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June 30, 2014

Office of Pesticide Programs
Environmental Protection Agency,
Mailcode 28221 T,
1200 Pennsylvania Ave, NW,
Washington, DC 20460

Re: 2,4-D: New Use on Herbicide-Tolerant Corn and Soybean.
Docket No.: EPA-HQ-OPP-2014-0195

Dear Sir/Madam,

We are submitting these comments to advise the U.S. Environmental Protection Agency (EPA) against amending 2,4-D's registration to include 2,4-D choline salt use on 2,4-D tolerant corn and soybeans. EPA is considering the registration of the product, Enlist Duo,™ which contains glyphosate and the choline salt of 2,4-D, for use on corn and soybeans genetically engineered (GE) to tolerate 2,4-D. Enlist™ is the 2,4-D choline salt formulation to be exclusively used on 2,4-D tolerant corn and soybeans containing DAS-68416-4 genetic trait. As evidenced with other GE crops, the use of 2,4-D-tolerant crops will simultaneously increase 2,4-D use in the environment, leading to unreasonable adverse risks that EPA must consider before allowing an unprecedented increase in 2,4-D use. Given that 2,4-D is currently undergoing registration review, the agency must first complete a full evaluation of all aggregate and cumulative uses of 2,4-D before a consideration of expanded use.

Earlier this year, Beyond Pesticides submitted comments to the U.S. Department of Agriculture (USDA) against the proposal to deregulate 2,4-D-tolerant corn and soybeans. These GE crops not only have the potential to contaminate non-GE crops, native plant species, and waterways, but will lead to, according to some estimates, 2,4-D use at 1.75-3 times current use.[1] This would increase the risk of inducing 2,4-D-resistant weeds, and cause direct and indirect adverse impacts on human health and the environment due to corresponding increases in drift, and the contamination of food and water. The scientific literature makes it clear that 2,4-D is highly toxic, as it is linked to numerous adverse health effects, including increased risk of birth defects, reduced sperm counts, increased risk of non-Hodgkin

[1] 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. pp133.

lymphoma, Parkinson's disease, and endocrine disruption. As a result, there is grave concern about the impending expansion of 2,4-D use, and we urge the agency to use its statutory authority to limit 2,4-D uses.

FEDERAL OVERSIGHT HISTORICALLY LACKING

USDA oversees the regulation of GE crops, while EPA oversees herbicide applications on these crops under environmental law. Both agencies have a statutory responsibility to safeguard the environment from any potential adverse effects from these actions. However, the proliferation of herbicide resistant weeds, contamination of non-GE crops and native plants, as well as surface water contamination has proven that adequate oversight is lacking. USDA notes several times in its 2013 proposal for deregulation that the potential for adverse impact to the environment from the expected increased use of 2,4-D (direct and indirect impacts) are under the jurisdiction of EPA and the *Federal Insecticide, Fungicide and Rodenticide Act (FIFRA)*.[2] Additionally, USDA acknowledges that cumulative impact (of 2,4-D corn and soybean) results from the "combined action of USDA on the subject of petitions and of the EPA's action to register 2,4-D for use on Enlist™ corn and soybean."[3] USDA is assuming that herbicide applications associated with its action to deregulate 2,4-D-tolerant GE corn and soybeans will be fully evaluated by EPA , and that possible exposure patterns, including drift, will be mitigated by registration requirements established by the agency.

Allowance Should Not Precede Full Registration Review:

EPA's *Environmental Risk Assessment of Proposed Label for Enlist (2,4-D choline salt)* is filled with ecological data gaps, and does not address concerns of 2,4-D induced weed resistance, potential water contamination, nor the potential synergistic and additive effects associated with 2,4-D and glyphosate mixture of Enlist Duo™.[4] Additionally, 2,4-D and its many salts are currently under registration review by the agency, where a registration decision is not expected before 2017.[5] No decision should be made on the choline salt before the final assessments on all human and ecological effects of the other 2,4-D forms, given the expected expansion of 2,4-D use patterns. Similarly, a *Food Quality Protection Act* (FQPA) analysis needs to be conducted given that dietary residues and exposures are expected to increase.[6]

Ecological exposures via drift, and the impact to non-target crops, especially to sensitive organic systems, have not been sufficiently addressed by the agency to date. While EPA acknowledges that there is a high level of public concern on this matter, and is moving to get feedback from stakeholders,

[2] Federal Insecticide, Fungicide and Rodenticide Act (FIFRA), 7 U.S.C. §§ 136-136Y.
[3] 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. US Department of Agriculture. Riverdale, MD.
[4] USEPA. 2013. EFED Environmental Risk Assessment of Proposed Label for Enlist (2,4-D Choline Salt), New Uses on Soybean with DAS 68416-4 (2,4-D Tolerant) and Enlist (2,4-D + Glyphosate Tolerant) Corn and Field Corn. Environmental Fate and Effects Division. Washington DC
[5] USEPA. 2012. 2,4-D Preliminary Work Plan. Reregistration Review: Initial Docket Case No. 73. Office of Pesticide Programs. Washington DC.
[6] *See* 21 U.S.C. § 346a.

the agency must also recognize the above reasons for concern and not usher in increased 2,4-D levels into the environment.

Previous decisions to deregulate GE crops (Roundup Ready crops) without the proper considerations of ecological risks have led to an increase in resistant weeds, also known as "superweeds," brought on by increased selection pressure due to a reliance on herbicides in these GE systems. [7,8] Now Enlist is being marketed to combat the surge in glyphosate-resistant weeds brought on by previous errors in federal decision making. Both USDA and EPA must now realize that it is counterintuitive and futile to mitigate the failures of GE technology with more GE crops, increased herbicide use, and a retrogression to older pesticidial chemistries. Instead, it is time for both agencies to focus on other sustainable, integrated methods for long-term weed management, which allow our nation's agricultural economy to get off the toxic treadmill and meet the standard to protect in the short- and long-term against "unreasonable adverse effects" under the *Federal Insecticide, Fungicide and Rodenticide Act* (FIFRA).[9]

INCREASED 2,4-D USE TRIGGERS NEW TOLERANCE ASSESSMENTS

2,4-D choline salt is being registered for use on GE corn and soybeans –the two most widely grown crops in the U.S., with 84 and 73.8 million acres harvested in 2011, respectively.[10] Additionally, there are over 100 food commodities that have established tolerance levels for 2,4-D in general.[11] Currently, the vast majority of GE crops are chemically managed with glyphosate, due to their glyphosate tolerance. Introducing a new use pattern for 2,4-D, through a stacked 2,4-D and glyphosate tolerance, would therefore increase 2,4-D residues on corn and soybeans, leading to increased dietary exposures. Corn and soybeans are cornerstone ingredients in the American diet, and increased 2,4-D residues on these GE crops will contribute significantly to human exposures.

According to the *Food Quality Protection Act* (FQPA), EPA's review and assessment of tolerances must include a consideration of aggregate risks of non-occupational sources of pesticide exposure, whether there is increased susceptibility to infants and children, and the cumulative effects of pesticides with a common mechanism of toxicity. A pesticide tolerance may only be promulgated or left in effect by EPA if the tolerance is "safe."[12] "Safe" is defined as "a reasonable certainty that no harm will result from aggregate exposure to the pesticide chemical residue, including all anticipated dietary exposures and all other exposures for which there is reliable information."[13]

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[7] 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.
[8] 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.
[9] *See* 7 U.S.C. §§ 136-136a.
[10] USEPA. 2013. Major crops grown in the U.S. http://www.epa.gov/oecaagct/ag101/cropmajor.html
[11] 40 CFR 180.142.
[12] See 21 U.S.C. 346a(b)(2)(A)(i).
[13] See 21 U.S.C. 346a(b)(2)(A)(ii)

A safety finding can only be made when it is determined that aggregate risks are not of concern and there is a reasonable certainty of no harm from aggregate exposure. In its analysis of residue data, EPA states that the maximum residues in field trial data for 2,4-D choline do not exceed the current 2,4-D tolerances on corn commodities, and has therefore not issued any new tolerances.[14] Not surprisingly, the registrant Dow AgroSciences proposed to the agency that existing corn and corn feed tolerances for 2,4-D were adequate to cover new uses of 2,4-D choline. However, the documents provided by EPA for this action in the Federal Register do not show a proper tolerance assessment that considers all the above concerns. How can the agency come to this conclusion when a proper tolerance assessment has not been conducted, and is not expected until the 2,4-D registration review period is completed in 2017?[15] Given that 2,4-D is now slated to be used on millions of acres of corn and soybeans, what is the basis for the agency's belief that existing corn tolerance levels can still apply?

Theoretically, tolerance limits help ensure that pesticide applications do not exceed federal application rates, and that the human population is not exposed to residues that can adversely impact health. These set limits must be based on human health data and should not be amended without complete information, or to simply accommodate a new use pattern.

Given that a recent study investigating GE crops and glyphosate residues found that GE soybeans sprayed with Roundup during the growing season take up and accumulate glyphosate (and its metabolite, AMPA) at levels higher than conventional non-GE and organic soybeans,[16] it can be inferred that 2,4-D residues can or will accumulate in or on GE crops in a similar manner. EPA must therefore conduct a proper dietary assessment under FQPA to satisfy its federal mandate, and reexamine tolerance levels.

VOLATILITY, DRIFT CONTINUE TO GO UNDERESTIMATED

The major marketing spin for Enlist Duo is the promise that the choline salt of 2,4-D is significantly less volatile than other forms of 2,4-D. EPA's information regarding this is based on a field study submitted by the registrant that is still under review.[17] The vapor pressure for the 2,4-D acid is $1.4x10^{-7}$mmHg, DMA salt: $1x10^{-7}$mmHg, and EHE salt: $3.6x10^{-6}$mmHg, while that of 2,4-D choline salt is not provided. The environmental risk assessment, however, provides the preliminary volatility flux data for the choline, DMA, and EHE salts of 2,4-D (Appendix H). No information on the flux rate of the acid is provided, even though, according to EPA, under most environmental conditions, various forms of 2,4-D degrade rapidly to form 2,4-D acid. Appendix H shows that the volatility flux rate –used to estimate dissipation from the soil over time– of the choline salt is less than the DMA and EHE salts. It is not clear what field conditions

[14] USEPA. 2011. 2,4-D. Summary of Analytical Chemistry and Residue Data for Use of 2,4-D Choline in/on Herbicide Tolerant Field Corn Containing the Aryloxyalkanoate Dioxygenase-1 (ADD-1) Gene. Office of Pesticide Programs. Washington DC.
[15] USEPA. 2012. 2,4-D Preliminary Work Plan. Reregistration Review: Initial Docket Case No. 73. Office of Pesticide Programs. Washington DC.
[16] Bøhn, T et al. 2014. Compositional differences in soybeans on the market: Glyphosate accumulates in Roundup Ready GM soybeans. *Food Chemistry.* 153(15):207–215.
[17] USEPA. 2013. EFED Environmental Risk Assessment of Proposed Label for Enlist (2,4-D Choline Salt), New Uses on Soybean with DAS 68416-4 (2,4-D Tolerant) and Enlist (2,4-D + Glyphosate Tolerant) Corn and Field Corn. Environmental Fate and Effects Division. Washington DC.

existed, e.g. temperature, soil moisture content etc, and so this data does not provide very meaningful information.

Volatility is dependent on several environmental conditions, including temperature and humidity. The vapor pressure of the 2,4-D acid ($1.4x10^{-7}$mmHg) indicates that 2,4-D has a relatively low volatility, but historical evidence of 2,4-D drift and damage to non-target sites demonstrates that the chemical can in fact enter the atmosphere (volatilize) and travel significant distances (drift). Thus, claims of the 2,4-D choline salt's comparatively lower volatility does not appear to mean much in the real world when different environmental and application variables play a part in whether the chemical will remain on site or travel off site.

When it comes to spray drift, local climatic conditions and topography are also important contributing factors. Climate conditions across the U.S. vary widely; for instance, conditions in the Northwest are markedly different than those in the Southwest, and it is expected that drift in different areas will depend on local conditions. In recent comments to the agency on the Spray Drift Risk Assessment,[18] and its work with the AgDRIFT model, Beyond Pesticides identified several of these variables that we believe the agency has not taken into consideration fully for evaluating drift, which must be addressed in this 2,4-D assessment.

As mentioned, 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[19] and 2,4-D drift has been known to damage tomatoes, grapes, and other plants. Drift can injure plants half a mile or more from the application site, and concentrations 100 times below the recommended label rates have even been reported to cause injury to grapes.[20] In addition to non-target plants, 2,4-D drift can impact species listed under the *Endangered Species Act* (ESA). In 2011, the National Marine Fisheries Service (NMFS) identified 2,4-D as likely to jeopardize all listed salmonid, based on current registration and label directions.[21] 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).[22] Non-target plants in these areas and others are therefore also at risk. Likewise, 2,4-D is toxic to aquatic plants, and is more toxic to vascular plants than to non-vascular plants.

Claims that the 2,4-D choline salt is somehow safer for the environment due to its supposed lower volatility, and thus, is less prone to drift is yet to be proven. Moreover, the surfactants and solvents added to commercial mixtures can substantially alter volatility. Environmental conditions, which can vary tremendously, affect volatility and drift, and will play a role in the off-site movement of the 2,4-D choline salt formulation. These have not been adequately addressed by EPA, given 2,4-D's reputation for off-site movement. There is an expectation that EPA label use restrictions for 2,4-D will mitigate the potential (non-target) risks from exposure. But, pesticide product label directions have been shown to

[18] FR docket number: EPA-HQ-OPP-2013-0676-0104.
[19] Hales, R. 2010. Herbicide Injury a Problem on Plants. Colorado State University Cooperative Extension.
[20] Ball, D.A, Parker, R, et al. 2004. Preventing Herbicide Drift and Injury to Grapes. Oregon State University Extension Service
[21] NMFS. 2011. Endangered Species Act Section 7 Consultation Biological Opinion: 2,4-D, Triclopyr, Diuron, Linuron, Captan, and Chlorothalonil. National Marine Fisheries Service.
[22] USEPA. 2005. 2,4-D RED Facts. Available at http://www.epa.gov/oppsrrd1/REDs/factsheets/24d_fs.htm.

have no effect on decreasing spray drift. In fact, EPA has acknowledged this and is attempting to review and revise pesticide labeling guidance.[23]Additionally, given that certain data gaps still exist for evaluating 2,4-D drift impact on sensitive crops like grapes and cotton, the agency still has a lot of work to do on its assessment of 2,4-D volatility and drift, and cannot afford to underestimate risks posed by an increased use of 2,4-D.

DIOXIN CONTAMINATION STILL UNRESOLVED

2,4-D's contamination with dioxins has long been a part of 2,4-D's history. According to the agency's ecological assessment, "Polychloro dibenzo-p-dioxin (PCDD) and polychloro dibenzo-p-furans (PCDF) may be formed during the manufacture of 2,4-D and can remain in the products as impurities." 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. EPA mentions that, "No PCDD and PCDF were detected above 30% of the limit of quantitation (LOQ) in the registered sources of the active ingredients for 2,4-D choline," and that, "2,4-D choline salt use in corn and soybean is not expected to pose risk to terrestrial organisms since the [toxicity equivalence]for 2,4-D choline is 4.8 times lower than the formulated products of 2,4-D acid and EHE." While dioxin contamination may be the lowest it has been in 2,4-D formulations, the levels have not been reduced to zero. While levels may be very low, expected increases in 2,4-D use means that the frequency of low level dioxin residues entering the environment will also increase.

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. Dioxins have notoriously long half-lives, are bioaccumulative, and present broadly significant health risks developmentally and postnatally, including increased risk of heart disease and diabetes.[24] EPA , while acknowledging reduced dioxin contamination in 2,4-D, ignores projected increased use of 2,4-D and underestimates the possibility of increased dioxin contamination to fields using 2,4-D, and the threat to environmental health.

INCREASED SELECTION OF 2,4-D RESISTANT WEEDS IS A MAJOR CONCERN

The proliferation of glyphosate-resistant weeds presents an ever-growing economic concern to farmers, since a widespread distribution of hard-to-control weeds has the potential to cause significant economic losses. Scientists studying the phenomenon agree that it is of economic concern, and have advised against the dependence on herbicides, and advocate for the use of crop rotations and the rotation to non-GE crops.[25] It is inevitable that the introduction of 2,4-D tolerant crops will result in 2,4-D resistant weeds. USDA in its draft Environmental Impact Statement (DEIS) recognizes that the adoption of 2,4-D corn and soybean can have a "potentially significant environmental impact," on the proliferation of resistant weeds, due to changes in farming practices, i.e., increased reliance on 2,4-D for weed control.

[23] USEPA. 2009. Pesticide Spray and Dust Drift. Available at http://www.epa.gov/pesticides/factsheets/spraydrift.htm.
[24] 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.
[25] Culpepper, A. S. 2006. Glyphosate-Induced Weed Shifts. *Weed Technology*, 20(2), 277–281.

The DEIS states, "If 2,4-D resistant weeds were to be selected as a result of these combined actions, growers who rely on 2,4-D for effective control and inexpensive weed control are likely to experience increased socioeconomic impacts from more costly and restrictive weed control alternatives."[26] USDA concedes that, given the prevalence of glyphosate-resistant weeds, it is "very likely" that 2,4-D resistant weeds will occur, and is aware that weed resistance to 2,4-D has already been identified in other countries.[27] This phenomenon is also expected in the U.S. with an expansion of 2,4-D use. Thus far, 28 species across 16 plant families have already evolved resistance to the synthetic auxin herbicides, the mode of action to which 2,4-D belongs, with 16 known to be resistant specifically to 2,4-D.[28] Experts have already predicted that with the introduction of herbicide-tolerant genes, plants carrying multiple resistances will become common after commercial GE release. [29]

Contrary to industry promises of an overall increase in agricultural productivity with a decrease in chemical use for GE crops, one published report, which utilized data from USDA, shows that GE crops have been responsible for an increase of 404 million pounds of herbicide use in the U.S. over the first 16 years of commercial use of GE crops (1996-2011).[30] Another survey of farmers' herbicide use patterns found that herbicide use continues to increase, with many farmers making one to three post-applications per year.[31] Given that resistant weeds are the direct result of herbicide overuse, the problem will not be resolved simply by adding new herbicide-resistance traits into our agriculture. According to data published by Purdue University Extension, resistant weeds species have several negative effects on a farm, including increased labor, increased costs, and increased risk of crop injury. [32]

Under FIFRA, EPA must meet a no "unreasonable adverse effect" standard. FIFRA defines the term ''unreasonable adverse effects on the environment'' as "any unreasonable risk to man or the environment, taking into account the economic, social, and environmental costs and benefits of the use of any pesticide."[33] Certainly, the reliance of herbicides on corn and soybeans has costs that far outweigh the perceived benefits. EPA must consider the onset of weed resistance as an environmental and economic consequence of expanded 2,4-D use, and find that 2,4-D poses an "unreasonable risk" to the environment.

HAZARDS TO PUBLIC AND FARMWORKER HEALTH MUST NOT BE IGNORED

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[26] 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. US Department of Agriculture. Riverdale, MD.

[27] APHIS. 2011. Plant Pest Risk Assessment for DAS-40278-9 Corn. U.S. Department of Agriculture.

[28] Egan JF, Maxwell BD, Mortensen DA, et al. 2011. 2,4-Dichlorophenoxyacetic acid (2,4-D)-resistant crops and the potential for evolution of 2,4-D-resistant weeds. Proc Natl Acad Sci. 108(11): E37.

[29] 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.

[30] 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.

[31] Givens, W. A., Shaw, D. R., Johnson, W. G., Weller, S. C., Young, B. G., Wilson, R. G., Owen, M. D. K., & Jordan, D. 2009. A Grower Survey of Herbicide Use Patterns in Glyphosate-Resistant Cropping Systems. *Weed Technology*, 23(1), 156-161.

[32] Boerboom, C and Owen, M. Facts About Glyphosate Resistant Weeds. The Glyphosate, Weeds, and Crops Series. Purdue Extension.

[33] 7 U.S.C. § 136(bb).

EPA must ensure that any expansion of 2,4-D's aggregate uses do not pose risks to human health. Despite industry claims that 2,4-D has been used "safely" for years, the scientific database says otherwise. 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.[34] A study found that 2,4-D is indeed cytotoxic and induces apoptosis via direct effect on mitochondrial membranes.[35] Changes to maternal behavior in rats, along with increased catecholamine levels and a drastic decrease in indolamine levels have also been observed.[36] 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."[37] 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.[38] One study of agricultural workers found an increased risk of gastric cancer among those who worked in areas where 2,4-D was applied.[39] Others found that those exposed to 2,4-D had poor semen quality.[40,41] Higher rates of birth defects were also observed in farmers with long-time exposure to 2,4-D.[42]

Laboratory studies have observed the hormone effects of 2,4-D exposure, including estrogenic activity in various organisms exposed to 2,4-D,[43] decreases in the thyroid gland transport and production functions, and impairment of hormone iodination in the thyroid glands of laboratory rats.[44] A study investigating developmental toxicity in mice of a common commercial formulation of an 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.[45] Other studies have found that 2,4-D promotes the proliferation of androgen-sensitive cells by acting synergistically with its main

[34] 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.
[35] 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.
[36] 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.
[37] U.S. EPA. 2005. Reregistration Eligibility Decision for 2,4-*D*. Office of Prevention Pesticides and Toxic Substances. Washington DC.
[38] 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.
[39] Mills PK and Yang RC. 2007. Agricultural exposures and gastric cancer risk in Hispanic farm workers in California. Environ Res. 104(2):282-9.
[40] 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.
[41] 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.
[42] 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.
[43] 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.
[44] 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.
[45] 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.

metabolite, 2,4-dichlorophenol (DCP), also known for its endocrine disrupting effects. [46,47] This heightened androgen-sensitive cell population may be linked to the recent escalation of polycystic ovary syndrome in reproductively aged women[48] that results in reproductive impairment due to inability to ovulate and carry young to term.

The scientific literature confirms that farmers, farmworkers, and their families face extraordinary risks from pesticide exposures. Application and pesticide drift result in dermal, inhalation, and oral exposures that are typically underestimated. According to a study by Arcury et al.,[49] 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. The Centers for Disease Control's Fourth *National Report on Human Exposure to Environmental Chemicals,* which analyses pesticides residues in the U.S. population via the National Health and Nutrition Examination Survey *(*NHANES*),* notes that occupational exposure to 2,4-D *(*production plant workers and forestry workers) results in urinary levels several hundred to several thousand times higher than the 95th percentiles of the NHANES subsamples. In farm families, the average urinary levels of 2,4-D are highest in the farmers who applied 2,4-D; other family members had levels also ranging higher than the U.S average.[50] Others studies have also reported 2,4-D detections in a majority of samples including those of pregnant workers.[51,52] A 2004 study detected agricultural pesticides in the homes near to agricultural fields.[53]

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 the homes sampled in this study contains 2,4-D.[54] 2,4-D, detected in the semen of farmworkers in Canada, could be toxic to sperm cells and can be transported to the woman and developing embryo/fetus.[55] Phenoxyacetic acid herbicides, specifically 2,4-D, is associated with non-Hodgkin lymphoma (NHL) and a high incidence of NHL has been

[46] 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.
[47] 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.
[48] Mason, H, Colao, A, et al. 2008. Polycystic ovary syndrome (PCOS) trilogy: a translational and clinical review. Clinical Endocrinology, 69(6): 831–844.
[49] 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.
[50] Centers for Disease Control and Prevention (CDC). *Fourth National Report on Human Exposure to Environmental Chemicals. 2013 Update.* Available at URL:http://www.cdc.gov/exposurereport/
[51] 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.
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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.[56] 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.[57] Despite industry attempts to downplay these findings and claim that 2,4-D has low toxicity, farmers and farmworkers continue to bear the brunt of these exposures and chronic health effects. 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.[58]

CONCLUSION

2,4-D has a well-documented history of environmental contamination and adverse human health effects. Knowing this, U.S. agriculture should be moving away from 2,4-D, as we have with older, more toxic pesticides (organophosphates, organochlorines). The proposed expansion of 2,4-D uses cannot be done before all aggregate and cumulative risks have been analyzed. This includes dietary and human toxicity assessments. 2,4-D use of GE corn and soybeans is not a solution for the problems created by glyphosate-resistant weeds. There is no meaningful evidence to show that the 2,4-D choline salt poses less of a threat to the environment and human health than other forms. In lieu of this information, EPA must not move forward this expanding 2,4-D uses, and uphold its statutory mandate.

Respectfully,

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