BEYOND PESTICIDES
701 E Street, SE ▪ Washington DC 20003
202-543-5450 phone ▪ 202-543-4791 fax
info@beyondpesticides.org ▪ www.beyondpesticides.org

June 30, 2020

Biotechnology Regulatory Services
Animal and Plant Health Inspection Service (APHIS)
Station 3A-03.8
4700 River Road Unit 118
Riverdale, MD 20737-1238

Re: Docket No. APHIS–2020–0021
Determinations of Nonregulated Status for Multi-Herbicide-Tolerant MON 87429 Corn

Dear Sir/Madam,

We are writing to comment on the U.S. Department of Agriculture's (USDA) Animal and Plant Health Inspection Service (APHIS) determination of nonregulated status for genetically engineered (GE) plant variety, MON 87429 corn, that has been engineered to be tolerant of the herbicides dicamba, glufosinate, aryloxyphenoxypropionate (AOPP) acetyl coenzyme A carboxylase (ACCase) inhibitors (so called "FOPs" herbicides such as quizalofop) and 2,4-dichlorophenoxyacetic acid (2,4-D), and to provide tissue-specific glyphosate tolerance to facilitate the production of hybrid maize seeds. Monsanto's petition to deregulate and allow into the environment yet another GE variety that would inevitably lead to damaging effects on non-GE crops, native plant species, and environmental biodiversity required for plant health. It can also lead to the propagation of noxious, resistant weeds, and cause direct and indirect adverse impacts on the environment.

According to Monsanto, the primary purpose of MON 87708 soybean and MON 88701 cotton is "to offer maize growers multiple choices for effective weed management including tough to control and herbicide resistant broadleaf and grass weeds. The combination of dicamba, glufosinate, quizalofop and 2,4-D tolerance offers multiple herbicide sites-of-actions and provides an effective weed management system for maize production in the U.S." As we mentioned in previous comments to the agency regarding similar GE varieties (2,4-D GE corn and soybeans, dicamba GE cotton and soybeans), introducing crops resistant to other chemical technologies may provide short-term relief from resistant weeds, but is not a long-term, sustainable solution to burgeoning weed resistance.

Dicamba

Recent history

Dicamba is a selective benzoic acid herbicide similar in structure and mode of action to phenoxy herbicides like 2,4-D. We have concerns that increased use of dicamba will lead to elevated human and environmental exposures, and especially via contamination of waterways. Concerns

about dicamba drift have already proved to be valid. First registered in the late 1960s, dicamba has been linked to cancer,[1] reproductive effects, neurotoxicity, birth defects, and kidney and liver damage. It is also toxic to birds, fish and other aquatic organisms, and is known to leach into waterways after an application.[2] It is a notoriously drift-prone herbicide. Studies and court filings show dicamba able to drift well over a mile off-site after an application.

Bayer's Monsanto thought it could solve this problem. The "Roundup Ready" GE agricultural model the company developed, with crops engineered to tolerate recurrent applications of their flagship glyphosate weedkiller, was in trouble. Repeated glyphosate spraying on the same plots put natural selection into overdrive and fueled rapid and widespread weed resistance.

Rather than move to an alternative model, Monsanto doubled down and determined that the solution to weed resistance was to bring more herbicides into the mix. GE agriculture allows chemical companies to increase profits by vertically integrating seed and chemical divisions; glyphosate's failure is a business opportunity for the industry. The company's new line of seeds would see dicamba use in agriculture explode from roughly one million pounds to nearly 10 million per year.

There were problems from the start. Bayer's Monsanto had developed new dicamba-tolerant seeds and received approval to sell them from the U.S. Department of Agriculture in 2015. But EPA was not as fast to register the company's patented "vapor grip" formulation of dicamba and glyphosate (Xtendimax), intended to be sprayed on its GE seeds. Nonetheless, Monsanto urged farmers to plant its seed because it claimed they would increase yields. The results of this were predictable: farmers began to use older, unapproved dicamba formulations on their new GE seeds, and reports of damage began to spring up throughout the U.S.

Non-soybean farmers began taking action. Bader Farms, the largest peach farm in Missouri, filed suit against Bayer's Monsanto seeking compensation for damage and defoliation of its trees after illegal dicamba use. The dicamba scandal pitted farmer against farmer, tearing apart many agricultural communities. As reported by NPR, one Arkansas farmer was killed in a dispute with his neighbor that involved use of dicamba herbicides. That state became one of the first to consider regulatory action, with the Arkansas Plant Board voting 12-0 to move forward on measures to restrict agricultural use of dicamba and stop illegal spraying.

By the end of 2016, EPA had approved the company's new "low volatility" herbicide formulation under a two year conditional registration. The label required a range of restrictions

---

[1] Lerro, C.C., Hofmann, J.N., Andreotti, G., Koutros, S., Parks, C.G., Blair, A., Albert, P.S., Lubin, J.H., Sandler, D.P. and Beane Freeman, L.E., 2020. Dicamba use and cancer incidence in the agricultural health study: an updated analysis. *International Journal of Epidemiology*.

[2] Cox, C. 1994. Dicamba Factsheet. https://d3n8a8pro7vhmx.cloudfront.net/ncap/pages/26/attachments/original/1428423357/dicamba.pdf?1428423357.

intended to minimize drift. However, by the end of 2017, according to court records and reporting from Reuters,[3] state agriculture departments were fielding over 2,600 incident reports and scientists estimated over 3.6 million acres of non-GE soybean crops had been damaged by dicamba drift – likely an underestimate according to EPA's own staff.

Despite accumulating data to the contrary, Monsanto continued to blame crop damage on farmers using older dicamba formulations. Environmental groups (National Family Farm Coalition, Center for Food Safety, Center for Biological Diversity, and Pesticide Action Network North America) filed their first lawsuit against EPA in early 2017, and by the end of the year Arkansas and Missouri banned the sale and use of over-the-top (OTT) dicamba. In October 2017, EPA announced, alongside Monsanto and other chemical companies, further label restrictions on OTT dicamba use.

With the bad press rampant, Bayer's Monsanto made plans to cover more than half the cost of its Xtendimax dicamba herbicide as an incentive to get farmers to plant its GE seeds. By the beginning of 2018, Arkansas had announced an official ban on dicamba use during the growing season, the toughest restrictions from any state to date. The company sued, but quickly lost a court battle, as the judge cited recent precedent holding that the state cannot be made a defendant in court.

The new label language did little to abate the damage the herbicide was causing, and another lawsuit was filed in 2018 by a Kansas farmer alleging damage to his row crops. In mid-August an investigative report found indications as to why new labels were insufficient: EPA let Monsanto write the new rules themselves.

In late 2018, prior to the expiration of its conditional registration, EPA announced it would renew registration of dicamba products conditionally for another two years, alongside yet more label changes intended to address "potential concerns." As a result, a federal court ruled that conservation groups' 2016 lawsuit was moot, but the groups quickly repetitioned the court in January 2019.

One key aspect of the 2018 label changes was the implementation of a buffer zone of 57 feet. An investigative report from the Arkansas Democrat and Chronicle (ADC) found that number to be far smaller than what scientists and EPA staff had recommended. Emails retrieved by ADC found that Monsanto worked closely with University of Arkansas weed science Professor Jason Norsworthy, PhD, on a field study to assess dicamba drift from its Xtendimax product. The collaboration was copacetic until results of the study showed that a 443 ft buffer would be required to avert adverse impacts. After disputes with the company, EPA's scientific staff agreed. However, even in the face of earlier press coverage on how the agency let Bayer's Monsanto write its own rules, it appears that political staff and then-Acting

[3] https://www.reuters.com/article/us-usa-pesticides-epa-exclusive/exclusive-epa-eyes-limits-for-agricultural-chemical-linked-to-crop-damage-idUSKCN1BG1GT.

EPA Administrator Andrew Wheeler overruled the science again in favor of the chemical industry's economic benefit.

Subsequent independent studies have found that the combination of glyphosate with dicamba is likely to increase the probability that dicamba will drift. "…[O]ur data shows the addition of glyphosate to a dicamba spray solution increased dicamba detection in the atmosphere which would point to increased volatilization," said Tom Mueller, PhD, a professor in the University of Tennessee Department of Plant Sciences. Synergy between dicamba and glyphosate had already been shown to damage the DNA of toads.

Drift and environmental damage continued throughout 2019, with July seeing reports of soybean field research plots damaged in several states, including Missouri, Kansas, Nebraska, and Arkansas, making it nearly impossible to carry out public research on non-GE crop varieties. Not only did drift harm public research, it eroded the market for non-GE soybeans, as growers saw GE dicamba seeds as their only way to avoid dicamba damage to their farm.

A report in late 2019 by Arkansas Audubon found widespread impacts to the habitat of birds and other wildlife. The organization wrote that it "predicts that in a landscape full of GMO crops [genetically modified organisms] (on which dicamba is typically used), the atmospheric loading of volatile dicamba could be enough to cause landscape scale damage to our state natural areas, wildlife management areas, national wildlife refuges, family farms, and the wildlife they harbor."

In 2020, the tide finally began to turn away from chemical industry damage and destruction, and toward compensation and comeuppance. In February 2020, Missouri's Bader Farms was awarded $265 million in compensation from Monsanto and BASF (another maker of a GE dicamba-based herbicide) for the damage caused to their peach farm. Critically, the jury determined that the joint venture between the two companies amounted to a conspiracy to create an "ecological disaster" in the name of profit. Then in June, a federal court vacated EPA's 2018 conditional registration of three dicamba weed killer products for use on an estimated 60 million acres of DT (dicamba-tolerant through genetic modification/engineering) soybeans and cotton.

The written court ruling by the Ninth Circuit released in early June clearly spells out the violations of federal pesticide law (Federal Insecticide Fungicide and Rodenticide Act) by EPA in re-approving OTT dicamba under another conditional registration. The court ruling was made on the basis that "EPA substantially understated the risks it acknowledged and failed entirely to acknowledge other risks."

Among the violations cited by the court were EPA's understatement of the amount of dicamba tolerant seed planted, whether formal complaints were accurately reported, and its complete refusal to estimate actual damage. Instead of estimating damage in real numbers, the court chastised the agency for referring to dicamba damage as "potential" or "alleged," an

approach that lines up with the gaslighting the chemical industry perpetrated on affected farmers.

The judge also took EPA to task in three areas rarely considered under FIFRA. First, EPA's failure to acknowledge that the iterative tightening of dicamba's label language over the years effectively made it "difficult if not impossible to follow for even conscientious users." Second, that EPA failed to consider the "anti-competitive economic effects" of GE dicamba on the non-GE cotton and soybean markets. And lastly, that the agency failed to consider how "OTT dicamba use would tear the social fabric of farming communities." These critical components provide important precedent for future lawsuits challenging egregious abuses under federal pesticide law.

"This is a massive victory that will protect people and wildlife from uses of a highly toxic pesticide that never should've been approved by the EPA," said Lori Ann Burd, director of the Center for Biological Diversity's environmental health program. "The fact that the Trump EPA approved these uses of dicamba despite its well-documented record of damaging millions of acres of farmland, tree groves and gardens highlights how tightly the pesticide industry controls EPA's pesticide-approval process. But this ruling is a powerful rejection of their lawlessness." As the court acknowledged, vacating all OTT dicamba registrations (including those by Monsanto, BASF, and Corteva [DowDupont]) would result in difficulties to some growers (the court noted it was not growers' fault), but was compelled to do so as a result of "the absence of substantial evidence to support the EPA's decision."

We offer the above extended chronicle of recent events regarding dicamba in the hope that USDA will avoid the next GE debacle.

Environmental and Health Effects

Dicamba is highly soluble, and along with its metabolites, has the potential to leach into, and contaminate groundwater. Although the half-life of dicamba in water is < 7 days, residues have been detected in surface-water more than 6 months after application.[4] However, dicamba is routinely detected in surface waters in the U.S.[5] and has been frequently measured in California.[6] Additionally, dicamba is toxic to aquatic organisms and its presence in waterways therefore poses risks to these organisms. According to the U.S. Geological Survey, dicamba has been measured in waterways at levels that did not exceed EPA benchmarks. However, with an expected increase in use on millions of acres of corn, would dicamba not only be more frequently detected in U.S. waters, at levels that may exceed aquatic and human health benchmarks? In the 2006 Reregistration Eligibility Decision for dicamba no mitigation measures

[4] Caux PY, Kent RA, Taché M, et al. 1993. Environmental fate and effects of dicamba: a Canadian perspective. *Rev Environ Contam Toxicol*. 133:1-58.

[5] Gilliom, R et al. 2007. The Quality of Our Nation's Waters- Pesticides in the Nation's Streams and Ground Water, 1992-2001. U.S. Geological Survey Circular 1291,172 p.

[6] Ensminger MP, Budd R, et al. 2013. Pesticide occurrence and aquatic benchmark exceedances in urban surface waters and sediments in three urban areas of California, USA, 2008-2011. *Environ Monit Assess.* 185(5):3697-710.

were put in place for drinking water, or residential exposures to dicamba, despite the fact that dicamba can contaminate groundwater as a result of its high mobility in soils.[7]

The 2006 RED also raised concerns over the risks to terrestrial animals. At that time, EPA recommended reducing application rates of dicamba for all use patterns, in order to mitigate potential risks. Dicamba has been associated with adverse health risks that should concern applicators and the general public. A Canadian agricultural study found that pre-conception exposure to dicamba was associated with increased risk of birth defects in male offspring.[8] Dicamba has also been associated with a decrease in fecundity.[9] Similarly, dicamba alone or combined with other herbicides has been observed to induce significant levels of apoptosis in developing embryos,[10] raising concerns about the health consequences for humans. In minnows, dicamba has been observed to result in changes in sex hormone levels, and alterations of hormone-related gene expression, implying that dicamba may act as an endocrine disruptor.[11]

2,4-D

2,4-D is a phenoxy herbicide that is known for its propensity to drift. Many environmental, farmworker and consumer groups are concerned about the inevitable increase in 2,4-D use that this deregulation decision would bring. This means that potential adverse impacts and contamination from this highly toxic herbicide will also increase, along with the demonstrated plant-damaging effects. The scientific literature has shown that 2,4-D is far from being a safe chemical. Over the decades of its use, 2,4-D has been linked to an increased risk of birth defects, reduced sperm counts, increased risk of non-Hodgkin lymphoma, Parkinson's disease, and hormone disruption, as well as other health problems.

Similarly, 2,4-D drift is a major concern, especially for those who live adjacent to and near agricultural areas. 2,4-D is known to drift into homes, where it can stay in the indoor environment for up to a year,[12] further exposing these communities to 2,4-D. The risk from drift that will occur under a best case and worst case scenario cannot go ignored.

Environmental Effects

2,4-D is one of the most widely used herbicides for the control of broadleaf weeds for commercial agriculture and residential landscapes in the U.S. An increase in the application of 2,4-D in the environment would increase environmental harm. According to EPA, under most

---

[7] US EPA. 2006. Reregistration Eligibility Document for Dicamba and Associated Salts. Office of Pesticide Programs. Washington, DC

[8] Weselak M, Arbuckle TE, Wigle DT, et al. 2008. Pre- and post-conception pesticide exposure and the risk of birth defects in an Ontario farm population. *Reprod Toxicol.* 25(4):472-80.

[9] Curtis KM, et al. 1999. The effect of pesticide exposure on time to pregnancy. *Epidemiology.* 10(2):112-7.

[10] Greenlee AR[1], Ellis TM, Berg RL. 2004. Low-dose agrochemicals and lawn-care pesticides induce developmental toxicity in murine preimplantation embryos. *Environ Health Perspect*. 112(6):703-9.

[11] Zhu L, Li W, Zha J, Wang Z. 2014. Dicamba affects sex steroid hormone level and mRNA expression of related genes in adult rare minnow (Gobiocypris rarus) at environmentally relevant concentrations. *Environ Toxicol*. doi: 10.1002/tox.21947

[12] Nishioka MG, Burkholder HM, Brinkman MC, Gordon SM. 1996. Measuring lawn transport of lawn applied herbicide acids from turf to home: Correlation of dislodgeable 2,4-D turf residues with carpets dust and carpet surface residues. *Environmental Sci and Tech*. 30:3313-3320.

environmental conditions, various forms of 2,4-D will degrade rapidly to form 2,4-D acid. While 2,4-D acid degrades fairly quickly in soils, it is relatively persistent in anaerobic aquatic environments (half-life ranges from 41 to 333 days).[13] This will have implications for fragile wetland areas, especially those under conservation. According to Donald et al., concentrations of herbicides in water from wetlands where herbicides are not used are as high as those from locations where herbicides are used.[14] Non-target plants in these areas and others are also at risk. 2,4-D is toxic to aquatic plants and is more toxic to vascular plants than to non-vascular plants.

2,4-D drift has long been a known problem to off-site locations, endangered species, and non-target crops. Many forms of 2,4-D volatilize above 85°F[15] and 2,4-D drift has been known to damage tomatoes, grapes, and other plants. Herbicide concentrations 100 times below the recommended label rate have been reported to cause injury to grapes. Drift can injure plants half a mile or more from the application site.[16] In addition to non-target plants, 2,4-D can impact species listed under the jurisdiction of the Endangered Species Act (ESA). In 2011, the National Marine Fisheries Service (NMFS) identified 2,4-D as likely to jeopardize all listed salmonids, based on current registration and label directions.[17]

APHIS cannot rely on EPA label use restrictions for 2,4-D to mitigate the potential (non-target) risks from exposure. Label directions have been shown to have no effect on decreasing spray drift. In fact, EPA has acknowledged this and has attempted to review and revise pesticide labeling guidance.[18]

2,4-D's contamination with dioxins has long been a part of 2,4-D's history. While recent manufacturing advancements have reduced dioxin levels in 2,4-D, the threat of dioxin contamination is still very much a consequence of 2,4-D use. The science is very clear that dioxins are a carcinogenic class of chemicals that have left a toxic legacy for human health and environmental protection across the U.S due to their persistence and toxicity. The issue of 2,4-D contaminants such as dioxins that are present in formulations, has been ignored and is probably much more serious in terms of degradation issues than the "active ingredient." Dioxins have notoriously long half-lives, are bioaccumulative, and present broadly significant health risks developmentally and postnatally, including increased risk of heart disease and

---

[13] USEPA. 2005. 2,4-D RED Facts. Available at http://www.epa.gov/oppsrrd1/REDs/factsheets/24d_fs.htm.
[14] Donald DB, Gurprasad NP, Quinnett-Abbott L, Cash K. 2001. Diffuse geographic distribution of herbicides in northern prairie wetlands. Environ Toxicol Chem. 20(2):273-9.
[15] Hales, R. 2010. Herbicide Injury a Problem on Plants. Colorado State University Cooperative Extension.
[16] Ball, D.A, Parker, R, et al. 2004. Preventing Herbicide Drift and Injury to Grapes. Oregon State University Extension Service.
[17] NMFS. 2011. Endangered Species Act Section 7 Consultation Biological Opinion: 2,4-D, Triclopyr BEE, Diuron, Linuron, Captan, and Chlorothalonil. National Marine Fisheries Service.
[18] USEPA. 2009. Pesticide Spray and Dust Drift. Available at http://www.epa.gov/pesticides/factsheets/spraydrift.htm.

diabetes.[19] APHIS must take into account the possibility of increased dioxin contamination to fields using 2,4-D and the threat to environmental health.

2,4-D is Hazardous to Human Health

2,4-D is neurotoxic, mutagenic, and genotoxic, and poses serious risks to human health. In sub-chronic laboratory studies, rats exposed to 2,4-D experienced decreases in red cell mass, decreases in ovary and testes weights, and increases in liver, kidney, and thyroid weight.[20] A study found that 2,4-D is indeed cytotoxic and induces apoptosis via direct effect on mitochondrial membranes.[21] Changes to maternal behavior in rats, along with increased catecholamine levels and a drastic decrease in indolamine levels have also been observed.[22] 2,4-D is also an endocrine disruptor and is known to interfere with the thyroid hormone. According to EPA, current data "demonstrate effects on the thyroid and gonads following exposure to 2,4-D, [and] there is concern regarding its endocrine disruption potential."[23] EPA researchers found that persons with urinary 2,4-D presence have low levels of thyroid hormone. Their results also indicate that exposure to 2,4-D was associated with changes in biomarkers that have been linked to risk factors for acute myocardial infarction and type-2 diabetes.[24] One study of agricultural workers found an increased risk of gastric cancer among those who worked in areas where 2,4-D was applied.[25] Others found that those exposed to 2,4-D had poor semen quality.[26,27] Higher rates of birth defects were also observed in farmers with long-time exposure to 2,4-D. [28]

Laboratory studies have observed the hormone effects of 2,4-D exposure, including estrogenic activity in rainbow trout[29] exposed to 2,4-D, decreases in the thyroid gland transport

---

[19] NIEHS. 2011. Environmental Health Topics: Dioxins. National Institutes of Health. Research Triangle Park, NC. Available at http://www.niehs.nih.gov/health/topics/agents/dioxins/index.cfm.

[20] Charles, J.M., Cunny, H.C., Wilson, R.D., and Bus, J.S. 1996. Comparative Subchronic Studies on 2,4-Dichlorophenoxyacetic Acid, Amine, and Ester in Rats. *Fundamental and Applied Toxicology* 33, 161-165.

[21] Oakes, D.J., and Pollak, J.K. 2000 The in vitro evaluation of the toxicities of three related herbicide formulations containing ester derivatives of 2,4,5-T and 2,4-D using sub-mitochondrial particles. *Toxicology* 151, 1-9.

[22] Stürtz, N., Deis, R.P., Jahn, G.A., Duffard, R., and Evangelista de Duffard, A.M. 2008. Effect of 2,4-dichlorophenoxyacetic acid on rat maternal behavior. *Toxicology* 247, 73-79.

[23] U.S. EPA. 2005. Reregistration Eligibility Decision for 2,4-*D*. Office of Prevention Pesticides and Toxic Substances. Washington DC.

[24] Schreinemachers DM. 2010. Perturbation of lipids and glucose metabolism associated with previous 2,4-D exposure: a cross-sectional study of NHANES III data, 1988-1994. Environ Health. 9:11.

[25] Mills PK and Yang RC. 2007. Agricultural exposures and gastric cancer risk in Hispanic farm workers in California. Environ Res. 104(2):282-9.

[26] Swan SH, Kruse RL, Liu F, Barr DB, et al. 2003. Semen quality in relation to biomarkers of pesticide exposure. Environ Health Perspect. 111(12):1478-84.

[27] Lerda, D., and Rizzi, R. 1991. Study of Reproductive Function in Persons Occupationally Exposed to 2,4-Dichlorophenoxyacetic Acid (2,4-D). *Mutation Research* 262, 47-50.

[28] Garry, V.F., Schreinemachers, D., Harkins, M.E., and Griffith, J. 1996. Pesticide Appliers, Biocides, and Birth Defects in Rural Minnesota. *Environmental Health Perspectives* 104, 394-399.

[29] Xie, L.T., Thrippleton, K., Irwin, M.A., Siemering, G.S., Mekebri, A., Crane, D., Berry, K., and Schlenk, D. 2005. Evaluation of estrogenic activities of aquatic herbicides and surfactants using an rainbow trout vitellogenin assay. *Toxicol. Sci*. 87, 391-398.

and production functions, and impairment of hormone iodination in the thyroid glands of laboratory rats.[30] A study investigating developmental toxicity in mice of a common commercial formulation of herbicide containing a mixture of 2,4-D noted a decrease in litter size associated with a decrease in the number of implantation sites, at very low and low environmentally relevant doses.[31] Other studies have found that 2,4-D promotes the proliferation of androgen-sensitive cells by acting synergistically with its main metabolite, 2,4-dichlorophenol (DCP), also known for its endocrine disrupting effects. [32,33] This heightened androgen-sensitive cell population may be linked to the recent escalation of polycystic ovary syndrome in reproductively aged women[34] that results in reproductive impairment due to inability to ovulate and carry young to term. Occupational exposure to 2,4-D is also associated with an increased risk of Parkinson's disease. 2,4-D has effects on dopaminergic neurons in experimental settings and is associated with more than a 3-fold increased risk of disease.[35] The scientific literature confirms that farmers, farmworkers, and their families face extraordinary and disproportionate risks from pesticides, making the expansion of pesticide use an issue of environmental justice. Application and pesticide drift result in dermal, inhalation, and oral exposures that are typically underestimated. According to a study by Arcury et al.,[36] workers experience repeated exposures to the same pesticides evidenced by multiple pesticides routinely detected in their bodies. This study of 196 farmworkers found that 86 percent of them contained 2,4-D in their urine. Others have also reported 2,4-D detections in a majority of samples including those of pregnant workers.[37,38] A 2004 study detected agricultural pesticides in the homes near to agricultural fields.[39]

Researchers from the National Cancer Institute and the National Institutes of Health found that increasing acreage of corn and soybean fields within 750 meters of homes is associated with significantly elevated odds of detecting agricultural herbicides. 95 percent of

---

[30] Malysheva, L.N., and Zhavoronkov, A.A. 1997. Morphological and histochemical changes in the thyroid gland after a single exposure to 2,4-DA herbicide. *Bull. Exp. Biol. Med.* 124, 1223-1224.

[31] Cavieres, M,F, Jaeger, J and Porter, W. 2002. Developmental toxicity of a commercial herbicide mixture in mice: I. Effects on embryo implantation and litter size. *Environ Health Perspect*. 110(11): 1081–1085.

[32] Kim, H.-J., Park, Y.I., and Dong, M.S. 2005. Effects of 2,4-D and DCP on the DHT-Induced Androgenic Action in Human Prostate Cancer Cells. *Toxicological Sciences*. 88(1), 52–59 pp. 52-59.

[33] McKinlay, R., Plant, J.A., Bell, J.N.B., and Voulvoulis, N. 2008. Endocrine disrupting pesticides: Implications for risk assessment. Environment International 34, 168-183.

[34] Mason, H, Colao, A, et al. 2008. Polycystic ovary syndrome (PCOS) trilogy: a translational and clinical review. Clinical Endocrinology, 69(6): 831–844.

[35] Tanner CM, Ross GW, Jewell SA, et al. 2009. Occupation and risk of parkinsonism: a multicenter case-control study. Arch Neurol. 66(9):1106-13.

[36] Arcury, T, Grzywacz, J, Talton, J, et al. 2010. Repeated Pesticide Exposure among North Carolina Migrant and Seasonal Farmworkers. *Am J Ind Med*. 53(8): 802–813.

[37] Arcury, T, Grzywacz, J, et al. 2009. Seasonal Variation in the Measurement of Urinary Pesticide Metabolites among Latino Farmworkers in Eastern North Carolina. Int J Occup Environ Health.15(4): 339–350.

[38] Cooper, S, Burau, K, Sweeney, A, et al. 2001. Prenatal exposure to pesticides: A feasibility study among migrant and seasonal farmworkers. Am. J. Ind. Med. 40:578–585.

[39] Quandt SA, Arcury TA, Rao, P, et al. 2004. Agricultural and residential pesticides in wipe samples from farmworker family residences in North Carolina and Virginia. Environ Health Perspect. 112(3): 382–387.

the homes sampled here contain 2,4-D.[40] 2,4-D has also been detected in the semen of farmworkers in Canada, which could be toxic to sperm cells and can be transported to the woman and developing embryo/fetus.[41] Phenoxyacetic acid herbicides, specifically 2,4-D, are associated with non-Hodgkin lymphoma (NHL) and a high incidence of NHL has been reported among farmers and other occupational groups working with 2,4-D. According to the National Cancer Institute, frequent use of 2,4-D, has been associated with 2- to 8-fold increases of NHL in studies conducted in Sweden, Kansas, Nebraska, Canada, and elsewhere.[42] Farmers using 2,4-D are associated with an increased risk of NHL in 131 lymphohematopoietic cancers (LHC) in a case-control study embedded in a cohort of 139,000 members of United Farm Workers of America (UFW) diagnosed in California between 1988 and 2001.[43] Despite industry attempts to downplay these findings and claim that 2,4-D has low toxicity, farmworkers continue to bear the brunt of these exposures and chronic health effects. APHIS must look at the increased occupational risks posed by 2,4-D. The agency therefore cannot make a determination for DAS-40278-9 corn until occupational health is specially considered.

Glyphosate

Glyphosate (N-phosphono-methyl glycine) is a broad spectrum, post-emergent, non-selective systemic herbicide used on non-cropland, as well as a variety of crops. It has seen the largest use in crops that are genetically engineered to be tolerant to it, where it can kill most grassy and broadleaved plants. Glyphosate products, such as Monsanto's Roundup®, are formulated with surfactants and other ingredients to increase its effectiveness. Glyphosate's major metabolite is aminomethyl phosphonic acid (AMPA).

Glyphosate is translocated to meristematic tissues in the plant (where active cell division occurs.) There it blocks the activity of the enzyme 5-enolpyruvylshikimate-3-phosphate synthase (EPSPS), a key enzyme in the shikimate pathway of production of aromatic amino acids, ultimately leading to the plant's death by starvation.[44] Since the shikimate pathway occurs in plants, but not animals, this mode of action has been used to support claims of safety for glyphosate.

---

[40] Ward MH, Lubin J, Giglierano J, et al. 2006. Proximity to crops and residential exposure to agricultural herbicides in Iowa. Environ Health Perspect. 114(6):893-7.
[41] Arbuckle TE, Schrader SM, et al. 1999. 2,4-Dichlorophenoxyacetic acid residues in semen of Ontario farmers. Reprod Toxicol. 13(6):421-9.
[42] Zahm SH and Blair A. 1992. Pesticides and non-Hodgkin's lymphoma. Cancer Res. 52(19 Suppl):5485s-5488s.
[43] Mills PK, Yang R, Riordan D. 2005. Lymphohematopoietic cancers in the United Farm Workers of America (UFW), 1988-2001. Cancer Causes Control. 16(7):823-30.
[44] Industry Task Force on Glyphosate, 2017. Glyphosate: mechanism of action. http://www.glyphosate.eu/glyphosate-mechanism-action.

Glyphosate use and residues are increasing

The use of glyphosate has been increasing steadily.[45] As a result, glyphosate residues are being detected in tissues and excretions of farm animals, as well as human urine.[46] Bøhn et al. found that glyphosate accumulates in Roundup Ready® soybeans and also contained a different nutritional profile from organic and non-genetically engineered soybeans.[47]

Glyphosate risk assessment[48]

EPA's risk assessments—based on data submitted by Monsanto—rate glyphosate's acute toxicity as "relatively low." EPA bases its assessment of chronic risks on Monsanto's developmental tests on glyphosate. In developmental toxicity studies using pregnant rats and rabbits, glyphosate caused treatment-related effects in high dose groups, including diarrhea, decreased body weight gain, nasal discharge and death.[49,50]

EPA classifies glyphosate as a Group E carcinogen—evidence of non-carcinogenicity for humans—based on the lack of convincing evidence of carcinogenicity in studies submitted to the agency by Monsanto.

Problems with risk assessment --#1

EPA's risk assessment of glyphosate is based on direct effects of the active ingredient alone, as demonstrated in laboratory tests. The chemical must demonstrate a toxic effect that is related to the dose received. As we will see, when this model is applied to glyphosate, it fails to identify the most important impacts of glyphosate as it is used. The first problem is that glyphosate is not used alone.

"Inert" ingredients in glyphosate products

Surfactants and other ingredients added to glyphosate products to make them more effective as herbicides include: 5-chloro-2-methyl 3(2H)-isothiazolone, FD&C Blue No. 1, glycerine, 3-iodo-2-propynyl butyl carbamate, light aromatic petroleum distillate, methyl p-hydroxybenzoate, polyoxyethylene alkylamine, propylene glycol, sodium sulfite, sodium benzoate, sodium salt of o-phenylphenol, and sorbic acid. Some health effects that are associated with these so-called "inert" ingredients are: genetic damage, reduced fertility,

---

[45] Data from supplemental tables from Benbrook, C.M., 2016. Trends in glyphosate herbicide use in the United States and globally. *Environmental Sciences Europe*, *28*(1), p.3. https://enveurope.springeropen.com/articles/10.1186/s12302-016-0070-0.

[46] Krüger, M., Schledorn, P., Schrödl, W., Hoppe, H.W., Lutz, W. and Shehata, A.A., 2014. Detection of glyphosate residues in animals and humans. *Journal of Environmental & Analytical Toxicology*, *4*(2), p.1.

[47] Bøhn, T., Cuhra, M., Traavik, T., Sanden, M., Fagan, J. and Primicerio, R., 2014. Compositional differences in soybeans on the market: glyphosate accumulates in Roundup Ready GM soybeans. *Food chemistry*, *153*, pp.207-215.

[48] For more information, see the Beyond Pesticides factsheet on glyphosate: http://www.beyondpesticides.org/assets/media/documents/pesticides/factsheets/Glyphosate.pdf.

[49] EPA. 1993. Reregistration Eligibility Decision (RED) Document: Glyphosate. Office of Pesticide Programs.

[50] EPA, 2006. Glyphosate Human Health Risk Assessment for Proposed Use on Indian Mulberry and Amended Use on Pea, Dry. PC Code: 417300, Petition No: 5E6987, DP Num: 321992, Decision No. 360557.

thyroid damage, eye irritation, anemia, reduced survival of offspring, and skin irritation.[51] Polyethoxylated tallowamine or POEA—a surfactant used in Roundup® and other herbicidal products—has been identified as particularly toxic. [52]

Hazards of glyphosate products

In contrast to the results of the manufacturer's tests of glyphosate alone, an increasing number of studies have found that formulated glyphosate products (e.g., Roundup®) are more toxic than glyphosate alone. Symptoms following acute exposure to glyphosate formulations include: swollen eyes, face and joints; facial numbness; burning and/or itching skin; blisters; rapid heart rate; elevated blood pressure; chest pains, congestion; coughing; headache; and nausea.[53] Glyphosate and its formulated products adversely affect embryonic, placental and umbilical cord cells, and affect fetal development.[54] Chronic exposure to glyphosate-based herbicides can result in significant liver and kidney damage.[55]

Human cell endocrine disruption has also been observed to occur at concentrations well below those considered "acceptable," including disruption at the androgen receptor, inhibition of transcriptional activities on estrogen receptors on HepG2, decreased aromatase activity, DNA damage, and cytotoxic effects.[56]

Roundup and Monsanto on trial

Recent reviews of glyphosate and glyphosate-based herbicides demonstrate a growing scientific consensus and concern about their health, environmental, and social impacts. A group of well-known and respected scientists collaborated on a consensus "Statement of Concern" stating glyphosate is more persistent in the environment than previously believed and that evidence has accumulated over the past two decades showing that glyphosate-based herbicides have serious impacts on human health and the environment, the extent of which has yet to be determined.[57]

---

[51] Caroline Cox, 2004. Northwest Center for Alternatives to Pesticides Factsheet: Glyphosate.

[52] Tsui, M., & Chu, L. 2003. Aquatic toxicity of glyphosate-based formulations: comparison between different organisms and the effects of environmental factors. *Chemosphere*., 52(7), 1189-1197.

[53] Caroline Cox, 2004. Northwest Center for Alternatives to Pesticides Factsheet: Glyphosate.

[54] Paganelli, A., Gnazzo, V., Acosta, H., López, S.L. and Carrasco, A.E., 2010. Glyphosate-based herbicides produce teratogenic effects on vertebrates by impairing retinoic acid signaling. *Chemical research in toxicology*, *23*(10), pp.1586-1595.

[55] Mesnage, R., Arno, M., Costanzo, M., Malatesta, M., Séralini, G.E. and Antoniou, M.N., 2015. Transcriptome profile analysis reflects rat liver and kidney damage following chronic ultra-low dose Roundup exposure. *Environmental Health*, *14*(1), p.70.

[56] Gasnier, C., et al. 2008. Glyphosate-based herbicides are toxic and endocrine disruptors in human cell lines. *Toxicology*, doi:10.1016/j.tox.2009.06.006. Defarge, N., Takács, E., Lozano, V.L., Mesnage, R., Spiroux de Vendômois, J., Séralini, G.E. and Székács, A., 2016. Co-formulants in glyphosate-based herbicides disrupt aromatase activity in human cells below toxic levels. *International Journal of Environmental Research and Public Health*, *13*(3), p.264.

[57] Myers, J.P., Antoniou, M.N., Blumberg, B., Carroll, L., Colborn, T., Everett, L.G., Hansen, M., Landrigan, P.J., Lanphear, B.P., Mesnage, R. and Vandenberg, L.N., 2016. Concerns over use of glyphosate-based herbicides and risks associated with exposures: a consensus statement. *Environmental Health*, *15*(1), p.19.

The International Monsanto Tribunal heard evidence resulting in a legal opinion of the activities of Monsanto with respect to international human rights and environmental law. The Tribunal concluded that Monsanto has engaged in practices which have negatively impacted the right to a healthy environment; practices that have negatively impacted the right to food; practices that negatively impacted the right to health conduct that negatively affects the right to freedom indispensable for scientific research; activities that if a crime of ecocide were recognized in international criminal law, may fall within its definition. The Tribunal also stated the need to assert the primacy of international human and environmental rights law and the need to hold non-state actors responsible within international human rights law.[58]

Glyphosate and cancer

Contrary to EPA's finding of evidence of non-carcinogenicity, epidemiological studies–in which exposure is to formulated products rather than the technical grade active ingredient glyphosate—have found a positive association between exposure to glyphosate-based herbicides and cancer. On March 20, 2015, the International Agency for Research on Cancer (IARC) announced that it had classified glyphosate as a class 2A carcinogen, as "probably carcinogenic to humans." [59] This category is the most definitive of any based on standard laboratory animal testing.

New science and glyphosate

Besides looking at the total formulation in addition to the active ingredient, newer scientific studies have looked in greater depth at glyphosate's mode of action and the implications for human and ecological health. As mentioned above, because glyphosate's mode of action is disruption of a crucial pathway for manufacturing aromatic amino acids in plants–but not animals—many have assumed that it does not harm humans. However, many bacteria do use the shikimate pathway, and 90% of the cells in a human body are bacteria. The destruction of beneficial microbiota in the human gut (and elsewhere in and on the human body) is, therefore, a cause for concern –and a major contributor to disease. In addition, the destruction of soil microbiota leads to unhealthy agricultural systems with an increasing dependence on agricultural chemicals. Looking even deeper at the mode of action of glyphosate, other scientists have found that it starves and sickens the very crop plants that it is supposed to protect.

It is dangerous to base the review of chemicals on the assumption that microbiota is irrelevant to assessing dangers. It is well known that taking a course of antibiotics disturbs microbes that help digest food, but disturbing the microbiota has greater consequences than a bout of diarrhea. It can contribute to a whole host of "21st century diseases," including diabetes, obesity, food allergies, heart disease, antibiotic-resistant infections, cancer, asthma,

---

[58] International Monsanto Tribunal, 2017. Summary of the advisory opinion of the International Monsanto Tribunal.

[59] The IARC monograph is here: http://monographs.iarc.fr/ENG/Monographs/vol112/mono112-10.pdf. Also see the Beyond Pesticides article "Glyphosate Causes Cancer" at https://www.beyondpesticides.org/assets/media/documents/GlyphosateCausesCancer.pdf for more information.

autism, irritable bowel syndrome, multiple sclerosis, rheumatoid arthritis, celiac disease, inflammatory bowel disease, and more.

The human gut and 21st century diseases

The 90% of human cells that are microbial in origin are (mostly) not pathogenic, nor are they (mostly) just along for the ride. They are (mostly) symbionts who help the human function as it should. The human body, rather than being a distinct organism, is a biological community or "superorganism," the product of coevolution. The microbial community in the mammalian gut reflects the coevolution of host and microbiota, resulting in a mutually beneficial balance. As well as aiding the nutrition of the host human (or other mammal), microbiota contribute to developing and maintaining a healthy immune system. In return, the human host provides a niche in which the individual microbes and their community can persist, providing essential nutrients and habitat. As one review summarized current science, "Recent studies have provided firm evidence that skewing of the commensal community, often referred to as 'dysbiosis,' can result in inflammatory diseases not only of the intestine, but also of organs at distal sites. Such diseases can be triggered not only by pathogenic microbes, but also by otherwise harmless commensal microbes or those that are normally held in check by the microbial ecosystem and/or the metabolic state and immune response of the host. Thus, disturbance of this homeostasis by intrinsic or extrinsic influences, e.g., treatment with broad-spectrum antibiotics, can result in life-threatening dysbiosis."[60]

Not all disturbance in the microbiota comes from the conscious use of antibiotics. Swanson et al. have recently documented that the rise in these same diseases is tightly correlated with the use of the herbicide glyphosate.[61] They have also shown that glyphosate exposure can result in the inflammation that is at the root of these diseases. All of this is not surprising, since glyphosate has been patented as an antibiotic.[62]

Glyphosate and gut dysbiosis

Researchers Samsel and Seneff, starting with documents obtained from EPA through the Freedom of Information Act (FOIA), synthesized mountains of peer-reviewed research relating to health effects driven by glyphosate's mode of action. They and others have shown that the long list of 21st century diseases are linked to imbalances in the human gut connected to pervasive exposure to glyphosate.[63] Although Samsel and Seneff have speculated about the

---

[60] Littman, D.R. and Pamer, E.G., 2011. Role of the commensal microbiota in normal and pathogenic host immune responses. *Cell host & microbe*, *10*(4), pp.311-323.

[61] Swanson, N.L., Leu, A., Abrahamson, J. and Wallet, B., 2014. Genetically engineered crops, glyphosate and the deterioration of health in the United States of America. *Journal of Organic Systems*, *9*(2), pp.6-37.

[62] U.S. Patent number US7771736 B2. Glyphosate formulations and their use for the inhibition of 5-enolpyruvylshikimate-3-phosphate synthase. https://www.google.com/patents/US7771736.

[63] See, for example, Anthony Samsel and Stephanie Seneff, "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. Anthony Samsel and Stephanie Seneff, " Glyphosate, pathways to modern diseases II: Celiac sprue and gluten intolerance." *Interdiscip Toxicol.* 2013; 6(4): 159-184. Anthony Samsel and Stephanie Seneff. "Glyphosate, pathways to modern diseases III: Manganese, neurological diseases, and associated pathologies." *Surgical*

precise mechanisms involved in the causation of these diseases, the evidence for a causal link is strong. The evidence comes from two directions –first, that glyphosate causes dysbiosis in the gut microbiota, and second, that gut dysbiosis is a causal factor in many 21st century diseases. The patent for glyphosate as an antibiotic provides the first piece of evidence. It contains a long list of families of susceptible microorganisms.[64] Scientists have described the interaction between glyphosate and the shikimate pathway "in atomic detail."[65] Those who have looked at the impacts on the microbiota of poultry and cattle have found that glyphosate appears to have more negative impacts on beneficial bacteria, allowing pathogens to flourish.[66] For example, Shehata et al. found that "highly pathogenic bacteria as *Salmonella entritidis*, *Salmonella gallinarum*, *Salmonella typhimurium*, *Clostridium perfringens* and *Clostridium botulinum* are highly resistant to glyphosate. However, most beneficial bacteria such as *Enterococcus faecalis*, *Enterococcus faecium*, *Bacillus badius*, *Bifidobacterium adolescentis* and *Lacto-bacillus* spp. were found to be moderate to highly susceptible."[67]

Gut dysbiosis and 21st century diseases

Normally, the human gut is host to an ecosystem composed of anaerobic bacteria that are (mostly) non-pathogenic and (mostly) serve a number of beneficial functions, including assisting in the absorption of nutrients, producing short-chain fatty acids and vitamins, synthesizing amino acids, detoxifying xenobiotics, contributing to host immunity, preventing pathogenic infection, and maintaining the health and integrity of the colon wall. Some of these organisms live only in the human intestinal tract, which suggests a coevolved relationship.[68]

The imbalance (dysbiosis) of bacteria in the gut has been associated with many modern diseases. They include diarrhea, inflammatory bowel disease, activation of HIV infection, allergies, infection by *Clostridium difficile* and other pathogenic bacteria, autism, liver disease, atherosclerosis, pancreatitis, diabetes, obesity, fibromyalgia, polycystic ovary syndrome, and

---

Neurology International 2015, 6:45. Anthony Samsel and Stephanie Seneff. "Glyphosate, pathways to modern diseases IV: cancer and related pathologies," *The Journal of Biological Physics and Chemistry.* A. Samsel and S Seneff. "Glyphosate pathways to modern diseases V: Amino acid analogue of glycine in diverse proteins," *Journal of Biological Physics and Chemistry* 2016;16: 9-46. Robert M. Davidson, and Stephanie Seneff, "The Initial Common Pathway of Inflammation, Disease, and Sudden Death," *Entropy* 2012, 14, 1399-1442.

[64] U.S. Patent number US7771736 B2. Glyphosate formulations and their use for the inhibition of 5-enolpyruvylshikimate-3-phosphate synthase. https://www.google.com/patents/US7771736.

[65] Schönbrunn, E., Eschenburg, S., Shuttleworth, W.A., Schloss, J.V., Amrhein, N., Evans, J.N. and Kabsch, W., 2001. Interaction of the herbicide glyphosate with its target enzyme 5-enolpyruvylshikimate 3-phosphate synthase in atomic detail. *Proceedings of the National Academy of Sciences*, *98*(4), pp.1376-1380.

[66] Shehata AA, Schrödl W, Aldin AA, Hafez HM, Krüger M. 2013. The effect of glyphosate on potential pathogens and beneficial members of poultry microbiota in vitro. Curr Microbiol 66(4):350-8. Krüger, M., Shehata, A.A., Schrödl, W. and Rodloff, A., 2013. Glyphosate suppresses the antagonistic effect of Enterococcus spp. on Clostridium botulinum. Anaerobe, 20, pp.74-78. Schrödl, W., Krüger, S., Konstantinova-Müller, T., Shehata, A.A., Rulff, R. and Krüger, M., 2014. Possible effects of glyphosate on Mucorales abundance in the rumen of dairy cows in Germany. Current microbiology, 69(6), pp.817-823.

[67] Shehata AA, Schrödl W, Aldin AA, Hafez HM, Krüger M. 2013. The effect of glyphosate on potential pathogens and beneficial members of poultry microbiota in vitro. Curr Microbiol 66(4):350-8.

[68] Ding, H.T., Taur, Y. and Walkup, J.T., 2016. Gut Microbiota and Autism: Key Concepts and Findings. *Journal of Autism and Developmental Disorders*, pp.1-10.

others.[69] The fact that such diseases are linked to dysbiosis of the gut does not in itself prove that glyphosate causes them. However, the increase in these diseases is correlated tightly with increases in the use of glyphosate. Glyphosate is the most widely used antibiotic in agriculture, and agricultural use of antibiotics dwarfs the use of antibiotics in human medicine.[70]

Antibiotic Resistance

The spread of antibiotic resistance is a health care crisis of major proportions. The Centers for Disease Control and Prevention (CDC) call it "one of the world's most pressing public health problems."[71] Many bacterial infections are becoming resistant to the most commonly prescribed antibiotics, resulting in longer-lasting infections, higher medical expenses, and the need for more expensive or hazardous medications, and inability to treat life-threatening infections. The development and spread of antibiotic resistance is the inevitable effect of the use of antibiotics.[72] Bacteria evolve quickly, and antibiotics provide strong selection pressure for those strains with genes for resistance.

With the explosion of antibiotic resistance in the U.S. and worldwide, antibiotic use in crop and livestock production is a major public health issue. Use of antibiotics like glyphosate in agriculture allows residues of antibiotics and antibiotic-resistant bacteria to emerge on agricultural lands, move through the environment, contaminate waterways, and ultimately reach consumers in food. Both the human gut and contaminated waterways provide incubators for antibiotic resistance.

Glyphosate is the most widely used antibiotic. In addition to the promotion of weed resistance by widespread application of glyphosate and use of glyphosate-resistant genes in agriculture, there is evidence that glyphosate at levels used in agriculture results in bacterial resistance to antibiotics important in fighting human pathogens and infections.[73] It may not be widely appreciated that use of antibiotics in agriculture can contribute to resistance to antibiotics in human pathogens. The human pathogenic organisms themselves do not need to be sprayed by the antibiotic because movement of genes in bacteria is not solely "vertical"–that is from parent to progeny– but can be "horizontal –from one bacterial species to another. Thus, a pool of resistant soil bacteria or commensal gut bacteria can provide the genetic material for resistance in human pathogens. The use of glyphosate has an impact on the pool of antibiotic-

---

[69] Sekirov, I., Russell, S.L., Antunes, L.C.M. and Finlay, B.B., 2010. Gut microbiota in health and disease. *Physiological reviews*, *90*(3), pp.859-904. Parker, J., 2015. A new hypothesis for the mechanism of glyphosate induced intestinal permeability in the pathogenesis of polycystic ovary syndrome. *Journal of the Australasian College of Nutritional and Environmental Medicine*, *34*(2), pp.3-7.

[70] Shistar, T. and Curle, C., 2017. Agricultural uses of antibiotics escalate bacterial resistance. *Pesticides and You*, Winter 2016-2017, pp. 9-15.

[71] CDC, "Get Smart: Know When Antibiotics Work." http://www.cdc.gov/getsmart/antibiotic-use/fast-facts.html.

[72] Thomas F. O'Brien, 2002. Emergence, Spread, and Environmental Effect of Antimicrobial Resistance: How Use of an Antimicrobial Anywhere Can Increase Resistance to Any Antimicrobial Anywhere Else, Clinical Infectious Diseases 2002; 34(Suppl 3):S78–84.

[73] See *GMOs, Glyphosate, and Antibiotic Resistance* below.

resistant bacteria. Furthermore, residues of glyphosate in the soil may be taken up by treated or untreated plants and affect bacteria.[74]

The gut of humans and other animals provides an efficient incubator for antibiotic resistance. Antibiotic resistance increases first in commensal bacteria–the bacteria that naturally live within our bodies–and may then be transferred to pathogens. Thus, the absence of human pathogens in fields sprayed with glyphosate is irrelevant to the actual development and spread of resistant bacteria. The number of bacteria in the gut is large–often more than 10^{14} bacteria of several hundred species–with a large gene pool offering many mechanisms of resistance, and every exposure to antibiotics providing new opportunities for selection for resistance.[75]

Glyphosate used on crops is also washed into waterways, where it finds another environment perfect for encouraging the growth of antibiotic-resistant bacteria. Aquatic environments are rich in bacteria and provide opportunities for pathogens to obtain genes for resistance.

Glyphosate is the most widely used antibiotic in agriculture. Although it is registered as an herbicide, glyphosate works by attacking the shikimate pathway, part of the mechanism for manufacturing certain amino acids in both plants and microbes. The Monsanto patent for glyphosate as an antibiotic claims efficacy against the malaria plasmodium and other protozoan parasites.[76] Other research supports this claim and identifies the shikimate pathway as a target for *Mycobacterium tuberculosis*, the cause of tuberculosis.[77] Thus, two of the most troublesome

---

[74] K. Kumar, S.C. Gupta, Y. Chander, and C.J. Rosen, 2005. Antibiotic Uptake by Plants from Soil Fertilized with Animal Manure. J. Environ. Qual. 34:2082–2085 (2005). W.D. Kong, Y.G. Zhu,,, Y.C. Liang, J. Zhang, F.A. Smith, and M. Yang, 2007. Uptake of oxytetracycline and its phytotoxicity to alfalfa (Medicago sativa L.). Environmental Pollution, Volume 147, Issue 1, May 2007, Pages 187-193. RC Sinha and EA Peterson, 1972. Uptake and persistence of oxytetracycline in aster plants and vector leafhoppers in relation to inhibition of clover phyllody agent, Phytopathology 62: 50-56. MJ Daniels, 1982. Editorial: Possible effects of antibiotic therapy in plants. Reviews of Infectious Diseases 4 (Supp): 167-170.

[75] Chee-Sanford, J.C., Mackie, R.I., Koike, S., Krapac, I.G., Lin, Y.F., Yannarell, A.C., Maxwell, S. and Aminov, R.I., 2009. Fate and transport of antibiotic residues and antibiotic resistance genes following land application of manure waste. *Journal of environmental quality*, *38*(3), pp.1086-1108.

[76] U.S. Patent number US7771736 B2. Glyphosate formulations and their use for the inhibition of 5-enolpyruvylshikimate-3-phosphate synthase. https://www.google.com/patents/US7771736.

[77] Schönbrunn, E., Eschenburg, S., Shuttleworth, W.A., Schloss, J.V., Amrhein, N., Evans, J.N. and Kabsch, W., 2001. Interaction of the herbicide glyphosate with its target enzyme 5-enolpyruvylshikimate 3-phosphate synthase in atomic detail. *Proceedings of the National Academy of Sciences*, *98*(4), pp.1376-1380. http://www.pnas.org/content/98/4/1376.full. McConkey, G.A., 1999. Targeting the shikimate pathway in the malaria parasite Plasmodium falciparum. *Antimicrobial agents and chemotherapy*, *43*(1), pp.175-177. http://aac.asm.org/content/43/1/175.full.pdf+html. Blanco, B., Prado, V., Lence, E., Otero, J.M., Garcia-Doval, C., van Raaij, M.J., Llamas-Saiz, A.L., Lamb, H., Hawkins, A.R. and González-Bello, C., 2013. Mycobacterium tuberculosis shikimate kinase inhibitors: design and simulation studies of the catalytic turnover. *Journal of the American Chemical Society*, *135*(33), pp.12366-12376. http://s3.amazonaws.com/academia.edu.documents/42326626/Mycobacterium_tuberculosis_Shikimate_Kin20160207-9459-

human diseases may be susceptible to antibiotics using glyphosate's mode of action. The use of glyphosate can thus be a contributor to the spread of resistance to medically important antibiotics. In addition, glyphosate (along with some other herbicides) at environmentally relevant levels facilitates the development of resistance to antibiotics. [78] Broadcasting this antibiotic on grain crops–and spreading genes for resistance through genetically engineered crops dependent on glyphosate–contributes to the problem of antibiotic resistance.
Since, as EPA stated concerning another antibiotic, if "bacterial resistance to oxytetracycline from pesticidal use occurs, it is most likely that it would be caused by development of resistance from non-pathogenic bacteria in orchards which later transferred their resistance to human bacterial pathogens," [79] risk assessment based on toxic effects in animal and human models is inadequate for the assessment and management of the risk of antibiotic resistance promoted by glyphosate use.

Micronutrient imbalance

Some researchers have dived more deeply into the mechanisms by which glyphosate achieves its toxic effects. A recent review article questions whether disruption of the shikimate pathway is sufficient to kill plants and suggests, "As a metal chelator, glyphosate could deprive plants of important nutrients which have major roles as enzymatic co-factors and biomolecular constituents."[80] In addition, several scientists have suggested that through interactions with rhizosphere microorganisms, glyphosate causes diseases that kill plants–including glyphosate-resistant crops. Glyphosate varies in its impacts on microbes–some species are inhibited by glyphosate, some are resistant, and still others may use glyphosate or its metabolite AMPA as a food source.[81] The impacts of glyphosate's interactions with the microbiota of the root zone are various. For example, soybeans are legumes and hence harbor nitrogen-fixing bacteria in root nodules. There are reports that glyphosate interferes with nitrogen fixation in glyphosate-resistant soybeans.[82] Several researchers have documented a number of diseases that increase in frequency or severity when grown in soil in which glyphosate was used to burn down weeds or cover crops prior to planting or applied to the previous year's crop. These diseases include

---

1poojjb.pdf?AWSAccessKeyId=AKIAJ56TQJRTWSMTNPEA&Expires=1481730295&Signature=u%2FmuxakG13p%2BHNbhsxeMQZhikIg%3D&response-content-disposition=inline%3B%20filename%3DMycobacterium_tuberculosis_Shikimate_Kin.pdf.

[78] Kurenbach, B., Marjoshi, D., Amábile-Cuevas, C. F., Ferguson, G. C., Godsoe, W., Gibson, P., & Heinemann, J. A. 2015. Sublethal exposure to commercial formulations of the herbicides Dicamba, 2, 4-Dichlorophenoxyacetic acid, and Glyphosate cause changes in antibiotic susceptibility in Escherichia coli and Salmonella enterica serovar Typhimurium. *MBio*, *6*(2), e00009-15.

[79] USEPA. 2006. "Report of the Food Quality Protection Act (FQPA) tolerance reassessment progress and risk management decision (TRED) for oxytetracycline."

[80] Gomes, M.P., Smedbol, E., Chalifour, A., Hénault-Ethier, L., Labrecque, M., Lepage, L., Lucotte, M. and Juneau, P., 2014. Alteration of plant physiology by glyphosate and its by-product aminomethylphosphonic acid: an overview. *Journal of experimental botany*, *65*(17), pp.4691-4703.

[81] Kremer, R.J. and Means, N.E., 2009. Glyphosate and glyphosate-resistant crop interactions with rhizosphere microorganisms. *European Journal of Agronomy*, *31*(3), pp.153-161.

[82] Zobiole, L.H.S., Kremer, R.J. and Constantin, J., 2012. Glyphosate effects on photosynthesis, nutrient accumulation, and nodulation in glyphosate-resistant soybean. *Journal of Plant Nutrition and Soil Science*, *175*(2), pp.319-330.

Corynespora root rot of soybean, take-all of cereal crops, diseases caused by *Xylella fastidiosa*, and *Fusarium* diseases. Mechanisms observed for these increases in plant diseases include reduction in plant defensive compounds and reduced plant nutrition.[83] The reduced nutrition reaching plants from their microbial partners also affects the nutritional content of the crop, which has led to concern about impacts on the animals eating the crop.[84]

Ecological impacts

In addition to recent science showing the much greater toxicity of glyphosate products than the technical active ingredient to aquatic and semi-aquatic organisms,[85] an important finding is that glyphosate-resistant plants release glyphosate into the soil, where it has a continued impact. Glyphosate is also released to the soil by dead plants. "Once in soil, glyphosate may be adsorbed onto soil particles, degraded by microbes, or transferred to deeper soil horizons, migrating via soil pores or root canals. However, some agricultural practices, such as phosphorous amendment, may re-solubilize glyphosate in soils, making it available for leaching and to the rhizosphere of non-target plants."[86] Glyphosate adsorbed to soil particles may move in wind or water, affecting organisms off the target field. Its use in agriculture has had a significant impact on monarch butterfly populations through the reduction of milkweed stands.[87] However, the potentially much greater impact of glyphosate through its effects on soil microbiota is unknown and require long term studies.[88]

Other herbicides

Glufosinate

The Northwest Center for Alternatives to Pesticides summarizes the effects of glufosinate:

> Glufosinate is a broad-spectrum herbicide that kills plants by inhibiting the enzyme glutamine synthetase, an enzyme also found in animals, including humans. Glufosinate chemically resembles glutamine, a molecule used to transmit nerve impulses in the brain. Neurotoxic symptoms observed in laboratory animals following ingestion, dermal exposure, or inhalation of glufosinate include convulsions, diarrhea, aggressiveness, and

---

[83] Johal, G.S. and Huber, D.M., 2009. Glyphosate effects on diseases of plants. *European Journal of agronomy*, *31*(3), pp.144-152.

[84] Jefferson Dodge, 2011. Expert: GMOs to blame for problems in plants, animals. Boulder Weekly, August 11, 2011. http://gmwatch.org/index.php?option=com_content&view=article&id=13366. Zobiole, L.H.S., de Oliveira, R.S., Huber, D.M., Constantin, J., de Castro, C., de Oliveira, F.A. and de Oliveira, A., 2010. Glyphosate reduces shoot concentrations of mineral nutrients in glyphosate-resistant soybeans. Plant and Soil, 328(1-2), pp.57-69.

[85] For example: Tsui, M.T. and Chu, L.M., 2003. Aquatic toxicity of glyphosate-based formulations: comparison between different organisms and the effects of environmental factors; *Chemosphere*, *52*(7), pp.1189-1197. Relyea, R.A., 2005. The lethal impact of Roundup on aquatic and terrestrial amphibians. *Ecological applications*, *15*(4), pp.1118-1124.

[86] Gomes, M.P., Smedbol, E., Chalifour, A., Hénault-Ethier, L., Labrecque, M., Lepage, L., Lucotte, M. and Juneau, P., 2014. Alteration of plant physiology by glyphosate and its by-product aminomethylphosphonic acid: an overview. *Journal of experimental botany*, *65*(17), pp.4691-4703.

[87] Pleasants, J.M. and Oberhauser, K.S., 2013. Milkweed loss in agricultural fields because of herbicide use: effect on the monarch butterfly population. *Insect Conservation and Diversity*, *6*(2), pp.135-144.

[88] Kremer, R.J., 2017. Soil and environmental health after twenty years of intensive use of glyphosate. Adv Plants Agric Res 2017, 6(5): 00224.

disequilibrium. Dogs appear to be the laboratory animal most sensitive to glufosinate. Ingestion of glufosinate for two weeks caused heart and circulatory failure resulting in death. Exposure of pregnant laboratory animals to glufosinate caused an increase in premature delivery, miscarriages, the number of dead fetuses, and arrested development of fetal kidneys. Concentrations of a glufosinate-containing herbicide of less than one part per million cause mortality of oyster and clam larvae. Several species of disease-causing fungi are resistant to glufosinate, while a beneficial fungi that parasitizes disease-causing fungi is very susceptible to glufosinate. This means that use of glufosinate can have "important microbiological consequences.[89]

Quizalofop

Quizalofop is a developmental and reproductive toxin and recognized as an endocrine disruptor by the EU.[90] It carries the signal word "Danger" and requires full protective equipment. The label warns, "DANGER! Causes irreversible eye damage. Harmful if swallowed, inhaled, or absorbed through the skin. Avoid contact with eyes, skin, or clothing. Avoid breathing vapor or spray mist."

The label also warns of environmental hazards: "This pesticide is toxic to fish and invertebrates. Do not apply directly to water, or to areas where surface water is present, or to intertidal areas below the mean high water mark. … This product may contaminate water through drift of spray in wind. This product has a potential for runoff for several months or more after application. Poorly drained soils and soils with shallow water tables are more prone to produce runoff that contains this product."

Extent of use poses great risks

Approximately 97 million acres of corn are predicted to be planted in 2020.[91] This indicates that a vast amount of U.S. farmland would be sprayed with these toxic herbicides should this GE variety be deregulated, leading to possible increased weed resistance, environmental contamination, and increased public health risks in these regions. Contrary to industry propaganda and misinformation, providing these GE "tools" to farmers only keeps them on a perpetual chemical treadmill which continues to propagate resistant weeds, endanger our environment, health, and agricultural economy.

As we have done previously, we urge APHIS to use its full statutory authority to (1) protect the environment and all agricultural interests from unsustainable technologies that induce weed resistance, (2) consider the environmental and human health risks increased herbicide use resulting from this latest GE variety will pose, and (3) deny the petitioner's request for deregulation.

---

[89] Cox, C. 1996. Glufosinate Factsheet. https://d3n8a8pro7vhmx.cloudfront.net/ncap/pages/26/attachments/original/1428423375/glufosinate.pdf?1428423375.

[90] http://www.pesticideinfo.org/Detail_Chemical.jsp?Rec_Id=PRI5533.

[91] http://ethanolproducer.com/articles/17040/usda-projects-8-increase-in-us-corn-acreage-for-2020.

Responsibilities Under the Law

The *Plant Protection Act of 2000 (PPA)* sets out that GE organisms must not pose a plant pest or noxious weed risk.[92] APHIS is mandated to regulate these organisms when there is the potential for "unacceptable" risk.[93] APHIS's mission to "protect and promote U.S. agricultural health"[94] is one that must provide "leadership in ensuring the health and care of plants and animals . . . improves agricultural productivity and competitiveness, and contributes to the national economy and the public health."[95] However, this petition on GE crops tests the agency's compliance with the statute and commitment to its mission. We would view an inadequate analysis of the full spectrum of environmental impacts as an accommodation to special interests and a narrow exercise of its legal responsibilities.

According to section 7712(a) of the PPA, APHIS must prohibit and/or restrict any plant or plant product that may introduce or disseminate a plant pest or noxious weed within the U.S.[96] A "noxious weed" is defined as any "plant or plant product that can directly or indirectly injure or cause damage to crops….or other interest of agriculture…. the public health, or the environment."[97] Resistant weeds, like those resistant to glyphosate (Roundup®), have ballooned in recent years, due particularly to the expansion of Roundup-Ready® crops, including soybeans and corn. Increased selection pressure from widespread use and reliance on glyphosate, and the simultaneous reductions in the use of sustainable weed management practices have resulted in glyphosate-resistant weeds.[98] The introduction of resistance to dicamba and other herbicides is predictable by this mechanism. These resistant weeds present an ever-growing economic concern to farmers, since a widespread distribution of hard-to-control weeds has the potential to cause significant agricultural economic losses underestimated in the APHIS analysis.

Under a previous National Environmental Policy Act (NEPA) review, APHIS acknowledges the following unavoidable environmental impacts:

> Herbicides represent a tool that allows for the economical production of corn and soybean. As long as herbicides are used to produce corn and soybean, weeds will develop resistance to the herbicides used. *Under all four [NEPA] Alternatives, the selection of herbicide-resistant weeds is an unavoidable impact.* Growers may mitigate

---

[92] Plant Protection Act of 2000 (PPA), 7 U.S.C. § 7702.
[93] PPA, 7 U.S.C. §§ 7701(7), 7711, 7712.
[94] APHIS. About APHIS. Available at http://www.aphis.usda.gov/wps/portal/banner/aboutaphis
[95] USDA. USDA agencies and Offices overview: http://www.usda.gov/wps/portal/usda/usdahome?navid=AGENCIES_OFFICES
[96] PPA, 7 U.S.C. § 7712(a).
[97] PPA, 7 U.S.C. § 7702(10).
[98] APHIS. 2012. Dow AgroSciences Petition (09-349-01p) for Determination of Nonregulated Status of Event DAS-68416-4. US Department of Agriculture.

the rate at which weeds develop resistance by adopting best management practices as described in Section 5.3.2.[99]

Despite acknowledgment of the inevitable propagation of herbicide-resistant weeds, APHIS continues to deregulate GE crops which utilize herbicides that induce resistance. The deregulation of GE crops like MON 87429 corn poses an unacceptable noxious weed propagating risk, in violation of the PPA and NEPA.[100] Resistant weeds must be interpreted as "noxious weeds" that are directly and indirectly causing undue burden to U.S. agricultural interests in terms of additional costs, economic burden to farmers (especially organic farming systems), and impact to overall agricultural productivity, as well as contaminating the environment. APHIS therefore can and must use its authority to restrict further spread of these resistant, "noxious weeds" to prevent further impact on U.S. agricultural systems. Introducing into the environment GE material, the very agent which is reliant on herbicides that promote the spread of resistant weeds, violates section 7712(a) of the PPA, and poses "unacceptable" risk to plant health and an unreasonable risk to the environment.

Deregulation of these crops only serves to undermine U.S. agricultural interests in the long-term. In addition, the continued allowance of GE technology and chemical-intensive practices raises a severe economic threat to non-GE plant systems, such as crops certified under the USDA organic standards.

Weed Resistance Continues to Proliferate

As with the recently approved dicamba-tolerant cotton and soybeans and corresponding dicamba use, there is concern that the increased use of all of these herbicides will induce multi-herbicide resistant weeds. The idea behind GE crops is to pair them with their complementary herbicide to control weeds without significant crop damage. Data has shown that since the advent of GE crops, herbicide use has remarkably increased.[101] This widespread glyphosate use on glyphosate-resistant GE crops has vastly increased the prevalence of glyphosate-resistant weeds.[102,103] In a previous Draft Environmental Impact Statement, APHIS states that "Weed resistance is not a consequence of the use of herbicide resistant crops," even though the agency acknowledges that "a lack of diversity of weed management practices…have contributed significantly to the selection of resistant biotypes."[104] The agency goes on to note

---

[99] APHIS. 2013. Draft Environmental Impact Statement. Dow AgroSciences Petitions (09-233-01p, 09-349-01p, and 11-234-01p) for Determinations of Nonregulated Status for 2,4-D Resistant Corn and Soybean Varieties. Biotechnology Regulatory Services. U.S. Department of Agriculture. Riverdale, MD, at 148.

[100] NEPA, 42 U.S.C. § 4332.

[101] Benbrook, C. 2012. Impacts of genetically engineered crops on pesticide use in the U.S. -- the first sixteen years. *Environmental Sciences Europe*, 24:24 doi:10.1186/2190-4715-24-24.

[102] Eastham, K., and Sweet, J. 2002 Genetically modified organisms (GMOs): The significance of gene flow through pollen transfer. Assessing the Impact of GM Plants (AIGM) programme for the European Science Foundation and the European Environment Agency Environmental issue report.

[103] Benbrook, C. 2012. Impacts of genetically engineered crops on pesticide use in the U.S. -- the first sixteen years. *Environmental Sciences Europe*, 24:24 doi:10.1186/2190-4715-24-24.

[104] USDA-APHIS. Draft Environmental Impact Statement- 2014. Monsanto Petitions (10-188-01p and 12-185-01p) for Determinations of Nonregulated Status for Dicamba-Resistant Soybean and Cotton Varieties. p180-181.

that if growers rely on dicamba and glyphosate for weed control, "resistance might be selected quickly." While the agency's statements are somewhat contradictory, it is clear that current weed management practices—i.e., over-reliance on chemical inputs—spawn weed resistance, and that continuing such practices with dicamba, 2,4-D, glyphosate, quizalofop, and glufosinate will only lead to an increased occurrence of resistant weeds.

It is inevitable that once the herbicides are released into the environment, selection pressure due to herbicide reliance induces the development of resistance among weed species. Taking a 'wait and see' approach to resistance is one that is designed to fail. Once resistant populations are identified it is already too late to prevent these traits from being passed to successive generations. Scientists studying weed resistance agree that it is of economic concern to farmers, have advised against the dependence on herbicides, and advocate for the use of crop rotations and a shift to non-GE crops.[105] APHIS should act quickly to support this shift by disallowing the introduction of all new GE crops in the marketplace.

According to Weed Science Society of America, over 10 plants species have developed resistance to dicamba (over 200 for glyphosate).[106] If new dicamba-resistant crops are approved, it is predicable that this number will increase. While APHIS and EPA may hope to rely on mitigation measures to control the spread of resistance, the only sustainable solution is to refrain from deregulating yet another GE variety of corn. Failure to do so only serves to compound growing weed resistance problems which go against the APHIS's mission to "protect American agriculture."

Volatility and Drift Endanger the Environment

Dicamba and 2,4-D vapor drift and subsequent crop injury to sensitive broadleaf crops have been frequent problems.[107] Abnormal leaf growth, floral development, reduced yield, and reduced quality have all been observed from dicamba drift.[108] These impacts have severe economic consequences for non-GE and organic farmers. The burden should not be placed on these farmers to protect themselves from drift with best management practices.

APHIS cannot assume that the environmental impacts associated with herbicide drift will be mitigated by the registration requirements established by EPA on pesticide labels. Unfortunately, label directions have been shown to have no effect on decreasing spray drift. In fact, EPA has acknowledged this and has attempted to review and revise pesticide labeling guidance.[109] EPA believes that it can mitigate against potential risks from drift by requiring buffer zones and application restrictions, which have proven ineffective.

---

[105] Culpepper, A. S. 2006. Glyphosate-Induced Weed Shifts. *Weed Technology*, 20(2), 277–281.

[106] Weed Science Society of America. Weeds Resistant to the Herbicide Dicamba. International Survey of Resistant Weeds.

[107] Egan JF, and Mortensen DA. 2012. Quantifying vapor drift of dicamba herbicides applied to soybean. *Environ Toxicol Chem*. 31(5):1023-31.

[108] Cox, C. 1994.Herbicide factsheet; Dicamba. *Journal of Pesticide Reform*. Vol.14, No.1.

[109] USEPA. 2009. Pesticide Spray and Dust Drift. Available at http://www.epa.gov/pesticides/factsheets/spraydrift.htm.

Conclusion

APHIS has a responsibility under the law to prohibit and/or restrict any plant or plant product that poses a risk to the environment. APHIS must meet its statutory duty to fully review the salient impacts of multi-herbicide-tolerant MON 87429 corn, and the expected increase in herbicide use. Therefore, we urge the agency to reject the petition for deregulation. To allow new GE material into the environment against the backdrop of documented problems created by other herbicide-tolerant GE crops is taking U.S. agriculture in a wrong and hazardous direction. GE gene flow in the environment and increased herbicide dependency has been left unchecked for many years, resulting in an increasing population of resistant weeds and insects that are becoming more and more difficult and costly to control.

GE crops are not the solution for glyphosate resistant weeds created by glyphosate-resistant GE crops. Had a proper environmental assessment been conducted by APHIS on previous GE decisions, the economic and environmental threat of resistant, noxious weeds may have been avoided. It is time for the agency to focus on other sustainable, integrated methods for long-term weed management, which allow our nation's farmers to get off the toxic treadmill.

As we have done in previous comments to the agency, we urge APHIS to use its full statutory authority and reject the petition to deregulate multi-herbicide-tolerant MON 87429 corn by citing the plant-damaging and noxious-weed propagating risks that have not been fully evaluated by the petitioner when considered alongside the accompanying use of these herbicides. We urge APHIS to consider both the environmental effects and human health effects this dangerous combination will pose and to deny petitioner's request for deregulation. We urge the agency not to escalate the American agricultural economy's broad reliance on herbicides because of the failure of glyphosate GE- technologies. Now is the time to concede that GE technologies have not lived up to their promises and encourage our nation's farmers to return to more sustainable methods of farming.

Thank you for your attention to these comments.

Respectfully,

Terry Shistar, Ph.D.
Board Member, Beyond Pesticides