 aquatic herbicides that FWC uses regularly has sparked opposition from environmentalists and the general public due to its wide usage and **known adverse effects**. According to FWC data, 12,263 pounds of glyphosate-based herbicides were used on Florida's Lake Okeechobee in 2017. About 175,000 people have signed North Palm Beach photographer and wildlife advocate Jim Abernathy's **petition** titled "Stop The State-Sanctioned Poisoning of Our Lakes and Rivers!". The petition decries the use of glyphosate to kill invasive aquatic plants and warns of subsequent nutrient pollution caused by decay. An excess of nutrients (e.g. nitrogen and phosphorus) in water bodies contribute to algal blooms. Eutrophication can eventually result in oxygen depletion and thereby decrease biodiversity. FWC denies that the invasive species management program contributes to either red tide (discoloration caused by an explosion of algae) or blue/green algae build up, citing lack of evidence and asserting that keeping low populations of the plant reduces buildup of decaying plant material.

Invasive aquatic plants, such as **water hyacinth** and **hydrilla,** plague Florida's waterways. They displace native plant communities and disrupt recreation – particularly waterhyacinth, which can get so thick as to be impassable. Water hyacinth is a free-floating aquatic plant native to Amazon River in Brazil. Mature plants reproduce rapidly through horizontal stolons; populations can double in as little as 6-18 days. Mechanical means of management are difficult, as dense populations can weigh as much as 400 tons per acre. The plant then needs to be taken away from the waterway, and disposal can be expensive and time consuming. In response to the question, "Why can't the FWC just use mechanical control and eliminate the use of herbicides?," FWC noted:

"*Research and tests conducted on Lake Okeechobee and other waterways throughout the state have consistently shown that mechanical harvesters alone are ineffective for large-scale control of these fast-growing exotics. In past tests, when harvesters replaced chemicals on Lake Okeechobee, the plants multiplied faster than they could be harvested, lake conditions became unsuitable for navigation and recreation, and there was a significant loss of native*

habitat. One crew applying herbicide can cover approximately 10 acres a day, whereas a crew operating a harvester can typically clear only .5 acre a day. Some biological controls can have moderate success on some types of plants but, despite many research efforts, we have not found a biological control agent that provides good results on floating plants such as water hyacinths."

Those who use alternatives say that employing nonchemical strategies requires different approaches than chemical-intensive strategies. For example, timing of harvesting and the use of biological controls becomes an important factor in efficacy of these non-chemical approaches. Additionally, economists evaluating the cost of pesticide use in comparison with nonchemical approaches have evaluated secondary costs, such as those associated with adverse health effects, contamination, clean-up costs, weed resistance, and more. In most cases, chemical-intensive approaches are inherently more expensive.

Florida residents are concerned about the impact on people and wildlife of chemicals used, while FWC responds to this apprehension with the position that, "Herbicides registered for use in aquatic environments undergo years of rigorous evaluation with the U.S. Environmental Protection Agency (EPA)." Additionally, FWC states that it works with universities and research institutions for "environmentally compatible and cost-effective strategies to apply herbicides to control target vegetation while conserving or enhancing non-target plants and animals." However, with industry-influenced research and a history of negligence regarding the potential harm associated with undisclosed pesticide product ingredients (inerts), independent critiques have found EPA's pesticide evaluation process to be inadequate.

While not ending herbicide use entirely, FWC is "recommitting to employing methods that minimize the quantity of herbicides needed to achieve the desired level of control." A **news release** from March 1, 2019 details their improvements as:

- Accelerating the development of habitat management plans for individual lakes.
- Forming a Technical Assistance Group consisting of staff, partners and stakeholders.
- Improving the timing of herbicide-based invasive aquatic plant treatments.
- Exploring ways to better integrate and increase the strategic use of mechanical aquatic plant harvesting.
- Exploring new methods and technologies to oversee and increase accountability of aquatic plant control contractors.
- Developing pilot projects to explore better integrated plant management tools.
- Improving agency communication regarding plant management activities.

Read Beyond Pesticides' 2018 article "**Meeting the 'Invasive Species' Challenge**" or our "**Least-toxic Control of Weeds**" for more information about Beyond Pesticides' approach to weed management.

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21)••USGS. 2017. **Common Weed Killer is Widespread in the Environment**
https://toxics.usgs.gov/highlights/2014-04-23-glyphosate_2014.html

U.S. Geological Survey (USGS) scientists report that glyphosate and its degradation product AMPA (aminomethylphosphonic acid) are transported off-site from agricultural and urban sources and occur widely in the environment. This study is the largest and most comprehensive assessment of the environmental occurrence of glyphosate and AMPA in the United States conducted to date, summarizing the results of 3,732 environmental samples collected between 2001 and 2010 from 38 states.

- Glyphosate and, or AMPA were detected commonly in surface waters (59 percent of 470 sites), and infrequently in groundwater or soil water (8.4 percent of 820 sites).
- Glyphosate was detected in more than 50 percent of soil and sediment samples, and water samples from ditches and drains, precipitation, large rivers, and streams.
- Glyphosate was detected in less than 40 percent of water samples from lakes, ponds, wetlands.
- AMPA was detected more frequently than glyphosate in all environmental settings except lakes, ponds, and wetlands.

- AMPA was detected in more than 80 percent of wastewater treatment plant samples; while glyphosate was detected in only about 10 percent of those samples.
- Data from nine surface-water sites sampled repeatedly indicate that glyphosate and AMPA detection frequency, median concentrations, and loads are higher late in the study period (2006-2010) than early (2001-2005).

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22)••LL Alonso, PM Demetrio, M Agustina Etchegoyen & DJ Marino. 2018. **Glyphosate and atrazine in rainfall and soils in agroproductive areas of the pampas region in Argentina.** *Sci Total Environ*. 2018 Dec 15;645:89-96. doi: 10.1016/j.scitotenv.2018.07.134.
The presence in the atmosphere of glyphosate (GLP) and atrazine (ATZ) was investigated-those pesticides dominating the market in Argentina-through rain, as the main climatic phenomenon associated with wet deposition, both through analyzing source-receptor relationships with soil along with the climatic influences that may condition that transport and through estimating the annual deposition on the surface of the Argentine pampas. Rainwater samples (n = 112) were collected throughout each rainfall in urban areas of the pampas having different degrees of land use and with extensive crop production plus subsurface-soil samples (n = 58) from the relevant periurban sites. The herbicides-analyzed by liquid-chromatography-mass-spectrometry-were detected in >80% of the rain samples at median-to-maximum concentrations of 1.24-67.3 μg·L-1 (GLP) and 0.22-26.9 μg·L-1(ATZ), while aminomethylphosphonic acid (AMPA) was detected at 34% (0.75-7.91 μg·L-1). In soils, GLP was more frequently registered (41%; 102-323 μg·kg-1) followed by ATZ (32%; 7-66 μg·kg-1) and then AMPA (22%; 223-732 μg·kg-1). The maximum GLP concentrations quantified in rainwater exceeded the previously reported levels for the USA and Canada. No associations were observed between soil and rainwater concentrations in the same monitoring areas-despite the soil's action as a source, as evidenced through the AMPA present in rainwater. Median GLP concentrations were significantly associated with isohyets, in an increasing gradient from the east to the west-as such in an inverse pattern to that of the annual rainfall volumes; whereas ATZ-rainwater levels exhibited no characteristic spatial configuration. The estimated annual deposition of GLP by rainfall indicated that more than one source of a herbicide can lead to its presence in the atmosphere and points out the relevance of rainfall's contribution to the surface levels of a pollutant.

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23)••Grosa P, A Ahmed, O Kühn & P Leinwebera. 2017. **Glyphosate binding in soil as revealed by sorption experiments and quantum-chemical modeling**. *Sci Tot Envir* 586: 15 May 2017; 527-535. https://doi.org/10.1016/j.scitotenv.2017.02.007
The herbicide glyphosate (GLP) is supposed to be rapidly degraded or adsorbed strongly by soil solids but findings in soil years after application and concentrations in waters above legal limits question a harmless disappearance. Therefore, we conducted batch sorption experiments with 23 thoroughly characterized arable surface soils, correlated isotherm coefficients with numerous inorganic and organic soil parameters, and investigated GLP-SOM-complexes by quantum-chemical modeling. The Freundlich sorption model yielded the best fits, and coefficients *Kf* and nf were correlated positively with the contents of clay/silt. The contents of organic C (Corg) and of the mass-spectrometrically determined SOM-compound classes carbohydrates, phenols/lignin monomers, lignin dimers, lipids, alkylaromatics, non-amide N and amides and sterols all were strongly positively correlated with the Freundlich coefficients. Quantum-chemical modeling showed that both GLP phosphonic and carboxylic functional groups interact similarly with the polar SOM functional groups via H-bond formation but the GLP phosphonic moiety is most important in the GLP-SOM-interaction. Moreover, the interaction mechanism between GLP and every modeled SOM-compound class was explored indicating the importance of the polarity, electron density, and site of attack of the SOM fragments in the GLP-SOM-interaction. Partial binding energies were combined to a total binding energy (*EB,tot*) of GLP to the SOM, considering the mass spectrometrically quantified compound classes for each individual soil sample. The resulting strongly positive correlation

between the *EB,tot* and the Corg provided compelling new experimental-theoretical evidence for the importance of SOM on the GLP binding and its behavior in the environment. In conclusion, the multitude of binding mechanisms to clay minerals and organic colloids make the occurrence of free GLP rather unlikely but a leaching of GLP complexes via preferential flow path through soil and transfer to waterways rather likely.

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24)••Hébert, Marie-Pier , V Fugère & A Gonzalez. 2019. **The overlooked impact of rising glyphosate use on phosphorus loading in agricultural watersheds.** *Front Ecol Envir* 17 (issue 1): 48-56.

Glyphosate is the most extensively used pesticide worldwide. In addition to raising ecotoxicological concerns, the use of glyphosate adds phosphorus (P) to agricultural landscapes, influencing the accumulation and cycling of P in soil and nearby surface waters. Yet pesticides have been largely ignored when monitoring anthropogenic sources of P in agricultural watersheds. Estimating the supply of P derived from glyphosate use, both globally and in the US alone, we show that trends have markedly increased over the past two decades. Across the US, mean inputs of glyphosate-derived P increased from 1.6 kg P km–2 in 1993 to 9.4 kg P km–2 in 2014, with values frequently exceeding 20 kg P km–2 in areas planted with glyphosate-resistant crops. Although still a minor source of P relative to fertilizers, P inputs from glyphosate use have now reached levels comparable to those from sources for which P regulations were initiated in the past. We thus argue for greater recognition of glyphosate's influence on P flow in watershed research and management.

In a nutshell:

- The herbicide glyphosate dominates the global pesticide market, with applied tonnage increasing steadily worldwide
- Glyphosate's capacity to degrade rapidly is often used to argue against potential toxicological effects, but the phosphorus (P) it contains persists in the environment and can influence soil P accumulation and losses to surrounding freshwater systems, which are prone to nutrient pollution
- Although pesticides are typically regarded as negligible sources of nutrients, we argue that the recent and rapid rise in glyphosate use has magnified its relative importance as a source of anthropogenic P, especially in areas of intensive corn, soybean, and cotton cultivation
- Glyphosate inputs should be considered in P assessments and sustainable management programs in agricultural watersheds; with glyphosate use increasing globally, it is imperative that we broaden the discourse of its environmental impacts

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25)••Pesticide Action Network/Europe. 2017. **New Study: Glyphosate persists! And European top soils are contaminated with it.** PAN/Eur Press Release: October 13, 2017

(Contact: PAN Europe, Angeliki Lysimachou, +32 496 392930)

Research from the European Commission's Joint Research Centre and two Dutch laboratories shows that 45% of Europe's top soil contains glyphosate residues, demonstrating the over-reliance of the EU agricultural model on this harmful herbicide chemical. In contrast to what its manufactures[2] purport, glyphosate persists in soils affecting not only soil fertility and crop quality, but also human and environmental health

The -research by the Dutch University of Wageningen and Rikilt laboratories, jointly with the JRC, reveals that among 317 EU soil samples of arable land, 42% contained AMPA, the most toxic metabolite of glyphosate, while glyphosate was found in 21% of the soils; 18% of the samples had both. The study was conducted in six crop systems along 11 EU member states comprising soils under different geographical and climatic conditions. Denmark, the UK and Portugal are the worst in this spectrum, with the highest detection frequency, while Italy and Greece seem to be the ones using less glyphosate on their crops. However, and most notably, these 2 molecules could be found in every tested member state. All tested crops presented glyphosate and AMPA residues. By far, the worst case was that of Portuguese vineyards, while no crops exhibited patterns of reduced reliance on glyphosate compared to others. The results

prove that the accumulation and persistence of glyphosate in soil is underestimated by European authorities, as is the harm it may cause to environmental ecosystems. The concentrations of glyphosate and AMPA found in the study have been shown to be toxic to soil organisms such as earthworms, beneficial bacteria and fungi, as glyphosate weakens down plants' natural defences making them susceptible to pathogens[. These substances that get adsorbed by soil particles are not immobile, but can propagate through wind or rainfall, leading to air pollution and exposure through the atmosphere as well as contamination of surface and ground waters. The application of fertilisers may also release a fraction of the glyphosate and AMPA bound in particles, making it directly bioavailable for uptake by plants and organisms.
Angeliki Lyssimachou, PAN Europe's ecotoxicologist said: 'This study clearly contradicts the predictions of European Authorities that glyphosate does not persist in the environment. In fact European agriculture is highly reliant on a toxic substance that is not even properly regulated in the EU, putting everyone at risk. Policy makers must stop the use of these harmful chemicals in the production of our food. It is more than time to implement all existing non-chemical alternatives to herbicides'.
Henriette Christensen, PAN Europe's agriculture policy officer added 'Over the last years, a growing body of evidence shows that soil health is one of the main drivers of growing healthy crops that will resist to pest attacks. Glyphosate destroys soil health and leads to more pesticide uses. Our farmers must leave this vicious circle'.

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26)••Martinez DA, UE Loening & MC Graham. 2018. **Impacts of glyphosate-based herbicides on disease resistance and health of crops: a review.** *Environ Sci Eur* (2018) 30: 2.
https://doi.org/10.1186/s12302-018-0131-7
Based on experimental data from laboratory and field, numerous authors have raised concern that exposure to glyphosate-based herbicides (GBHs) may pre-dispose crops to damage by microbial pathogens. In this review, we distinguish and evaluate two principal pathways by which GBHs may affect the susceptibility of crops to disease: pathway 1—via disruptions to rhizosphere microbial ecology, and pathway 2—via restriction of nutrients to crops. We conclude that GBHs have the potential to undermine crop health in a number of ways, including: (i) impairment of the innate physiological defences of glyphosate-sensitive (GS) cultivars by interruption of the shikimic acid pathway; (ii) impairment of physiological disease defences has also been shown to occur in some glyphosate-resistant (GR) cultivars, despite their engineered resistance to glyphosate's primary mode of action; (iii) interference with rhizosphere microbial ecology (in particular, GBHs have the potential to enhance the population and/or virulence of some phytopathogenic microbial species in the crop rhizosphere); and finally, (iv) the as yet incompletely elucidated reduction in the uptake and utilisation of nutrient metals by crops. Future progress will best be achieved when growers, regulators and industry collaborate to develop products, practices and policies that minimise the use of herbicides as far as possible and maximise their effectiveness when used, while facilitating optimised food production and security.

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