CENTER FOR FOOD SAFETY

Dicamba: New Use on Herbicide-Tolerant Cotton and Soybeans
Environmental Protection Agency, Mailcode 28221T
1200 Pennsylvania Ave., NW
Washington, D.C. 20460

Docket No. EPA-HQ-OPP-2016-0187

Comments on the Proposed Unconditional Registration for the New Uses of Dicamba on Genetically Engineered, Dicamba-Resistant Soybean and Cotton

The Center for Food Safety (CFS) hereby submits the following comments on the United States Environmental Protection Agency (EPA or the Agency)'s proposed unconditional registration for the new uses of the herbicide dicamba on genetically engineered (GE), dicamba-resistant soybean and cotton. The proposed new uses will be added to Monsanto Company's currently registered herbicide product M1691 (EPA Registration No. 524-582), which contains 58.1% of the active ingredient dicamba, diglycolamine salt (dicamba or dicamba DGA) for both pre- and post-emergence applications to Monsanto's dicamba-resistant soybean and cotton.

CFS is a national, nonprofit public interest and environmental advocacy organization working to protect human health and the environment by curbing the use of harmful food production technologies. In furtherance of this mission, CFS uses legal actions, groundbreaking scientific and policy reports, books and other educational materials, and grassroots campaigns, on behalf of its nearly 750,000 members. CFS is a recognized national leader on the issue of GE organisms and pesticides, and has worked on improving their regulation and addressing their impacts continuously since the organization's inception in 1997.

The comments submitted by CFS herein also incorporate by reference and supplement the detailed legal and scientific comments and supporting reference materials and studies that CFS submitted at earlier stages of this agency proposal, specifically, the 2012 notice of receipts of new use applications published by EPA, Docket No. EPA-HQ-OPP-2012-0841. CFS will not duplicate and repeat comments that it has already submitted numerous times, nor the detailed critiques and demands for lawful compliance and proper scientific analysis that EPA has yet to answer, address, or explain. Rather, these comments will incorporate previously unaddressed points and add to them with further deficiencies in EPA's proposed new use registration.

As explained in detail in CFS's previous comments and the comments submitted herein, EPA's proposed registration of dicamba for use on dicamba-resistant cotton and soybean violates all applicable statutes, specifically, the Agency's duties under the Federal

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Insecticide, Fungicide, and Rodenticide Act (FIFRA), the Federal Food, Drug, and Cosmetic Act (FFDCA), the Migratory Bird Treaty Act (MBTA), and the Endangered Species Act (ESA). EPA's assessment underestimates the true costs of the proposed new use registration, relies on erroneous assumptions and uncertainties, as well as unenforceable mitigation measures. EPA has not made the requisite finding, mandated under FIFRA, to approve the proposed registration of dicamba on dicamba-resistant GE cotton and soybean. Similarly, EPA's approach to assessing effects to listed species is contrary to the ESA's legal mandate. EPA's current assessment fails to consider available data and literature that identify the significant environmental, human health, and socioeconomic risks of the proposed new uses, as well as effects to listed species and their critical habitats. The proposed registration of dicamba for use on dicamba-resistant cotton and soybean would not only result in unreasonable adverse effects to the environment, but will also jeopardize federally protected species and their critical habitats. Rather than approving the proposed new uses of dicamba on dicamba-resistant, GE cotton and soybean, EPA must cure the numerous legal and scientific deficiencies in their current risk assessments.

RELEVANT LEGAL STANDARDS

The Federal Insecticide, Fungicide, and Rodenticide Act

FIFRA authorizes EPA to regulate the registration, use, sale, and distribution of pesticides in the United States. FIFRA defines pesticides broadly to include herbicides—"any substance or mixture of substances intended for use as a plant regulator, defoliant, or desiccants."[1] Under FIFRA, EPA is "charged to consider the effects of pesticides on the environment."[2]

Pursuant to FIFRA, EPA oversees both initial registration of an active ingredient as well as any new uses of the registered active ingredient of a pesticide. FIFRA mandates that prior to approving any pesticide registration and any new uses of the pesticide, EPA consider the "impacts on human health, occupational risks, and environmental risks"[3] of the proposed pesticide formulation and its proposed uses. FIFRA "protects human health and prevents environmental harms from pesticides" by requiring EPA to conduct a risk-benefit analysis of the pesticides.[4] Under FIFRA, EPA cannot register the pesticide unless EPA concludes that the proposed new use "will not generally cause unreasonable adverse effects on the environment" when "perform[ing] its intended function" and "when used in accordance with widespread and commonly recognized practice."[5] FIFRA defines "unreasonable adverse effects on the environment" as "<u>any</u> unreasonable risk to man or the environment, taking into account the economic, social, and environmental costs and

[1] 7 U.S.C. § 136(u)(2).
[2] *Fairhurst v. Hagener*, No. CV-03-67-BU-SHE, 2004 U.S. Dist. LEXIS 30161, at *49 (D. Mont. Mar. 24, 2004).
[3] EPA, Overview of Risk Assessment in the Pesticide Program (May 9, 2012), at http://www.epa.gov/pesticides/about/overview_risk_assess.htm.
[4] *Wash. Toxics Coalition v. EPA*, 413 F.3d 1024, 1032 (9th Cir. 2005).
[5] 7 U.S.C. § 136a(c)(5).

benefits of the use of any pesticide."[6] FIFRA defines "environment" broadly to include "water, air, land, and all plants and man and other animals living therein, and the interrelationships which exist among these."[7] In sum, FIFRA's broad statutory definition of the phrase "unreasonable adverse effects on the environment" mandates that EPA consider all economic, social and environmental risks, including risks that are interrelated and indirect results of the proposed registration, in the agency's review of a proposed registration.

Section 3(c) of FIFRA states that a manufacturer must submit an application to register the use of a pesticide.[8] Section 3(c) of FIFRA outlines two types of pesticide use registrations: unconditional or conditional.[9] Under Section 3(c)(5) of FIFRA, EPA shall register a pesticide if the agency determines that the pesticide "will perform its intended function without unreasonable adverse effects on the environment" and that "when used in accordance with widespread and commonly recognized practice[,] it will not generally cause unreasonable adverse effects on the environment."[10] EPA may also conditionally register a pesticide or proposed new use conditionally, under section 3(c)(7) of FIFRA. Of relevance to the present applications to register dicamba for uses on dicamba-resistant, GE cotton and soybean, EPA may conditionally amend the existing dicamba registration if EPA determines that "the pesticide and proposed use are identical or substantially similar to any currently registered pesticide and use therefor, or differ only in ways that would not significantly increase the risk of unreasonable adverse effects on the environment," and that "approving the registration or amendment in the manner proposed by the applicant would not significantly increase the risk of any unreasonable adverse effect on the environment."[11] Alternatively, EPA "may conditionally amend the registration of a pesticide to permit additional uses of such pesticide," but only if EPA concludes that "the applicant has submitted satisfactory data pertaining to the proposed additional use," and that "amending the registration in the manner proposed by the applicant would not significantly increase the risk of any unreasonable adverse effect on the environment."[12]

Alternatively, where there are data gaps and missing information, EPA can register a pesticide with conditions (conditional registration) under Section 3(c)(7) of FIFRA "for a period reasonably sufficient for the generation and submission of required data," but only if EPA also determines that the conditional registration of the pesticide during that time period "will not cause any unreasonable adverse effect on the environment, and that use of the pesticide is in the public interest."[13]

FIFRA also mandates that, as part of the registration of a pesticide and its proposed

[6] 7 U.S.C. § 136(bb) (emphasis added).
[7] 7 U.S.C. § 136(j).
[8] 7 U.S.C. § 136a(c)(1); 40 C.F.R. § 152.42.
[9] 7 U.S.C. § 136a(c)(5), (7).
[10] 7 U.S.C. § 136a(c)(5).
[11] 7 U.S.C. § 136a(c)(7)(A).
[12] 7 U.S.C. § 136a(c)(7)(B).
[13] 7 U.S.C. §136a(c)(7)(C).

uses, EPA shall classify the pesticide and its use as either "general use" or "restricted use."[14] Under FIFRA, EPA must classify a pesticide and its proposed use as "restricted use" if "the pesticide, when applied in accordance with its directions for use, warnings and cautions and for the uses for which it is registered, or for one or more of such uses, or in accordance with a widespread and commonly recognized practice, may generally cause, without additional regulatory restrictions, unreasonable adverse effects on the environment, including injury to the applicator."[15]

The culmination of the registration process is EPA's approval of a label for the pesticide, including use directions and appropriate warnings on safety and environmental risks. It is a violation of FIFRA for any person to sell or distribute a "misbranded" pesticide.[16] A pesticide is misbranded if the "labeling accompanying it does not contain directions for use which … if complied with … are adequate to protect health and the environment."[17]

The Federal Food, Drug, and Cosmetic Act

The FFDCA[18] prohibits the introduction of "adulterated" food into interstate commerce.[19] The Act requires that where use of a pesticide will result in any pesticide residue being left on food, the EPA must either set a "tolerance" level for the amount of allowable pesticide residue that can be left on the food, or set an exemption of the tolerance requirement.[20] The tolerance or exemption requirements apply to raw agricultural commodities such as dicamba-resistant cotton and soybean.[21]

The FFDCA mandates EPA to "establish or leave in effect a tolerance for a pesticide chemical residue in or on a food only if the EPA Administrator determines that the tolerance is safe".[22] For a tolerance level to be "safe," the statute requires EPA determine "that there is a reasonable certainty that no harm will result from aggregate exposure to the pesticide chemical residue, including all anticipated dietary exposures and all other exposures for which there is reliable information."[23] "Aggregate exposure" includes not only dietary exposure through food consumption, but also exposure from all nonoccupational sources, including "exposures through water and residential uses," as well as the cumulative effects of the particular pesticide's residues "and other substances that have a common

[14] 7 U.S.C. § 136a(d)(1)(A).
[15] 7 U.S.C. § 136a(d)(1)(C).
[16] 7 U.S.C. § 136j(a)(1)(E).
[17] 7 U.S.C. § 136(q)(1)(F).
[18] 21 U.S.C. § 301 *et seq.*
[19] 21 US.C. § 331.
[20] 21 U.S.C. § 346a(1).
[21] 21 U.S.C. § 321(r) defines "raw agricultural commodities" as "any food in its raw or natural state, including all fruits that are washed, colored or otherwise treated in their unpeeled natural form prior to marketing."
[22] 21 U.S.C. § 342a(2)(A) (emphasis added); *see also* 40 C.F.R. § 180.1(f).
[23] 21 U.S.C. § 346a(2)(A)(ii).

mechanism of toxicity." [24] The Act further requires that, in determining the "safe" tolerance level, EPA must specifically consider potential routes of exposure to infants and children, and apply additional margin of safety for the pesticide residue and other sources of exposure to ensure that the tolerance level will be safe for infant and children.[25]

The 1996 passage of the Food Quality Protection Act ("FQPA"), Pub. L. No. 104-170, 110 Stat. 1489, amended EPA's statutory duties under both FIFRA and the FFDCA. Specifically, the FQPA mandates that EPA gives extra consideration to account for risks to infants and children from pesticide exposure.[26] As such, the FFDCA directs that in determining the tolerance level, "an additional tenfold margin of safety for the pesticide residue and other sources of exposure shall be applied … with respect to exposure to toxicity to infants and children."[27] However, the presumptive 10X FQPA safety factor is not always required; the FFDCA provides that the EPA "*may* use a different margin of safety for the pesticide chemical residue," but "only if, on the basis of reliable data, such margin will be safe for infants and children."[28]

Endangered Species Act

As recognized by the Supreme Court, the ESA is "the most comprehensive legislation for the preservation of endangered species ever enacted by any nation."[29] The ESA's statutory scheme "reveals a conscious decision by Congress to give endangered species priority over the 'primary missions' of federal agencies."[30] Federal agencies are obliged "to afford first priority to the declared national policy of saving endangered species."[31]

Section 7(a)(2) of the ESA requires every federal agency to consult the appropriate federal fish and wildlife agency—Fish and Wildlife Service (FWS), in the case of land and freshwater species and the National Marine Fisheries Service (NMFS) in the case of marine species—to "insure" that the agency's actions are not likely "to jeopardize the continued existence" of any listed species or "result in the destruction or adverse modification" of critical habitat.[32]

The ESA's implementing regulations broadly define agency action to include "all activities or programs of any kind authorized, funded or carried out … by federal agencies," including the granting of permits and "actions directly *or* indirectly causing modifications to the land, water or air."[33] The scope of an action, or "action area," is also broadly defined,

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[24] 21 U.S.C. § 346a; *see Natural Res. Def. Council v. Whitman*, No. C 99-03701-WHA, 2001 WL 1221774 (N.D. Cal. Nov. 7, 2001).
[25] 21 U.S.C. § 346a(c).
[26] *See* 21 U.S.C. § 346a(b)(2)(C).
[27] *Id.*
[28] *Id.* (emphases added).
[29] *Tenn. Valley Authority v. Hill*, 437 U.S. 153, 180 (1978).
[30] *Id*. at 185.
[31] *Id.*
[32] 16 U.S.C. § 1536(a)(2); *see also* 50 C.F.R. § 402.01(b).
[33] 50 C.F.R. § 402.02 (emphasis added).

and includes "all areas to be affected directly or indirectly by the federal action and not merely the immediate area involved in the action."[34] The potential "effects" of an action that an agency must consider are similarly broad, and include both "direct" and "indirect" effects of the action and all activities "interrelated or interdependent" with that action.[35] Finally, a species' "critical habitat" includes those areas identified as "essential to the conservation of the species" and "which may require special management considerations or protection."[36]

FWS and NFMS have adopted joint regulations governing the Section 7(a)(2) consultation process. Every federal agency, using the "best scientific and commercial information available,"[37], must first determine whether its actions—here, EPA's proposed registration of dicamba use on dicamba-resistant GE cotton and soybean—"may affect" any listed species or designated critical habitat, and if so initiate a Section 7(a)(2) consultation with NMFS or FWS.[38] The threshold for a "may affect" determination is very low, and includes "any possible effect, whether beneficial, benign, adverse, or of an undetermined character."[39]

The ESA requires each federal agency that plans to undertake an action to request information from the expert agency "whether any species which is listed or proposed to be listed [as an endangered species or a threatened species] may be present in the area of such proposed action."[40] If FWS/NMFS advises the agency that listed species or species proposed to be listed may be present, the agency must then prepare a biological assessment for the purpose of identifying any such species that are likely to be affected by the proposed agency action.[41] If, based on a biological assessment, an agency determines that its proposed action may affect any listed species and/or their critical habitat, the agency generally must engage in consultation with FWS/NMFS.[42]

ESA consultation may in some cases be informal.[43] If, after informal consultation, the expert federal wildlife agency concurs in writing that the action is "not likely to adversely affect" any listed species or critical habitat, the process ends.[44] Otherwise, the agency must enter formal consultation.[45] Formal consultation "is a process between the Service and the [f]ederal agency that commences with the [f]ederal agency's written request for consultation under section 7(a)(2) of the Act and concludes with the Service's issuance of

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[34] *Id.*
[35] *Id.*
[36] 16 U.S.C. § 1532(5)(A).
[37] 16 U.S.C. § 1536(a)(2).
[38] 50 C.F.R. § 402.14(a).
[39] *See* 51 Fed. Reg. 19,926, 19,949 (June 3, 1986) (Codified at 50 C.F.R. pt. 402).
[40] 16 U.S.C. § 1536(c)(1); *see also* 50 C.F.R. § 402.12(c).
[41] *Id.*
[42] 50 C.F.R. § 402.14.
[43] 50 C.F.R § 402.13(a).
[44] 50 C.F.R. § 402.14(b).
[45] 50 C.F.R. § 402.14(a).

the biological opinion under section 7(b)(3) of the Act."[46] At the end of the formal consultation, FWS/NMFS must provide the agency with a "biological opinion" detailing how the proposed action will affect the threatened and endangered species and/or critical habitats.[47] If FWS/NMFS concludes that the proposed action will jeopardize the continued existence of a listed species or result in the destruction or adverse modification of critical habitat, the biological opinion must outline "reasonable and prudent alternatives" to the proposed action that would avoid violating ESA section 7(a)(2).[48]

Pending the completion of formal consultation with the expert agency, an agency is prohibited from making any "irreversible or irretrievable commitment of resources with respect to the agency action which has the effect of foreclosing the formulation or implementation of any reasonable and prudent alternative measures."[49]

Migratory Bird Treaty Act

The Migratory Bird Treaty Act (MBTA) implements the obligations of the U.S. under several international treaties and conventions for the protection of migratory birds.[50] The MBTA mandates that proposed projects must avoid the take of migratory birds entirely and must minimize the loss, destruction, and degradation of migratory bird habitat.[51] The vast majority of U.S. native birds are protected under the MBTA, even those that do not participate in international migrations.[52] Under the MBTA, "[n]o person may take, possess, import, export, transport, sell, purchase, barter, or offer for sale, purchase, or barter, any migratory bird, or the parts, nests, or eggs of such bird except as may be permitted under the terms of a valid permit."[53]

COMMENTS

As analyzed in detail below and CFS's previously-submitted comments and supporting documents to Docket No. EPA-HQ-OPP-2012-0841, EPA's proposed new use registration of dicamba for use on Monsanto's dicamba-resistant GE cotton and soybean mark a significant departure from existing use patterns of dicamba on existing varieties of cotton and soybean. The novelty of the proposed new use on two widely planted agricultural crops in the United States demands that EPA carefully consider all of the "economic, social, and environmental costs" against any purported benefits associated with the proposed new uses in its risk assessments.[54] Under FIFRA, EPA cannot approve the proposed new use of dicamba on dicamba-resistant GE cotton and soybean if the Agency's assessment reveals that the proposed registration may result in unreasonable adverse

[46] 50 C.F.R. Id. § 402.02.
[47] 16 U.S.C. § 1536(b); 50 C.F.R. § 402.14.
[48] 16 U.S.C. § 1536(b)(3)(A).
[49] 16 U.S.C. § 1536(d).
[50] 16 U.S.C. § 701.
[51] *Id.* § 701–12.
[52] *See* 50 C.F.R. § 10.13.
[53] *Id.* § 21.11.
[54] 7 U.S.C. §136(bb).

effects on the environment. EPA must also ensure that "there is a reasonable certainty that no harm to humans, including sensitive populations, will result from aggregate exposure" to dicamba.[55]Separately, the ESA requires that EPA consult the appropriate federal expert agency to "insure" that the agency's actions are not likely "to jeopardize the continued existence" of any listed species or "result in the destruction or adverse modification" of critical habitat.[56] The MBTA mandates that proposed projects must avoid the take of migratory birds entirely and must minimize the loss, destruction, and degradation of migratory bird habitat.[57] EPA's current assessments fail to meet these statutory duties. To the contrary, EPA's assessments demonstrate that the proposed new uses of dicamba would result in unreasonable adverse effect on the environment, to the detriment of threatened and endangered species and their critical habitats. EPA must revise and supplement its current risk assessments, and conduct the requisite ESA consultation, before moving forward with the proposed approval of dicamba use on dicamba-resistant GE cotton and soybean.

I. EPA's Assessment of the Impacts to Threatened and Endangered Species from the Proposed New Uses of Dicamba on Dicamba-Resistant GE Cotton and Soybean Is Legally Deficient.

EPA's assessment of the potential risks to federally listed threatened and endangered species from the proposed approval is legally deficient, in violation of the ESA and FIFRA. EPA's current assessment is unlawful because the Agency improperly assumed that some level of effect to listed species is acceptable. Despite initially finding that exposure to the proposed new uses of dicamba carried great risks for numerous federally listed and threated species, the Agency unilaterally eliminated its "may affect" finding and instead switched to "no effect" determinations by narrowing the "action area" and relying on unrealistic mitigation measures such as buffer zones. EPA's approach here violates the ESA, as well as the agency's stated approach in assessing pesticide risks to listed species. EPA also failed to adequately consider various direct and indirect effects to non-target species, including listed species, such as exposure to dicamba from drift, volatilization, other forms of dicamba degradation and contamination of the environment, as well as synergistic effects of dicamba toxicity when used with other pesticides.[58] EPA's lack of sufficient analysis violates the Agency's duty under the ESA and FIFRA.

First, EPA's current approach to considering potential impacts to threatened and endangered species is legally deficient, in violation of the ESA. EPA uses "levels of concern" and "risk quotients" to determine if listed species will be effected throughout its ESA risk assessments, from screening level through more refined assessments. For example, "EPA determines that there is "no effect" on listed species if, at any step in the screening level assessment, no levels of concern are exceeded. If, after performing all the steps in the screening level assessment, a pesticide still exceeds the Agency's levels of concern for listed

[55] 21 U.S.C. § 346a.
[56] 16 U.S.C. § 1536(a)(2); *see also* 50 C.F.R. § 402.01(b).
[57] *Id.* § 701–12.
[58] *Id.*

species, EPA then conducts a species-specific refined assessment to make effects determinations for individual listed species…."[59] At the species-specific level, EPA also uses "levels of concern" and "risk quotients" based on modeling exposure to predicted environmental exposure.[60]

These determinations are not based on whether there is any effect at all, but on whether any effects predicted are of concern to EPA. This is contrary to the ESA's definition of "may affect," which is broadly defined to include "any possible effect, whether beneficial, benign, adverse, or of an undetermined character."[61] EPA's current approach, relying on "risk quotients" and "levels of concern," falls short of the agency's duty under the ESA.

Second, EPA's current approach is also unlawful because EPA improperly switches from a "may affect" to a "no effect" finding after unilateral analysis. EPA's own policy provides that where a screening level assessment shows the risk threshold is exceeded for a listed species, EPA may conduct further refined analysis, but such refined analysis will not determine "no effect" and avoid consultation. Instead, the agency's refined assessment is only used to make the "not likely to adversely affect"/"likely to adverse effect" determination, which then can be used to allow EPA to forego formal consultation, but only if the expert wildlife agency concurs in writing with EPA's determination after informal consultation. [62]

Here, EPA's initial assessments of the various states concluded that there are numerous species that may be directly or indirectly affected by dicamba use. EPA switched to "no effect" findings after the agency's unilateral further analyses with three "refined endangered species assessments" for soybean and cotton, for 3 different sets of states. In these documents, EPA drills down to particular listed species and their habitats and requirements to determine ESA "no effect" or "may effect" designations:

- In the Addendum Assessment for 16 states, 183 listed species were identified as occurring in counties where soybeans and cotton are grown. At the screening level, EPA concluded that 10 of these species would be expected to occur on the fields themselves where they would be exposed to dicamba and its metabolites, triggering a "May Affect" determination under the ESA. Yet, EPA proceeded with unilateral further refined analysis, whereby EPA reverted to "no effect" findings for 9 of the species. EPA only gave 1 of these

[59] EPA, *Addendum to Dicamba Diglycolamine Salt (DGA) and its Degradate, 3,6-dichlorosalicylic ac id (DCSA) Section 3 Risk Assessment: Refined Endangered Species Assessment for Proposed New Uses on Herbicide-Tolerant Soybean and Cotton in 16 states (Arkansas, Illinois, Iowa, Indiana, Kansas, Louisiana, Minnesota, Mississippi, Missouri, Nebraska, North Dakota, Ohio, Oklahoma, South Dakota, Tennessee, and Wisconsin)* 2-3 (Mar. 24, 2016) [hereinafter *Addendum Assessment for 16 States*].
[60] *See, e.g.,* EPA, *Addendum Assessment for 16 States*, at 7.
[61] *See* 51 Fed. Reg. 19,926, 19,949 (June 3, 1986) (Codified at 50 C.F.R. pt. 402).
[62] EPA, *Overview of the Ecological Risk Assessment Process in the Office of Pesticide Programs, U.S. Environmental Protection Agency. Listed and Threatened Species Effects Determinations* (2004); *see also* EPA, *Assessing Pesticides under the Endangered Species Act,* http://www2.epa.gov/endangered-species/assessing-pesticides-under-endangered-species-act.

species a "May Affect" determination, and "Likely to Adversely Affect": Spring Creek Bladderpod, found only in Wilson County, TN.[63]

- For its assessment of risks to listed species in the 7 states (Alabama, Georgia, Kentucky, Michigan, North Carolina, South Carolina, and Texas),[64] of 307 listed species in cotton and soybean counties, EPA concluded that 10 species would be expected to occur on the fields themselves and thus be exposed and may be affected. During refined assessments, EPA gave all but 1 "No effect" determinations.[65] The Eskimo Curlew (bird) was given a "May Affect" determination, and although potentially found in 23 counties in Nebraska and 1 in Texas, is "presumed extinct," so was designated "Not Likely to Adversely Affect."

- For its assessment of risks to listed species in 11 states (Arizona, Colorado, Delaware, Florida, Maryland, New Mexico, New Jersey, New York, Pennsylvania, Virginia and West Virginia),[66] of 322 listed species in cotton and soybean counties, EPA concluded that 14 species would be expected to occur on the fields themselves and thus be exposed and may be affected. During refinement, all but 1 were given "No effect" determinations by EPA.[67] The Audubon Crested Caracara (bird) was given a "May Affect" and "Not Likely to Adversely Affect" determination for Palm Beach County in Florida, only.

- For all three ESA refined assessments, all critical habitats were given a "No Modification" determination. Most "No Modification" determinations were based EPA's assessment that the associated listed species did not use cotton or soybean fields and hence cannot be impacted by on-field exposure to dicamba DGA. For the few critical habitats of species that EPA determined do use cotton or soybean fields, EPA first assumed there may be modification, then unilaterally arrived at a "No Modification" determination after a more refined analysis that focused on the species' exposure to dicamba within cotton and soybean fields, and that assumed there would be an acceptable

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[63] EPA, *Addendum Assessment for 16 States*, at 3-4.
[64] EPA, *Addendum to Dicamba Diglycolamine Salt (DGA) and its Degradate, 3,6-dichlorosalicylic acid (DCSA) Section 3 Risk Assessment: Refined Endangered Species Assessment for Proposed New Uses on Herbicide-Tolerant Soybean and Cotton in 7 states (Alabama, Georgia, Kentucky, Michigan, North Carolina, South Carolina, and Texas)* 3-4 (Mar. 24, 2016) [hereinafter *Addendum Assessment for 7 States*].
[65] *Id.*
[66] EPA, *Addendum to Dicamba Diglycolamine Salt (DGA) and its Degradate, 3,6-dichlorosalicylic ac id (DCSA) Section 3 Risk Assessment: Refined Endangered Species Assessment for Proposed New Uses on Herbicide-Tolerant Soybean and Cotton in 11 states (*Arizona, Colorado, Delaware, Florida, Maryland, New Mexico, New Jersey, New York, Pennsylvania, Virginia and West Virginia) 4 (Mar. 24, 2016) [hereinafter *Addendum Assessment for 11 States*].
[67] *Id.* at 4.

threshold of impact based on the Agency's "risk quotients" and "levels of concern."[68]

EPA cannot unilaterally undo a "may affect" finding as it did here in refining assessments. EPA's most-recent guidance on assessing pesticide risks to listed species notes that "any species or critical habitat that overlaps with the action area *will be considered a 'May Affect.'*"[69] The guidance confirms unequivocally: "For species and critical habitats that do overlap with the action area, the call *will be 'May Affect,'* and the analysis *will proceed* with [informal consultation with FWS]."[70] Here, EPA reached "may affect" findings for 24 unique listed species based on habitat co-occurrence with dicamba use on cotton and soybean fields and did not consult the expert agencies, in contravention of the ESA's legal triggers and the Agency's own guidance on ESA assessments.

In addition, EPA determined that there would be no effect on almost all of the hundreds listed species identified at the screening level as co-occurring in counties where cotton and soybeans are grown by unrealistically narrowing the "action area" to only within GE cotton or GE soybean fields that had been sprayed with dicamba DGA. EPA similarly concluded that there would be no modification to listed species' critical habitats solely based on the fact that the species did not use cotton or soybean fields. EPA's approach is unlawful under the ESA.

As detailed below, EPA's approach is arbitrary and capricious, and scientifically indefensible, in violation of the agencies' duties under ESA and FIFRA.

1. Exposure to listed species from off-site movement of dicamba

EPA's rationale for limiting the potential impacts of dicamba on listed species to within the boundaries of treated fields is based on putting mitigation measures in the label language that EPA states will result in no direct dicamba exposure outside of those fields (terrestrial species), or exposure below EPA's level of concern (critical habitats, aquatic species).[71]

EPA's rationale is faulty. EPA's own calculations of movement of dicamba do in fact predict that this registration action will result in off-site dicamba transport, and thus potentially expose those listed species and critical habitats that occur outside of treated fields, requiring a "may effect" finding for more species than EPA has so far determined.

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[68] EPA, *Addendum Assessment for 7 States*, at 29-31; EPA, *Addendum Assessment for 11 States*, at 25-26; EPA, *Addendum Assessment for 16 States*, at 100-101.

[69] EPA, *Interim Approaches for National-Level Pesticide Endangered Species Act Assessments Based on the Recommendations of the National Academy of Sciences April 2013 Report*, at 4, *available at* http://www2.epa.gov/sites/production/files/2015-07/documents/interagency.pdf.

[70] *Id.*

[71] EPA, *Addendum Assessment for 11 States*, at 6.

For example, in the Proposed Registration Document,[72] EPA describes how the proposed buffer distances were determined, and concludes that "[u]sing these buffers, expected residues at the field's edge from spray drift would be below apical endpoints for the most sensitive tested species (i.e. NOAEC for soybean plant height)."

For volatilization, EPA admits that it doesn't have enough information to determine if the proposed in-field buffers are sufficient.[73] Rather than require more data before taking this registration action, and ignoring incident data showing injury to sensitive crops well beyond its chosen buffer distances, EPA is going to reconsider the efficacy of the buffer distances "if" it receives more volatility data.[74] In the meantime, listed species far away from application sites may be affected by exposure to dicamba from volatilization. This violates EPA's duties under both ESA and FIFRA.

EPA finds that dicamba residues will leave treated fields into surrounding waterways via runoff, where many kinds of aquatic and semi-aquatic organisms could be directly exposed,[75] and also terrestrial plants[76] Terrestrial animals also may come into contact with dicamba-contaminated runoff.

In fact, EPA shows over and over throughout the environmental assessments in the docket,[77] that even with mitigation measures in place, some dicamba is expected outside of field boundaries due to spray drift, volatilization and runoff.[78] Stating categorically that terrestrial species outside of field boundaries are "not expected to be directly exposed to dicamba DGA" is thus at odds with EPA's own models and calculations - assessments EPA has done for this very registration action, and is contrary to the agency's legal mandates under the ESA.

For aquatic organisms, EPA's rationale for "no effect" determinations based on exposures below levels of concern is unlawful, as discussed above, since EPA does estimate particular levels of dicamba in runoff. In addition, EPA has estimated an environmental

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[72] EPA, *Proposed Registration of Dicamba on Dicamba-Tolerant Cotton and Soybean* 17 (Mar. 31, 2016) [hereinafter *Proposed Registration Document*].
[73] *See* EPA, *Proposed Registration Document*, at 17; EPA, *Dicamba DGA: Second Addendum to the Environmental Fate and Ecological Risk Assessment for Dicamba DGA Salt and Its Degradates, 3,6-dichlorosalicylic acid (DCSA) for the Section 3 New Use on Dicamba-Tolerant Soybean* 10 (Mar. 24, 2016) [hereinafter *Second Addendum to Ecological Risk Assessment for Dicamba Use on Dicamba-Tolerant Soybean*].
[74] EPA, *Proposed Registration Document*, at 17.
[75] *See* EPA, *Second Addendum to Ecological Risk Assessment for Dicamba Use on Dicamba-Tolerant* Soybean, at 21, 31-33; EPA, *Ecological Risk Assessment for Dicamba DGA Salt and Its Degradates, 3,6-dichlorosalicylic acid (DCSA), for the Proposed Post-Emergence New Use on Dicamba-Tolerant Cotton (MON87701)* 14 (Mar. 24, 2016) [hereinafter *Ecological Risk Assessment for Dicamba Use on Dicamba-Tolerant Cotton*].
[76] EPA, *Addendum Assessment for 16 States* at 6.
[77] *See* EPA, *Second Addendum to Ecological Risk Assessment for Dicamba Use on Dicamba-Tolerant Soybean* at 2-11 (especially, using new data on drift and volatilization)
[78] *See* EPA, *Proposed Registration Document*, at 16-18.

concentration for surface waters from dicamba applications to dicamba-resistant cotton[79] that is much higher than concentrations shown to cause endocrine effects in fish.[80]

Besides offsite movement of dicamba admitted by EPA, there are deficiencies in EPA's assumptions about off-field exposure to dicamba and dicamba metabolites that lead to underestimates of exposure for both terrestrial and aquatic species.

For example, EPA assumes that terrestrial mammals and birds will only ingest DCSA, a toxic metabolite of dicamba, if those animals are within sprayed fields: "Based on the available plant metabolism data for DCSA on non-DT plants, EFED assumed that any exposure for terrestrial vertebrates occurs as a result of feeding solely on DCSA in DT soybean and no exposure to DCSA is expected for terrestrial vertebrates feeding off the field, even if dicamba residues should occur following spray drift or volatilization. This is because the conversion of dicamba to DCSA in plants is only expected to occur in crops modified to be tolerant to dicamba."[81]

EPA does not consider exposure to dicamba and DCSA from ingestion of dicamba-resistant crop material that leaves the field via wind or runoff, even though detritus from crop fields is well known to move away from fields and to persist in the environment, and to serve as a reservoir of pesticides and metabolites in aquatic and terrestrial areas.[82] This is a serious omission, and may affect both terrestrial and aquatic animals.

Insects and other arthropods that have fed on dicamba-resistant crop tissues and thus are contaminated with dicamba and DCSA[83] could be consumed by animals outside of the field boundaries. Many insects come and go from crop fields. EPA did not include this likely occurrence when assessing risks to listed species. Both terrestrial and aquatic animals that eat insects may be affected.

Increases in total dicamba usage are likely, and will result in higher levels of exposure to more listed organisms.[84] This is a cumulative impact that EPA did not adequately consider, as it is not taken into account in EPA's risk assessment models. For example, rivers and streams in watersheds where dicamba is used on dicamba-resistant crops are likely to have higher dicamba contamination levels, but this is not taken into account.

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[79] EPA, *Ecological Risk Assessment for Dicamba Use on Dicamba-Tolerant Cotton*, at 14.
[80] Zhu et al. 2015.
[81] *See* EPA, *Second Addendum to Ecological Risk Assessment for Dicamba Use on Dicamba-Tolerant Soybean* at 14; *see also* EPA, *Proposed Registration Document* at 20.
[82] *See, e.g.,* Tank et al. 2010 and other studies of Bt in corn detritus cited in CFS's previously-submitted comments.
[83] *See* EPA, *Proposed Registration Document* at 20.
[84] *See* Exhibit B, at 74 (attached) (01/18/2013 CFS's Science Comments to EPA's Notice of Receipt of Application to Register New Use of Dicamba on Monsanto's Dicamba- and Glufosinate-Resistant MON 88701 Cotton, Docket No. EPA-HQ-OPP-2012-0841).

Dicamba contamination is already widespread in surface waters in the US and EPA must consider the cumulative impacts on both terrestrial and aquatic species of increased dicamba use in watersheds where it is already applied to other crops.[85]

For all these reasons, EPA's assumption that exposure of terrestrial and aquatic species will be confined to fields where applications occur is scientifically indefensible and legally erroneous.

2. EPA's fails to adequately consider effects to listed species of using dicamba formulations on dicamba-resistant cotton and soybeans because toxicity of all the components of likely end-use products has not been considered.

In addition to the toxicity of the each ingredient, EPA must consider possible additive and synergistic effects from various components of the end-use product formulation. If synergy is present, there can be greater effects from the same exposure to the pesticide than predicted, and thus effects at longer distances from the application site.

Although EPA is only considering registration of Monsanto's dicamba DGA salt formulation in this action, it is well known that Monsanto plans to combine dicamba with glyphosate, and perhaps with other herbicides such as glufosinate, to apply in fields planted with crops that have multiple herbicide resistance traits. Monsanto is already marketing such crops for 2016. Therefore EPA needs to consider impacts of likely mixtures of herbicide active ingredients now in order to understand complete costs and benefits.

Synergy can result from combining any of the components in the formulation, including synergy from combining different active ingredients and also between inerts (surfactants and other components added to the formulation before sale), adjuvants (surfactants and other components added to the formulation by applicators, as in tank mixes), and other components of the formulation and the active ingredient(s).

Synergy concerns are not limited to premixes and tank mixes where the components are applied to fields simultaneously. It is also relevant for pesticides applied on the same field before or after dicamba formulations are applied. For example, in a patent, Monsanto describes synergy between dicamba and glyphosate applied at different times:[86]

> In accordance with the invention, methods and compositions for the control of weeds are provided comprising the use of plants exhibiting tolerance to glyphosate and auxin-like herbicides such as dicamba. As shown in the working examples, <u>dicamba and glyphosate allow use of decreased amounts of herbicide to achieve the same level of control of glyphosate-tolerant weeds</u> and thus this embodiment

[85] *See* Exhibit A (attached), at 54-55 (09/21/2012 CFS's Science Comments to EPA's Notice of Receipt of Application to Register New Use of Dicamba on Dicamba-Resistant Soybean, Docket No. EPA-HQ-OPP-2012-0841); Exhibit B, at 62-63.
[86] Feng and Brinker 2014, at 9.

provides a significant advance for the control of herbicide tolerance in commercial production fields. In one embodiment, a tank mix of glyphosate and dicamba is applied pre- and/or post-emergence to plants. Glyphosate and dicamba may additionally be applied separately. In order to obtain the ability to use decreased amount of herbicide, the glyphosate and dicamba are preferably applied within a sufficient interval that both herbicides remain active and able to control weed growth.

This embodiment therefore allows use of lower amounts of either herbicide to achieve the same degree of weed control as an application of only one of the herbicides.

EPA admits that there are uncertainties regarding impacts of mixtures of different herbicide active ingredients, and has added a mitigation measure to compensate for the uncertainty: a requirement that no other herbicides be tank-mixed with dicamba DGA.[87] However, this is an inadequate mitigation measure for several reasons: 1) other types of pesticides than herbicides, such as insecticides and fungicides, could also interact synergistically in the formulation and are not included in the tank mixing restriction, 2) adjuvants that do not increase spray drift are allowed to be tank mixed without consideration of synergistic toxicity even though adjuvants are often chosen specifically because they synergistically enhance toxicity of the active ingredient,[88] and 3) synergism can occur between pesticides that are applied before or after each other in addition to being applied concurrently.[89]

EPA's failure to consider synergistic effects between dicamba and other chemicals is unlawful in light of the Agency's recognition that the proposed new use would be used concurrently with glyphosate and other pesticides on soybean and cotton. Under FIFRA, EPA must consider "any unreasonable risk to man or the environment, taking into account the economic, social, and environmental costs and benefits of the use of any pesticide" prior to approving a pesticide use. Here, EPA improperly segmented its cost-benefit analysis and neglected to consider the environmental costs associated with the use of the dicamba on GE soybean and cotton resistant to both dicamba and glyphosate. As a result of EPA's improper segmentation, EPA fails to consider the increased costs associated with the synergistic and additive effects of using both glyphosate and dicamba together.

3. EPA's conclusion that the proposed buffer zones would effectively reduce exposure of listed species to dicamba is unsupported

[87] EPA, *Proposed Registration Document* at 22; M1691 Herbicide DT Cotton Label M1691 EPA Reg. No. 524-582, EPA Docket ID EPA-HQ-OPP-2016-0187-0014, at 22; M1691 Herbicide DT soybean Label - EPA Reg. No. 524-582, EPA Docket ID EPA-HQ-OPP-2016-0187-0015, at 4.
[88] Sun 2012.
[89] Feng and Brinker 2014 at 9.

Finally, assumptions EPA used to design mitigation measures—buffer zones—to reduce exposure of listed species to dicamba DGA are unrealistic.[90] For example, EPA does not analyze how often applicators are likely to spray when wind speeds are greater than allowed, when weather conditions are unpredictable, or how often rain events occur when not forecast. Nor does EPA assess the likelihood that nozzles will be adjusted improperly, or buffer zone distances miscalculated. Without a realistic assessment of mitigation measures, risks cannot be predicted accurately and are likely to be underestimated.

II. EPA's Assessment Neglects Any Potential Impacts on Migratory Birds.

Based on the same reasoning above, EPA's current risk assessment is also unlawful under the MBTA. EPA's own risk assessments acknowledged that the proposed registration of dicamba use on dicamba-resistant, GE cotton and soybean poses potential risks to avian species, including numerous listed migratory avian species, yet EPA failed to properly consider and disclose its obligations to migratory birds, never even mentioning its responsibilities under the MBTA. The MBTA prohibits the take of migratory birds entirely and mandates that the loss, destruction, and degradation of migratory bird habitat must be minimized. Under EPA's proposed approval, dicamba would be used in fields visited by hundreds of species of birds protected under the MBTA. Rather than determining whether the proposed use of dicamba on dicamba-resistant GE cotton and soybean would have adverse effects on species protected under the MBTA, EPA simply ignores this significant issue. EPA must cure this defect by conducting a new risk assessment.

III. EPA's Current Assessment Does Not Adequately Consider Unreasonable Adverse Effects and Potential Risks to Pollinator Species.

EPA's current assessments regarding potential adverse effects to honey bees, other bees and pollinator species, and other beneficial terrestrial invertebrates, is also legally deficient under FIFRA. A recent study of dicamba impacts on nectar resources found that very low levels of dicamba, such as occur during drift of dicamba into areas adjacent to treated fields, caused reduced and delayed flowering and fewer visits by honey bees to the dicamba-injured plants.[91] Given the importance and imperilment of beneficial invertebrates such as pollinators, EPA needs to do a full assessment before taking this registration action instead of delaying until the upcoming dicamba registration review that won't be completed for several years.[92]

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[90] For detailed analysis, see previous comments for similar mitigation measures in Exhibit C (attached) (01/30/2014 CFS's comments to EPA on the Proposed New Use of Enlist Duo on 2,4-D-Resistant Crops, Docket No. EPA-HQ-OPP-2014-0195), and Exhibit D (attached) (12/15/2014 CFS's comments to EPA on the Proposed New Use of Enlist Duo on 2,4-D-Resistant Crops in Ten Additional States, Docket No. EPA-HQ-OPP-2014-0195).

[91] Bohnenblust et al. 2016.

[92] EPA, *Second Addendum to Ecological Risk Assessment for Dicamba Use on Dicamba-Tolerant Soybean* at 16-17.

EPA's own *Guidance for Assessing Pesticide Risks to Bees* sets out a risk assessment process for assessing potential risks to honey bees and other pollinators.[93] Here, EPA admitted that the initial 2011 risk assessment for the proposed uses "included no quantitative analysis of the risks" to beneficial insects and pollinators, and recognized that since then, EPA itself has "identified additional honeybee life stage testing and longer duration effects tests for adults [bees]…as potentially important to the risk assessment process."[94] Nonetheless, EPA fails to adhere to its current guidance and require all the necessary data and studies in order to adequately assess the potential risks to honey bees and other insects, including pollinators and federally listed terrestrial invertebrates, as part of the current risk assessment. Without these data and studies, EPA cannot ascertain that the proposed use of dicamba would not have "unreasonable adverse effects to the environment" or that it would not affect listed terrestrial invertebrates, in violation of FIFRA and the ESA.

For assessment of impacts to pollinators, there are important data gaps. For example, there are no data on levels of dicamba residues and metabolites in parts of the crops that pollinators use, such as pollen, nectar, or guttation fluids, without which no risk assessment can be meaningfully conducted.[95] There are no data on toxicity of the major metabolite of dicamba in dicamba-resistant crop tissues, glucosylated DCSA, which has not been tested for toxicity to any species. Also, toxicity data from studies of surrogate species used by EPA are unreliable because of vastly different life histories.[96]

These and other deficiencies in EPA's pollinator risk assessments are discussed by CFS for dicamba use with dicamba-resistant soybean and cotton at length in previous comments.[97]

IV. EPA's Current Assessment Entirely Fails to Consider Toxicity of Conjugated Metabolites of Dicamba.

All of EPA's risk assessments that involve animals, including listed animals, which may ingest dicamba-treated, dicamba-resistant crop tissues are deficient because toxicity of the major metabolite of dicamba is unknown and unaccounted for.

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[93] EPA, *Guidance for Assessing Pesticide Risks to Bees* (2014), *available at* https://www.epa.gov/sites/production/files/2014-06/documents/pollinator_risk_assessment_guidance_06_19_14.pdf

[94] EPA, *Second Addendum to Ecological Risk Assessment for Dicamba Use on Dicamba-Tolerant Soybean* at 16.

[95] *See, e.g.,* EPA, *Second Addendum to Ecological Risk Assessment for Dicamba Use on Dicamba-Tolerant Soybean* at 20, where EPA uses levels of DCSA in seeds instead.

[96] *See, e.g.,* EPA, *Second Addendum to Ecological Risk Assessment for Dicamba Use on Dicamba-Tolerant Soybean* at 18 - 20, where aquatic invertebrates are used as surrogates for chronic effects of dicamba exposure, and then this assessment is extended to all terrestrial invertebrates.

[97] *See* Exhibit A (attached), at 62-64; Exhibit B (attached), at 70-73; Exhibit E (attached), at 15-23 (10/10/2014 CFS's Science Comments to USDA's Draft Environmental Impact Statement on Monsanto Petitions (10-188-01p and 12-185-01p) for Determinations of Nonregulated Status for Dicamba-Resistant Soybean and Cotton Varieties, Docket No. APHIS 2013-0043).

By far the most common metabolite present at the highest level after spraying dicamba on dicamba-resistant soybeans or cotton is a conjugate of DCSA that has been modified by the addition of a sugar: glucosylated (also called glycosylated) DCSA (. This metabolite is a novel addition to the food supply for both humans and animals that eat dicamba-treated, dicamba-resistant crops, particularly forage and fodder, and also perhaps other plant-derived foods such as nectar, pollen, guttation fluids.[98]

EPA does not report any toxicology studies of glucosylated DCSA for any kind of organism. Based on studies with other conjugated metabolites, during digestion toxic DCSA could be released as the sugar is cleaved from the glucosylated form. CFS discusses this in previous comments.[99]

Given the novelty of glucosylated DCSA in the food and feed supply, and the fact that it is the major metabolite of dicamba in dicamba-resistant crops, EPA's risk assessments are incomplete, and may significantly underestimate adverse effects.

V. EPA Lacks Sufficient Information to Make the No "Unreasonable Adverse Effects" Finding Required Under FIFRA.

The Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) mandates that EPA can register a pesticide use only if it can ensure that the use will not cause unreasonable adverse effects on man or the environment, taking into account the economic, social, and environmental costs and benefits of the pesticide's use.[100] Here, EPA has failed to assess and account for several significant economic and social costs of the proposed uses, in violation of FIFRA.

1. EPA's assessment of dicamba resistance in Weeds

EPA acknowledges that weeds resistant to glyphosate and other heavily used herbicides have imposed "yield and economic losses" on farmers. In fact, the chief benefit claimed for the proposed uses of dicamba is to facilitate better control of these resistant weeds.[101]. However, EPA also acknowledges that these new uses on dicamba-resistant soybeans and cotton could lead to "expansion of dicamba-resistant weeds and the development of [dicamba] resistance by some additional weed species."[102] Dicamba-resistant weeds, like those resistant to glyphosate, would impose costs on growers. Therefore, EPA must assess any potential benefits of the new uses (i.e. controlling

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[98] *See* EPA, *Dicamba. Section 3 Registration for the Amended Use of Dicamba on Dicamba-Tolerant Cotton. Summary of Analytical Chemistry and Residue Data* 19 (Mar. 29, 2016); *Second Addendum to Ecological Risk Assessment for Dicamba Use on Dicamba-Tolerant Soybean* at 14.
[99] *See* Exhibit A (attached), at 58-61; Exhibit B (attached), at 65-70; Exhibit E (attached), at 26-28.
[100] *See* 7 U.S.C. § 136a(c)(5).
[101] EPA, *Review of Benefits as Described by the Registrant of Dicamba Herbicide for Postemergence Applications to Soybean and Cotton and Addendum Review of the Resistance Management Plan as Described by the Registrant of Dicamba Herbicide for Use on Genetically Modified Soybean and Cotton* 2 (Mar. 20, 2016) [hereinafter *Benefits Analysis*].
[102] *Id.* at 4.

glyphosate-resistant weeds) and weigh them against costs (emergence of dicamba resistance).

However, EPA's Benefits Analysis that is supposed to address weed resistance is deficient in several respects. In brief:

1) It only describes purported benefits, not costs;
2) The treatment of weed resistance is extremely cursory and descriptive in nature, erroneous in certain respects, and entirely lacking any quantitative or semi-quantitative analysis of the dicamba-resistant weed threat;
3) EPA explicitly limits itself to the registrant's viewpoints and information, neglecting relevant scientific literature, a key assessment by the US Department of Agriculture, and public comments that EPA was aware of;
4) EPA's failure to properly assess the dicamba-resistant weed threat has led it to propose an herbicide resistance management plan that will be ineffective and unworkable.

EPA's description of the purported benefits of the new dicamba uses is just six pages (minus appendices), with no accounting of costs.[103] It is explicitly keyed to "benefits as described by the registrant" and "Monsanto's submitted information." Only two peer-reviewed studies on weed resistance are cited, and a handful of farm press articles and extension publications. Even in those few instances where EPA cites non-registrant studies or data, it does so in a way that inexplicably minimizes resistance issues. For instance, EPA cites Godar et al. (2015) and Sandell et al. (2012) for the statement that "glyphosate-resistant kochia populations have been identified in Kansas … and Nebraska." However, Godar et al. (2015) actually report glyphosate-resistant [GR] kochia not just in Kansas and Nebraska, but in ten states and three Canadian provinces: "As of 2014, presence of GR kochia populations has been reported in ten Great Plains states (Colorado, Idaho, Kansas, Montana, Nebraska, North Dakota, Oklahoma, Oregon, South Dakota, and Wyoming) and three Canadian provinces (Alberta, Saskatchewan, and Manitoba).[104]

EPA provides no discussion of the resistance-promoting features of herbicide-resistant crop systems in general or the news uses with dicamba-resistant soybeans or cotton in particular. EPA also fails to provide any quantitative or semi-quantitative assessment of the factors conducing to weed resistance, or of the extent or costs of dicamba-resistant weeds that the proposed uses would foster. Though EPA makes regular use of quantitative projections and modeling in assessing new uses of pesticides, and has done so in certain respects with dicamba,[105] such analysis is entirely lacking here with respect to weed resistance.

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[103] EPA, *Benefits Analysis* at 1-6.

[104] Godar et al. 2015. EPA's citation to this study (*see EPA Benefits Analysis* at 12, with first author's name misspelled as "Bodar") specifies the abstract "(abstr.)." Thus, EPA may have missed the statement quoted here, which appears in the body of the paper, by scanning only the title and abstract.

[105] For instance, EPA used drift modeling software to provide quantitative estimates of how far and what concentrations dicamba would drift.

This cursory treatment contrasts sharply with the approach taken by others to assess the issue of herbicide- and dicamba-resistant weeds. For instance, weed scientist Paul Neve has created a quantitative simulation model to assess how rapidly weed resistance would evolve under various herbicide usage scenarios.[106] Neve found that using an herbicide as it is typically used with an herbicide-resistant crop "very substantially increases risks of resistance evolution" relative to typical uses of the same herbicide with conventional crops. While the cited paper focuses on glyphosate, the model is applicable to other herbicides.

The U.S. Department of Agriculture (USDA) provided a detailed, quantitative assessment of dicamba use in its Environmental Impact Statement on Monsanto's petition to deregulate dicamba-resistant (DR) soybeans and cotton, based in part on data provided by Monsanto.[107] This assessment is highly relevant to the dicamba-resistant weed threat posed by the new uses on DR crops. USDA's assessment was based on quantitative estimates of acreage planted to dicamba-resistant soybeans and cotton and sprayed with dicamba; the number of dicamba applications per season to each DR crop, and the rate (i.e. lbs./acre) at which dicamba would be applied. Based on these projections, tens of millions of acres of DR crops would receive two to three applications of dicamba per season. Because resistance risk generally rises with the frequency of application, and most herbicides are applied just once per season, dicamba-resistant weeds are likely to emerge rapidly on millions of acres of DR cropland (see analysis in Exhibit F[108]). USDA deregulated DR soybeans and cotton without restriction despite its conclusion that doing so would increase selection pressure for dicamba-resistant weeds.[109] USDA took this action in the expectation that EPA was "thoroughly analyzing" the weed resistance impacts of the proposed new uses of dicamba, and would establish effective weed resistance management requirements as part of its registration.[110] Yet EPA makes no reference to this clearly relevant USDA assessment, despite the fact that the two agencies are supposed to be collaborating to address weed resistance risks associated with herbicide-resistant crop systems.

Mortensen et al. (2012) discuss many implications of the introduction of soybeans genetically engineered for resistance to dicamba (Monsanto) and 2,4-D (Dow). They provide quantitative projections of DR/2,4-D-resistant soybean acreage and associated

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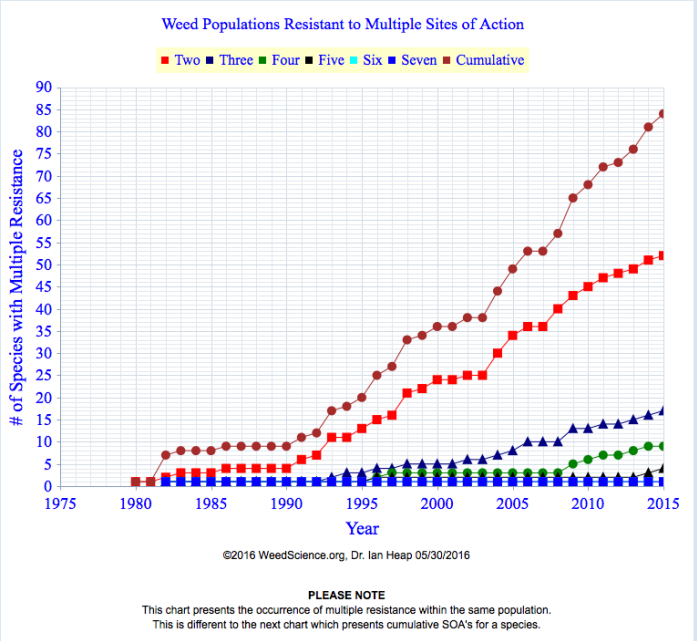
[106] Neve 2008.
[107] USDA, *Monsanto Petitions (10-188-01p and 12-185-01p) for Determinations of Nonregulated Status for Dicamba Resistant Soybean and Cotton Varieties Final Environmental Impact Statement* (December 2014), *available at* https://www.aphis.usda.gov/brs/aphisdocs/dicamba_feis.pdf. [hereinafter *USDA Dicamba FEIS*].
[108] Exhibit F (attached) (10/10/2014 CFS's Science I Comments to USDA's Animal and Plant Health Inspection Service on the Agency's draft Environmental Impact Statement on Monsanto Petitions (10-188-01p and 12-185-01p) for Determinations of Nonregulated Status for Dicamba-Resistant Soybean).
and Cotton Varieties, Docket No. APHIS-2013-0043).
[109] USDA, *Record of Decision, Monsanto Petitions (10-188-01p and 12-185-01p) for Determinations of Nonregulated Status for Dicamba Resistant Soybean and Cotton Varieties 20* (2015), *available at* https://www.aphis.usda.gov/brs/aphisdocs/dicamba_feis_rod.pdf. [hereinafter *USDA Dicamba ROD*].
[110] *USDA Dicamba ROD*, at 21.

usage of dicamba/2,4-D. They discuss the weed resistance risk posed by introduction of these crops. Among their relevant findings are that weeds resistant to dicamba and/or 2,4-D (closely related "auxin" herbicides) are more common than generally recognized, and that the new uses of dicamba (and 2,4-D) pose a high risk of generating dicamba/2,4-D-resistance in weeds already resistant to glyphosate, resulting in weeds resistant to both herbicides. They also discuss the dramatically increasing prevalence of such multiple herbicide-resistant weeds in U.S. and world agriculture (see graph below), which increases weed control costs as much as six-fold.[111] Additional dicamba-resistance in weeds already resistant to glyphosate (and sometimes other herbicides) will limit weed management options for farmers,[112] are often more difficult and costly to control, and more likely to be managed with soil-eroding tillage, as discussed below.



Source: International Survey of Herbicide Resistant Weeds. http://www.weedscience.com/Graphs/MultipleResistance.aspx, 3/30/16.

EPA's cursory review makes no reference to this much-cited study; nor does it provide any assessment of the threat posed or costs imposed by multiple herbicide-resistant weeds generated by the proposed uses. In fact, EPA appears unaware that populations of the damaging weed kochia that have evolved resistance to dicamba in Kansas (mentioned at EPA Benefits Analysis on page 4) already have multiple resistance to glyphosate and other classes of herbicide as well as dicamba[113], illustrating EPA's general failure to consider the threat of multiple herbicide-resistant weeds.

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[111] Service 2013.

[112] Following Monsanto, EPA states that registration of dicamba "would expand weed management options for growers by providing an additional MOA [mode of action] in the growing season" (EPA Benefits Analysis, t 2). However, EPA fails to discuss the limitation of weed management options that will result with the evolution of dicamba- and multiple-herbicide resistant weeds.

[113] HR Kochia 1 & 2 (2015).

Finally, EPA itself has provided careful quantitative projections of the resistance risks associated with toxins introduced into first-generation genetically engineered corn and cotton that target above-ground pests like European corn borer. EPA conducted rigorous analysis, and consulted independent scientific literature in making these projections, and in establishing mandatory insect resistance management plans to prevent (or greatly delay) emergence of insect pest resistance to these toxins.[114] Weed resistance shares many characteristic features with insect resistance, yet EPA has provided nothing approaching this level of analysis of weed resistance risks in its cursory "benefits" memorandum or its proposed registration. As discussed below, EPA has also failed to require effective measures to prevent or greatly delay emergence of dicamba resistance.

Dicamba-resistant weeds that evolve with the proposed uses will likely spread to the fields of other farmers via seed dispersal and cross-pollination, including farmers who use other forms of dicamba on non-DR crops. This spread of dicamba resistance would likely impose increased weed control costs on such farmers, costs which EPA has not assessed or even mentioned. For instance, wheat growers who use dicamba may be forced to replace/supplement dicamba use with more costly/additional herbicides. EPA has failed to assess this issue. In contrast, USDA provided a quantitative assessment of such costs imposed on other farmers in a precisely analogous case: that is, costs associated with the projected spread to wheat farmers' fields of 2,4-D-resistant weeds fostered by the use of Enlist Duo on 2,4-D-resistant corn and soybeans.[115]

The discussion above is far from comprehensive, and is meant only to suggest the wealth of relevant resources and facts that EPA ignored in its cursory description of weed resistance, and to highlight assessment approaches and factors that EPA must employ or consider in projecting the costs of dicamba-resistant weeds under the proposed uses.

2. EPA's assessment failure undermines proposed herbicide resistance management plan

EPA has proposed an herbicide resistance management plan that will very likely be ineffective and unworkable, a predictable outcome given the Agency's failure to assess the very problem it purports to address, as discussed above. CFS has provided a detailed discussion of the flaws of EPA's herbicide-resistance management plan for the new uses, based on the Agency's plan for Enlist Duo, upon which the dicamba plan is closely modeled.[116] We provide a brief summary of these comments below, and also address elements that are new and specific to EPA's proposed herbicide-resistance management plan for the new dicamba uses.

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[114] *See, e.g.* EPA IRM 2001.

[115] USDA, *Final Environmental Impact Statement on Dow AgroSciences Petitions (09-233- 01p, 09-349-01p, and 11-234-01p) for Determinations of Nonregulated Status for 2,4-D-Resistant Corn and Soybean Varieties* (2014), *available at* https://www.aphis.usda.gov/brs/aphisdocs/24d_feis.pdf, [hereinafter *USDA 2,4-D FEIS*].

[116] Exhibit F (attached), at 32-35.

1) EPA fails to require any effective measures to prevent or substantially delay emergence of weed resistance to dicamba. The most effective measures would involve reducing selection pressure by limiting the frequency with which dicamba is applied, in a single season and/or over years, in line with the recommendations of many weed scientists. In the analogous case of inhibiting evolution of glyphosate resistance, scientists recommend annual rotation between a Roundup Ready and non-Roundup Ready crop, with glyphosate applied every other year instead of every year.[117] Syngenta's Chuck Foresman similarly recommended limiting glyphosate use to two applications in a two-year period.[118] EPA does not discuss or even mention the possibility of placing limits on the frequency of dicamba use as a condition of the proposed registration.

2) EPA's plan relies on farmers detecting weed resistance once it has already occurred by scouting their fields both before and after application of dicamba. It is unreasonable to expect busy growers who often farm thousands of acres to make the substantial time commitment thorough scouting would entail; to the extent such scouting occurs, it is often difficult to detect resistance until it is far advanced, and too late to effectively control.

3) EPA delegates most authority for implementing this plan to the registrant; yet Monsanto has failed to properly implement a very similar insect resistance management plan for genetically engineered Bt corn targeting corn rootworm, resulting in broad emergence of resistant pests. To the limited extent the plan has value, it is unlikely to be properly implemented due to the registrant's conflicts of interest.

4) EPA's resistance management recommendations rely heavily on use of dicamba sequentially with different types of herbicide, which are supposed to inhibit evolution of dicamba resistance. However, use of multiple herbicides is increasingly ineffective with the rapid emergence of multiple herbicide-resistant weeds (e.g. kochia resistant to two and four herbicide modes of action in Kansas, discussed above), which EPA fails to consider. For a fuller discussion of this issue, including examples of the failure of the multiple herbicide approach to forestalling weed resistance.[119]

5) EPA relies heavily on a recommendation that growers of DR crops use non-dicamba pre-emergence herbicides with residual activity to kill emerging weeds six to eight weeks after application to help forestall dicamba resistance.[120] However, this is extremely unlikely to occur in the case of DR soybeans, for several reasons:

[117] *See, e.g.*, Heap 1997.
[118] NGSF I 2004, at 26.
[119] *See* Exhibit F (attached), at 15-30; *see also* Mortensen et al. (2012).
[120] EPA, *Benefits Analysis*, at 3.

a. Soybean farmers have already shifted away from use of pre-emergence herbicides with residual activity in favor of reliance on glyphosate, which does not have residual activity;
b. USDA's more robust assessment of DR soybeans directly contradicts EPA's assumption on this point. USDA projects that "….substantive PRE [pre-emergence] non-glyphosate applications ***will likely be eliminated***, as may more than half of POST non-glyphosate applications."[121] The upshot of USDA's analysis is that most DR soybean farmers will rely entirely on dicamba and glyphosate[122] (to which DR soybeans are also resistant), generating intense selection pressure for evolution of dicamba resistance, often in weeds already resistant to glyphosate.
c. EPA fails to appreciate that dicamba has (limited) residual activity, as indicated by the waiting intervals for its pre-emergence use on conventional crops,[123] and is thus a likely choice for those growers who choose to make pre-emergence applications. This is also indicated by the fact that the proposed registration permits one or more pre-emergence applications of dicamba.
d. EPA's failure to conduct a proper real-world assessment of herbicide use practices and consult USDA's more robust assessment has led it to rely heavily on an herbicide resistance management method that will for the most part not be implemented.

6) EPA has proposed a minimum rate of 0.5 lb./acre per application of dicamba for post-emergence (in-crop) use as a resistance management measure for both DR soybeans and DR cotton.[124] Normally, the Agency prescribes only maximum pesticide rates. However, there is disagreement in the scientific literature on the utility of using "full herbicide rates" to inhibit weed resistance. In a comprehensive review of the effects of using reduced herbicide rates, Blackshaw et al. (2006) found that "reduced doses of herbicides are likely to have a neutral effect on weed resistance development, especially if used within an integrated weed management system." Beckie & Kirkland (2003) found that reducing ACCase inhibitor herbicide rates "decreased the proportion of resistant [wild oat] individuals in the population," especially when reduced rates were combined with increasing crop competition with a higher seeding rate. This suggests that prescribing a high minimum dicamba rate of 0.5 lb./acre might actually exacerbate rather than reduce resistance problems. Using the label-recommended (full rate) of glyphosate with Roundup Ready crops has always been Monsanto's chief recommendation for reducing the emergence of glyphosate-tolerant and glyphosate-resistant weeds, but

[121] *USDA Dicamba FEIS*, at 143 (emphasis added). For detailed discussion, *see* Exhibit F (attached).
[122] These two herbicides are not permitted to be used together in a tank mix, according to the proposed registration, but there is no bar to a farmer using them sequentially.
[123] Waiting intervals of two to four weeks between application of dicamba and planting of conventional soybeans and cotton are imposed for pre-emergence uses to allow dicamba to degrade or dissipate to levels that will not kill or damage the emerging crop (EPA, *Benefits Analysis*, Table 1). This same residual activity provides some level of weed control during these intervals.
[124] EPA, *Proposed Registration Document*, at 3.

many weed scientists disagree with this approach. At the National Glyphosate Stewardship Forum, a meeting convened specifically to address the emerging threat of glyphosate-resistant weeds, Iowa State University weed scientist Micheal Owen found that "reduced glyphosate rates, at times, may increase returns without increased weed problems."[125] In addition, glyphosate-resistant weeds have emerged in epidemic fashion despite Monsanto's "full rate" exhortations, and despite steadily increasing glyphosate use rates. Thus, prescribing a minimum rate of dicamba would be unlikely to inhibit emergence of dicamba resistance, and could exacerbate the problem.

7) USDA data show that dicamba, to the very limited extent it is used in soybeans, is currently applied to soybean fields on average at less than half the minimum rate proposed by EPA (0.1 to 0.2 lbs./acre).[126] Prescribing more than double the usual rate for post-emergence new use applications would likely increase farmer dicamba use and expenditures beyond, and perhaps well beyond, what they would otherwise be. The rate of herbicide needed to provide acceptable weed control varies dramatically in particular regions and fields based on numerous factors: which weed species are present, the number and size of the weeds, environmental factors like weather, crop production practices (tillage, seeding rate, etc.), which other herbicides (if any) are used, and the farmer's "tolerance" for weed presence. Weed scientists find that reduced herbicide rates are consistent with maintaining yield and increased overall production returns, even in cases where there is increased weed seed production.[127] This is particularly true when reduced rates are part of an integrated weed management program that involves cultural practices like higher crop seeding rates, diverse crop rotations, specific fertilizer placement and cover crops.[128] Thus, prescribing a high minimum rate of dicamba would likely increase farmer production costs and reduce farmer returns, without accomplishing the intended purpose of inhibiting resistance. In addition, this high minimum rate would also likely have negative environmental costs, for instance reductions in populations of field-edge flowering plants, given dicamba's propensity to drift and high efficacy on broadleaf weeds.

8) EPA's resistance management plan relies heavily on inclusion of various items of information and directions regarding weed resistance management on the dicamba label. However, weed resistance management statements similar though less extensive than those recommended now by EPA have been included on herbicide product labels since at least 2004,[129] and have obviously been ineffective, especially with respect to inhibiting glyphosate-resistant weed development. Participants at

[125] NGSF I 2004, at 18.
[126] *See* https://quickstats.nass.usda.gov/results/2513DF3C-9C21-3487-A36B-BA460678756C#0DC606AB-2494-3C85-8F7E-1C6920C4BA7A. One reason for the low rate is that dicamba is sometimes applied in mixtures with other herbicides.
[127] Hamill et al. 2004.
[128] Beckie & Kirkland 2003, Blackshaw et al. 2006.
[129] NGSF I 2004, at 36-37.

the second National Glyphosate Stewardship Forum, which included weed scientists, farmers and representative of commodity groups and industry, found that resistance management statements on labels have "low impact" at inhibiting resistance to glyphosate.[130] EPA provides no empirical evidence to support the efficacy of label statements concerning resistance management, and no empirical assessment of the factors (e.g. economic, time constraints) that influence farmers' real-world herbicide choices and the degree to which they do or do not implement herbicide resistance management directions. For instance, as discussed above several recommendations involve use of additional herbicides that represent additional production costs that growers may find excessive, or scouting for potential resistance that many farmers will not have time for.

9) EPA proposes a "5-year time limited registration … so that any unexpected weed resistance issues that may result from the proposed uses can be addressed before granting an extension…."[131] This time period is too long. Weed resistance to dicamba will likely emerge within this five-year time limit, and perhaps on an extremely widespread basis that inflicts significant costs on growers. Two considerations support this. First, EPA is greatly overestimating the efficacy of the herbicide resistance management plan, as discussed above. Second, weed resistance is known to evolve very rapidly when an herbicide is used as part of an herbicide-resistant crop system. For instance, glyphosate-resistant horseweed emerged within just three years in Delaware fields planted continuously to glyphosate-resistant soybeans treated with glyphosate.[132] Similarly, glyphosate-resistant (GR) horseweed was first reported in Tennessee cotton and soybean fields in 2001, and by 2004, just three years later, it had infested an estimated 1.5 million acres of Tennessee cropland.[133] Stahlman et al. (2013) found that "[g]lyphosate-resistant kochia spread rapidly ***throughout the central U.S. Great Plains within 4 years of discovery***" (emphasis added). These examples illustrate how quickly resistant weeds have evolved and spread in glyphosate-resistant crop systems, and suggest a similar potential for rapid and widespread evolution of resistance with the new uses of dicamba. EPA provides no rationale for choosing a 5-year time limit, and provides no assessment of the speed or extent of resistant weed evolution or spread, as modeled for example by Neve (2008).

3. Dicamba-Resistant Cotton Will Compromise Boll Weevil Eradication Efforts

Both volunteer cotton and cotton stalks remaining after harvest can harbor boll weevil larvae. Thus, cotton growers in several states (e.g. Texas, Tennessee) are legally required to control cotton volunteers and destroy cotton stalks as part of boll weevil eradication efforts. Agronomists have found this task to be more difficult with the advent of glyphosate- and glufosinate-resistant cotton varieties, and anticipate still greater problems

[130] NGSF I 2004, at 36-37.
[131] EPA, *Proposed Registration* Document, at 28.
[132] VanGessel 2001.
[133] NGSF I 2004, at 60.

with the introduction of Monsanto's dicamba, glyphosate- and glufosinate-resistant cotton and Dow's 2,4-D-, glyphosate- and glufosinate-resistant cotton. This is because glyphosate, 2,4-D, dicamba and glufosinate are among the few herbicides that provide effective control of volunteer cotton and cotton stalks. Registration of the new dicamba use on cotton would encourage farmer adoption of DR cotton, and hence potentially compromise boll weevil eradication efforts, or substantially increase the associated costs. This subject is addressed in more detail, with citations, in the attached Exhibit B, at 38-40. EPA did not address this issue in its proposed registration documents.

4. Increased tillage and soil erosion

Typical herbicide use patterns with herbicide-resistant crops foster rapid evolution of herbicide-resistant weeds, which in some cases are controlled through the use of tillage. Tillage in turn renders the soil more prone to erosion. A National Research Council committee reported increased use of tillage by farmers to control glyphosate-resistant weeds fostered by Roundup Ready cropping systems.[134] Many farmers employed tillage to control glyphosate-resistant horseweed infesting 1.5 million acres of Tennessee cropland, leading to a dramatic 50% reduction in the use of conservation tillage in Tennessee cotton, and a 30% reduction in the state as a whole.[135] Reduced use of conservation tillage due to GR weeds has also been reported in Missouri and Arkansas. A decline in no-till acreage in U.S. cotton and corn from 2007-2010 and in soybeans from 2008-2010 was attributed to greater use of tillage to control glyphosate-resistant weeds.[136] USDA reported a drop in the use of conservation tillage in soybeans from 2006 to 2012, which likely reflects more tillage to combat glyphosate-resistant weeds.[137]

As weeds with resistance to multiple herbicides continue to emerge and expand, herbicidal management options will continue to decline, meaning more and more farmers will turn to tillage for weed control. For instance, Godar & Stahlman (2015) report higher than expected use of tillage in Kansas to control kochia, which "might indicate failure to control kochia with herbicides." They report that the efficacy of glyphosate + dicamba on kochia has declined dramatically since 2007, as confirmed by reports of kochia with verified resistance to dicamba, glyphosate and other herbicides in Kansas.[138]

By promoting the emergence of weed resistance to dicamba (often in combination with resistance to glyphosate and other herbicides), registration of the proposed new uses will exacerbate the trend to increased use of tillage and soil erosion in American agriculture. Soil erosion on U.S. cropland is already occurring at rates far above soil formation rates,[139] meaning an ongoing loss of valuable topsoil that poses an extremely

[134] NRC 2010.
[135] NGSF I 2004, at 60.
[136] Owen 2011, Table 1.
[137] Based on USDA Agricultural Resource Management Surveys (ARMS). Data accessible at: http://www.ers.usda.gov/data-products/arms-farm-financial-and-crop-production-practices/tailored-reports-crop-production-practices.aspx.
[138] HR Kochia 1 & 2 (2015).
[139] Montgomery 2007, USDA NRCS 2015.

serious long-term threat to American agriculture and American society more broadly. The increased soil erosion expected with the new dicamba uses are significant social costs that EPA has not considered in its assessment of the proposed registration.

5. Dicamba, DR crops and land consolidation

Economists have found that herbicide-resistant crop systems tend to reduce labor needs on the farm.[140] USDA agricultural economists MacDonald et al. agree: "HT [herbicide-tolerant] seeds reduce labor requirements per acre."[141] MacDonald's team examined factors responsible for the continuing increase in farm size in American agriculture. They found that innovations like herbicide-resistant seeds that reduce the amount of labor required for field operations allow farming more acres. Large growers of herbicide-resistant crops are generally in a better position to absorb the costs of buying or leasing additional land for expansion, and so outcompete small and medium-size growers, who are thereby put at a competitive disadvantage and potentially out of business. Thus, MacDonald et al. find that herbicide-resistant seeds are a likely contributor to increased consolidation among field crop farmers since 1995.[142]

EPA should assess the impacts of the proposed new uses of dicamba on labor, farm size, land consolidation, welfare of small to medium-size farmers, and the economic health of rural communities. The discussion above suggests that registration of the new uses could have significant social costs.

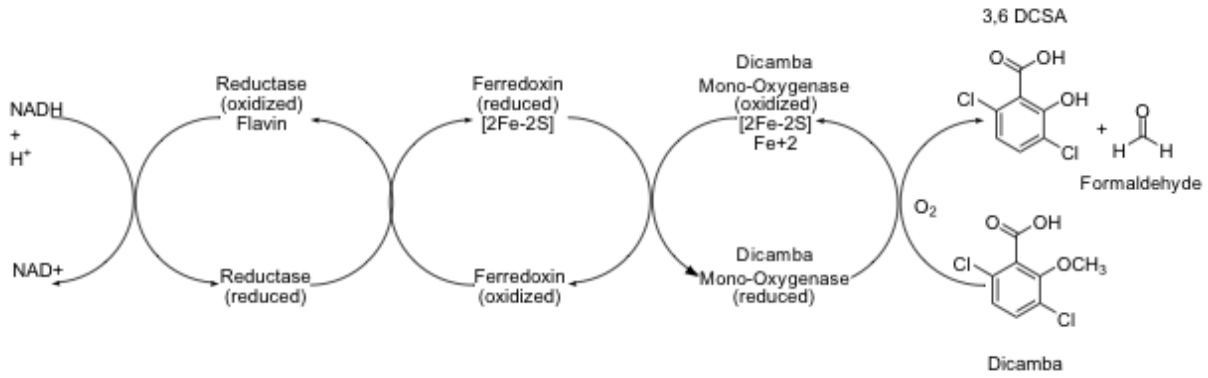
Under FIFRA, EPA cannot approve a proposed registration or proposed use if there would be "unreasonable adverse effects on the environment" from the pesticide use, defined as "any unreasonable risk to man or the environment, taking into account the economic, social, and environmental costs and benefits of the use of any pesticide." Yet, EPA's Benefits Analysis fails to affirm or assess Monsanto's claimed benefits, and entirely fails to show that the purported benefits outweigh the unreasonable adverse effects of the proposed use. Instead, as explained above, EPA's assessment fails to critically assess numerous unreasonable adverse effects of approving the proposed use. EPA also failed to quantitatively or meaningfully assess the significant environmental and economic costs of these adverse effects against the purported benefits of the propose use. EPA's Benefits Analysis failed to make the requisite legal finding that the benefits of the proposed approval would outweigh its risks such that approving the proposed dicamba use on dicamba-resistant cotton and soybean would not have "unreasonable adverse effects on the environment." EPA must critically reassess the potential benefits of the proposed use against its numerous significant environmental and economic costs.

VI. EPA's Assessment of Human Health Risks Violates FIFRA and the FFDCA.

[140] Gardner et al. 2009.
[141] MacDonald et al. 2013, p. 28.
[142] MacDonald et al. (2013).

Monsanto's genetically engineered, dicamba-resistant soybeans and cotton enable the entirely novel uses of dicamba that EPA has proposed to register: spraying the herbicide at high levels directly on growing dicamba-resistant soybeans or cotton to kill nearby weeds throughout the growing season. Because of dicamba's toxicity to conventional soybeans and cotton, it is little used in conventional production of these crops. When used, it is applied primarily "pre-emergence" to clear a field of weeds prior to crop "emergence" to avoid crop injury.

Dicamba resistance is conferred by genetically engineering a gene encoding an enzyme, dicamba mono-oxygenase (DMO), into dicamba-resistant (DR) soybeans and cotton. This DMO enzyme, derived from a soil bacterium, is expressed in the DR crops and demethylates dicamba to form metabolites, chiefly 3,6-dichlorosalicylic acid (DCSA) and formaldhyde, that are generated at levels that are not toxic to the plant, as depicted below. DCSA is not found, or only at extremely low levels, in conventional crops that come into contact with it.



EPA's Assessment of the Carcinogenicity of Dicamba

Animal experiments

EPA describes two animal studies (rat and mouse) on the potential carcinogenicity of dicamba.[143] In the rat study, four groups of 60 animals of each sex were either untreated (control) or fed one of three doses of dicamba for 115 (male) or 117 (female) weeks. Seven percent (4 of 60) of the male rats in each of the two higher-dose groups contracted malignant lymphomas, while no lymphomas were found in the control group or low-dose group (each 0 of 60). In addition, 0/60, 2/60 and 5/60 male rats in the low, medium, and high-dose groups, respectively, contracted thyroid parafollicular cell carcinomas, along with 1/60 males in the control group.

[143] EPA, Dicamba and Dicamba BAPMA Salt: Human Health Risk Assessment for Proposed Section 3 New Uses on Dicamba-tolerant Cotton and Soybean 74-76 (Mar. 29, 2016) [hereinafter *Human Health Risk Assessment*].

EPA notes that: "The Cochran-Armitage trend test showed a statistically significant ($p \leq 0.05$) tendency for the proportion of animals with tumors to increase steadily with increase in dose." Thus, for two forms of cancer, the study exhibited "dose-response," an important indicator that the tumors are related to the treatment (dicamba) rather than due to chance. However, EPA dismissed the statistically significant trends for both cancers because a second statistical test involving pairwise comparisons did not show statistical significance.

EPA followed accepted practice in analyzing the carcinogenicity data with a trend test, and the Cochran-Armitage test is most commonly used for this purpose. It is also accepted practice to make a pairwise comparison of the incidences of animals with tumors in the high dose and control groups.[144] However, the highest dose used in the study should be based on the "maximum tolerated dose,"[145] which was not the case here. In the context of carcinogenicity experiments, the maximum tolerated dose (MTD) is defined as "[t]he highest dose … which, when given for the duration of the chronic study, is just high enough to elicit signs of minimal toxicity without significantly altering the animal's normal lifespan due to effects other than carcinogenicity."[146]

However, no toxicity other than cancers was observed in this experiment. EPA notes that the rats treated with dicamba did not exhibit ***any*** signs of systemic toxicity,[147] that the animals would likely have tolerated substantially higher doses, and that "an MTD was not achieved." Thus, EPA's dismissal of the statistically significant trend of increasing number of tumors with increasing dose of dicamba based on lack of statistical significance in the pairwise comparison of control and high-dose groups is not legitimate, because the study did not incorporate a maximum tolerated dose as demanded by accepted protocol for animal carcinogenicity experiments with chemicals.

In the mouse study, five groups of mice of each sex were either untreated (control group) or received one of four doses of dicamba for 89 (males) or 104 (females) weeks. Of the 10 groups (5 male, 5 female), EPA reports the number of animals with tumors for only two. Eight of the 52 female mice (15%) that were fed the second-lowest dose of dicamba contracted lymphosarcomas, compared to only 2 of 52 (4%) in the control group. The pairwise comparison of these two groups shows a statistically significant increase in lymphosarcomas, but EPA dismissed this finding due to a lack of dose-response (the presence of which was dimissed in the rat study), and because different groups of untreated control mice from entirely different studies tended to have a higher incidence of the tumor than the control group in this study (concurrent control). As in the rat study, the mouse study did not incorporate a maximum tolerated dose. EPA notes that in 1995, its RfD/Peer Review Committee had found that this "mouse carcinogenicity study was not tested at a high enough doses [sic] to evaluate carcinogenicity in the mouse." However, this

[144] Rahman & Armitage 2012.
[145] NRC 1993;FDA 2008; Rahman & Armitage 2012.
[146] FDA 2008 (citing the U.S. Interagency Staff Group on Carcinogens, 1986).
[147] "Treatment had no adverse effect on survival, body weight, body weight gain, food consumption, hematology, clinical chemistry, urinalysis, organ weights or gross pathology."

determination was overturned here, without explanation, and the study will not be repeated.

Both studies revealed statistically significant evidence of carcinogenicity. EPA dismissed the significant dose-response trend of increasing tumors with increasing dicamba dose in male rats because pairwise comparisons were not significant. A significant pairwise comparison result in the mouse study was dismissed because dose-response was not significant. Neither study incorporated a maximum tolerated dose, which is critical for legitimate application of the pairwise comparison test. Unless or until studies that incorporate maximum tolerated doses are conducted and their results definitively refute the present findings, based on existing evidence EPA should properly find that dicamba is carcinogenic.

Human evidence

Epidemiological studies have associated dicamba exposure with increased incidence of a number of cancers in pesticide applicators. In 1992, epidemiologists with the National Cancer Institute (NCI) found that Iowa and Minnesota farmers who were first exposed to dicamba prior to 1965 had increased incidence of non-Hodgkin's lymphoma (NHL) relative to controls, with an odds ratio of 2.8.[148] A subsequent study in Canada also found an association between exposure to dicamba and NHL.[149] A study of cancer in Iowa farmers associated exposure to benzoic herbicides[150] with increased risk of multiple myeloma,[151] which has since been identified as a subtype of non-Hodgkin's lymphoma.[152] A comprehensive meta-analysis of epidemiology assessing non-Hodgkin's lymphoma and exposure to agricultural pesticides also found an association with dicamba exposure.[153]

Exposure to pesticides has long been suspected as a risk factor in non-Hodgin's lymphoma due to a striking fact. While farmers are generally healthier, and have lower ***overall*** cancer rates than the general population, they have higher than average risk of contracting NHL and several other cancers.[154] This fact lends weight to epidemiology studies that find correlations between these cancers and and specific pesticides, such as dicamba. EPA does not discuss the increased incidence of NHL or any other cancer in farmers or pesticide applicators.

EPA fails to assess these studies, though CFS brought most of them to the Agency's attention several years ago.[155] Neither does EPA remark on or assess the commonality in cancer type (lymphatic system) in animal experiments and epidemiology: malignant lymphomas (male rats), lymphosarcomas (female mice), and non-Hodgkin's lymphoma

[148] A 2.8-fold higher risk of cancer than the unexposed control group. *See* Cantor et al 1992, Table 6.
[149] McDuffie et al 2001.
[150] Dicamba is the most widely used benzoic acid herbicide.
[151] Burmeister 1990.
[152] Schinasi and Leon 2014.
[153] Schinasi and Leon 2014.
[154] Blair & Zahm 1995.
[155] *See* Exhibit B (attached).

(pesticide applicators). This may well indicate that dicamba has a common mechanism of action targeting the lymphatic system in animals and humans.

The only epidemiology study assessed by EPA in its six-sentence treatment of epidemiology data.[156] is from the Agricultural Health Study,[157] Samanic et al. found found suggestive associations between dicamba exposure and both lung and colon cancer, with statistically significant exposure-response trends in both cases.[158] EPA's cursory review of Samanic et al. (2006) is biased, incomplete and erroneous, failing to report even the specific types of cancer – lung and colon – for which the authors found dicamba dose-response trends when the referent group was low-exposed applicators. EPA reports that they found a significant trend (p = 0.02), failing to specify this trend was between dicamba exposure and **lung** cancer. Contrary to EPA, this lung cancer trend was ***not*** "largely due to elevated risk at the highest exposure level." The authors identified a still more significant trend for **colon** cancer (p = 0.002), and it is this trend that was largely due to elevated risk at the highest exposure level. Samanic et al. describe their results in part as follows:

> "When the reference group comprised low-exposed applicators, we observed a positive trend in risk between lifetime exposure days and lung cancer (p = 0.02), but none of the individual point estimates was significantly elevated. We also observed significant trends of increasing risk for colon cancer for both lifetime exposure days and intensity-weighted lifetime days, although these results are largely due to elevated risk at the highest exposure level."

EPA also fails to assess a previous Agricultural Health Study[159] that likewise found "a positive trend in risk for lung cancer with lifetime exposure days for dicamba…" (as quoted in Samanic et al. 2006).

Samanic et al. find that "the patterns of association observed for lung and colon cancers warrant further attention" and propose to re-examine dicamba "when larger numbers will allow for a more comprehensive evaluation of lung and colon cancer, as well as additional cancer cites." With registration of the proposed new uses, many more farmers would be exposed to higher levels of dicamba than ever before, providing epidemiologists with additional cancer cases to analyze.

EPA has failed to properly assess either animal or human evidence of dicamba's potential carcinogenicity, or to consider the implications of the common cancer types (lymphatic system) found in animal studies and human epidemiology studies.

<u>*EPA's Assessment of the Chronic Toxicity of Dicamba and its Metabolites*</u>

Point of Departure based on the DSCA study

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[156] EPA, *Human Health Risk Assessment*, at 29-30,
[157] Samanic et al. 2006.
[158] Weichenthal et al 2010.
[159] Alvanaja et al. 2004.

EPA assessed a number of animal feeding studies with dicamba and its major metabolite (DCSA) in dicamba-resistant soybeans and cotton to establish a purported "safe" level of chronic (long-term) human dietary exposure. The studies were submitted by the registrant, and involved long-term administration of dicamba or DCSA to rats, rabbits or dogs at various levels to assess potential reproductive, developmental or neurological toxicity, among other endpoints.[160] Consistent with its standard practice, EPA chose the registrant-submitted study that revealed adverse effects at the lowest dose as its "point of departure" for calculating the highest level of long-term dietary exposure to dicamba that is presumed "safe" for human beings, known as the chronic reference dose (cRfD).

The "point of departure" study chosen by EPA was a two-generation rat reproduction study involving DCSA. In this study, following pre and/or post-natal exposure, rat pups exhibited signs of toxicity (decreased body weight) at levels of DSCA that were approximately ten-fold lower than did adult rats.[161] EPA established the lowest observed adverse effect level (LOAEL) at 37 mg/kg/day, and the no observed adverse effect level (NOAEL) at 4 mg/kg/day.[162] After applying the standard 100X uncertainty factor to the NOAEL for application of these findings to humans (10X for interspecies extrapolation; 10X for intraspecies variation), EPA established a chronic reference dose (cRfD) of 0.04 mg/kg/day. Even though rat pups were 10-fold more sensitive to DCSA than adults, EPA did not apply the additional 10X safety factor demanded by the Food Quality Protection Act (FQPA) when toxicology tests demonstrate that the young are more susceptible than adults. Thus, based on the findings in the DCSA point of departure study, EPA should have applied the FQPA safety factor and set the cRfD at 0.04 x 0.1 = 0.004 mg/kg/day rather than 0.04 mg/kg/day.

Point of Departure based on beagle study not considered by EPA

EPA failed to consider another study in its database that the Agency once used to establish a still lower cRfD. In this study, beagle dogs were administered dicamba in their diets for two years at three different doses, in addition to an untreated control group. The doses of 5, 25 or 50 ppm corresponded to 0.125, 0.625 or 1.25 mg/kg/day. Based on the observation of reduced body weight in males at the 25 ppm = 0.625 mg/kg/day dose, EPA identified an NOAEL of 5 ppm = 0.125 mg/kg/day based on this study. After application of a standard uncertainty factor of 100X, EPA established a chronic reference dose of 0.0013 mg/kg/day.[163] A National Research Council committee recommended a very similar acceptable daily intake (ADI) level (equivalent to cRfD) for dicamba of 0.00125 mg/kg/day,[164], as noted by EPA.[165]

[160] EPA, Human Health Risk Assessment, Tables A.2.4, A.2.5, A.2.6.
[161] EPA, *Human Health Risk Assessment*, at 21.
[162] EPA, *Human Health Risk Assessment*, at 21, 25.
[163] EPA 1987.
[164] NRC 1977.
[165] EPA 1987.

EPA provides no assessment of this study in any of the registration documents, though it was brought to the Agency's attention three years ago by CFS.[166]

Estimated exposure relative to alternative cRfD values

EPA provides estimates of human dietary exposure (food + water) to dicamba and its metabolites that greatly exceed both alternative cRfD values discussed above. Chronic dietary exposure to dicamba is estimated at 0.006319 mg/kg/day for the general U.S. population and 0.016988 mg/kg/day for the most highly exposed subgroup, children 1-2 years of age.[167] Below we compare these exposure levels to the alternative cRfD values.

Population	**Dietary exposure**	**DCSA study (adj. 10X FQPA)**		**Beagle study (EPA 1987)**	
		cRfD	**% exceedance**	**cRfD**	**% exceedance**
General U.S.	0.006319	0.004	58%	0.0013	386%
1-2 yrs. old	0.016988	0.004	325%	0.0013	1207%

Based on the DSCA study with application of the 10X FQPA safety factor and EPA's estimates of human dietary exposure to dicamba, the general U.S. population and children 1-2 years old are exposed to levels of dicamba that exceed the cRfD by 58% and 325%, respectively. Based on the beagle study that EPA used to set a chronic reference dose in 1987, the estimated exposure of the U.S. population and 1-2 year old children to dicamba is nearly 400% and 1200% greater than the cRfD, respectively. Thus, Americans' exposure to dicamba as estimated by EPA is far above the level the Agency formerly regarded as safe.

Unfortunately, this would not be the first time the Agency has sharply increased the level of exposure to a pesticide it regards as safe, based on unexplained dismissal or dubious reinterpretation of old studies in favor of newer ones that sharply raise the "safe" level of exposure. For instance, EPA radically and unjustifiably altered its interpretation of a key study on the herbicide 2,4-D to accommodate the greatly increased use and exposure that would result from rising use of 2,4-D on corn and soybeans engineered to resist it.[168] In the case of glyphosate, EPA has raised the maximum "safe" level of exposure 17.5-fold since just 1983.[169]

Formaldehyde exposure

Formaldehyde is generated as a byproduct when dicamba is metabolized in DR soybeans and cotton to DCSA (see figure above). EPA should consider potential human health impacts from exposure to formaldehyde in food or feed derived dicamba-resistant soybeans and cotton that has been treated with dicamba.

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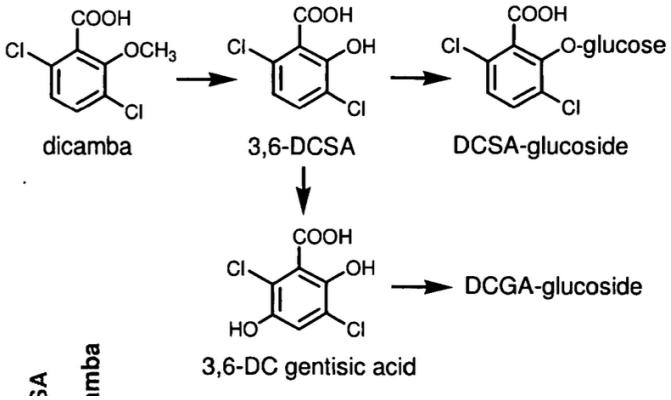
[166] *See* Exhibit B (attached).
[167] EPA, *Human Health Risk Assessment*, at 37 Table 5.4.6.
[168] Callahan 2015.
[169] EPA 1983; *see also* CFS 2015, *Glyphosate and cancer risk: frequently asked questions*, *available at* http://www.centerforfoodsafety.org/files/glyphosate-faq_64013.pdf.

Metabolites of dicamba

When dicamba is applied to dicamba-resistant soybeans and cotton, the herbicide is absorbed and translocated internally to various plant tissues. The novel DMO enzyme expressed in DR soybeans and cotton converts dicamba to 3,6-DSCA and formaldehyde, as discussed above. DCSA in turn undergoes a process known as conjugation – the attachment of sugar molecules to the chemical to form compounds known generically as glycosides. When the sugar molecule that is attached is glucose, the "conjugates" are known glucosides. In dicamba-resistant soybeans, a metabolism study using radioactively labeled dicamba shows that the major dicamba metabolite is DCSA-glucoside (see figure below).

> "A new metabolism study submitted by the registrant on dicamba resistant soybean shows that the identified dicamba metabolites were DCSA glucoside (60.32-74.48% of TRR), which was the major component in dicamba-tolerant soybean, DCSA HMGglucoside (1.14-7.62% of TRR), DCGA glucoside (0.75-4.32%), DCGA malonylglucoside (0.73-5.46% of TRR), DCSA (1.54- 4.08% of TRR), in addition to two minor un-identified metabolites characterized as mixtures of unknown DCSA and DCGA conjugates, each constituted less than 2.0% of the TRR."[170]



Source: Feng, PCC (2013). Methods and composition for improving plant health. U.S. Patent 2013/0217576 A1, August 22, 2013. Figure 11: Metabolism of 14C-dicamba to DCSA and conjugation to glucoside in whole plant studies.

DCSA glucoside represents roughly 60-74% of the total recovered radioactivity (TRR); that is, 60-74% of the radioactively labeled dicamba that was applied to the plant and recovered when the plants were analyzed. In contrast, DCSA in its unconjugated or free form represents just 1.5-4% of the TRR, on the order of 20- to 40-fold less than DCSA glucoside.

[170] EPA, *Human Health Risk Assessment*, at 30.

It is well known that intestinal bacteria have the general capacity to split off the glucoside component of conjugated chemicals like DCSA glucoside, thus liberating the non-glucoside component (here, DCSA).[171] Thus, there is a clear potential for animals or human beings that consume feed or food derived from dicamba-resistant soybeans to be exposed not only to the relatively small amount of free DCSA they contain, but also to the much larger amount of DCSA that may be liberated from the DCSA-glucoside conjugate upon ingestion. The same is true of other conjugated metabolites of dicamba (e.g. DCGA-glucoside).

Thus, EPA must consider the potential exposure to DCSA and other metabolites of dicamba that are released from glucoside-conjugated forms of these metabolites when animals or humans consume food or feed derived from dicamba-resistant soybeans and cotton that have been treated with dicamba. This issue is also discussed in the context of potential environmental impacts in the section of our comments addressing potential risks to threatened and endangered species.

CFS addresses additional potential health concerns of the proposed new uses of dicamba in prior comments submitted to the Agency.[172]

CONCLUSION

For the reasons described above and discussed in detail in the attached exhibits and CFS's previously submitted comments, CFS requests EPA comply with FIFRA, FFDCA, MBTA, and the ESA by critically considering the effects to listed species and their critical habitats, as well as the numerous unreasonable adverse human health, environmental, and socioeconomic effects stemming from proposed new uses of dicamba on dicamba-resistant, GE cotton and soybean.

Submitted by,
Center for Food Safety

[171] Stella 2007.
[172] *See* Exhibits A-B (attached).

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