Appendix A

Center for Food Safety Comments
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2,4-D: New Use on Herbicide-Tolerant Corn and Soybean
Environmental Protection Agency, Mailcode 28221T
1200 Pennsylvania Ave., NW
Washington, D.C. 20460

Docket No. EPA-HQ-OPP-2014-0195

June 30, 2014

Comments to EPA on EPA's Proposed Registration of Enlist Duo™ Herbicide Containing 2,4-D and Glyphosate for New Uses on Herbicide-Tolerant Corn and Soybean

Part I: Altered use pattern, human health issues, economic and environmental costs
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Introduction

Center for Food Safety (CFS) appreciates the opportunity to comment on the EPA's proposed registration of Enlist Duo herbicide for use on Dow AgroSciences Enlist corn and soybeans.

CFS is the leading public interest organization on the science, regulation and impacts of genetically engineered (GE) crops. We have considerable scientific and legal expertise on the subject of GE herbicide-resistant crops. CFS has engaged the USDA in its review of Enlist corn and soybeans and the EPA in its review of Enlist Duo herbicide. In 2012, we authored an open letter to USDA Secretary Tom Vilsack and then EPA Administrator Lisa Jackson outlining the risks posed by Enlist crop systems that was co-signed by 153 other public interest organizations (CFS et al 2012). On June 22, 2012, CFS submitted extensive comments to EPA[1] on Dow's proposed registration of Enlist Duo herbicide for use on Enlist crops (CFS Enlist Duo 2012). In these comments, we assessed risks, explained EPA's statutory obligations, identified key data gaps and needs for further study, and made recommendations with regard to potential mitigation measures. Submission of these comments was

[1] 80 pages single spaced, with 177 references to scientific studies and other documents.

followed in the summer of 2012 by a meeting between CFS staff and Jim Jones and Stephen Bradbury to underscore our concerns and recommendations.

Despite these good faith efforts, the proposed registration and its supporting documents show no sign that EPA has given any consideration to the harms, data collection needs, or mitigation recommendations spelled out in CFS's comments. In most cases, EPA fails to mention, much less address, these serious issues.

Because EPA has ignored our prior input, we here make frequent reference to our previous comments to avoid repetition. We also call EPA's attention to new information that has come to light over the past two years. All scientific studies and other cited materials – both in these comments and in those of prior comments – are being submitted as supporting materials. CFS calls upon EPA to take the public input process seriously this time, confront the scientific issues raised in these and prior comments, and to make the decision demanded of it by federal law – rejection of the proposed registration. Alternately, as CFS has requested before, EPA should formally postpone any decision until it has completed the recently begun registration review of 2,4-D, which would allow for more thorough consideration of recent science on 2,4-D health harms and other matters that EPA has chosen to ignore in the Enlist Duo registration process.

Executive Summary

American agriculture stands at a crossroads. One path leads to more intensive use of old and toxic pesticides, increased rates of cancer and other diseases, environmental harms, more crop damage from herbicide drift, increasingly intractable weeds, and sharply rising farmer production costs. This is the path American agriculture will take with EPA approval of the proposed registration of Enlist Duo and USDA deregulation of Enlist crops. Another path is possible, but embarking upon it will take enlightened leadership from EPA.

Agricultural biotechnology firms have long promised less dependence on toxic pesticides. Instead, hundreds of millions of dollars are being invested to engineer crops for resistance to multiple herbicides (Kilman 2010). Herbicides represent two-thirds of overall pesticide use in American agriculture (EPA 2011), and two-thirds of genetically engineered (GE) crops pending deregulation by USDA are herbicide-resistant, including Monsanto's dicamba-resistant soybeans and cotton.[2] Dow officer John Jachetta welcomes these new crops as inaugurating "a new era" and "a very significant opportunity" for chemical companies (as quoted in Kilman 2010). As pesticide regulator, EPA determines whether, and if so how, herbicides can be applied to these "next-generation" GE herbicide-resistant crops, including the application of Enlist Duo to Dow's Enlist corn and soybeans, the subject of these comments.

EPA's assessment documents and the proposed registration reveal blindness to and in some cases willful ignorance of the real world facts and impacts of approval. For instance, nowhere in its assessment does EPA even mention, much less discuss, the three- to seven-fold increase in agricultural 2,4-D use projected by Dow and USDA if both crop and herbicide components of the Enlist crop system are approved. This fundamental assessment failure vitiates much of EPA's evaluation of Enlist Duo. With regard to overall herbicide use, our nation's pesticide regulator can say nothing more definite than that it will "change," making no reference to credible data and studies projecting that total herbicide use would increase dramatically along with 2,4-D.

While the herbicide product being considered for approval is a mixture of the active ingredients 2,4-D choline salt and glyphosate, as well as various additional inert ingredients, EPA in most cases assesses data only for 2,4-D. The combination of two potent herbicides may lead to synergistic adverse impacts on human health or the environment that are not caused by either one alone. In addition, most testing reviewed by EPA was not conducted on the formulation that farmers will actually use, which has additional, undisclosed inert ingredients that can be toxic in their own right or increase the toxicity of the active ingredients.

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[2] Petitions for Determination of Nonregulated Status, USDA APHIS, see top two tables at http://www.aphis.usda.gov/biotechnology/petitions_table_pending.shtml, last visited June 30, 2014.

In assessing human health impacts, EPA ignores the medical literature linking exposure to 2,4-D and herbicides of its class with the immune system cancer non-Hodgkin's lymphoma, as well as Parkinson's disease, among other health harms. We discuss a recent authoritative study that reaffirms the cancer connetction. EPA also ignores concrete instances of human harm reported to the Agency. Rather than conduct an integrated assessment that considers all of the data, including the most relevant studies and reports of human health effects, EPA relies entirely on flawed animal experiments conducted by Dow. In addition, EPA entirely ignores recent studies showing likely new health harms from 2,4-D that the Agency itself discusses in the context of the 2,4-D registration review process.

EPA's assessment of the potential for Enlist Duo to drift, causing damage to neighboring and distant crops, is an entirely model-based exercise that once again ignores the real world facts of the matter – namely, authoritative surveys by state pesticide control officers showing that even at current modest usage levels, 2,4-D and glyphosate are consistently the top culprits in drift-related crop injury, and scientific literature showing that 2,4-D is ubiquitous in air and rain. EPA's proposed mitigation measures – such as prohibitions against application under certain weather conditions – are vague, too open to loose interpretation, and will almost certainly fail on the ground, exposing growers of sensitive crops like vegetables, cotton, grapes and many other to substantial risk of devastating crop injury.

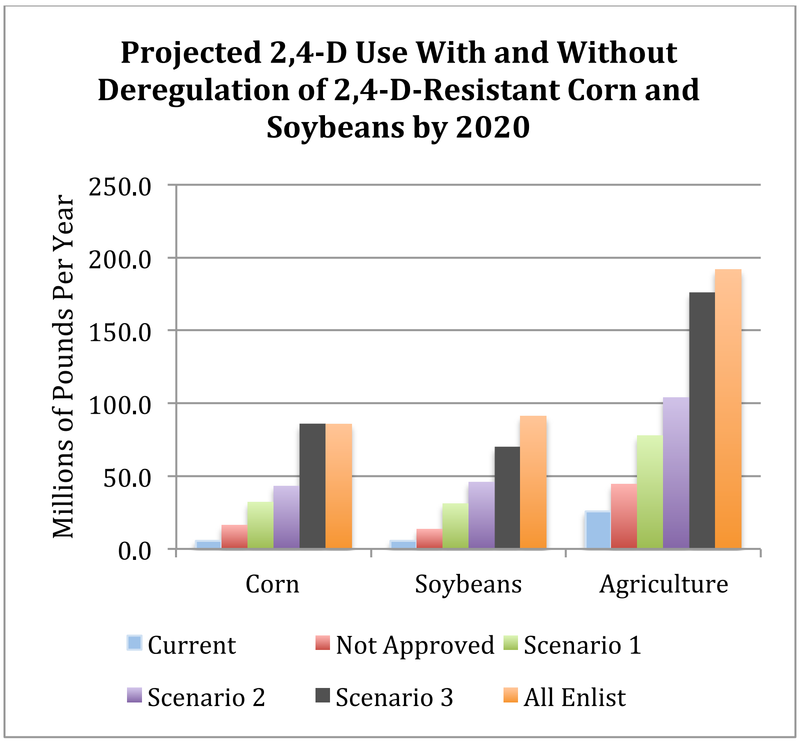
USDA and weed scientists agree that the Enlist crop system under the proposed registration would rapidly generate 2,4-D–resistance in weeds, often in weeds already resistant to other herbicides. Such multiple herbicide-resistant weeds will cost more for farmers to control, and will impose environmental costs in terms of the increasing number and quantity of herbicides deployed, and soil-eroding tillage operations carried out, to control them. EPA's weak attempt to assess this issue is un- and misinformed, revealing misconceptions about the nature and impacts of herbicide-resistant crops and weeds, perhaps because EPA's entire "benefits" discussion is based on a flawed and biased Dow submission. Here too, mitigation measures are inadequate and likely to fail. There are no mandatory requirements to prevent weeds from evolving resistance to 2,4-D, but rather only a monitoring program intended to detect resistant weeds once they have emerged. And EPA's delegation of nearly all responsibilities for implement the plan to Dow represents a clear conflict of interest. Dow's financial interests lie in ***not*** finding resistance.

In addition, public participation in the registration process has been greatly hindered by EPA's failure to make numerous key assessment documents and interagency memos available to the public in the docket, notably "confidential memos" on the dioxin content of 2,4-D, but many others as well.

CFS once again calls on EPA to deny the requested registration of Enlist Duo. This decision would be consistent with federal law, and also protect human health, the environment and the true interests of farmers and American agriculture as a whole. At the very least, EPA should postpone any decision until it has had the opportunity to conduct a comprehensive review of the proposed registration in the context of the ongoing 2,4-D registration review process.

1. EPA ignores the increased use and altered use pattern of 2,4-D that would result from approval of the proposed registration

EPA has completely failed to assess the sharply increased use of 2,4-D that would result from approval of the proposed registration. Dow AgroSciences and USDA have projected that annual agricultural use of 2,4-D would rise from a current level of 25.6 million lbs. to anywhere from 77.8 to 176 million lbs. by 2020 with approval of Enlist Duo on Enlist corn and soybeans (the Enlist system), depending on the extent to which farmers adopt Enlist crops (USDA EIS 2013, p. 134, see bar chart below).



Source: CFS Corn-Soy EIS Science I (2014), p. 10, based on projections made by Dow and adopted by USDA in its Environmental Impact Statement on on Enlist crops. Scenarios 1, 2 and 3 are based on progressively higher estimates of acreage planted to Enlist corn and soybeans by 2020.

Enlist Duo contains both glyphosate and 2,4-D. Glyphosate comprises a large majority (82%) of the herbicide active ingredient applied to soybeans today (USDA NASS 2013), and is the most heavily used herbicide on corn (USDA NASS 2011). Dow projects usage rates of Enlist Duo on Enlist crops that would maintain, largely unchanged, the amount of glyphosate currently applied to U.S. corn and soybeans (CFS 2,4-D Corn-Soy Science I 2014). Thus, 2,4-D applied as a component of Enlist Duo would not displace glyphosate, resulting in a large increase in overall herbicide use on corn and soybeans.

EPA provides no quantitative assessment of the huge increase in both 2,4-D and overall herbicide use that would result from approval of Enlist Duo and Enlist crops. "The total loading of herbicides has not been evaluated by the Agency" (EPA Benefits 2014, p. 9). EPA only concedes that herbicide use will "change," in a 4-sentence section of its "benefits" assessment incorrectly entitled "Reducing pesticide environmental loading" (Ibid, p. 9). In this 4-sentence "assessment," EPA does not cite a single figure on current or projected future use of 2,4-D, glyphosate, or for that matter any corn or soybean herbicide.

EPA's failure to recognize that Enlist Duo and Enlist crop approval would dramatically increase (not reduce) "pesticide environmental loading" is based entirely on completely uninformed wishful thinking, the notion that: "any increase in 2,4-D may offset some other herbicides that are currently used for these crops" (EPA Benefits 2014, p. 3). However, the authors do not name or assess a single herbicide that might be displaced by Enlist Duo; or to what extent such displacement might occur.

An informed assessment shows that one can expect very little displacement. The key factor here is that Enlist Duo is intended to be used as glyphosate is used today – post-emergence, that is, sprayed on the growing crop to kill later-emerging weeds, as EPA acknowledges (EPA Benefits, pp. 3-4). If post-emergence use were not intended, there would be no point to developing Enlist crops, which are engineered to enable precisely this use.

Enlist Duo would be little used pre-emergence,[3] and thus would displace little if any pre-emergence herbicide use. The reason is that farmers prefer herbicides that have "residual activity" (i.e. persist in the soil to kill weeds that sprout in the weeks after application) for pre-emergence applications. Glyphosate has no residual activity, while 2,4-D has very little.

In the case of soybeans, non-glyphosate herbicides comprise only 18% of total herbicide use by weight, and roughly half of this amount is comprised of herbicides identified by weed scientists as pre-emergence herbicides: flumioxazin, metolachlor, metribuzin, pendimethalin, S-metolachlor, sulfentrazone and trifluralin (Penn State 2014a, USDA NASS 2013). Thus there is very little non-glyphosate herbicide applied post-emergence that could be displaced by Enlist Duo.

In corn, pre-emergence herbicides such as atrazine, acetochlor, alachlor, pendimethalin, metolachlor and S-metolachlor continue to be popular, comprising over half of corn herbicide use (USDA NASS 2011). Glyphosate comprises a large majority of post-emergence corn herbicide use by weight. Thus, here too, one can expect little displacement of non-glyphosate herbicides by Enlist Duo. This is confirmed by the fact that from 2002 to 2010, the percent of corn acres treated with atrazine, acetochlor, metolachlor and S-metolachlor remained constant, despite the

[3] Application before the crop is planted, or after planting but before the crop seed sprouts.

enormous increase in corn acres treated post-emergence with glyphosate (9% in 2002, rising to 76% in 2010) as a result of increasing Roundup Ready corn adoption (USDA NASS 2003, USDA NASS 2011). This shows quite clearly that glyphosate complements, rather than displaces, other major corn herbicides that are used primarily pre-emergence.

Enlist soybeans are also resistant to a third herbicide, glufosinate, while Enlist corn is resistant to the class of "fops" grass herbicides, such as quizalofop. Use of these herbicides would also increase with approval of the Enlist Weed Control System, but to a lesser extent than 2,4-D. For a fuller discussion of the herbicide use impacts of approval, see CFS Corn-Soy EIS Science I (2014), pp. 9-18.

In short, approval of Enlist Duo and Enlist crops would lead to sharply increased 2,4-D use on corn and soybeans; continued heavy use of glyphosate at current levels; very little displacement of the non-glyphosate herbicides currently applied to corn and soybeans; additional use of glufosinate on soybeans and quizalofop on corn; and thus a substantial ***increase*** in overall "pesticide environmental loading."

EPA's failure to assess the increased 2,4-D and overall herbicide use enabled by the registration vitiates much of its analysis, as discussed below. One further point is important to consider. EPA recently began its registration review of 2,4-D. In comments to the Agency, CFS also urged EPA to consider the increased use of 2,4-D and total herbicides that would result from registration of Enlist Duo in the context of this parallel review process (CFS Reg Review 2013), which EPA anticipates will not be completed until 2017 (EPA Reg Review Work Plan 2012). Two EPA divisions responded that they are not doing so, at least at the present time (EPA Reg Review BEAD 2013; EPA Reg Review HED 2013). Thus, it appears that the Agency is willfully turning a blind eye to the most fundamental and important aspect of the proposed registration – vastly increased use of, and human and environmental exposure to, 2,4-D.

CFS has also found more generally that EPA's assessment of Enlist Duo is being conducted with no regard to important new scientific information – particularly in the area of human health harms – that is being given preliminary consideration in the context of 2,4-D registration review. This might be defensible if the new use under consideration here would enable only a minor increase in use of 2,4-D. However, it is completely indefensible in light of the enormous increase in exposure to 2,4-D that approval of Enlist Duo will enable.

2. Human health impacts of the proposed registration

This assessment failure is particularly concerning in the area of human health. Approval of Enlist Duo would mean many-fold more farmers will be using 2,4-D; they would be handling and applying it at substantially higher rates; and making more applications per season; than in the past. This all adds up to substantially broader and more intensive occupational exposure. Much more 2,4-D will also be released into the environment, exposing all of us to greater amounts of this herbicide in air, rainfall, water and as residues in food. These factors make it all the more necessary to conduct a thorough and comprehensive human health risk assessment.

2.1 EPA continues to ignore human epidemiology and "human incidents"

Much of the compelling evidence for human health harms of 2,4-D comes from human epidemiology studies and what EPA calls "human incidents" – reports of adverse health effects by exposed human beings. In our 2012 comments to EPA, CFS discussed studies linking 2,4-D exposure to non-Hodgkin's lymphoma (NHL), an often-fatal immune system cancer whose incidence has doubled since the 1970s; and Parkinson's disease (PD), an incurable, debilitating, degenerative nervous system disorder that afflicts an estimated 1 million Americans. Both diseases are more prevalent in farmers than the general population. CFS also critiqued EPA's dismissive attitude to epidemiological evidence in general, in favor of an approach that relies entirely on animal experiments and ideal-world human exposure estimates (CFS Enlist Duo 2012). We will not repeat that discussion here.

Neither the human health nor the occupational and residential exposure assessment addressed either NHL or PD, and neither document cited any human epidemiology study or any human incident report (EPA Human Health 2013, EPA Occupational 2013). Elsewhere, EPA stated only that: 1) It stands by its past contention that 2,4-D is not linked to cancer; 2) It would defer further consideration of cancer and PD epidemiology to the 2,4-D registration review process; and 3) It is presently "involved in many efforts to refine its risk assessment policies including ***establishing better methods for considering epidemiological research in the regulatory process***…" (EPA Registration 2014, p. 21-22, emphasis added).

CFS is encouraged to learn that EPA recognizes its approach to epidemiology is deficient, and that better methods are needed. However, it appears that little progress has been made on this front. In EPA Reg Review HED (2013), EPA's Health Effects Division points to a 2010 PowerPoint presentation that describes these efforts (Lowit 2010). This four-year old presentation outlines EPA's current animal experiment-based approach to assessing pesticides; but despite its title, it provides no framework for integrating human epidemiology or incident reports, merely raising questions about how they might be integrated at some point in the future. This was four years ago. As noted above, the relevant Enlist Duo assessments lack any reference to epidemiology or human incidents.

2.1.1 Epidemiology and cancer

EPA's position on 2,4-D and cancer is unsupportable, in clear contradiction to the views of the medical community (Arguello et al 2012), including scientists with our own National Institutes of Health, the National Academy of Sciences' Institute of Medicine, and international cancer researchers (reviewed in CFS Enlist Duo 2012). A recently published study further undermines EPA's denial of the strong epidemiological evidence linking 2,4-D and chlorophenoxy herbicide exposure to cancer.

Two scientists with the authoritative International Agency for Research on Cancer (IARC) just published an exhaustive meta-analysis of the last 30 years of epidemiology studies on non-Hodgkin's lymphoma and occupational exposure to agricultural pesticides (Schinasi and Leon 2014). They concluded, contrary to EPA, that phenoxy herbicides are "positively associated with NHL." The analysis further found that "diffuse B-cell lymphoma [a specific form of NHL] was positively associated with phenoxy herbicide exposure." 2,4-D is by far the most heavily and widely used of the phenoxy herbicide group. The meta-analysis found that 2,4-D exposure in particular was associated with a 40% greater risk of NHL, based on six studies, equivalent to the 40% increased risk from exposure to phenoxy herbicides as a group, based on 12 epidemiology studies (Ibid, abstract and Table 5).[4]

As CFS advised EPA in our comments, IARC's official position is that there is in fact evidence of a link between chlorophenoxy herbicides[5] and multiple cancers:

"It should be noted that EPA's classification of 2,4-D as a Category D chemical ("not classifiable as to human carcinogenicity") is out of line with assessments by other authoritative bodies that take epidemiology more seriously, not to mention those by leading epidemiologists at our National Institutes of Health. For instance, the governments of Norway, Sweden and Denmark have banned 2,4-D use (Boyd 2006), together with 2,4,5-T, largely on the basis of the epidemiological associations to non-Hodgkin's lymphoma and related cancers. The World Health Organization's International Agency for Research on Cancer (IARC) classifies the chlorophenoxy herbicide group, of which 2,4-D is by far the most widely used member, as "possibly carcinogenic to humans" (IARC 1987). WHO's IARC finds "limited evidence in humans" for chlorophenoxy herbicides as causative agents for multiple cancers (i.e. "multiple sites") (IARC 2012). EPA incorrectly states that IARC has not assessed chlorophenoxy herbicides for carcinogenicity (EPA 2007)." (CFS Enlist Duo 2012).

EPA is urged to correct the erroneous statement in EPA (2007), which is contradicted by IARC (1987) and IARC (2012).

2.1.2 Neurotoxicity: Parkinson's disease

CFS discussed a single high-quality study linking 2,4-D exposure to a 159% (2 ½ -fold) increased risk of PD in our prior comments (CFS Enlist Duo 2012, p. 59, citing Tanner et al (2009)). We have since found several additional epidemiological studies that link chlorophenoxy herbicides to PD, which are cited and discussed by

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[4] The study presents the 40% increased risk in standard epidemiological format as an "odds ratio" of 1.4. An odds ratio (OR) of 1 indicates no increased risk; an OR of 2 = 100% greater risk, etc., relative to an unexposed cohort.

[5] "Chlorophenoxy" is an alternative designation for "phenoxy," calling attention to the fact that herbicides of this class contain chlorine.

the Institute of Medicine. Committees of the Institute of Medicine of the National Academy of Sciences conduct exhaustive biennial reviews of the medical literature to ascertain associations between exposure to Agent Orange compounds[6] and disease in Vietnam veterans. In the last three reviews, the committees have found limited or suggestive evidence of an association with PD, largely on the basis of epidemiology studies showing increased risk of PD in those exposed to herbicides in general, and chlorophenoxy herbicides and 2,4-D in particular (IOM 2010, 2012, 2014). PD is a neurodegenerative disease. Below we discuss further evidence of 2,4-D's neurotoxic effects. The studies referred to in the following discussion are cited and discussed in CFS Registration Review (2013).

<u>2.1.3 Neurotoxicity: increased risk of fatal injuries</u>

Waggoner et al (2013) assessed pesticide use and fatal injury among farmers in the Agricultural Heath Study. Of the 49 pesticides investigated, the authors found strong evidence of an association with risk of fatal injury for only two herbicides: 2,4-D and cyanazine.[7] The authors found their results to be "unexpected," because "[t]ypically, insecticides rather than herbicides are associated with neurotoxicity… and neurotoxicity might predispose to higher rates of fatal injury."

However, examination of the common side effects of chlorophenoxy herbicide exposure may help to explain their results. Bradberry et al (2000) found that over 7,976 chlorophenoxy herbicide incidents were reported to poison control centers in the U.S. from 1996 to 1998, an average of over 2,600 per year. 2,4-D is by far the most heavily used chlorophenoxy herbicide in American agriculture. According to Bradberry et al (2000), chlorophenoxys have a broad range of adverse effects, many of them neurological and neuromuscular in nature. These include ataxia (loss of the ability to coordinate muscular movement), myopathic symptoms including limb muscle weakness, loss of tendon reflexes, and myotonia (tonic spasm or temporary rigidity of one or more muscles). Most effects were from ingestion of chlorophenoxys. But substantial dermal exposure to 2,4-D in particular has led to progressive mixed sensorimotor peripheral neuropathy; and peripheral neuromuscular symptoms have occurred after occupational inhalation exposure. As reported in Cox (2006), EPA has previously reported 2,4-D poisoning incidents as involving effects such as dizziness, headaches, and eye irritation. Neurological and neuromuscular symptoms of this sort may help explain the increased risk of fatal injury with exposure to 2,4-D in the dangerous business of farming, as found by Waggoner et al (2013).

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[6] The IOM considers studies that involve one or more components of Agent Orange – 2,4,5-T, 2,4-D and dioxins – which it calls "chemicals of concern" – as well as several other non-Agent Orange defoliants used in Vietnam.

[7] Cyanazine, once a heavily used herbicide, has been withdrawn from the market because after many years of use it was belatedly found to be a probable human carcinogen.

2.1.4 Neurotoxicity: 2,4-D-related human health incident reports

EPA compiles reports of adverse health effects from exposure to pesticides, including 2,4-D (discussed further below). In the 5.5 years from 2007 to mid-2012, EPA recorded 2,202 low severity incidents, which it regarded as a high number relative to other pesticides and thus meriting further evaluation (EPA Reg Review Human Incidents 2012, p. 3). Given the discussion above, many of these incidents likely involved neuromuscular symptoms that might help explain the increased risk of fatal injuries. Even "low severity" symptoms such as dizziness, that resolve quickly, could predispose to injuries.

EPA registered 459 more serious 2,4-D-related incidents over the same 5.5-year period. Six incidents issued in death. In the one incident described by EPA, "a 41 year old male sprayed diluted product earlier in the day. Later that day he experienced confusion, dizziness, conductive disturbance, and hypoglycemic shock. He was taken to the ER" (EPA Reg Review Human Incidents 2012, Table 1, p. 7). Confusion or dizziness is consistent with some of the chlorophenoxy herbicide effects noted above, and could be related to increased incidence of fatal injuries, for instance in operation of farm machinery. These data are discussed further below.

2.1.5 Neurotoxicity: animal experiments

EPA's limited assessment of 2,4-D's neurotoxicity for the proposed registration entirely ignores the human evidence discussed above: Parkinson's disease, increased risk of fatal injury, and numerous incidents involving neurological symptoms and neuromuscular deficits. Instead, EPA focuses narrowly on a handful of rat and rabbit experiments (EPA Human Health 2013, pp. 12-15). Interestingly, these experiments found neurological effects (e.g. gait abnormalities, discoordination, ataxia, loss of righting reflex) quite similar in nature to those experienced by human beings exposed to 2,4-D. However, these experiments were conducted by the registrant, and are used by EPA solely to establish a putative safe level of exposure rather than explore mechanism of action.

2.1.6 Neurotoxicity: potential mechanisms

2,4-D is neurotoxic, as shown both in in laboratory animals and more importantly in exposed human beings. The biological mechanisms by which 2,4-D and other chlorophenoxys cause these neurotoxic effects have not been fully elucidated, but may involve damage to cell membranes and membrane transport mechanisms, generation of free radicals, disruption of acetyl-CoA metabolism, and/or inhibition of microtubule assembly, among other proposed mechanisms (Bjorling-Poulsen et al 2008, Bradberry et al 2000). EPA fails to discuss any biological mechanism for 2,4-D's neurotoxicity (EPA Human Health 2013, EPA Occupational 2013).

2.1.7 Neurotoxicity: assessment failure

Rather than consider multiple lines of evidence – epidemiology, human incidents, animal experiments and biological mechanisms – in an integrated manner to assess the neurotoxicity of 2,4-D, EPA relies narrowly on registrant-conducted animal experiments whose sole purpose is to establish a putative safe level of exposure.

The result is an entirely inadequate assessment that merely serves to justify the proposed registration. A similar critique could be made of EPA's assessment of the other human health endpoints, such as developmental and reproductive toxicity, immunotoxicity, and organ toxicity, among others.

2.2 Exposure to 2,4-D in combination with glyphosate, other pesticides and inerts

2.2.1 Exposure to 2,4-D and glyphosate may increase risk of rhinitis and asthma
EPA approval of Enlist Duo would mean not only an enormous increase in exposure to 2,4-D, but also simultaneous exposure to glyphosate. Yet EPA's human health assessments focus solely on 2,4-D rather than the mixture. "Since no new use pattern and no new exposures for glyphosate are being considered with this registration action, no new assessment is needed for glyphosate" (EPA Registration 2014, p. 1). The point is not to do new assessments of glyphosate and 2,4-D, separately, but to assess the Enlist Duo formulation, the product that will be actually be used, because it is well known that multiple chemicals can act additively or synergistically to cause harm that is not caused (or only to a lesser degree) by either one alone. EPA's risk assessment process ignores such interactions, except in exceptional cases when Agency has determined that pesticides share a common mechanism of action.

Exposure to both 2,4-D and glyphosate in Enlist Duo may well lead to increased rates of occupational asthma in farmers and other exposed populations. Slager et al (2009) reviewed data from the Agricultural Health Study to investigate associations between exposure of commercial pesticide applicators to 34 pesticides and rhinitis. Significant positive associations were found for just five of the 34 pesticides. Exposure to both 2,4-D and glyphosate over the past year was associated with an over 40% greater risk of rhinitis (odds ratio 1.42), while exposure to either herbicide alone was not, suggesting the possibility that a "synergistic effect occurs in the upper airway with use of glyphosate and 2,4-D," though it remains to be determined whether this is in fact the case (Slager et al 2009).

Rhinitis is defined as "an inflammation of the lining of the nose, characterized by one or more of the following symptoms: nasal congestion, rhinorrhea, sneezing, and itching" (Moscato et al 2009). Some scientists regard rhinitis and asthma as different manifestations of the same underlying disease, affecting the upper and lower respiratory tract, respectively:

"Increasing scientific evidence shows that among the general population asthma and rhinitis might be a unique disease with manifestations in different sites of the respiratory system [2,5,7]. The 'united airway disease' model describes such a relationship as two clinical manifestations of a single disorder" (Moscato et al 2009).

Occupational rhinitis (OR) is thought to be 2-4 times more prevalent than occupational asthma (OA); symptoms of OR are often reported to develop before those of OA; and most who suffer from OA also exhibit symptoms of OR (Moscato et al 2009) – evidence consistent with the hypothesis that occupational rhinitis is a predisposing factor in contracting occupational asthma. Finally, a relatively high proportion of farmers with OR are also asthmatic:

"The incidence rate ratio for asthma in workers with occupational rhinitis varied across occupations, being highest for farmers and woodworkers [81]" (Moscato et al 2009).

Occupational asthma is a serious disease. According to the U.S. Occupational Safety & Health Administration:

"Occupational factors are associated with up to 15 percent of disabling asthma cases in the United States. Asthma is an illness characterized by intermittent breathing difficulty including chest tightness, wheezing, cough, and shortness of breath. It is frequently serious and sometimes fatal" (OSHA undated).

The Slager et al (2009) study suggests that exposure to Enlist Duo could increase the incidence of rhinitis, while other research points to potential for increased asthma, in farmers and other exposed populations. Taking into account intensity of exposure, the increase could be substantially greater than suggested by the study. Slager and colleagues defined the group exposed to both 2,4-D and glyphosate as those who had used both herbicides at some point over the past year. This definition encompasses a wide range of situations and exposure intensities, ranging from occasional use of each separately to frequent use of both in combination. Approval of Enlist Duo would lead to a dramatic increase in the number of farmers and applicators at the high intensity end of this spectrum, and thus potentially greater risk of rhinitis than found by these researchers. EPA did not evaluate or even mention this study in its assessment of Enlist Duo (EPA Human Health 2013, EPA Occupational 2013).

2.2.2 Exposure to 2,4-D or Enlist Duo and other pesticides

Just as 2,4-D apparently interacts with glyphosate to increase risk of rhinitis, so 2,4-D and glyphosate (either separately or as combined in Enlist Duo) may interact with still other pesticides (e.g. other herbicides, insecticides and/or fungicides) in ways that are harmful to human health. Fungicide use in corn and soybeans has increased dramatically in recent years, while there is also a recent upsurge in insecticide use in corn, increasing opportunities for such harmful interactions if Enlist Duo is approved.

Since 1992, EPA has compiled reports of adverse health effects from exposure to 2,4-D and other pesticides in its Incident Data System (IDS) (for following discussion, see EPA Reg Review Human Incidents 2012). In the 5.5 years from 2007 to mid-2012, EPA registered 2,661 health incidents that involved 2,4-D exposure, an average of 484 per year. No information is given for the 1992 to 2007 period. Of these incidents, 2,202 (83%) were of "low severity" and 459 (17%) of "higher severity." As noted above, EPA found the absolute number of low severity incidents to be high relative to other pesticides, and thus deserving of further evaluation. However, EPA provided no information on the nature of these incidents, and apparently has little detail on them itself:

"These incidents are reported by registrants only as counts in what are aggregate summaries. These aggregate summaries do not include any description of symptoms or circumstances of exposure" (EPA Reg Review HED 2013, p. 4).

Of the higher severity incidents, the vast majority (442, or 96%) involved exposure to another chemical as well as 2,4-D. Such episodes could be attributable to: 1) 2,4-D alone; 2) 2,4-D acting in concert with the other chemical; or 3) the other chemical.

CFS urged EPA to give full consideration to ALL of these numerous incidents (CFS Registration Review 2013). EPA said it will focus on the 17 involving 2,4-D alone: "Incidents involving one pesticide are typically focused on because they are considered to provide more certain information about the potential effects of the particular pesticide. … It is important to note that since most of these reported incidents involve more than one active ingredient (i.e. 2,4-D and another active ingredient), the incidents that were reported were not necessarily attributable to 2,4-D" (EPA Reg Review HED 2013). However, 2,4-D is very frequently used in mixtures with other herbicides – either premix products or tank mixtures. Premix products refer to off-the-shelf mixtures of two or more active ingredients. In a brief search, CFS found five commonly used premix products that contain 2,4-D (Penn State 2014b). Tank mixtures refer to applicator-prepared mixtures of individual active ingredients, a very common practice.

By discounting the vast majority of human incident data, EPA will almost certainly miss important adverse effects that are caused, in whole or in part, by 2,4-D. The priority for EPA risk assessment should be protecting human health, not pesticide use.

In any case, even the inadequate review of incident reports proposed by EPA will take place only in the preliminary phases of its registration review process, not scheduled for completion until 2017. Past EPA practice shows that the concrete instances of human harm represented by incident reports are heavily discounted in favor of much less relevant animal experiments. The proposed registration of Enlist Duo is a case in point. As with the other health studies discussed above, none of these incident data have been reviewed in the Enlist Duo assessment process.

2.2.3 Exposure to 2,4-D, Enlist Duo and formulation additives

It is well-known that pesticide formulations used by farmers include additives to increase the efficacy of the active ingredients, and that these so-called "inert" ingredients can be toxic in their own right, or increase the toxicity of the active ingredients (e.g. by increasing absorption of the a.i.). The animal experiment-based health data that EPA assessed for the Enlist Duo registration derive from studies conducted with the active ingredient 2,4-D alone, not as it will be used in practice as a component of Enlist Duo, which contains in addition both glyphosate and unspecified inerts. EPA must demand new studies that involve tests with the Enlist Duo formulation rather than the active ingredient 2,4-D alone.

2.3 Dioxin contamination of 2,4-D and the environment

Dioxins comprise a class of extremely toxic substances that cause a broad range of human health harms at exceptionally low levels. Dioxins are generated during the manufacture of 2,4-D and reside as contaminants in 2,4-D formulations. The adverse health effects of 2,4-D are often attributed to dioxin contaminants, although whether all can be blamed on dioxins is far from clear. Most tests that have been conducted find some level of dioxin content in 2,4-D, and there appears to be no baseline health data from tests on a hypothetically "pure, dioxin-free, 2,4-D."

CFS commented extensively on the important issue of 2,4-D-related dioxins in prior comments to the Agency on the Enlist Duo registration and on its 2,4-D registration review (CFS Enlist Duo 2012, pp. 63-65; CFS Registration Review 2013: Appendix B, pp. 53-56). We summarize the points made in those comments as follows:

EPA relies on registrant-conducted tests for information on the dioxin content of 2,4-D. The most recent publicly available data from such tests on 2,4-D in the late 1980s/early 1990s revealed substantial dioxin contamination. While industry assured EPA that it has reduced dioxin levels in 2,4-D since that time, tests by USDA and Australian researchers on 2,4-D from the mid 1990s and mid 2000s, respectively, reveal dioxin levels comparable to or exceeding those of the 1980s/early 1990s. EPA cannot rely on industry results, and should instead conduct or commission independent dioxin testing on a broad range of off-the-shelf 2,4-D formulations. EPA should also assess dioxins released into the environment during 2,4-D manufacture, and dioxins generated upon incineration of 2,4-D jugs with residual 2,4-D.[8] EPA must assess the increased environmental release of and human exposure to dioxins that would result from vastly increased 2,4-D use enabled by Enlist Duo approval. EPA must make this assessment in light of Part 1 of its assessment of dioxin toxicity (non-cancer risks), released in February 2012, which establishes a quite low "safe" level of lifetime dioxin exposure; and in light of the yet to be released Part 2, which addresses cancer risks. EPA should postpone its decision on Enlist Duo registration until it has the opportunity to fully assess 2,4-D-related dioxin issues in the context of the Agency's 2,4-D registration review. Further detail is provided in the comments cited above.

In the Enlist Duo assessment documents, EPA made no explicit response to the data, analysis or recommendations in CFS's comments. In a one-paragraph response on the issue of dioxins in general, it becomes clear that EPA still relies entirely on registrant-conducted tests for its data on dioxin levels in 2,4-D (EPA Registration, p.

[8] Such incineration tests have in fact been conducted by EPA research scientists.

21). The response also contains at least two factual errors. First, EPA strongly implies that dioxins are no longer present in today's 2,4-D, which is shown to be incorrect elsewhere in the assessment documents (see below). Second, EPA equates "dioxin," a large family of closely related compounds of varying toxicity, with the single form (congener) that is among the most toxic, 2,3,7,8-TCDD. In fact, one other dioxin compound (1,2,3,7,8-PeCDD) has equal toxicity to the one named by EPA, while a host of others have lesser but still considerable toxicity (Van den Berg et al 2006, Table 1). EPA data on dioxins in 2,4-D from the 1980s/1990s reveal the presence of many dioxin congeners; in fact, the 1,2,3,7,8-PeCDD congener that is as toxic as the EPA-named form - 2,3,7,8-TCDD – was detected more frequently and at substantially higher levels than the latter (EPA Dioxins undated).

The only other reference to dioxins found by CFS occurred in EPA's environmental assessment (EPA Environmental 2013a, p. 25), not in any of the human health assessment documents. There, EPA cites two "confidential memos," dated 2005 and 2012, that apparently contain data on dioxin levels in 2,4-D. The 2005 memo relates to dioxins in non-choline forms of 2,4-D, but it is not clear who conducted these tests. The 2012 memo refers to "recently submitted product chemistry data" for 2,4-D choline, which suggests that industry conducted the dioxin tests that generated these data. EPA does not report the absolute level of any dioxin congener, or dioxins as a whole, in either case. It is unclear to CFS why EPA does not report these data, or why they should be regarded as "confidential."

EPA's continued reliance on 2,4-D manufacturers' dioxins tests is extremely disappointing, given the great disparity in dioxin levels in 2,4-D found by USDA scientists and Australian researchers (higher) and those reported by industry (lower). CFS is also disappointed by EPA's failure to address any of the other serious issues we raised with respect to dioxins. We urge EPA once again to respond to our comments on 2,4-D-related dioxins and take positive action on our recommendations before any decision is made on Enlist Duo.

3. Economic, environmental and social costs of the proposed registration

A major deficiency in EPA's assessment is its failure to assess the economic, environmental and social costs of proposed registration. Below, CFS provides an assessment of three major costs: crop injury from herbicide drift, costs arising from the rapid evolution of 2,4-D- and multiple herbicide-resistant weeds; and the social costs of increasing consolidation of farmland.

3.1 Crop injury from herbicide drift

CFS addressed the issue of drift in our previous comments to EPA, which are incorporated here by reference (CFS Enlist Duo 2012, pp. 17-20). EPA made no meaningful response in the Enlist Duo assessment documents. We provide further comments below. Under the proposed registration, Enlist Duo would lead to a substantial increase in herbicide drift and associated damage to neighboring and distant crops, imposing huge economic costs on growers.

Summary
Herbicide drift is a serious and underreported problem. Herbicide-resistant crops lead to increased drift and associated crop damage by promoting intensive herbicide use later in the season when crops are more susceptible to drift damage. For this reason, glyphosate as used with Roundup Ready crops has become a leading culprit in drift-related crop damage. The chief predictor of drift and associated crop damage is intensity and timing of use, though drift is exacerbated when volatile herbicides are used. 2,4-D is volatile, drift-prone and can damage a wide range of crops. Even with modest use and extensive regulation, 2,4-D drift is a leading cause of crop injury. Glyphosate and 2,4-D are ubiquitous in air, water and rain. EPA's assessment of 2,4-D choline drift is vitiated by excessive reliance on models and failure to evaluate real-world data. EPA's proposed mitigation measures are unrealistic and unworkable, and it has a poor record of regulating drift, which further undermines confidence in them. By leading to a vastly more 2,4-D applied later in the season, approval of Enlist Duo would result in sharply increased crop damage and thus impose huge costs on growers of sensitive crops.

3.1.1 Herbicide drift

Herbicide drift comes in several forms. Spray drift refers to the movement of an herbicide off the field as it is being applied, and is affected by wind speed, application method and droplet size, among other factors. Some volatile herbicides can drift days to months after application, a phenomenon known as vapor drift. This occurs when an herbicide previously deposited on plant surfaces and the ground during the spray operation "volatilizes" (evaporates) and moves offsite, and is favored by hot conditions. Drift can also occur when herbicide-laden dust is carried by the wind.

Over the past two decades, two surveys of state pesticide regulatory agencies found that an average of over 2,100 pesticide drift complaints were received each year, most involving herbicides and crop damage (AAPCO 1999, 2005). However, the true number of drift episodes is certainly much higher, because many go unreported. According to EPA scientists who have studied pesticide drift for many years, farmers often settle drift cases without reporting them; and when lawsuits are filed, the majority are settled out of court, with confidentiality clauses that prevent disclosure even to the government (Olszyk et al. 2004, p. 225). It is often difficult to determine the source of damaging drift (Bennett 2006), which discourages farmers who would otherwise report in hope of obtaining compensation. All of these factors suggest that the true scope of herbicide drift is far greater than implied by the number of reported cases, which in any case is substantial. Experience with Roundup Ready crops shows clearly that drift becomes more frequent and damaging when an herbicide is used in the context of an herbicide-resistant crop system.

3.1.2 The Roundup Ready crop experience

Glyphosate has low volatility, and thus is not a drift-prone weed-killer (Lee et al. 2005, p. 135). Nevertheless, it has become one of the top two herbicides (along with 2,4-D) implicated in herbicide drift complaints nationwide since the Roundup Ready era began (AAPCO 1999, 2005). The high incidence of glyphosate drift injury is partly attributable to the expanded acreage and increased volume of use with Roundup Ready (RR) crops. However, the late application period – mid-season with RR crops versus early season with conventional varieties – is clearly a contributing factor. In a comprehensive study of the potential for herbicide drift to injure crops in Fresno, CA, EPA scientists found that:

> Increased use of herbicide-resistant technology by producers creates the possibility of off-site movement onto adjacent conventional crops. … Postemergence application of a herbicide to a genetically-modified (GM) crop often occurs when non-GM plants are in the early reproductive growth stage and are most susceptible to damage from herbicide drift (Ghosheh et al.,1994; Hurst, 1982; Snipes et al., 1991, 1992). Consequently, most drift complaints occur in spring and summer as the use of postemergence herbicide applications increases. (Lee et al. 2005, p. 15)

It is because Roundup Ready crops have enabled "large quantities" of glyphosate to be used "throughout the season" that it poses a greater threat than more damaging but lesser used herbicides like 2,4-D:

> "Glyphosate may be applied as a preplant or postplant postemergent herbicide. It is not as damaging to sensitive crops as 2,4-D and dicamba and other high potential risk herbicides but has greater potential to damage sensitive crops because it is applied throughout the year in large quantities." (Lee et al. 2005, p. 47)

The problem is not confined to California. Glyphosate drifting from application to Roundup Ready crops has repeatedly caused extensive damage to wheat (Baldwin 2011) and especially rice (Scott 2009) in Arkansas; to rice (Wagner 2011) and corn (Dodds et al. 2007) in Mississippi; to rice in Louisiana (Bennett 2008); and to tomatoes in Indiana and adjacent states (Smith 2010); to cite just a few of many examples.[9] Such episodes sometimes give rise to lawsuits, as when farmers won compensation for onions damaged by glyphosate applied to Roundup Ready soybeans in Ontario, Canada (Lockery vs. Hayter 2006).

Glyphosate drift injury can be extensive, damaging 30,000 to 50,000 acres of rice in Mississippi in 2006, for example (Wagner 2011). Glyphosate drift damage to wheat has prompted suggestions that the crop simply not be grown in Arkansas (Baldwin

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[9] A search of the online farm publication Delta Farm Press using the search term "glyphosate drift" turned up 127 articles (search conducted 6/5/14, www.deltafarmpress.com).

2011). Tomato growers in Indiana, Michigan and Ohio suffered over $1 million in glyphosate drift damage over four years (Smith 2010). Arkansas corn growers felt so threatened that they switched to Roundup Ready varieties out of "self-defense" against glyphosate drifting from Roundup Ready soybean and cotton fields (Baldwin 2010). While most drift damage occurs near treated fields, weed consultant Ford L. Baldwin has documented glyphosate drifting 0.5 to over 2 miles to damage rice in Arkansas (Baldwin 2008).

3.1.3 2,4-D drift today and yesterday

2,4-D is a volatile herbicide that is prone not only to spray drift (like glyphosate), but also to vapor drift, which is much more unpredictable and difficult to prevent and control. When 2,4-D was first introduced in Iowa, vineyard operators suffered substantial losses and lobbied unsuccessfully for restrictions on its use by corn growers (Anderson 2005). 2,4-D drift has been so problematic that many states did eventually restrict its use in areas where sensitive crops are grown, at certain times of year (Feitshans 1999). Drift problems were also one factor leading to sharp reductions in 2,4-D use in favor of less toxic and less drift-prone herbicides in the 1980s and 1990s. Despite restrictions and reduced use, however, problems continue.

2,4-D ranked 1st or 2nd in herbicide drift complaints in the six years from 1996-1998 and 2002 to 2004 (AAPCO 1999, 2005). Crops damaged by 2,4-D drift, often at quite low levels, include grapes, cotton (Egan et al 2014a), soybeans, sunflower, and many fruits and vegetables (Doohan et al. 2014). Though damage often occurs to crops in adjacent fields, area-wide impacts are not uncommon. For instance, in 2006 volatilization of 2,4-D damaged cotton on "upwards of 200,000 to 250,000 acres" in five counties in Arkansas, an impact likely due to multiple applications in the area and weather conditions that promoted vapor drift (Bennett 2006). In 2012, a single 2,4-D application damaged 15,000 acres of California cotton as well as a pomegranate orchard, with damage to cotton verified as far as 100 miles from the application site (Cline 2012).

Despite numerous restrictions on formulation types and application methods, 2,4-D drift continues to damage grapes, one of the most sensitive crop species:

> Grape vineyards, especially in regions of mixed cereal and minor crop production, have historically been exposed to auxin-type herbicides, presumably from a combination of local and regional transport. Banning dust and volatile ester formulations, restricting the timing of low volatile ester formulations, and prohibiting applications when drift is likely have all helped to minimize the damage to grapes. Unfortunately, episodic injury remains severe enough to cause economic losses to the grape industry. Our recent two years of field monitoring of 2,4-D residues supports the above assertion. The movement of these highly active substances from the target site as aerosols, on/in soil wind-blown particulates, or in the gas-phase are

> unfortunately difficult to predict and therefore more difficult to apply consistent label language. Moreover, post-application processes are beyond the direct control or influence of pesticide applicators. Because of the high potency, mitigating injury from the use of auxin-type herbicides to sensitive crops upwind will remain difficult. (Hebert 2004)

3.1.4 2,4-D, glyphosate and other herbicides ubiquitous in water, air and rain

The discussion above makes clear that while volatility can exacerbate drift, even non-volatile herbicides like glyphosate are problematic when used in large quantities. The same is true of herbicides polluting our water bodies, air and rain: the best predictor of presence is the amount used. As U.S. Geological Survey scientists concluded in an exhaustive analysis of pesticides in U.S. waters from 1992-2001: "[t]he pesticides detected most frequently in streams and ground water were primarily those with the greatest use…" as well as mobility and persistence in water (Gilliom et al. 2006, p. 10). Since 2003, 2,4-D has been detected in 47% of surface water samples tested by the U.S. Geological Survey, over twice the detection rate of prior samples (EPA Environmental 2013a, pp. 35-36). Vastly increased use of 2,4-D with approval of Enlist Duo would increase both the frequency and levels of detection.

Despite being both non-volatile and non-persistent in the environment, glyphosate is detected as or more frequently than other herbicides, and at equal or higher concentrations, in the air, rain and waterways of areas like Iowa and the Mississippi Delta where it is heavily used (Coupe et al 2012, Chang et al 2011). This underscores the overriding importance of usage level over physical properties such as volatility when assessing the potential for environmental pollution and associated harms.

Even so, high-level use combined with volatility will in most cases yield the worst outcomes. Pesticides like 2,4-D can "volatilize into the lower atmosphere, a process that can continue for days, weeks, or months after the application, depending on the compound" (USGS 2003), and are then brought back to earth when it rains.

In the Canadian Prairies, where 2,4-D use is common on wheat fields, measurable levels of 2,4-D and other herbicides are frequently found in the air and in rain (Turduri et al. 2006). At the high end of concentrations detected in rainfall in Alberta, Canada, a mixture of four herbicides (2,4-D, dicamba, MCPA and bromoxynil) was found to negatively impact test plants, leading the researchers to conclude that: "…based on our bioassay results and those of Kudsk et al. (1998), it is our opinion that the occasional high levels of herbicides detected in southern Alberta rainfall could adversely affect dry beans and tomatoes grown in the area" (Hill et al. 2002). The levels of 2,4-D found in air and rain would increase dramatically with the three- to seven-fold increased use enabled by Enlist Duo registration, increasing the incidence of "toxic rainfall" containing sufficient levels of 2,4-D (and other herbicides) to damage sensitive crops.

3.1.5 Modeling versus the real world

EPA's assessment of drift is vitiated by excessive reliance on models that rely unduly on 2,4-D choline's lesser volatility, presume use of drift-mitigating spray nozzles and proper equipment calibration, and assume perfect adherence to a host of unworkable mitigation measures that are discussed further below (EPA Environmental 2013a & 2013b, EPA Registration 2014, pp. 23-24, 27-28). The discussion above makes clear that glyphosate, an herbicide with much lower volatility than any form of 2,4-D, including the choline salt, is a leading cause of drift-related crop injury. EPA's spray drift model cannot account for, and would never predict, this indisputable real-world outcome. If EPA must rely on models, it should construct one that incorporates parameters based on real-world herbicide use practices, as well as data on ***actual*** occurrence of drift and crop damage, as for instance the AAPCO data discussed above. Until it does so, EPA's modeling exercises will be worthless as predictors of drift and other phenomena, and will continue to serve as little more than tools to provide false assurances and pretexts to approve hazardous pesticide uses, such as the one at issue here.

3.1.6 Proposed mitigation unrealistic and unworkable in the real world

EPA proposes a host of mitigation measures intended to reduce drift and associated crop damage, including: use of specific spray nozzles; spray pressures not to exceed 40 psi; minimizing the height of the groundboom; prohibition of aerial application; no application when wind speeds exceed 15 mph; and equipment calibration to produce larger droplets when applications are made under conditions of "low relative humidity." In addition, applicators are called upon to determine if wind speeds are less than 3 mph. If they are, applicators must further determine whether "conditions of temperature inversion exist," or "stable atmospheric conditions exist at or below nozzle height," in which case application is not to be made (EPA Registration 2014, pp. 27-28).

Furthermore, applicators are called upon to ascertain "circumstances" under which "spray drift may occur to food, forage, or other plantings that might be damaged or crops thereof rendered unfit for sale, use or consumption," and to abstain from applying Enlist Duo under such circumstances. In addition, they are to avoid contact of Enlist Duo "with foliage, green stems, exposed non-woody roots of crops, desirable plants, including including cotton and trees." Before making an application, EPA asks that applicators "please refer to your state's sensitive crop registry (if available) to identify any commercial specialty or certified organic crops that may be located nearby." Finally, applicators are told not to apply Enlist Duo when wind direction favors off-target movement [i.e. drift] onto commercially grown tomatoes and other fruiting vegetables, cucurbits and grapes (but apparently spraying is permitted if the vegetables are grown in a home garden) (EPA Registration 2014, p. 29).

The sheer number and complexity of the mitigation measures speaks volumes to the grave threats of crop injury posed by drift of Enlist Duo. As discussed above, past attempts to mitigate 2,4-D drift through such label language have failed to prevent it from being the top culprit in drift injury. It is still more certain that the measures proposed for Enlist Duo will fail.

Some of these mitigation measures are straightforward requirements, such as use of specific nozzles and spray pressures, and prohibition of aerial application. To what extent they would be followed is uncertain, but at least they are unambiguous. Most involve judgment calls. For instance, what constitutes "low relative humidity," "conditions of temperature inversion," or "stable atmospheric conditions"? Farmers and applicators are not meteorologists, and even those who are quite knowledgeable in this area will arrive at different assessments because the terms are inherently ambiguous. Wind restrictions seem straightforward, but winds continually vary in speed and direction, making them difficult to measure. And how many farmers carry anenometers to the field with them?

One must also consider real-world production constraints. Weed control must be undertaken during narrow windows (when weeds are small enough to be effectively controlled) and integrated into a sequence of other pressing farm tasks. This is particularly true on larger farms, and farms are getting larger in part thanks to herbicide-resistant crops. Commercial applicators who serve numerous farmers must meet both their farmer-clients' expectations of timely weed control and keep to their own busy schedules. The result is enormous pressure to bias weather assessments to permit spraying to fit tight schedules, and even to spray under clearly inappropriate conditions. EPA knows this to be true. As the Association of American Pesticide Control Officials (AAPCO) told the Agency in 2002, it "has experience that supports that there are numerous pesticide applications made when it is too windy" (AAPCO 2002).

Many of the mitigation measures appear to be redundant. Why the special plea to avoid spraying when "circumstances" would lead to spray drift damage to tomatoes, cucurbits, grapes, cotton, trees and "desirable plants" if the long list of mitigation measures would in fact be effective? Why should any farmer who follows EPA guidance need to consult a registry to find out if sensitive/organic crops are in his/her area? The reason is clear. EPA knows that its mitigation measures will ***not*** prevent substantial crop injury, both because of their inherent inadequacy and because many applicators will often ***not*** comply with them. One might be inclined to praise EPA for the special concern it shows for specialty crop growers, if it were not so obvious that they will not work, and that many growers will suffer substantial losses if the proposed registration is approved.

<u>3.1.7 Long-standing deficiencies in EPA's regulation of pesticide drift further undermine confidence in mitigation</u>

EPA has never effectively addressed the problem of pesticide drift. Recognizing that its regulations are inadequate, in 2001 EPA proposed more stringent limits on application equipment and methods, as well as conditions (e.g. maximum wind speeds) under which pesticides could be sprayed, to prevent harmful drift (Goldman et al. 2009). However, the proposed rule was never finalized, and is not in effect.

3.2 Environmental and economic costs of herbicide-resistant weeds

<u>Summary</u>

Use of Enlist Duo on Enlist crops (the Enlist system) would foster rapid emergence of weeds resistant to 2,4-D, as acknowledged by USDA and weed scientists. Because the Enlist system would be used primarily by farmers whose fields are infested with weeds resistant to glyphosate and often other herbicides, the result would be extremely intractable weeds immune to both herbicides. EPA ignores the many costs of 2,4-D and multiple herbicide-resistant weeds that would be generated by the Enlist system. These include greater use of toxic herbicides and associated human health and environmental harms; higher weed control costs for farmers; increased soil erosion from greater use of tillage; and reduced use of sustainable weed control practices that involve lesser reliance on herbicides. In anticipation of 2,4-D/glyphosate-resistant weeds, Dow has already added additional herbicide resistance traits to Enlist crops to permit high-level, post-emergence use of glufosinate and other weed-killers to control them. As weeds acquire resistance to these chemicals as well, Dow envisions adding multiple combinations of resistance to as many as nine classes of herbicide. This chemical arms resistance race between crops and weeds would ensure rapidly increasing use of additional toxic herbicides long into the future, generating substantial "benefits" for Dow and other pesticide firms, sharply rising weed control costs for farmers, and rising adverse impacts on human health and the environment.

EPA ignores these costs, and evaluates only putative benefits of the Enlist system. But even this limited assessment is invalidated by fundamental flaws. EPA lacked requisite cost data on the cost of Enlist Duo, Enlist seed, and alternative weed management programs, misunderstands how farmers would use the Enlist system, and relies entirely on a faulty and biased assessment by the registrant. A proper accounting shows that whatever fleeting economic benefits the Enlist system provide are swamped by the subsequent costs just a few years down the line. Dow's stewardship plan is no different than Monsanto's for Roundup Ready crops, and would be equally ineffective. EPA's proposed mitigation for 2,4-D resistant weeds – a monitoring program that entirely lacks any prevention component – would be also ineffective and unworkable. EPA should reject the proposed registration because the economic and environmental costs that would ensue are far greater than any short-term benefits.

CFS submitted extensive comments to EPA on the subject of 2,4-D and multiple herbicide-resistant weeds that would be triggered by the Enlist system (CFS Enlist Duo 2012, pp. 20-38), which are incorporated here by reference. EPA made no meaningful response to our comments. We will not repeat those comments, but rather summarize the major points, bring in new information, and point out major deficiencies in EPA's "benefits" assessment (Enlist Duo Benefits 2014) and its proposed mitigation for 2,4-D-resistant weeds (EPA Registration 2014, p. 29-31). Unless otherwise noted, page references refer to CFS Enlist Duo (2012).

3.2.1 Herbicide-resistant crops systems foster herbicide-resistant weeds

Herbicide-resistant crops can only be understood as crop ***systems*** comprised of the crop itself and application of the corresponding herbicide. The characteristic herbicide use pattern with resistant crops is particularly prone to spur rapid evolution of resistance in weeds. This use pattern involves heavy, frequent, and often exclusive reliance on the associated herbicide(s) to control weeds, and post-emergence application later in the growing season (pp. 23-26). Weeds evolve resistance on the same principle by which bacteria evolve resistance to overused antibiotics. The resistance-promoting effects of these crop systems is illustrated dramatically by Monsanto's Roundup Ready crops, resistant to glyphosate, which dominate corn, soybean and cotton production (pp. 26-28). Glyphosate-resistant weeds infest 50-62 million acres of U.S. cropland (Benbrook 2012), and the area infested is growing rapidly (Stratus 2013).

3.2.2 The Enlist crop system

The Enlist system is explicitly intended for farmers whose fields are infested with weeds resistant to glyphosate and other herbicides. USDA has found that the Enlist system would generate strong "selection pressure" for evolution of 2,4-D-resistance in weeds – often in weeds already resistant to glyphosate (CFS 2,4-D Corn-Soy Science I 2014). The result would be still more intractable weeds resistant to both herbicides (pp. 28-30). Multiple herbicide-resistant weeds are already a costly and growing problem for farmers, and the Enlist system would greatly accelerate their emergence (Mortensen et al 2012). The costs of such herbicide-resistant weeds include reduced yield; greater use of toxic herbicides and associated human health and environmental harms; higher weed control costs for farmers; increased soil erosion from greater use of tillage (pp. 21-23, 30-35); and reduced use of sustainable weed control practices that involve lesser reliance on herbicides (pp. 20-21; CFS 2,4-D Corn-Soy EIS Science I 2014, 32-35). Many of the weeds thus generated would be serious enough to rate the designation of noxious (CFS 2,4-D Corn-Soy EIS Science I 2014, pp. 22-28).

Enlist crops have also been engineered for resistance to other herbicides: glufosinate, triclopyr and fluroxypyr (soybeans); and "fops" class grass herbicides such as quizalofop (corn). These herbicides will likely be increasingly used as weeds evolve resistance to 2,4-D (CFS Corn-Soy EIS Science I 2014, pp. 13-18). Since weeds will inevitably evolve resistance to these weed-killers as well, Dow has obtained patents on Enlist corn (Cui et al 2011) and soybeans (Cui et al 2013) that envision adding multiple combinations of resistance to up to nine additional classes of herbicide.

> "Thus, the subject invention **[2,4-D-resistant soybeans]** can be combined with, for example traits encoding glyphosate resistance … glufosinate resistance … acetolactate synthase (ALS)-inhibiting

> herbicide resistance … bromoxynil resistance … resistance to inhibitors of HPPD … enzyme … resistance to inhibitors of phytoene-desaturase (PDS), resistance to photosystem II inhibiting herbicides (e.g. psbA) **[e.g. atrazine]**, resistance to photosystem I inhibiting herbicides **[e.g. paraquat]**, resistance to protoporphyrinogen oxidase IX (PPO)-inhibiting herbicides … resistance to phenylurea herbicides … dicamba-degrading enzymes … and others could be stacked [sic] alone or in multiple combinations to provide the ability to effectively control or prevent weed shifts and/or resistance to any herbicide of the aforementioned classes" (Cui et al 2013, section 0077, emphasis added).

The listed traits represent resistance to most major classes of herbicides, including those that include extremely toxic weed-killers like paraquat and atrazine. Other major biotechnology firms have quite similar patents. This chemical arms resistance race between crops and weeds would ensure rapidly increasing use of additional toxic herbicides long into the future, generating substantial "benefits" for Dow and other pesticide firms, sharply rising weed control costs for farmers, and rising adverse impacts on human health and the environment.

3.2.3 EPA's "benefits" assessment

FIFRA enjoins EPA to "tak[e] into account the economic, social and environmental costs and benefits" of a pesticide use in deciding whether or not it poses unreasonable adverse effects on the environment. In particular, EPA must consider economic costs as well as benefits.

EPA's assessment considers only putative benefits of Enlist Duo, and entirely ignores costs (EPA Benefits 2014), such as those arising from weed resistance, as discussed above. Even EPA's limited evaluation of putative benefits is invalid because it was undertaken in the absence of critical data, such as the cost of Enlist Duo, the cost of Enlist corn and soybean seed, and the cost of alternative weed control programs, and for other reasons discussed below. EPA makes numerous baseless assumptions in a failed attempt to conduct its assessment without these data. For instance, EPA assumes that the combined cost of Enlist Duo and Enlist seed would be equivalent to that of the cheapest alternative weed control program. On this basis, EPA then ascribes two benefits to the Enlist system: 1) A "convenience benefit," defined as "a measure of value to growers of the simplicity of managing weeds with the current glyphosate-based system, which allows a wide window for application, a single treatment of herbicide, an over the top application after the crop and weeds have emerged from the ground, as estimated by Marra and Piggot (2006);" and 2) Reduced need for tillage.

The so-called "convenience benefit" is based on an assessment of glyphosate-resistant crops that takes no account of the dramatically altered weed control practices and substantially increased weed control costs that have been triggered by glyphosate-resistant weeds generated by the Roundup Ready crop system "when used in accordance with widespread and commonly recognized practice." As discussed in our prior comments, referenced above, farmers are increasing the rate and number of glyphosate applications, often using additional herbicides, and utilizing more tillage operations to control epidemic emergence of glyphosate-resistant weeds. Ironically, it is the very "convenience benefit" of the Roundup Ready crop system – which involves excessive reliance on glyphosate – that generates what might be called the "convenience deficit" of glyphosate-resistant weeds. EPA does not assess the costs of glyphosate-resistant weeds, or provide any discussion of their prevalence. EPA has failed to learn the lesson taught by Roundup Ready crops, and so fails to apply it to the Enlist system, which would have precisely analogous effects if approved. The Enlist system would impose still greater costs on growers through facilitating the same unhealthy "convenience" that has undermined the efficacy of the Roundup Ready crop system.

It is important to understand that these costs would also be imposed on growers of non-Enlist crops, because once they have evolved, the pollen and seed of resistant weeds travel to spread resistance to near and sometimes distant fields, which undermines any individual farmer's incentive to undertake efforts to prevent evolution of resistance in his/her fields (CFS Enlist Duo 2012, pp. 37-38; CFS Corn-Soy EIS Science I 2014, pp. 25-26). In fact, USDA has found that 2,4-D-resistant weeds generated by Enlist crop systems would likely spread to fields of non-Enlist farmers, including wheat growers, who often use 2,4-D, but in ways that do not generally promote evolution of resistance; such weeds would increase weed control costs for wheat farmers by forcing them to use more expensive alternatives, and possibly encourage them to switch from wheat to some other crop, such as corn, which as normally cultivated is a much more environmentally damaging crop (CFS Corn-Soy EIS Science I 2014, pp. 7-9).

Similar considerations apply to the second putative benefit – reduced need for tillage. First, it must be emphasized that use of herbicide-resistant crops (e.g. Roundup Ready) does not drive adoption of reduced tillage farming practices, often called conservation tillage, one form of which is "no-till." CFS has addressed and refuted this common myth elsewhere, showing that the true causes of declining soil erosion in American agriculture – the major goal of conservation tillage – were federal farm policies first enacted in 1985 that provided strong financial incentives to farmers to adopt conservation tillage practices, and showing further that soil erosion rates in the Midwest stopped declining in 1997, around the time Roundup Ready crops were introduced (CFS Enlist Soy Science 2012, pp. 62-73). An updated and abbreviated analysis with respect to similar claims made for the Enlist system may be found at CFS Corn-Soy EIS Science I (2014), pp. 29-32. Second, it is indisputable that glyphosate-resistant weeds generated by the Roundup Ready crop system have led to greater use of tillage, not less (Neuman & Pollack 2010; NRC 2010; Owen 2011, Table 1), meaning increased soil erosion. The more intractable resistant weeds generated by the Enlist system would lead to still greater use of tillage and hence soil erosion.

In EPA's "benefits" assessment, the Enlist crop system is presented as a tool to "preserve the viability of glyphosate GE technology." This framing – adopted uncritically from Dow – obscures the precisely contrary truth of the matter. The Enlist system is entirely premised on ***the failure to preserve the efficacy of "glyphosate GE technology***." That is, no farmer would have any interest in Enlist crops if glyphosate as used with Roundup Ready crops were still an effective means to control weeds (see below). That glyphosate has become ineffective for a large and growing number of farmers thanks to glyphosate-resistant weeds is due in part to deceptive and unethical marketing by Monsanto, assuring farmers that they could rely entirely on glyphosate year after without risk of weed resistance (Hartzler et al 2004), EPA's and USDA's failure to impose sensible constraints on glyphosate use with Roundup Ready crops in the form of mandatory weed resistance measures; and farmer decisions. This false framing provides EPA with a pretext to recapitulate, with the Enlist system, its regulatory failure with Roundup Ready crops, leading to still worse weed resistance problems.

EPA's assessment is also internally inconsistent. When it comes to assessing "benefits," the Enlist system is understood correctly to be used by farmers as a convenient means to control glyphosate-resistant weeds. In this situation, however, glyphosate-resistant weeds would be exposed to just one effective mode of action, 2,4-D, and therefore would be quite likely acquire additional resistance to 2,4-D (Mortensen et al 2012). However, EPA also makes the contrary and false assumption that growers ***without*** glyphosate-resistant weeds would use the Enlist system to prevent their emergence (i.e. two effective modes of action). EPA makes the latter assumption despite its acknowledgement that it "is unable to determine whether growers will have a financial incentive to adopt the new system before glyphosate resistance becomes a problem" (EPA Benefits, p. 2). Clearly, EPA's shifting and contradictory assumptions are made to bias the assessment in favor of Enlist Duo, yet neither EPA nor growers can have it both ways. The Enlist system only becomes attractive when glyphosate is no longer effective; but when used in this situation, for convenient control of glyphosate-resistant weeds, the "convenience benefit" of the Enlist system will rapidly morph into the "convenience deficit" of weed resistance.

Another example of unresolved contradictions has to do with EPA's assumption that farmers who have glyphosate-resistant weeds and adopt the Enlist system would make use of a third "foundation herbicide" to prevent emergence of 2,4-D resistance. However, use of such a "foundation herbicide" (i.e. pre-emergence herbicide applied early in the season, with residual activity to control emerging weeds for several weeks or more) would be both more expensive than, and negate the convenience benefit of, relying on Enlist Duo, especially in the case of Enlist soybeans. Here again, EPA mistakenly assumes both a convenience benefit and prevention of weed resistance, when only one or the other is possible.

EPA also misunderstands basic features of herbicide-resistant crop systems, assuming falsely that their purpose is to permit spraying when weeds are small, more susceptible to control, and less likely to evolve resistance. In fact, glyphosate-resistant crops are designed to enable mid-season weed control, which generally occurs when weeds are larger, less amenable to control, and more likely to evolve resistance (CFS Enlist Duo 2012, pp. 25-26). Enlist Duo would be used in precisely the same way with Enlist crops, and is one factor that would promote rapid evolution of 2,4-D resistance (Ibid, pp. 30-34).

EPA's proposed mitigation for weed resistance is entirely inadequate and unworkable (EPA Registration 2014, pp. 29-31). Most importantly, there are no mandatory measures to ***prevent*** evolution of 2,4-D resistance in weeds, but rather only ***monitoring*** to detect them after they have emerged. Effective resistance prevention would require at the very least mandatory restrictions against post-emergence use of Enlist Duo on an Enlist crop every year on the same field. Every-year use of the Enlist system may well become common because the proposed registration encompasses use of Enlist Duo on both Enlist corn and Enlist soybeans, and rotation of corn and soybeans is extremely common throughout the Midwest. Every-year application of Enlist Duo, applied once to three times per season, would be the perfect recipe for weed resistance to emerge. We know this to be the case because this is precisely what has driven epidemic emergence of glyphosate-resistant weeds in the Midwest – every-year use of glyphosate on Roundup Ready soybeans and Roundup Ready corn. CFS has provided EPA with thoroughly documented discussions of these matters in our prior comments.

Even to the limited extent that monitoring for resistance after it has emerged would be useful, the proposed plan is undermined by EPA's delegation of virtually all responsibilities to Dow. Dow is put in charge of developing diagnostic tests used to evaluate potential resistance; investigating farmer reports of potential resistant weeds; collecting material for testing; eradicating weeds that Dow judges to be "likely resistant" based on its diagnostic tests; and informing growers and other stakeholders of likely and confirmed resistance. Dow is also required to report periodically to EPA on any findings of resistant weeds. Delegation of these responsibilities to Dow represents a clear conflict of interest. Dow's financial interests militate directly against any finding of resistance, for several reasons. First, 2,4-D resistant weeds would represent a failure of the Enlist system, which Dow is naturally motivated to sell to growers; sales would not be promoted, but could well suffer, if Dow were to determine that weeds are resistant to 2,4-D. This is all the more true since Dow is obligated to publicize local or widespread failure of the Enlist system to growers and other stakeholders. Second, a finding of resistance could lead to EPA modification or cancellation of Enlist Duo registration. While EPA would be extremely to undertake such an action, the possibility would further incentivize Dow to avoid finding resistant weeds in the first place, to avoid loss of Enlist Duo herbicide and/or Enlist crop seed sales.

The Dow-led implementation of the monitoring program would open up many possibilities for avoiding a 2,4-D resistance determination. For instance, Dow-developed diagnostic tests could be made intentionally insensitive; Dow could drag its feet in responding to grower reports of non-compliance; reports to EPA could be incomplete or doctored; to name just a few of the possibilities. These are not idle speculations. EPA has already had experience of such machinations in the context of insect resistance management (IRM) for GE corn resistant to the corn pest, corn rootworm. Here too, EPA delegates all responsibilities for IRM to the crop developer. Rootworm resistance to Monsanto's GE corn has emerged rapidly from at least 2008, but Monsanto – in charge of investigating grower complaints of potential resistance – delayed investigations, submitted incomplete reports to EPA, and set an inappropriately "high bar" for what exactly constituted "resistance." Rootworm resistant to Monsanto's GE corn were only confirmed in 2011, at least three years after their emergence, by public sector entomologists, not Monsanto. Monsanto then first denied the resistance finding, then when it became undeniable, downplayed its significance (for documented overview, see CFS Corn Rootworm 2013; see also Philpott 2011 and Gustin 2011).

Dow has already discounted the risks of 2,4-D resistance, even misrepresenting the basic fact that weeds resistant to 2,4-D and its synthetic auxin class of herbicides are already quite common (Egan et al 2011), which does not foster confidence in the firm's objectivity in this area.

Finally, while it might seem cynical to suggest, it is an indisputable fact that it is weed resistance that generates new markets for new herbicide-resistant crops that incorporate resistance to additional classes of herbicide. As recounted above, Dow has already incorporated resistance to glufosinate and quizalofop into Roundup Ready soybeans and corn, respectively, and envisions "stacking in" resistance to multiple additional herbicides in patents on Enlist crops. One must wonder why Dow would envision such stacking, which would have no purpose if 2,4-D resistant weeds were prevented and the Enlist system in its present form were to remain effective. CFS is not suggesting that Dow is intentionally planning to foster 2,4-D resistance; but rather only that the most profitable path for the company in the present is to maximize sales of Enlist Duo and Enlist seeds, which is also the path that would be most conducive to 2,4-D resistance, which in turn would open up new market opportunities.

4. Conclusion

In these comments and prior ones, CFS has presented reasonable and science-based arguments demonstrating that EPA should reject the proposed registration of Enlist Duo for use on Enlist corn and soybeans, to protect human health, the environment, and the true and sustainable economic interests of American farmers and U.S. agriculture. At the very least, any decision should be postponed until EPA can conduct the needed comprehensive and critical review in the context of the 2,4-D registration review process. CFS is confident that an objective, science-based review would necessitate denial of the requested registration.

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2,4-D: New Use on Herbicide-Tolerant Corn and Soybean
Environmental Protection Agency, Mailcode 28221T
1200 Pennsylvania Ave., NW
Washington, D.C. 20460

Docket No. EPA-HQ-OPP-2014-0195

June 30, 2014

Comments to EPA on EPA's Proposed Registration of Enlist Duo™ Herbicide Containing 2,4-D and Glyphosate for New Uses on Herbicide-Tolerant Corn and Soybean

Part II: Environmental Effects
Martha L. Crouch, Ph.D. Biology, for Center for Food Safety

EPA's assessment of adverse ecological effects of Enlist Duo used with Enlist corn and soybeans is inadequate and flawed.

Incredibly, EPA ignores impacts of the very large increases in use of 2,4-D that will occur if it registers Enlist Duo for use with Enlist corn and soybeans, discussed in detail in these comments in relation to use pattern, and CFS Enlist Duo 2012 at 10 – 17, 54 – 55; CFS Enlist EIS 2014a at 9 – 11). Because of this increase and specific changes in use pattern, a larger number of individuals of more species will be exposed to the herbicide at higher concentrations and by more routes of exposure, with or without mitigation procedures. In addition, EPA has underestimated risks to plants and other organisms by not testing toxicity of the actual formulation being registered, and by not requiring other important toxicity tests – to honeybees, for example – making it impossible for EPA to determine adverse effects on the environment, or to design and assess adequate mitigation measures. EPA does not weigh costs of adverse effects to beneficial organisms. And EPA makes indefensible assumptions about exposure of threatened and endangered species to Enlist Duo, claiming that no herbicide will leave the field of application, thus unduly limiting the risk assessment to only those listed species that directly inhabit corn and soybean fields.

EPA is unable to assess risks to the environment in part because of key deficiencies in its determination of adverse affects on non-target plants.

Terrestrial plants growing alongside Enlist corn and soybeans – weeds – are the intended targets of the herbicides in Enlist Duo. Therefore it is crucial that EPA carefully assess risks to non-target terrestrial plants of use of Enlist Duo with Enlist corn and soybeans because the formulation is optimized for killing that taxon.

Plants are also of utmost importance to functioning of ecosystems, forming the base of the food web, and providing habitat for most other species. Adverse effects to plants thus impact the environment as a whole. All crops are also terrestrial plants, and EPA must assess costs of harm to non-2,4-D resistant crops.

Given the central importance of plants to environmental and economic impacts of the registration action, EPA must require studies that provide information necessary to determine adverse effects. Without such information, assessment of risks to the environment and costs to society of using Enlist Duo with Enlist corn and soybeans cannot be determined, and EPA then cannot find that the registration action would not have an unreasonable adverse effect on the environment, or that benefits outweigh costs.

In fact, EPA's assessment of risks to non-target plants is insufficient, and EPA indeed cannot adequately determine impacts of the registration action on the environment or to other crops. EPA lacks information about toxicity to plants of the Enlist Duo formulation, and also does not determine impacts to plants at reproductive stages of development, or to a wide enough variety of plant species (EPA Environmental 2013a at 14, 68). Without this information, effective mitigation measures to protect non-target plants cannot be determined or assessed.

Enlist Duo formulation is likely to be more toxic to plants than the 2,4-D formulation used in toxicity tests

None of EPA's environmental assessments are based on studies performed with the actual formulation that is the subject of this registration action:

- EPA only assesses the 2,4-D component of the formulation. In addition to the herbicide 2,4-D, Enlist Duo contains the herbicide glyphosate that has a different mechanism of action. No impacts of the glyphosate component of the formulation are assessed, either alone or in combination with the other Enlist Duo ingredients.

- EPA does not consider any of the undisclosed so-called inert ingredients that affect the properties of the formulation and that may potentiate the impacts of 2,4-D and glyphosate.

- Not only are all of EPA's assessments based on 2,4-D alone, most are based on studies using other salts of 2,4-D rather than the 2,4-D choline being registered in this action. None of the plant studies were done with the choline salt.

In EPA's discussion of risks to non-target terrestrial plants, it does recognize that assessments based on toxicity of 2,4-D alone are deficient, and that "[f]or the 2,4-D choline salt-glyphosate formulation, it is anticipated that there could be additional toxicological effects (synergistic or additive) because of the presence of two herbicides" (EPA Environmental 2013a at 13). EPA further explains in their listing of data gaps and uncertainties:

> **Terrestrial Plant Seedling Emergence and Vegetative Vigor Tests (850.4100, 850.4150)**: Typical end-use data are required for terrestrial plants. In the case of the new 2,4-D choline salt registrations, no information is available for… the Enlist™ formulation, which is a mixture with glyphosate. For the 2,4-D choline salt-glyphosate formulation, it is anticipated that there could be additive, synergistic, or interference between the two herbicides, which could cause increased or decreased toxicological effects than are predicted by single ai [active ingredient] data. In lieu of these data, toxicity information from other 2,4-D formulations was used as a surrogate; however these surrogates did not contain glyphosate. This represents a point of uncertainty regarding the effects to terrestrial plants in the current analysis. (EPA Environmental 2013a at 67)

Although EPA expresses concern that additive or synergistic effects could operate with the combination of 2,4-D and glyphosate in Enlist Duo, it does not present support from the literature for this phenomenon. There are such studies. Flint and Barrett (1989) showed that the combination of glyphosate with 2,4-D resulted in greater uptake of 2,4-D and more accumulation of both herbicides in the roots of field bindweed (*Convolvulus arvensis*), resulting in more control of this perennial broadleaf weed with the mixture than with either herbicide alone. They stated that similar additive or synergistic weed control with glyphosate and 2,4-D combined had been reported for Canada thistle (*Cirsium arvense*) and honeyvine milkweed (*Ampelamus albidus*, now *Cynanchum laeve*). Considering either herbicide alone, as EPA does in assessing this registration action, would result in an underestimate of risks of the combination of 2,4-D and glyphosate to plants.

EPA briefly responds to commenters who expressed concern that glyphosate was not being assessed in combination with 2,4-D, and answers that glyphosate is already registered for use on corn and soybeans with the same use pattern proposed for Enlist Duo on Enlist corn and soybeans, so does not require additional review. EPA also states the public can comment during the general registration review of glyphosate, going on now (EPA Registration 2014 at 24 – 25). Although glyphosate is indeed registered for use on glyphosate-resistant corn and soybeans, if Enlist Duo is registered for use on Enlist corn and soybeans it will result in a new combination of herbicides being used. For corn, the current registration action would result in 2,4-D and glyphosate being applied together post-emergence later in the season than is allowed now, and for soybeans it will allow 2,4-D and glyphosate to be applied together post-emergence for the first time. This combination is a new use pattern and must be assessed.

Other formulation ingredients are ignored by EPA. EPA does not identify lack of information about impacts of surfactants and other so-called inert ingredients as a deficiency for assessing risks to plants or other organisms, nor does EPA discuss relevant scientific literature showing that such ingredients can increase the toxicity of herbicides. This is a serious omission, because many inert ingredients are added to herbicide formulations specifically to increase toxicity to plants:

> Adjuvants or surfactants are substances added or to be added to the active ingredients of pesticides. They are mostly used with herbicides to affect their behavior through changes in the pattern of the droplet spray deposition and by enhancing the retention and uptake efficiency of the active ingredient [13,14]. The addition of adjuvants/ surfactants can reduce the effective herbicide dose several fold [15,16], up to 10 times [17]. … While past research with a number of herbicides has shown that different formulations exert different effects on crops and weeds (and presumably on nontarget plant species) and can result in different toxicity between formulations [18–22], this has not been taken into account in phytotoxicity testing for regulatory risk assessment. (White and Boutin 2007 at 2634)

White and Boutin (2007) compared the toxicity of glyphosate active ingredient alone with a glyphosate formulation to variety of terrestrial plants, both crops and weeds. They used the inhibition concentration (IC25), defined as the dose that resulted in a 25% reduction in biomass, as a measure of toxicity:

> Table 2 shows the IC25 for each species and treatment with Round-Up Original [formulation] and glyphosate in active ingredient form. For all species for which it could be calculated, the IC25 was much lower for the formulated product than it was for the active ingredient alone, indicating that glyphosate is much less toxic to the species tested than the formulated product Round- Up Original. (White and Boutin 2007 at 2637)

Based on their own studies and on cited literature, these researchers conclude that toxicity testing with active ingredients alone likely underestimates risks:

> Nonetheless, the results gathered in the present study, together with previous research [15,16,19– 22], strongly suggest that pesticide registration guidelines should expand to consider the toxicity of the formulated products, along with any surfactants or adjuvants that may be added if these chemicals are listed on the herbicide label. Since active ingredients are not used alone and neither are the additives, toxicity data should consider the possible synergistic effects of these chemicals and expand to require data for the tankmix of formulated products; otherwise, their toxicity may be greatly underestimated. (White and Boutin 2007 at 2641)

Formulations have also been shown to be more toxic to animals, including humans, in some studies. According to Cox and Surgan (2006), in some cases, increased toxicity in formulations results from interactions between the active ingredient and adjuvants, in other cases increased toxicity is primarily due to adjuvants alone.

They conclude that inert "ingredients can increase the ability of pesticide formulations to affect significant toxicological end points, including developmental neurotoxicity, genotoxicity, and disruption of hormone function. They can also increase exposure by increasing dermal absorption, decreasing the efficacy of protective clothing, and increasing environmental mobility and persistence. Inert ingredients can increase the phytotoxicity of pesticide formulations as well as the toxicity to fish, amphibians, and microorganisms."

In the end, EPA's failure to consider increased toxicity of formulations and to test for such effects means that risks may be significantly underestimated, and thus mitigation measures cannot be relied upon.

For example, using data from other forms of 2,4-D as surrogates for 2,4-D choline salt and the 2,4-D choline and glyphosate formulation, EPA found that risk quotients for all terrestrial plants exceeded the level of concern:

> As is expected with herbicides, terrestrial plants are sensitive to 2,4-D residues. All terrestrial plant risk quotients exceeded the LOC (1.0). Risk quotients ranged from 1 to 90.62 for monocots and 12.35 to 1085.11 for dicots. Risk was attributed to both spray drift and runoff from treated fields. Thus, the risk quotient analysis indicates that effects are predicted from the proposed new uses of 2,4-D choline salt to terrestrial plants. (EPA Registration 2014 at 17)

EPA proposes to mitigate these predicted risks to plants by requiring a 30 foot buffer zone (EPA Registration 2014 at 29) and drift-reducing nozzles (EPA Registration 2014 at 27). As discussed in these comments in relation to drift, EPA has not adequately assessed these mitigation measures. Also, the proposed mitigation measures focus on spray drift, and do not address risks from runoff or vaporization. Fundamentally, though, EPA is unable to determine whether particular mitigation measures are adequate for plants because they do not have data on how toxic the formulation is to plants so cannot model protective measures.

As a result, not only are risks to plants unable to be determined, but also indirect risks to all other organisms are unable to be determined by EPA because all species depend on plants. EPA defines indirect effects to listed species, and the definition is the same for non-listed species:

> Indirect effects to a listed [or non-listed] species occur when its prey base is reduced or habitat is modified; <u>indirect effects are assumed for all taxa based on potential effects to terrestrial plants</u> and obligate relationships with birds and/or mammals. (EPA Environmental 2013a at 67)

In other words, EPA is unable to determine if there are adverse effects to animals if it cannot determine if there are adverse effects to plants. Reliance on mitigation measures that were determined using insufficient information is unacceptable.

Indirect effects are every bit as adverse as direct effects. For example, below we discuss the indirect adverse effects on monarch butterflies of glyphosate use on glyphosate-resistant corn and soybeans that has decimated the host plants of monarchs in their main breeding areas. The monarch butterfly population has declined precipitously as a result of this indirect effect of herbicide use on resistant crops (CFS Enlist Duo 2012 at 48 - 49, CFS Enlist EIS 2014b at 12 - 20).

EPA's proposal to register Enlist Duo for use on Enlist corn and soybeans is premature without being able to assess risks and determine adverse effects to plants, and thus indirect effects to all taxa.

Metabolism of 2,4-D within Enlist corn and soybeans creates a new route of exposure to residues and metabolites that EPA does not address.

If EPA registers Enlist Duo for use on Enlist corn and soybeans, there will be a new route of exposure to toxic 2,4-DCP for both terrestrial and aquatic organisms via 2,4-DCP conjugates that accumulate in the tissues of these plants.

Basically, the genetically engineered enzyme in Enlist corn and soybeans that confers resistance to 2,4-D does so by metabolizing 2,4-D to 2,4-DCP, which is then converted almost entirely to glycoside conjugates of DCP, as we describe in detail in previous comments (CFS Enlist Soybean 2012 at 84 – 92, CFS Enlist Duo 2012 at 39 - 43). The levels of conjugated DCP can be quite high. Free DCP is likely to be liberated from these conjugates during digestion in animals that eat the tissues, and by detrivores as the tissues are broken down during decay processes. EPA does not cite or discuss the relevant scientific studies that support inclusion of 2,4-DCP conjugates – the major metabolites of 2,4-D in Enlist corn and soybeans – in risk assessments.

Although independent peer-reviewed studies provide evidence that 2,4-DCP is released when animals digest conjugates, toxicity of the conjugates when delivered to animals via ingestion of plant tissues has not been studied. It is possible that the conjugates themselves are toxic, or that they are toxic only to the extent that 2,4-DCP is released during digestion (CFS Enlist Soybean 2012 at 87, CFS Enlist Duo 2012 at 41). This needs to be ascertained.

There are studies showing that insects may be more sensitive to 2,4-DCP than 2,4-D, potentially putting pollinators and other beneficial insects at risk (CFS Enlist Soybean 2012 at 88 – 89). Since 2,4-D is translocated throughout the plant from the site of application to growing tissues, and the engineered enzyme is likely to be expressed throughout the plant as well, we expect that DCP conjugates will accumulate in pollen, nectar, and guttation liquid, where honeybees and other pollinators will be exposed (CFS Enlist Duo at 44 – 48) .

Herbivores and detritivores will also be exposed to these new metabolites via 2,4-D resistant plant tissues (CFS Enlist Soybean at 87).

Therefore, in order to do an ecological risk assessment, EPA not only needs to know the fate and toxicity of 2,4-D, but also the fate and toxicity of the novel metabolites and degradates of 2,4-D in plant tissues engineered to be resistant to 2,4-D.

EPA must fill these data gaps in order to assess environmental risks. Levels of DCP conjugates in vegetative tissues at various times after 2,4-D applications need to be reported, along with fate of the DCP conjugates during tissue decomposition when leaves, stems and roots decay in soil or water. Levels of DCP conjugates in pollen, nectar, and guttation liquid need to be determined in order to assess risk to pollinators, comparing results to 2,4-D and metabolites in the same tissues of 2,4-D treated, non-engineered plants. Data needs also include toxicity of DCP conjugates to various taxa, with particular attention to toxicity to honeybees and other pollinators.

EPA does not consider risks to species beneficial to agriculture

In weighing costs of Enlist Duo use with Enlist corn and soybeans, EPA does not specifically consider effects on organisms beneficial to agriculture, in spite of the large social and economic impacts of this sector of the economy. For example, the registration action may affect, among other beneficial organisms, pollinators and other important insects, microorganisms such as nitrogen fixing bacteria, and mammals and birds important to agriculture.

<u>Beneficial microorganisms</u>

Beneficial microorganisms include species in the rhizosphere of corn and soybeans, and on leaf and stem surfaces that mediate nutrient relationships, diseases, and environmental stresses. Also, soil microbes are involved with decomposition, nutrient cycling, and other functions (Cheeke et al. 2013). EPA does not mention or consider beneficial microorganisms in any context, even though pesticides are known to affect them in some cases (e.g. Ahemad and Khan 2013).

Soybeans have a symbiotic relationship with the specific rhizobium bacterium *Bradyrhizobium japonicum* in the family Rhizobiaceae, which induces soybean roots to form nodules where the bacteria live and perform the reduction of atmospheric nitrogen into ammonia that can be used by plants. In fact, most soybean growers do not apply nitrogen fertilizers, since usually all nitrogen needed for plant growth is obtained from the association of soybeans with symbiotic rhizobia and nitrogen already available in the soil (Ruark 2009).

Enlist soybeans are the first broadleaved plant that will be sprayed directly with 2,4-D, and also the only genetically engineered crop that harbors symbiotic nitrogen-fixing bacteria. Therefore, it is crucial that EPA analyzes and assesses risks to rhizobium and the nitrogen fixation process of using Enlist Duo with Enlist soybeans under realistic field conditions.

Both 2,4-D and glyphosate have been shown to influence nitrogen fixation in some situations (as reviewed in Ahemad and Khan 2013). In fact, glyphosate use on glyphosate-resistant soybeans has been shown to impair nitrogen-fixing bacteria in some circumstances (Zablotwicz and Reddy 2007, Kremer and Means 2009, Zobiole et al. 2010, Bohm et al. 2009). The combination of 2,4-D and glyphosate in Enlist Duo applied to Enlist soybeans and then moving systemically to nodules may therefore have a greater impact on nitrogen fixation than either herbicide alone or and must be tested.

If new use of Enlist Duo with Enlist soybeans does lead to a reduction in nitrogen fixation in soybeans, then soybean growers may need to add more nitrogen fertilizer to their fields, with increased socioeconomic costs and environmental impacts.

<u>Beneficial mammals and birds</u>
Some mammals and birds are beneficial to agriculture, including corn and soybeans. For example, some rodents eat weed seeds, reducing the weed seed bank (EFSA 2005), or become food for predators that control pest species. Other mammals, such as bats, reduce insect pests, and may provide billions of dollars of services to US agriculture each year (Boyles et al. 2011, 2013). Some birds also control agricultural pests and provide other ecosystem services (Whelan et al. 2008).

EPA found that risks for mammals exceeded its level of concern (LOC) for both chronic and acute exposures (EPA Registration 2014 at 17):

> Risk quotients for mammals exceeded the Agency's LOCs for mammals for acute dose-based exposure and chronic dose-based and dietary-based exposure. The chronic dose-based LOC (1.0) was exceeded for all size classes of mammals consuming all food items except for seeds. The chronic dietary-based LOC (1.0) was exceeded for diets of short grass, tall grass, broadleaf plants, and arthropods for mammals…. The acute LOC (0.5) was exceeded only for small mammals consuming short grass.

EPA also predicted indirect effects for mammals, "based on the risk quotients that exceeded the non-listed mammal LOC, terrestrial plants, and birds. Indirect effects may occur when mammals depend on a terrestrial plant, bird, or other mammal that is adversely affected by 2,4-D choline salt. Terrestrial plants provide food and habitat for mammals." (EPA Environmental 2013a at 61)

EPA also found that risks for birds exceeded the LOC for acute exposures, with sublethal effects as well, and has identified data gaps related to bird toxicity studies

(EPA Environmental 2013a at 67). Indirect effects are also likely given dependence of birds on plants, and evidence that herbicides have already degraded and destroyed bird habitat in agricultural areas (e.g. Tappeser et al. 2014 at 37).

Although EPA expects the actual risks to mammals and birds are lower than its assessment (EPA Registration 2014 at 15-16), in fact, risks could be significantly higher since EPA only assessed dietary exposure to 2,4-D and not other routes of exposure, did not use the full Enlist Duo formulation, and did not include major metabolites 2,4-DCP and conjugates in toxicity testing or analysis. Also, as EPA notes, results of Endocrine Disruptor Screening are not yet available and have not been incorporated into the assessment (EPA Environmental 2013a at 68). In addition, EPA counts on spray drift mitigation measures to reduce both direct and indirect risks (EPA Registration 2014 at 17) without adequately assessing how effectively and reliably those measures will reduce risks, as discussed in these comments in relation to drift.

If new use of Enlist Duo with Enlist soybeans does adversely affect mammals and birds that benefit agriculture, then farmers may need to use more pesticides to control insects and other pests to replace services provided by mammals and birds, with increased socioeconomic costs and environmental impacts.

EPA does not adequately assess risks to honeybees, monarch butterflies, and other pollinators.

Pollinators are beneficial to agriculture and to natural areas, ensuring seed set and fruit development in a wide variety of crops and wild plants. Honeybees are the major domesticated pollinator, and many wild insects and other animals are important pollinators, as well. Pesticides, including herbicides, can affect pollinators by direct toxicity and indirectly via habitat changes. Therefore EPA must assess adverse affects on the environment and weigh the costs of impacts to pollinators of the proposed registration action.

In addition to FIFRA requirements to determine environmental risks and to weigh costs of pesticide registration actions, EPA has new responsibilities to assess impacts of pesticide registration actions on pollinators. The White House has now directed the EPA to work with other federal departments and agencies to create a "federal strategy to promote the health of honey bees and other pollinators", specifically including monarch butterflies:

> Pollinators contribute substantially to the economy of the United States and are vital to keeping fruits, nuts, and vegetables in our diets. Honey bee pollination alone adds more than $15 billion in value to agricultural crops each year in the United States. Over the past few decades, there has been a significant loss of pollinators, including honey bees, native bees, birds, bats, and butterflies, from the environment. The problem is serious and requires immediate attention to ensure the sustainability of our food production

systems, avoid additional economic impact on the agricultural sector, and protect the health of the environment.

> Pollinator losses have been severe. The number of migrating Monarch butterflies sank to the lowest recorded population level in 2013-14, and there is an imminent risk of failed migration. The continued loss of commercial honey bee colonies poses a threat to the economic stability of commercial beekeeping and pollination operations in the United States, which could have profound implications for agriculture and food. Severe yearly declines create concern that bee colony losses could reach a point from which the commercial pollination industry would not be able to adequately recover. The loss of native bees, which also play a key role in pollination of crops, is much less studied, but many native bee species are believed to be in decline. Scientists believe that bee losses are likely caused by a combination of stressors, including poor bee nutrition, loss of forage lands, parasites, pathogens, lack of genetic diversity, and exposure to pesticides.

EPA is co-chair along with USDA of President Obama's Pollinator Health Task Force. The White House specifically directs EPA to assess the effect of pesticides in order to support "increasing and improving pollinator habitat", and health:

> l. The Environmental Protection Agency shall assess the effect of pesticides… on bee and other pollinator health and take action, as appropriate, to protect pollinators... (Presidential Memorandum 2014 at 5 – 6)

This registration action by EPA impacts pollinators, including monarch butterflies, by potentially exposing them and their habitats to pesticides – the herbicides in Enlist Duo used with Enlist corn and soybeans. As CFS has noted in these comments in relation to monarch butterflies, in addition to possible direct impacts, pollinator habitat is likely to be adversely affected by changes in the use pattern of 2,4-D and glyphosate that result from this action. EPA must ensure that registration of Enlist Duo for use on Enlist corn and soybeans does not adversely affect pollinator habitat and that the action supports pollinator health.

Most pollinators are insects, although other taxa such as mammals and birds also pollinate some plants. EPA EPA Environmental 2013a determined that there would be no direct risks to terrestrial insects of the proposed use of 2,4-D choline salt on Enlist corn and soybeans. However, EPA's determination of no direct risks to insects is based on inadequate studies and assumptions, as discussed below. EPA also determined that there was insufficient information to determine if indirect effects are expected, such as habitat loss or degradation, because harm to non-target plants cannot be ascertained at this time (EPA Environmental 2013a at 2). Plants are key components of insect habitats, so EPA cannot find that registration of Enlist Duo would not have unreasonable adverse effects on pollinator habitat. In fact, important habitat for pollinators is likely to be at risk from this action, as we show in relation to monarch butterflies, below.

For environmental assessments, EPA considers insects to be an "ecological entity"– whose survival, growth and reproduction represent "an environmental value that is to be protected". However, the only study EPA uses for determining whether insects will be adversely affected is survival expressed as LD_{50}, based on acute contact toxicity to adult honeybees as surrogates for all terrestrial insects (EPA Environmental 2013a at 26). Only toxicity of the 2,4-D choline salt is considered; the major metabolites 2,4-DCP and conjugates are not included in the risk assessments (EPA Environmental 2013a at 25).

Results from the acute contact toxicity test with young adult honeybees led EPA to classify 2,4-D choline as "practically non-toxic" to terrestrial insects. However, there were several sublethal impacts of the contact exposure, including "lethargy, immobility, loss of equilibrium and hyper excitability" (EPA Environmental 2013a at 46). Sublethal impacts are of particular concern with honeybees and other pollinators, because pesticides have been shown to affect a wide range of processes, sometimes at very low concentrations. Exposure to sublethal concentrations of pesticides is implicated in Colony Collapse Disorder currently decimating honeybees in the US and elsewhere.

EPA does not routinely determine risk quotients for non-target terrestrial insects. EPA states that if they were to quantify such risks, assuming that insects were exposed to 2,4-D choline salt via residues on leaves or by direct contact during applications, "it is unlikely such exposures would be lethal…" (EPA Environmental 2013a at 57). This is the basis for EPA's determination that the registration action poses no direct risks to terrestrial insects.

There are several deficiencies in EPA's risk assessment of direct adverse affects on honeybees and other insects, including:

- Toxicity studies did not use the full formulation, or even a mixture of the two active ingredients, and thus may underestimate impacts of Enlist Duo.
-
- Only contact toxicity of the parent 2,4-D salt was tested, but honeybees and other insects are likely to also be exposed to Enlist Duo by ingestion of residues and metabolites on or within plant tissues and in drinking water. There may be differences in sensitivity to Enlist Duo based on different exposure routes.

- Both 2,4-D and glyphosate move systemically in exposed plants, and residues and metabolites are likely to be present in pollen, nectar and guttation fluid (CFS Enlist Duo 2012 at 45 – 48). There are no data on risks from consuming these plant parts.

- The major metabolites from 2,4-D in Enlist corn and soybeans are 2,4-DCP and its conjugates. Toxicity testing of these metabolites using the oral route of exposure has not been done with any honeybee life stage.

- Only adult honeybees were tested, whereas it is known that other life stages have different routes of exposure and sensitivities to pesticides.

- Sublethal effects were not taken into account, but are vitally important for bee health and fate of the colony.

- Honeybees are the only insect species tested and may not be an appropriate surrogate for all beneficial insects, or even for all bee species.

Many of these deficiencies are addressed in EPA's interim guidelines for assessing risks of pesticides to honeybees (EPA 2011). In addition, EPA submitted a white paper supporting a proposed risk assessment process for pesticide impacts on honeybees to the FIFRA Scientific Advisory Panel in September 2012, and gave specific recommendations (EPA SAP 2012). On June 23, 2014, EPA finalized the guidance for assessing pesticide risks to bees (2014), after this comment period opened. However, EPA did not implement any of the recommended pollinator-specific risk assessments from the interim guidelines or from their white paper in order to determine risks to pollinators of this registration action.

Given the sublethal toxicity of 2,4-D choline in the one test EPA required for honeybees, EPA should include more rigorous testing of Enlist Duo with honeybees in this new use registration. EPA has the flexibility to require additional testing to make up for the deficiencies listed above (40 CFS Part 158.30, as excerpted in NAS 2013 at 112), that would allow it to make an informed determination of whether the registration action will adversely affect honeybees.

Also, although Enlist Duo was registered for use on non-Enlist crop varieties in 2011, CFS has not found evidence of its commercial use, so there will have been no chance for incident reports. Incidents of non-target injury from herbicides are known to be under-reported in any case (CFS Enlist Duo 2012 at 19 – 20). EPA should use its flexibility to require field tests designed specifically to determine whether exposure of pollinators to Enlist Duo in realistic conditions has chronic, sublethal, reproductive or behavioral effects.

EPA did not assess risks to monarch butterflies of registering Enlist Duo for use with Enlist corn and soybeans, in spite of scientific evidence that herbicide use is a main factor in their decline

The recent decline of monarch butterflies (*Danaus plexippus*) is a clear example of harm to non-target organisms from past EPA registration allowing herbicide use on herbicide-resistant corn and soybeans, as CFS commented previously (CFS Enlist Duo 2012 at 48 – 49, CFS Enlist Soybean 2012 at 79 -80, CFS Enlist EIS 2014a at 12 - 20), yet EPA does not analyze adverse effects on monarchs of approving Enlist Duo for use on Enlist corn and soybeans in this registration action. In the time since CFS commented in 2012, the adverse effects on monarchs of herbicide use on herbicide-resistant crops have become even more apparent, as we describe in more detail here.

Monarch numbers in North America are at their lowest since records have been kept, and biologists are concerned that the monarch migration is in jeopardy (Brower et al. 2011, 2012). At their most recent peak in 1997, there were almost a billion monarch butterflies overwintering in oyamel fir trees in the central mountains of Mexico (Slayback et al. 2007). This year, counts indicate an overwintering monarch population of fewer about 33 million, by far the lowest ever measured (Réndon-Salinas and Tavera-Alonso 2014), continuing an alarming 20-year decline of more than 90% (Brower et al. 2011, 2012).

Although there are many factors at play, scientists have shown that the most critical driver of the recent steep decline in monarch butterfly numbers is loss of larval host plants in their main breeding habitat, the Midwest corn belt of the US, as CFS commented previously (CFS Enlist Duo 2012 at 48 – 49, Pleasants and Oberhauser 2012, Flockhart et al. 2014). Monarchs lay eggs exclusively on plants in the milkweed family, and the larvae that hatch from these eggs must consume milkweed leaves to complete the butterfly's lifecycle (Malcolm et al. 1993). Common milkweed (*Asclepias syriaca*) has been largely eradicated from corn and soybean fields where it used to be common (Hartzler 2010, Pleasants and Oberhauser 2012), depriving monarchs of the plant they require for reproduction.

<u>Glyphosate used with glyphosate-resistant corn and soybeans has removed common milkweed from corn and soybean fields, decimating the monarch population</u>

Common milkweed is a perennial plant with shoots that die back in the winter, but re-sprout from buds on spreading roots in the spring to form expanding colonies (Evetts and Burnside 1974, Martin and Burnside 1977/1984, Bhowmik 1994). Common milkweed also regrows when the plants are mowed, chopped by tillers, or treated with many kinds of herbicides that only kill aboveground plant parts, or are applied before milkweed shoots emerge in late spring (Bhowmik 1994). Thus, until recently, common milkweed has been found within and around corn and soybean fields in sufficient numbers to support a large population of monarch butterflies. In fact, in the late 1990s when monarch numbers were still high, almost half of the monarchs in Mexican winter roosts had developed on common milkweed plants in the Midwest corn belt, making this the most important habitat for maintaining the monarch population as a whole (Wassenaar and Hobson 1998).

Recently, though, the widespread adoption of genetically engineered, glyphosate-resistant corn and soybeans has triggered a precipitous decline of common milkweed, and thus of monarchs (Pleasants and Oberhauser 2012). Glyphosate moves throughout the plant – from sprayed leaves into roots, developing shoots and flowers – where it kills milkweed at the root and so prevents regeneration (Waldecker and Wise 1985, Bhowmik 1994).

Glyphosate is particularly lethal to milkweed when used in conjunction with glyphosate-resistant corn and soybeans (patterns of glyphosate use on resistant crops are described in detail in CFS Enlist Soybean 2012 at 6, 14 – 15, 21- 24). It is applied more frequently, at higher rates, and later in the season (during milkweed's most vulnerable flowering stage of growth) than when used with traditional corn and soybeans. The increasingly common practice of growing glyphosate-resistant corn and soybeans every year means that milkweed is exposed to glyphosate every year without respite, and has no opportunity to recover. In fact, in the 15 years since glyphosate-resistant soybeans, and then corn, were approved by APHIS, common milkweed has been essentially eliminated from corn and soybean fields in the major breeding area for monarch butterflies (Hartzler 2010).

The expanding acreage treated with glyphosate reflects the massive adoption of Roundup Ready crops, which in 2013 comprised roughly 90% of soybeans and over 80% of all corn grown in the U.S. (USDA ERS 2014). The rising intensity of glyphosate use (application rate times frequency) reflects farmers' response to the epidemic emergence of glyphosate-tolerant and –resistant weeds. There has also been a dramatic rise in the yearly frequency of acres treated every year with glyphosate**,** as farmers who once grew Roundup Ready soybeans in rotation with conventional corn have now transitioned to Roundup Ready corn as well (USDA ERS 2012, Fig. 3.4.2; USDA ERS 2013). Finally, glyphosate is applied to Roundup Ready crops two weeks to a month or more later in the season than when used with traditional crops (e.g. Monsanto 2009, Section 15.0 compared with Sections 9.2 and 9.8), a period when milkweed is in its most glyphosate-sensitive reproductive phases (Bhowmik 1982, Martin and Burnside 1977-1984, Loux et al. 2001).

This loss of habitat for monarch butterflies, because of near eradication of the only host plant that grows within corn and soybean fields in the Midwest, has been devastating. Fewer corn and soybean fields have milkweed plants, and where they do occur, the plants are more sparsely distributed. By 2012, it is estimated that just over 1% of common milkweed remained in corn and soybean fields in Iowa compared to 1999, just a few hundred combined acres (extrapolated from Pleasants and Oberhauser 2012). It is clear that other Midwestern states have experienced similarly devastating milkweed losses, based on comparable land-use patterns and other evidence.

Besides the small percentage of milkweeds still in corn and soybean fields, milkweeds remain outside of agricultural fields in the Midwest, but there aren't enough of them to support a viable monarch population. The combined area of roadsides, Conservation Reserve Program (CRP) land, and pastures is only about 25% of corn and soybean acreage in Iowa, which is representative of the Corn Belt as a whole (Pleasants and Oberhauser 2012).

In addition, monarchs produce almost four times more progeny per milkweed plant in corn and soybean fields than in non-agricultural areas (Monarch Larval Monitoring Project, as described in Pleasants and Oberhauser 2012), so agricultural milkweed is more valuable as habitat. Thus, even if non-crop lands have a higher density of milkweeds, they cannot begin to compensate for agricultural habitat lost to glyphosate use on glyphosate-resistant corn and soybeans.. Loss of habitat within corn and soybean fields must be reversed to save monarch butterflies.

EPA registration of Enlist Duo for use with Enlist corn and soybeans will continue adverse effects on monarchs from glyphosate in addition to new adverse effects from 2,4-D choline.

Enlist Duo is a mixture of 2,4-D choline and glyphosate, in addition to surfactants and other so-called inert ingredients (EPA Label 2014, EPA Environmental 2013a). Enlist corn and soybeans will therefore not only continue to be sprayed post-emergence with glyphosate, but also with 2,4-D, when common milkweed is in its most vulnerable reproductive stages (Bhowmik 1994). Enlist corn and soybeans are engineered to be extremely resistant to 2,4-D, resulting in farmers using higher application rates since they will not be concerned about harming their crops. Herbicides that cause limited damage to weeds when applied at lower rates are often much more damaging at higher rates. The combination of additional active ingredients applied post-emergence, and use of higher rates, can only accelerate the demise of common milkweed in corn and soybean fields while preventing its reestablishment, especially in view of the fact that glyphosate will continue to be used at rates similar to those used at present on crops resistant to glyphosate alone.

2,4-D is relatively little used in corn and soybean production at present (these comments, and CFS Enlist EIS 2014a at 9 – 11). Both the area treated with these herbicides and the rates used are expected to jump dramatically with registration of Enlist Duo for use on Enlist corn and soybeans.

<u>Efficacy of 2,4-D on common milkweed</u>
2,4-D is a in the synthetic auxin family of herbicides that mimic natural plant hormones and kill broadleaf plants by stimulating abnormal cell growth (EPA Environmental 2013a). 2,4-D is translocated to varying degrees throughout the plant and can suppress regrowth of perennials such as milkweed (Cramer and Burside 1981, Bhowmik 1982, Loux et al. 2001, Zollinger 1998). Although not consistently as effective as glyphosate, particularly for longer-term control, its efficacy is regarded as sufficient to merit recommendations for its use on common milkweed by experienced agronomists at several universities.

<u>Adverse effects of Enlist Duo used with Enlist corn and soybeans on common milkweed</u>

Use of Enlist Duo with Enlist corn and soybeans will greatly exacerbate the negative impacts of 2,4-D on common milkweed for several reasons: higher rates will be used; most applications will occur during milkweed's most vulnerable reproductive phase; most applications will be in combination with glyphosate; much more cropland will be sprayed; and the frequency of use will increase both within season and over years (CFS Enlist Duo 2012)._EPA does not consider these adverse effects on milkweed within the main monarch breeding habitat that will result from registration of Enlist Duo for use on Enlist corn and soybeans.

Herbicide drift injury from Enlist corn and soybean fields to nectar plants
Adult monarch butterflies derive nutrients from a wide variety of nectar-producing flowers (Tooker et al. 2002). They depend for energy on flowers that are in bloom in their breeding habitat during the spring and summer, and then along migration routes to winter roosts (Brower and Pyle 2004, Brower et al. 2006).

Use of herbicides in agricultural landscapes has resulted in changes in flowering plant populations within and around crop fields, with impacts felt throughout ecosystems. It has been shown that "[b]etween 5% (commonly) and 25% (occasionally) of the applied herbicide dose is expected to reach the vegetation in field margins and boundaries (e.g. hedgerows, woodlots, etc.) (Holterman et al., 1997; Weisser et al., 2002)." (Boutin et al. 2014).

Registration of Enlist Duo for use on Enlist corn and soybeans has an even greater potential for causing drift injury, as discussed in these comments, and is likely to have severe impacts on nectar resources used by monarchs and other pollinators (Brower et al. 2006). Hugely increased spray drift, volatilization and runoff from the much greater use of herbicides if Enlist Duo is registered for use on Enlist corn and soybeans, as discussed in these comments, are likely to alter the very habitats important for biodiversity in agroecosystems, such as hedgerows, riparian areas, unmanaged field margins, and other areas where wild organisms live near fields (Freemark and Boutin 1995, Boutin and Jobin 1998, Olszyk et al. 2004, Gove et al. 2007, Blackburn and Boutin 2003). These areas harbor nectar plants for adult monarchs as well as milkweeds for larvae. Also, use of Enlist Duo with Enlist corn and soybeans over a longer span of the growing season will overlap a wider range of developmental stages of nearby plants, hitting them when they may be more sensitive to injury (CFS Enlist Soybean 2012 at 78).

<u>Herbicide drift can alter the composition of plant communities</u>
Particular species of plants are more or less sensitive to specific herbicides (Olszyk et al. 2013, Boutin et al. 2004), and at different growth stages (Carpenter and Boutin 2010, Boutin et al. 2014), so that exposure can change plant population dynamics in affected areas. 2,4-D and other auxin-like herbicides such as dicamba are particularly potent poisons for many species of plants (Rasmussen 2001, US-EPA 2009), especially dicotyledons (broadleaf plants) that are sensitive to very low drift levels. Even monocots such as members of the grass and lily families can be killed

by higher doses of 2,4-D, and suffer sub-lethal injuries from drift levels at certain times in their life cycles (Nice et al. 2004).

Plants – both crop and wild species –are often very sensitive to herbicide injury as flowers and pollen are forming (Olszyk et al. 2004). This has been clearly shown with dicamba and injury to tomato plants (Kruger *et al.* 2012) and soybeans (Griffin et al. 2013), and with glyphosate injury to rice flowers (Wagner 2011). Drift levels of dicamba have also been shown to affect asexual reproduction in potatoes (Olszyk et al. 2010a,b), and seed production in peas (Olszyk et al. 2009), sometimes without accompanying vegetative injury. Glyphosate drift to potato plants has been responsible for causing potato shoots arising from seed potatoes in the next generation to grow abnormally or not at all (Worthington 1985), without always affecting the growth of the potato plants that were actually hit with the herbicide (Potato Council 2008). There are many other examples of differential sensitivity to particular herbicides (Boutin et al. 2014). Injury affecting flowers and vegetative propagules but not the rest of the plant can easily go undetected, nevertheless having a large impact on reproduction and thus subsequent generations.

Differential sensitivity to herbicides can lead to changes in species composition of plant communities. For example, as noted in CFS comments (CFS Enlist Soybean 2012 at 81), 2,4-D movement away from crop fields in mid-spring may kill sensitive dicotyledonous wildflowers at seedling stages, cause male sterility in less sensitive grasses about to flower, and have little effect on younger grasses or still-dormant perennials (Olszyk et al. 2004). These impacts can cause long-term changes in the mix of plant species, favoring annual weeds and grasses over native plants and perennial forbs (broadleaved plants), for example (Boutin and Jobin 1998, Boutin et al. 2008). And if there are herbicide resistant plants in these habitats, they will of course be better able to withstand drift and may become more abundant (Watrud et al. 2011).

Pollinators are at particular risk from changes in plant populations and flowering behavior. Recently published comparisons of flowering plants in natural areas around fields that have been exposed to herbicides on a regular basis versus those near fields managed without herbicides show striking differences in the types and abundance of plants in flower, and also in the time of plant flowering (Boutin et al. 2014). Hedgerows next to organic farms had more species, and many of them flowered earlier in the season and for a longer time span than hedgerows near herbicide-treated fields. These field observations confirmed greenhouse studies that showed significant delays in flowering of several species after exposure to herbicides (Boutin et al. 2014).

Such changes in which plants flower, and when, could affect monarchs as they breed and migrate, disrupting coordination between the butterflies and needed resources (Boutin 2014).

Herbicides selective for broadleaved plants such as 2,4-D adversely affect nectar plants

Herbicides such as 2,4-D that selectively kill dicots may deprive many insects of nectar and pollen, especially with frequent application over a broad area, as would occur with Enlist Duo use with Enlist corn and soybeans. A study of pesticide effects on butterflies in agricultural areas of England makes this point:

> The frequency and number of pesticide applications, the spatial scale of treatment and the degree of field boundary contamination during each spray occasion will determine the extent of damage to butterfly habitats and populations, and the rate at which populations will return to their original densities. (Longley and Sotherton 1997).

These scientists conducted experiments to determine whether restricting the use of "persistent broadleaf herbicides" near field edges would result in more butterflies in the landscape. In one experiment, they sprayed the bulk of the field with the usual complement of pesticides, but modified the spraying apparatus such that only selective grass-killing herbicides were applied to the field edges. They found that there were indeed more butterflies after implementing this measure, and also that there were more flowering plants, "thereby increasing the availability of nectar resources for butterfly species," as well as more biodiversity in general (Longley and Sotherton 1997, pp. 8-9).

The implications of this butterfly study in England are clear for use of Enlist Duo with Enlist corn and soybeans: 2,4-D selectively kills broadleaf plants, the main nectar source for adult butterflies, including monarchs. Enlist Duo also likely to be used more often during a season, more extensively in an area, and more continuously over years with resistant crops than they are currently used in agriculture. This is precisely the use pattern that the studies discussed above suggest would have long-term, harmful effects on butterflies and other species.

In a new study, scientists concerned by the potential impacts of dicamba use on dicamba-resistant crops – an herbicide with a similar mode of action to 2,4-D – tested the effects of dicamba drift on plant and arthropod communities in agricultural "edge" habitats (Egan et al. 2014). These researchers applied a range of dicamba doses to simulate different levels of drift to field margins and to plots within old fields. They sprayed dicamba once each year for two consecutive years, and surveyed plant and arthropod communities throughout the growing seasons, before and after dicamba applications. Egan and colleagues found that low drift levels of dicamba did in fact affect plant and arthropod communities, but in complex ways, depending on the initial successional status of the plant community, and environmental conditions such as water stress during herbicide application. Impacts, including a reduction of broadleaf plants that could lead to less nectar, were observed at substantially lower levels – about 1% of the dicamba field application rate – than have been reported to affect plant communities in other studies.

This study was conservative in design: dicamba alone was applied just once per year over two years, while farmers often make multiple applications of several different herbicides consistently over many years. Thus, the authors urge "a precautionary emphasis on limiting non-target herbicide exposures" while further research is conducted to better simulate agricultural practice. For instance, research is needed on the impacts of simultaneously applying dicamba and glyphosate two to three times per year, since Monsanto will offer a pre-mix formulation of the two herbicides, which could be applied up to three times per year according to the proposed label (CFS 2012c).

Similar cautions apply to Enlist Duo use with Enlist corn and soybeans. By far the best way to protect important nectaring habitat for monarchs is to restrict post-emergence use of such herbicides.

<u>Complementary action of premix herbicide components</u>
Enlist Duo with both 2,4-D and glyphosate will generally kill or injure a broader range of plants more effectively, and over a wider span of plant growth stages, than either herbicide alone. For instance, standard tests conducted for the EPA show that 2,4-D poses a 400- fold greater risk than glyphosate in suppressing seedling emergence of non-target plants; and a 12-fold greater risk of reducing vegetative vigor (Peterson and Hulting 2004). Conversely, glyphosate is more effective than 2,4-D on grass weeds and perennials. In addition, a mixture of 2,4-D and glyphosate has been shown to act synergistically or additively against field bindweed (Flint and Barrett 1989) and Brazil pusley (Sharma and Singh 2001), both perennial broadleaf plants. Surfactants also increase toxicity (Sharma and Singh 2001), as discussed above. Off-site movement of Enlist Duo will thus cause greater harm to field-edge plant communities than herbicides containing either component alone.

EPA regulations do not protect nectar plants from herbicide drift injury
The EPA is charged with regulating the use of pesticides in a manner that protects the environment. However, the frequent occurrence of herbicide drift injury to both sensitive crops and wild plants, as discussed above, demonstrates clearly that EPA regulation is inadequate (see also, Lee et al. 2005, Pfleeger et al. 2012).

In addition to failure of mitigation measures, discussed in detail in these comments in relation to drift, EPA guidelines for protecting non-target plants from drift injury are based on toxicity tests that include too few species, tested at only a few points in their vegetative development, without using the specific end-use formulation, and therefore underestimate the range of sensitivities in communities of wild species throughout their lifecycles (Pfleeger et al. 2012, White and Boutin 2007, Olszyk et al. 2013, Boutin et al. 2014). These deficiencies in assessment of herbicide impacts will put the monarch's nectaring and larval habitats at further risk should EPA register Enlist Duo for use on Enlist corn and soybeans.

Therefore, in order to comply with FIFRA, EPA must take action to reduce adverse effects of herbicide use on herbicide resistant crops. Areas that will yield the greatest expected benefits for monarchs include corn and soybean fields themselves, as these were the most productive breeding areas before glyphosate use on glyphosate resistant corn and soybeans. For pollinators in general, nectar plants and other habitat must be protected.

EPA does not adequately assess risks to federally listed threatened and endangered species

EPA's Memorandum, "Addendum to 2,4-D Choline Salt Section 3 Risk Assessment: Refined Endangered Species Assessment for Proposed New Uses on Herbicide-Tolerant [sic] Corn and Soybean" (EPA ESA 2014), in which EPA incorporates spray drift mitigation measures in its assessment of risk to listed species, concludes that none of the endangered species identified as potentially at-risk in the screening level assessment will be affected given proposed mitigation. This is an invalid determination.

<u>EPA should assess risks to listed species in all relevant states incorporating recent recommendations</u>

First, it is premature for EPA to make "effects" determinations for endangered species in this registration action. EPA plans to do an ESA assessment for registration of Enlist Duo with Enlist corn and soybeans, presumably for all states (Hopkinson 2014, NAS 2013).

National Academy of Sciences published a report "Assessing risks to endangered and threatened species from pesticides" from the Committee on Ecological Risk Assessment Under FIFRA and ESA; Board on Environmental Studies and Toxicology; Division on Earth and Life Studies; and National Research Council (NAS 2013). This report was requested by EPA and the Services to provide guidance on how to come together to assess impacts of pesticides on listed species, using common assumptions and methods that are scientifically sound. It appears that EPA has not used the new process for these six states in this registration action, since key recommendations from that report have not been implemented or acknowledged. Specifically, risks associated with pesticide mixtures have not been assessed, nor have sublethal, indirect and cumulative effects, and surrogate species been analyzed using NAS-suggested criteria (NAS 2013).

For example, EPA is advised to consider cumulative effects as defined ecologically, "in which a cumulative effect is 'the incremental [effect] of [an]action when added to other past, present, and reasonably foreseeable future actions.' In other words, cumulative effects are ones that 'interact or accumulate over time and space, either through repetition or in combination with other effects' (NRC 2003, p. 2)." (NAS 2013 at 72 – 73).

An example of cumulative effects of Enlist Duo use relevant to listed species is the toxicity to pollinators of residues and metabolites of 2,4-D and glyphosate in pollen, nectar and guttation fluids when combined with other toxins present in those foods. For example, many pesticides are commonly found together in pollen (Mullin et al. 2010).

Another example of cumulative effects has to do with aquatic exposure to 2,4-D and glyphosate when these herbicides are used on different crops in the same watershed during a season. EPA's aquatic exposure models (NAS 2013 at 38) estimate environmental concentrations of herbicides and metabolites that may occur from use on crops adjacent to the water body, but "the pesticide fate and transport models do not provide information on the watershed scale; they are intended only to predict pesticide concentrations in bodies of water at the edge of a field on which a pesticide was applied. Different hydrodynamic models are required to predict how pesticide loadings immediately below a field are propagated through a watershed or how inputs from multiple fields (or multiple applications) aggregate throughout a watershed." (NAS 2013 at 41). This is particularly important given the large increase in acreage that will be treated with 2,4-D if EPA registers Enlist Duo for use on Enlist corn and soybeans that will have watershed-level impacts, as discussed in these comments in relation to use patterns and health.

The use of surrogate species to determine risks of Enlist Duo use to other species in a taxon that has many species, is problematic for listed species:

> For example, examination of earlier EPA assessments has revealed a need for EPA to include and consider all available information about the life history of a listed species early in the process, ideally during planning and scoping (Item 1.1.4 in Box 2-1). Although assessment end points might ultimately involve only common surrogate or test species, the inclusion of natural life-history information on the listed species and critical habitat would at least enable a qualitative assessment of the similarities and differences between the listed species and the identified surrogates. (NAS 2013 at 27)

EPA should thus seek out studies that use a variety of crop and wild plant species, such as Carpenter and Boutin (2010), for risk assessments (e.g. NAS 2013 at 93 – 95). Also, EPA needs to call for studies of species other than the designated surrogate when preliminary evidence indicates these species may have different life histories that are subject to different exposures, for example (NAS 2012 at 98).

EPA should uniformly assess risks to listed species in all states that it plans to register Enlist Duo for use on Enlist corn and soybeans, using rigorous, up-to-date procedures informed by NAS recommendations. Therefore, the ESA assessment in this proposed registration action for six states should be withdrawn, and a new comment period instated when the new ESA assessment is complete.

EPA's current ESA assessment for six states is deeply flawed.

EPA assumes that with mitigation measures in place, listed species that are not directly within the fields to which Enlist Duo is applied will not be impacted because all of the herbicide will be confined to these fields: "The assessment assumes spray drift will remain confined to the field and that the action area is limited to the 2,4-D choline treated field." (EPA ESA 2014 at 3). This assumption is invalid, as discussed in our comment section on drift and mitigation.

EPA has determined that without mitigation measures all listed taxa are potentially at risk from direct or indirect effects of using Enlist Duo on Enlist corn and soybeans (EPA Environmental 2013a at 66, Table 32), either because levels of concern are exceeded, or because there is insufficient information to determine risk (EPA Environmental 2013a at 68). Therefore, it is crucial that EPA determine the efficacy and reliability of mitigation measures.

From EPA's decades of experience regulating pesticides, and as abundantly illustrated in the scientific literature, EPA must be aware that mitigation measures do not eliminate off-site movement of pesticides. Proposed mitigation measures are mainly focused on reducing spray drift at the time of application, but significant off-site movement occurs via runoff, wind-blown soil and dust, vaporization, and in rain. In addition, mitigation measures fail at some frequency for a variety of reasons. EPA repeatedly asserts that spray drift will be reduced by proposed buffers, nozzle types, label language regarding weather conditions, and so on, but makes no effort to determine to what level off-site movement will be reduced, taking into account realistic failure rates for spray drift mitigation and all routes by which Enlist Duo will move.

EPA's unrealistic assumption, contrary to scientific evidence, that all Enlist Duo sprayed on Enlist corn and soybeans will remain in the treated fields allows EPA to reduce the number of listed species that could be impacted from 53 listed species that "were identified as potentially at risk (direct or indirect effects) in the six states as a result of the screening-level assessment" (EPA ESA 2014 at 3), to just 4 listed species with habitat directly overlapping Enlist corn and soybean fields. In other words, the majority of listed species that could be injured by spray drift, volatilization or runoff, and that are found in the vicinity of corn and soybean fields but not within the boundaries of the fields, are assumed by EPA to be outside of the "action area."

EPA does not take into account the full Enlist Duo formulation, so direct and indirect risks from surfactants and other so-called "inert" ingredients are ignored, as are risks from glyphosate and any synergistic or additive impacts of the glyphosate and 2,4-D mixture. In particular, mitigation measures protective of listed species cannot be determined or assessed without knowledge of toxicity of Enlist Duo formulation to terrestrial plants, several of which are listed, and upon which many listed species depend, as discussed in relation to environmental effects to non-listed species, above.

Even EPA's assessment of risks to the 4 listed species that they determined inhabit corn and soybean fields is flawed. For example, the analysis of the diet of endangered whooping cranes does not include corn seeds and seedlings (EPA ESA 2014 at 4-5) – foods well known to be consumed by cranes, including whooping cranes (Austin 2012, Lovell 2012, Schramm et al. 2010, ICF 2014), and likely to be highly contaminated with residues, metabolites and other formulation ingredients after spraying. EPA does not consider likely routes of exposure, such as direct exposure American burying beetles may experience when brushing against sprayed foliage, or burrowing in contaminated soil (EPA ESA 2014 at 5). Nor does EPA consider populations of its four identified listed species that are being reintroduced or expanding ranges into areas of the six states where corn and soybeans are grown, such as whooping cranes in the eastern migrating population (Operation Migration 2014), or American burying beetles being reintroduced in Ohio and other states (FWS 20l4).

EPA underestimates risks to listed species such as the Indiana bat of eating contaminated insect prey, because EPA does not take into account toxicity of 2,4-DCP conjugates that may accumulate in insects that eat sprayed foliage (as discussed above in relation to risks to non-listed species and to beneficial organisms; EPA ESA 2014 at 11).

In conclusion, EPA's entire ESA assessment should be redone in light of new EPA procedures that take into account National Academy of Sciences recommendations (NAS 2013), and also because the current ESA assessment is not based on sound science and makes unwarranted assumptions that significantly underestimate risks to listed species.

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