

IN THE
UNITED STATES COURT OF APPEALS
FOR THE NINTH CIRCUIT

Natural Resources Defense Council,)	
Inc.)	
)	
Petitioner,)	
)	
v.)	Case No. 14-73353
)	
United States Environmental Protection)	
Agency,)	
)	
Respondent.)	

Center for Food Safety, et al.,)	
)	
Petitioners,)	
)	
v.)	Case No. 14-73359
)	
United States Environmental Protection)	
Agency, et al.,)	
)	
Respondents.)	

**DECLARATION OF DR. KRISTI PULLEN IN SUPPORT OF
PETITIONER NATURAL RESOURCES DEFENSE COUNCIL’S
MOTION FOR STAY PENDING REVIEW**

I, DR. KRISTI PULLEN, do hereby affirm and state:

1. This declaration is based on my personal knowledge, information, and belief.

2. I submit this declaration in support of Petitioner Natural Resources Defense Council (NRDC)'s motion for stay pending review of Respondent U.S. Environmental Protection Agency (EPA)'s decision to register the pesticide Enlist Duo.

3. NRDC is a not-for-profit environmental and public health advocacy organization.

4. I was hired by NRDC in January 2014 as a staff scientist in NRDC's health program. My primary role is to evaluate the potential health impacts of chemicals that people are exposed to through the food they eat, the air they breathe, the beverages they drink, and the products they use. More specifically, I read and evaluate scientific literature, analyze data from large datasets to understand chemical toxicity at the molecular level, and determine the potential impacts of various chemicals on human (and sometimes ecosystem) health. My work focuses primarily on how systems in the human body (for example, the endocrine system, immune system, or neurological system) can be changed by chemicals, including pesticides. My pesticide work at NRDC has centered on the evaluation of the pesticide 2,4-D, and the use of molecular, cellular, animal, and epidemiological data to determine its potential impacts to humans of various ages.

5. I have extensive undergraduate and graduate training in biochemistry and molecular biology, as well as postdoctoral training in public health. I received

a Bachelor of Science degree in biochemistry and molecular biology from the University of Maryland, Baltimore County in 2000. I was awarded a Ph.D. from the University of California, Berkeley in 2006. For my postdoctoral studies, I was a Robert Wood Johnson Foundation Health and Society Scholar at the Harvard School of Public Health, where I investigated the ways that threats outside of the human body can alter the functions within the body at the molecular level. I have had course work or training in biochemistry, molecular biology, computational biology, epidemiology, biostatistics, and population health.

6. I understand that on October 15, 2014, EPA registered the pesticide Enlist Duo under the Federal Insecticide, Fungicide, and Rodenticide Act. Enlist Duo contains the pesticide 2,4-D, a chemical that is used to kill weeds on agricultural and residential land. Living in areas with high use of 2,4-D and other similar herbicides is associated with higher risk of birth defects,¹ Type 2 diabetes,² and biomarkers associated with heart disease.³ Occupational exposure to 2,4-D in

¹ Dina M. Schreinemachers, *Birth Malformations and Other Adverse Perinatal Outcomes in Four U.S. Wheat-producing States*, 111 *Envtl. Health Persp.* 1259, 1259-64 (2003).

² D. M. Schreinemachers, *Mortality from Ischemic Heart Disease and Diabetes Mellitus (Type 2) in Four U.S. Wheat-producing States: A Hypothesis-generating Study*, 114 *Envtl. Health Persp.* 186-93 (2006).

³ Dina M. Schreinemachers, *Perturbation of Lipids and Glucose Metabolism Associated with Previous 2,4-D exposure: A Cross-sectional Study of NHANES III Data, 1988-1994*, 9 *Envtl. Health* 11 (2010).

male farm workers has been associated with decreased sperm counts and increases in spermatid abnormalities.⁴ Peer-reviewed studies also indicate that 2,4-D exposure can interfere with processes important for brain development,⁵ alter breast feeding ability,⁶ and disrupt various pieces of the endocrine system—especially through heightened impacts on the thyroid system.

7. Thyroid hormones play an essential role in the maintenance of body temperature, metabolism, cell differentiation, and fetal and postnatal brain development. The thyroid is particularly important in developing bodies, like those of fetuses, infants, and children. Suppression of thyroid hormones during development can damage the developing brain, resulting in developmental delays, lower IQ level, and behavioral issues. These impacts are permanent and irreversible. EPA’s own Science Advisory Board has noted in comments on another rulemaking that “[i]nterference with the thyroid and available thyroid

⁴ D. Lerda & R. Rizzi, *Study of Reproductive Function in Persons Occupationally Exposed to 2,4-Dichlorophenoxyacetic Acid (2,4-D)*, 262 *Mutation Res.* 47, 49 (1991); Shanna H. Swan et al., *Semen Quality in Relation to Biomarkers of Pesticide Exposure*, 111 *Envtl. Health Persp.* 1478, 1484 (2003).

⁵ Ricardo Duffard et al., *Central Nervous System Myelin Deficit in Rats Exposed to 2,4-Dichlorophenoxyacetic Acid Throughout Lactation*, 18 *Neurotoxicology & Teratology* 691, 691-96 (1996).

⁶ Nelson Stürtz et al., *Effect of 2,4-Dichlorophenoxyacetic Acid on Milk Transfer to the Litter and Prolactin Release in Lactating Rats*, 271 *Toxicology* 13, 13-20 (2010).

hormones is known to produce adverse effects on neurodevelopment in humans, with fetuses and infants being most vulnerable.”⁷ The Science Advisory Board additionally suggests that even small changes in thyroid hormone levels can be harmful to the developing brain of a fetus.⁸

8. Mounting scientific evidence demonstrates that 2,4-D can adversely impact the thyroid system. Epidemiological studies in humans have shown that farm workers exposed to 2,4-D are at increased risk of developing hypothyroidism, or underactive thyroid, compared to farm workers who were not exposed to 2,4-D.⁹ Studies in zebrafish, an important vertebrate animal model for studying developmental, reproductive, and neurological health impacts, provide further evidence that 2,4-D can decrease thyroid hormone levels.¹⁰ EPA itself has acknowledged that 2,4-D can impair thyroid functioning in rats and dogs.¹¹

⁷ U.S. EPA Science Advisory Board, SAB Advice on Approaches to Derive a Maximum Contaminant Level Goal for Perchlorate (May 29, 2013), at 2.

⁸ *See id.*

⁹ Whitney S. Goldner et al., *Hypothyroidism and Pesticide Use Among Male Private Pesticide Applicators in the Agricultural Health Study*, 55 J. Occupational Env'tl. Med. 1171, 1171-78 (2013).

¹⁰ Demetrio Raldúa & Patrick J. Babin, *Simple Rapid Zebrafish Larva Bioassay for Assessing the Potential of Chemical Pollutants and Drugs to Disrupt Thyroid Gland Function*, 43 Env'tl. Sci. &Tech. 6844, 6847-50 (2009).

¹¹ U.S. EPA, Human Health Risk Assessment for a Proposed Use of 2,4-D Choline on Herbicide-Tolerant Corn and Soybean (Aug. 8, 2013), at 13-14,

Scientists commonly use animal studies to identify the potential effects a chemical can have on humans. The toxic effects observed in animals and adult farmworkers exposed to 2,4-D show that 2,4-D exposure poses a risk of adversely impacting the thyroid function of humans— including fetuses, infants, and children— exposed to Enlist Duo.

9. EPA has not yet released the administrative record on which it based its decision to register Enlist Duo. Based on the agency documents that are available, including EPA's proposed and final registration decisions, EPA's analysis of Enlist Duo is flawed. It fails to account fully for the adverse impacts of 2,4-D on the thyroid, refuses to build in a statutorily required safety factor, and may underestimate the extent to which humans will be exposed to 2,4-D through the use of Enlist Duo. When EPA releases the full administrative record, I may revise some of these critiques, and may also uncover new ones.

10. First, EPA erred by overestimating the highest dose of 2,4-D to which an organism can be exposed without suffering adverse effects (the so-called no observed adverse effect level, or NOAEL), based on a mischaracterization of a key scientific study measuring the impacts of a chemical across generations (also known as an Extended One Generation Reproductive Toxicity Study). The study, which measured 2,4-D's effects on mother rats and their pups, showed that

available at <http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPP-2014-0195-0007> [hereinafter EPA Human Health Risk Assessment].

mothers and pups exhibited both decreased levels of thyroid hormone and increased levels of thyroid stimulating hormone after the pregnant mothers were exposed to 2,4-D. Both of those changes are signs of adverse impacts to the thyroid. Pups were also found to be more sensitive to the impacts of 2,4-D than mothers— they exhibited changes in thyroid hormone production at even lower doses.¹² However, EPA assumed that effects associated with the lower doses were not “adverse” but merely “adaptive” and accordingly set the NOAEL for 2,4-D exposure above the dose at which those changes occurred.¹³ In so doing, EPA ignored the possibility that the toxic effects of 2,4-D could have a non-linear (or, “non-monotonic”) relationship with the dose received— in other words, EPA ignored that peaks of chemical toxicity can occur at any dose, or multiple doses, within a living body, including at relatively low exposure levels. Current scientific understanding of hormone disrupting chemicals does not support EPA’s assumption. In fact, in its *Review of the Environmental Protection Agency’s State-of-the-Science Evaluation of Nonmonotonic Dose-Response Relationships as they*

¹² See Comments of the Natural Resources Defense Council on Dow Agrosciences’ Application to Register Enlist Duo Herbicide Containing the Choline Salt of 2,4-D and Glyphosate (June 30, 2014), at 22-25 (attached as Ex. D to Colangelo Decl.) [hereinafter NRDC Comments].

¹³ U.S. EPA, Response to Comments Regarding Registration of Enlist Duo (Oct. 14, 2014), at 3 (attached as Ex. E to Colangelo Decl.) [hereinafter EPA Response to Comments].

Apply to Endocrine Disruptors, the National Research Council of the National Academies of Sciences, a body dedicated to providing independent, authoritative, and expert scientific advice to decision-makers, warned that EPA should use caution when assuming that alterations are “adaptive” rather than “adverse,” noting that “effects that are adaptive in some people are adverse in others.”¹⁴ The National Research Council additionally noted that, “consideration should be given to potential windows of susceptibility (for example, during fetal development), sensitive populations (for example, those with pre-existing health conditions), and other factors (such as multiple chemical exposures) in making these [adaptive versus adverse] distinctions.”¹⁵ EPA did not adequately consider the factors urged by the National Research Council in setting the NOAEL in this case. As a result, one of the benchmarks it used to determine the safety of Enlist Duo was insufficiently protective of human health.

11. Second, EPA erred in not incorporating an important safety factor, or margin of error, into its analysis of whether Enlist Duo would expose humans to unsafe levels of 2,4-D. EPA is required under the Food Quality Protection Act to

¹⁴ National Research Council of the National Academies, *Review of the Environmental Protection Agency’s State-of-the-Science Evaluation of Nonmonotonic Dose-Response Relationships as They Apply to Endocrine Disruptors* (2004), at 8.

¹⁵ *Id.*

use an additional tenfold safety factor when evaluating pesticides, to ensure that the health of infants and children is adequately protected from harm. Despite evidence that developing bodies are more susceptible to the adverse effects of 2,4-D than adults (as shown by the animal study described above), and despite evidence that disruption of the thyroid system can cause irreversible damage to the developing brain, EPA did not use the required tenfold safety factor when it analyzed whether the 2,4-D in Enlist Duo will adversely affect humans. EPA's own analysis shows that, if it had treated the dose of 2,4-D that produced thyroid effects in rat pups in the study described above as the NOAEL, and had applied the tenfold safety factor, the agency would have been forced to conclude that Enlist Duo was unsafe.¹⁶

12. EPA also appears to have underestimated the exposure of fetuses, infants, and children to 2,4-D in a variety of ways— meaning that these vulnerable populations may be at even greater risk than the agency has acknowledged. For example, infants and children may be exposed to 2,4-D through breast milk. Indeed, EPA acknowledged in its human health risk assessment for 2,4-D that pregnant rats can transfer 2,4-D to offspring through maternal milk, suggesting that

¹⁶ See EPA Response to Comments at 8. Though the agency's comments state that the risks for all age groups are acceptable even assuming the lower NOAEL and incorporating the tenfold safety factor, this statement is based on a miscalculation. The safety factor and lower NOAEL would result in exposures 550% higher than the level of concern for risk assessment in children ages one to two.

breast milk could be a significant contributor to dietary 2,4-D exposure in human infants, as well. However, to estimate how much 2,4-D people ingest through their diets, EPA relied heavily on a dataset that focuses on the dietary intake of populations two-years-old and above— above the age of breastfeeding infants. It is thus not clear what infant exposure to 2,4-D through breast milk is, and likewise not clear whether EPA's analysis sufficiently accounts for that exposure. It is precisely this type of missing exposure information that the FQPA safety factor is required to account for.

13. In addition to dietary exposures, vulnerable populations can be exposed to 2,4-D via spray drift, which occurs when small particles of a pesticide are carried by the wind to areas far away from the application site. When pesticide particles move away from the original area of application, infants and children can inhale the chemical, or ingest it through the food they eat or by placing hands contaminated with 2,4-D directly into their mouths. EPA underweighted the chance of exposure via spray drift, because it assumed users of Enlist Duo would follow label instructions when applying the pesticide to fields, thereby minimizing spray drift.¹⁷ However, 2,4-D has been found to reach locations distant from its

¹⁷ EPA Human Health Risk Assessment at 35.

application site, including homes.¹⁸ This suggests that either the label instructions on which EPA relies are inadequate to prevent exposure through spray drift, or that people frequently fail to follow those instructions correctly. Thus, infants and children could inhale or ingest more 2,4-D due to spray drift than EPA's analysis of Enlist Duo assumes.

14. For all the foregoing reasons, EPA's conclusion that the 2,4-D in Enlist Duo is safe for sale is critically flawed. Taken together, the increased susceptibility of developing bodies, along with data gaps in important routes of exposure, require the maintenance of the tenfold safety factor. If Enlist Duo nonetheless goes on the market, people— especially fetuses, infants, and children— may be exposed to unsafe levels of 2,4-D. Overexposure to 2,4-D could result in changes to both the maternal and infant thyroid system. Even small changes in the delicately balanced thyroid system can result in serious, irreparable harm to the developing brain and body, making adequate consideration of thyroid toxicity prior to a pesticide entering the market absolutely critical.

¹⁸ NRDC Comments at 30-31; *see also* Marsha K. Morgan et al., *Adult and Children's Exposure to 2,4-D from Multiple Sources and Pathways*, 18 J. Exposure Sci. & Env'tl. Epidemiology 486, 486-94 (2008); M. G. Nishioka et al., *Distribution of 2,4-D in Air and on Surfaces Inside Residences After Lawn Applications: Comparing Exposure Estimates from Various Media for Young Children*, 109 Env'tl. Health Persp. 1185, 1185-91 (2001).

I declare under penalty of perjury that the foregoing is true and correct.

Executed this 18 of December, 2014 in Washington, D.C.



Dr. Kristi Pullen