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FOOD SAFETY

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Comments to EPA on Notice of Receipt of Application to Register New Use of Dicamba on Monsanto's Dicamba-Resistant MON 87708 Soybean

Center for Food Safety, Science Comments

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Notes on science comments

These comments submitted by Center for Food Safety are one of two sets of comments from our organization. Legal comments are also being submitted. The references cited have been uploaded as supporting materials. The filenames for these documents match the citations in the text (e.g. Benbrook 2009a). Full citations are included at the end.

The impact of the proposed registration on herbicide use

Summary of herbicide use

The proposed registration would permit the use of dicamba herbicide on Monsanto's MON 87708 soybean, which is genetically engineered to withstand direct application of high rates of dicamba without risk of crop injury. Like many other herbicide-resistance genes used or envisioned for herbicide-resistant crops, the dicamba-resistance gene is derived from a soil bacterium that was originally intended for bioremediation. Public sector research intended to ameliorate pesticide pollution has been "repurposed" by pesticide-biotech firms to increase it. At present, dicamba is little used in American agriculture, and hardly at all in soybean production, with drift-related crop injury a major deterrent to wider use. The proposed registration in combination with deregulation of MON 87708 would sharply erode inhibitions that currently constrain use of this drift-prone herbicide, facilitating a sharp increase in agricultural use of dicamba: a projected 50 million lbs. on soybeans and an additional 8 million lbs. on corn. The anticipated introduction in several years of dicamba-resistant varieties of corn and cotton would drive dicamba use still higher. This increased dicamba use is unlikely to displace much if any of the glyphosate that currently dominates weed control in soybeans, meaning that overall herbicide use will rise sharply as well. The proposed registration for dicamba use on MON 87708 poses serious threats with respect to drift injury and herbicide-resistant weeds that EPA should give careful consideration.

Introduction

The Monsanto Company seeks registration of dicamba herbicide, glycolamine salt, for use on MON 87708 soybean, a variety genetically engineered to withstand direct application of high rates of dicamba (3,6-dichloro-2-methoxybenzoic acid). Dicamba resistance[1] is conferred by an enzyme, dicamba mono-oxygenase (DMO), that demethylates dicamba to form the non-phytotoxic 3,6-dichlorosalicylic acid (DCSA) as well as formaldhyde, as depicted below.

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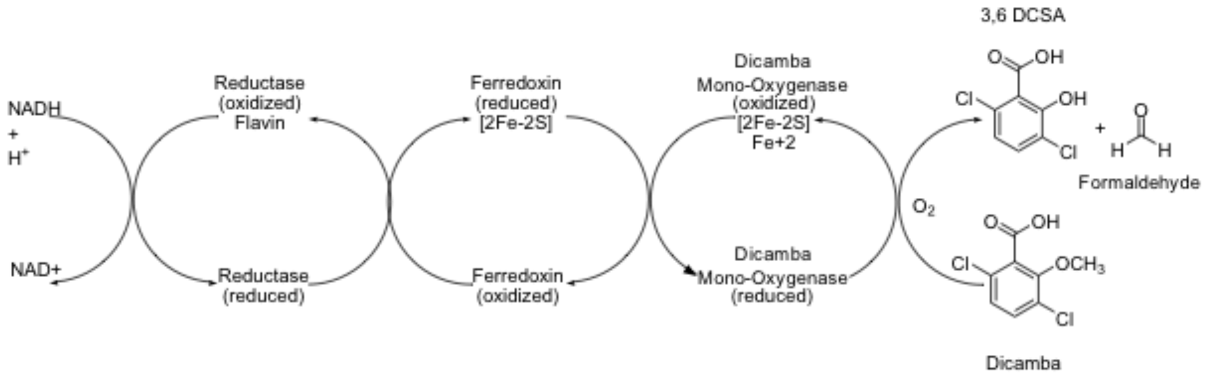
[1] Monsanto follows the biotechnology industry practice of misidentifying its crop as "dicamba-tolerant." The Weed Science Society of America has officially defined crops of this sort as "herbicide-resistant," while "herbicide-tolerance" refers to a natural species attribute. See WSSA (1998). For two of many examples of consistent, standard scientific usage of the term "herbicide-resistant" in reference to crops with this attribute, see Kruger et al (2010a) and the following book: Nandula, VK (ed.). *Glyphosate Resistance in Crops and Weeds: History, Development, and Management*, John Wiley & Sons, Inc. 2010. EPA is urged to follow standard scientific usage and to refer to Monsanto's crop correctly as "dicamba-resistant" rather than "dicamba-tolerant" in all regulatory documents.



DMO was initially purified from strain DI-6 of *Stenotrophomonas maltophilia*, found in soil and water samples obtained from storm water retention ponds at a dicamba manufacturing plant in Beaumont, Texas (Krueger et al 1989[2]). In this paper, Krueger and colleagues envisioned the use of this *S. maltophilia* strain as follows:

"Organisms capable of degrading dicamba and/or its 3,5-isomer … may be useful for facilitating the rapid dissipation of both isomers from the environment" (p. 534).

In the presence of this organism: "…dicamba is metabolized to ***compounds that are less of an environmental concern***. Complete mineralization of dicamba would result in reduced environmental exposure to degradation products and reduced potential for leaching of dicamba or its metabolites to groundwater" (p. 538, emphasis added).

Chakraborty et al (2005), who isolated and purified DMO from this same organism,[3] also make passing reference to the function of such bacteria as "useful in the bioremediation of harmful pollutants" (p. 20). Paradoxically, in the same paper, they note that DMO "has recently been utilized to develop transgenic plants that are tolerant to dicamba levels that are 10 to 20 times higher than the typical field application rate" (p. 27).

This discussion highlights a general phenomenon. There was a spate of research undertaken in the 1980s and 1990s to isolate or engineer microorganisms for bioremediation of pesticides and other toxic compounds in soils and water (e.g. at toxic waste dumps). Much of this research was funded by the public sector with the goal of reducing human and environmental exposure to toxic compounds, for instance by the

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[2] Krueger et al (1989) identified the source bacterium as a Pseudomonas species. In 1993, it was reclassified as S. maltophilia. See http://www.uptodate.com/contents/stenotrophomonas-maltophilia.

[3] Which they incorrectly named *Pseudomonas maltophilia*, apparently unaware of the 1993 reclassification to *S. maltophilia* noted in the previous footnote. Interestingly, most papers regarding DMO engineered into dicamba-resistant plants make the same mistaken identification of the source organism. For one of many examples, se: Behrens MR et al (2007). While perhaps oversight, it is also possible that the misidentification stems from a wish to avoid any association of DMO with *S. maltophilia*, which has emerged as a serious opportunistic pathogen in immunocompromised patients, a pathogen whose control is made difficult by the organism's acquisition of resistance to numerous classes of antibiotics.

Swiss government (Zipper et al 1999) and the EPA (Short et al 1991). To the best of our knowledge, none of these well-intentioned research efforts bore fruit in terms of successful bioremediation applications.

However, knowledge gained in this research has more recently been applied by pesticide companies and their university collaborators for the precisely contrary purpose of fostering much greater use of herbicides, which of course leads to greater pollution of the environment. For instance, Monsanto derived the EPSPS gene/enzyme utilized in most glyphosate-resistant crops from the CP4 strain of *Agrobacterium* originally isolated from the grounds of its Louisiana glyphosate manufacturing plant (Charles 2001, pp. 68-69). *Sphingobium herbicidovorans*, originally researched as a potential candidate for bioremediation of phenoxyalkanoic acid herbicides (Kohler 1999), has been utilized by Dow Chemical Co. to genetically engineer a corn variety resistant to phenoxy auxin broadleaf and AOPP ("fops") grass herbicides (Wright et al 2010).

In fact, it has now become abundantly clear that the major focus of pesticide-biotechnology industry R&D efforts is to exploit the herbicide resistance that has evolved in soil bacteria from past use of their products to facilitate many-fold higher rates of application to plants engineered with the resistance-conferring microbial genes. Fourteen of 19 GE crops awaiting deregulation by the U.S. Dept. of Agriculture are resistant to one to three herbicides each (USDA APHIS 2012). DuPont-Pioneer scientists recently sketched out the industry-wide strategy of engineering multiple herbicide-resistant crops to be utilized in combination with premix formulations of the corresponding herbicides (Green et al 2007). This same paper compiles a list of transgenes that await deployment in herbicide-resistant crops, most derived from microbes, and presumably soil microbes (see Table 1 below).

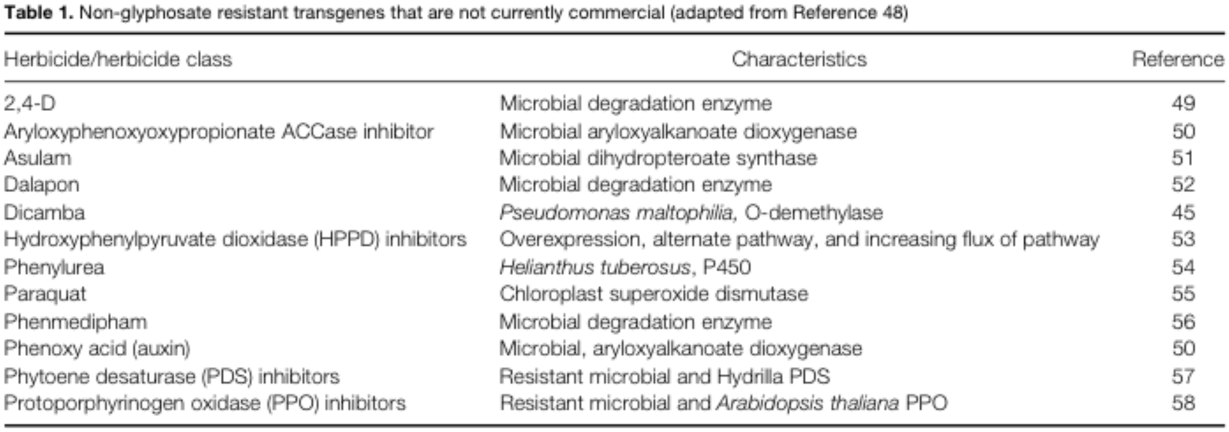

Table 1. Non-glyphosate resistant transgenes that are not currently commercial (adapted from Reference 48)

Herbicide/herbicide class	Characteristics	Reference
2,4-D	Microbial degradation enzyme	49
Aryloxyphenoxyoxypropionate ACCase inhibitor	Microbial aryloxyalkanoate dioxygenase	50
Asulam	Microbial dihydropteroate synthase	51
Dalapon	Microbial degradation enzyme	52
Dicamba	*Pseudomonas maltophilia*, O-demethylase	45
Hydroxyphenylpyruvate dioxidase (HPPD) inhibitors	Overexpression, alternate pathway, and increasing flux of pathway	53
Phenylurea	*Helianthus tuberosus*, P450	54
Paraquat	Chloroplast superoxide dismutase	55
Phenmedipham	Microbial degradation enzyme	56
Phenoxy acid (auxin)	Microbial, aryloxyalkanoate dioxygenase	50
Phytoene desaturase (PDS) inhibitors	Resistant microbial and Hydrilla PDS	57
Protoporphyrinogen oxidase (PPO) inhibitors	Resistant microbial and *Arabidopsis thaliana* PPO	58

From: Green et al (2007).

In short, government and university-funded research originally undertaken to ameliorate pesticide pollution has been "repurposed" by industry to greatly increase it. The pesticide-biotech industry is guiding American agriculture into an era of much increased use of and dependence on pesticides, contrary to widespread misconceptions on this point.

Herbicide-resistant (HR) crops are weed control systems involving one or more post-emergence applications of the HR crop-associated herbicide(s). Dow describes its 2,4-D-resistant corn and soybeans as the "Enlist Weed Control System" (DAS 2011a), with the brand name "Enlist" referring to both the HR trait and Dow's proprietary 2,4-D herbicide. Monsanto describes its HR crops in similar terms: "The utilization of Roundup agricultural herbicides plus Roundup Ready soybean, collectively referred to as the Roundup Ready soybean system..."[4] Likewise, Monsanto speaks of integrating dicamba-resistant soybean event MON 87708 "into the Roundup Ready soybean system" (Monsanto 2010 at 211). As discussed further below, the intended effect of marketing the HR crop and corresponding herbicide(s) as a packaged "system" is to foster an entirely unsustainable approach to weed control that leads directly to rapid evolution of weed resistance.

The proposed registration would lead to sharply increased and unprecedented use of dicamba in American agriculture

Dicamba a little used herbicide

Dicamba is used very little in American agriculture. According to figures from the agricultural consulting firm AgroTrak, as reported by Monsanto, agricultural use of dicamba has ranged from 2.7 to 9.4 million lbs./year from 1990 to 2008 (Monsanto 2010 at 198). Dicamba thus represents just 0.5-1.6% of all herbicides applied in U.S. agriculture during this period.[5] AgroTrak data also shows relatively little acreage treated with dicamba, ranging from just 17.4 to 36.3 million acres (Id.), or roughly 4-8% of total U.S. cropland during this period.[6]

Registered uses of dicamba include asparagus, barley, corn, cotton, fallow cropland, hay, oats, proso millet, pasture, rangeland, sorghum, soybean, sugarcane and wheat (BASF 2010).

Agricultural use of dicamba has declined over the past 15 years, peaking in 1994 at 9.4 million lbs., and declining to less than 30% of that level by 2008 (2.7 million lbs.). These figures from AgroTrak agree reasonably well with EPA estimates of dicamba's agricultural use. Acreage treated has fallen by roughly half, from 36.3 to 20.2 million acres. In 2007, dicamba was applied to just 5% of American cropland.

Dicamba is both an effective and inexpensive broadleaf herbicide. It controls a wide range of annual, biennial, perennial and woody weeds. Treatment with a typical dose of 1 pt./acre (0.25 lb/acre) costs just $3.50 to $6.44, making dicamba one of the cheaper

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[4] From: "Petition for the Determination of Nonregulated Status for Roundup Ready2Yield Soybean MON89788," submitted to USDA by Monsanto on June 27, 2006 (revised November 3, 2006), APHIS Docket No. APHIS-2006-0195, p. 4.

[5] Total agricultural herbicide use ranged from 498-583 million lbs. from 1990-2007 (EPA Pesticide Use 2011).

[6] Based on USDA Agricultural Census data from 1992 to 2007, showing 406 to 435 million acres of "total cropland" during this period. Since a major use of dicamba is on rangeland, which is not included in "total cropland," these percentages may be slight overestimates.

herbicides on the market.[7] This raises the dual questions of why dicamba has never been widely used, and further why its use has declined steeply over the past 15 years.

One important reason dicamba has had little use is its high potential to drift and volatilize, causing crop injury. This is likely a factor influencing farmers in switching from dicamba to sulfonylurea herbicides in wheat, and to new broadleaf herbicides in corn (Monsanto 2010 at 197). This is discussed further below.

Current use of dicamba in soybeans

There is practically no use of dicamba in soybeans. Because of the crop's great sensitivity to injury from this herbicide, usage is limited to preplant applications. The label for Clarity, BASF's diglycolamine salt of dicamba, advises farmers to use from 0.125 to 0.5 lb. dicamba per acre for this purpose (BASF 2010). Due to dicamba's residual activity, use of 0.25 lb./acre or less requires a waiting interval of 14 days and minimum rainfall of 1" prior to soybean planting to avoid injury to emerging soybeans; use of 0.5 lb./acre requires a waiting interval of 28 days and at least 1" rainfall prior to planting. The need for waiting intervals and rainfall to avoid crop injury likely explains why so little dicamba is used in soybean production. On average, just 1.0 application of 0.25 lb./acre dicamba was applied to roughly 64,000 soybean acres in 2006, for overall use of just 16,000 lbs. dicamba (USDA NASS AgChem 2006).

The dicamba label also permits a preharvest application of dicamba, with recommended rates from 0.25 to 1 lb./acre. Soybeans cannot be harvested until 7 days after a preharvest application, and soybean fodder and hay cannot be fed to livestock. California prohibits preharvest applications. Because of these restrictions, and the fact that preharvest applications are made only as rescue treatments in those unusual situations where weeds have gotten completely out of hand, such applications are rare. The data above confirm that very few growers use dicamba for this purpose.

Dicamba use under the proposed label

According to information from Monsanto 2010 (p. 208), the proposed label would permit up to 1 lb./acre preemergence, in one or several applications, on MON 87708, with elimination of the planting restrictions (waiting intervals and rainfall). The label also proposes two postemergence applications of up to 0.5 lb./acre each through the R1/R2 bloom stage. The maximum annual amount of dicamba would be 2 lbs./acre. It is unclear whether the proposed label provides for a preharvest application, as does the current label.[8]

i. Dicamba use on soybeans

Perhaps the major impact of the proposed registration on dicamba use would be to facilitate a switch from Roundup Ready soybeans to MON 87708 stacked with Roundup Ready. While EPA has no control over MON 87708, this soybean variety would not be

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[7] Based on price data for Banvel and Clarity in U. of Tenn (2011).

[8] If a preharvest application continues to be allowed, growers who do not make full use of the 2 lbs./acre maximum annual rate in pre- and postemergence use could apply the difference before harvest.

commercially introduced or grown without EPA registration of dicamba for use on MON 87708.

MON 87708 soybeans remove the biological constraint of crop injury that has virtually precluded any use of this herbicide in soybean production. In terms of preemergence use, farmers would be much more likely to use dicamba if they did not have to wait 14 to 28 days from application to planting, or depend on rainfall to reduce dicamba concentrations below phytotoxic levels. Dicamba's residual activity would then prove to be a benefit in controlling early-season weeds rather than a threat to the emerging soybean seedling. Farmers would likely make one or two applications of dicamba, one shortly before or at crop planting to maximize residual weed control benefits. Although Monsanto plans to recommend that growers use a soil residual herbicide in addition to both dicamba and glyphosate for the purpose of forestalling resistance to either herbicide, farmers are very unlikely to take on this added expense. First, soil residual herbicides have become very unpopular with the majority of growers who use a total postemergence program with Roundup Ready crops. Second, those growers who might consider a soil residual herbicide application are likely to regard it as redundant, given dicamba's at least limited residual activity in suppressing weeds that emerge within several weeks of application.

A much bigger impact of the proposed registration for MON 87708 would be to enable entirely new post-emergence use of dicamba, up to 1 lb./acre/year. In 2011, fully 94% of U.S. soybean acreage was planted to Roundup Ready varieties. Roundup Ready soybeans have fostered a huge shift to weed control programs that rely exclusively or primarily on post-emergence use of glyphosate. Growers who are already accustomed to growing RR soybeans, and who then switch to adopt MON 87708 stacked with the Roundup Ready trait, would be likely to make substantial use of the post-emergence portion of the label, particularly to control glyphosate-resistant weeds.

ii. Dicamba use on other crops

The proposed registration would also facilitate significant increases in dicamba use on other crops. Cereal crops are naturally tolerant of dicamba, and together with pasture and rangeland represent the major uses of dicamba at present. In 2010, just over 1 million lbs. of dicamba were applied to 6.0 million acres of corn, 7% of total field corn acres (USDA NASS AgChem 2010). In 2009, dicamba was applied to 5.9 million acres of wheat, 10% of wheat acres.[9] The other major uses of dicamba include fallow land, pasture and sorghum (Monsanto 2010 at 199, Table VIII-12).

Dicamba is rated highly for control of typical broadleaf weeds in corn and wheat, and as noted above is very inexpensive. The major factor limiting its much wider use in these crops is the high risk of crop injury to soybeans and other sensitive crops from dicamba spray drift. Widespread adoption of MON 87708, as facilitated by granting the proposed registration, would greatly erode the major obstacle to expanded use of dicamba in

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[9] Calculated from USDA NASS pesticide use data for spring wheat, durum; spring wheat, excl. durum and winter wheat for 2009, from tables at http://www.nass.usda.gov/Data_and_Statistics/Pre-Defined_Queries/2009_Wheat_Chem_Usage/index.asp.

American agriculture. Steve Smith, the Director of Agriculture at Red Gold, an Indiana-based tomato processor which sources tomatoes from family farmers in Indiana, Ohio and Michigan, explains the situation well:

> "The use of dicamba is not new. It has been a labeled product for use on corn for decades. It has been proven effective for many uses and is not particularly vulnerable to developing resistant strains of weeds. It is economical to apply.
>
> So many may be wondering why a product that is effective, proven, and economical is not the number one herbicide in use today. The answer is simple. Dicamba has proven itself to move off-target and cause injury and yield reductions to soybeans and so in a large sense, it is rarely used. Farmers respect their neighbors and know they are at risk of causing injury if they use dicamba, so it is not widely and routinely used in corn production. However, when soybeans become tolerant to dicamba, it is very likely that the amount of dicamba used in corn production will skyrocket when the fear of soybean injury is eliminated. As an example, when glyphosate soybeans were first introduced, there was significant injury due to drift on corn the first few years. It didn't take long for applicators and farmers to gain a higher degree of respect for the injury that could occur. But once the widespread use of glyphosate resistant corn became common, that level of caution began to erode because it didn't really matter if you drifted onto your neighbor, because their crop was also glyphosate resistant. I also predict a similar fate for dicamba use once soybeans are made tolerant. With no fear of soybean injury, the use of dicamba on corn acreage will dramatically increase, raising the overall exposure of sensitive crops to injury. Because dicamba is deadly to weeds and cheap to use, it is a sure prediction that dicamba use will increase dramatically, followed by escalating crop losses."
> (Smith 2010)

Mr. Smith's assessment deserves serious consideration. He has extensive experience in Midwestern agriculture, having grown up on an Indiana family farm. He also has a degree in Agriculture from Purdue University, is a Certified Crop Advisor, and served as Regional Sales Manager for a seed corn and soybean company, in addition to his 22 years of experience with Red Gold.

Smith's assessment of the threat that expanded dicamba use poses to soybean and specialty crop production is supported by surveys of herbicide drift damage conducted by state pesticide control officers, which over two three-year periods (1996-1998 and 2002-2004) consistently found dicamba to be the 3rd most frequent culprit in crop damage from herbicide drift, behind only 2,4-D (#1) and glyphosate (#2). The frequency of dicamba drift damage is all the more remarkable given its limited use in comparison to 2,4-D and glyphosate. In 2007, 27 million lbs. of 2,4-D and 183 million lbs. of glyphosate were used agriculturally (EPA Pesticide Use 2011), 10-fold and 67-fold greater use, respectively, than dicamba.

iii. Projection of dicamba and 2,4-D use on soybeans based on Mortensen et al. (2012)

A recent peer-reviewed publication in the journal BioScience by Penn State weed scientist David Mortensen and colleagues offers a projection of increased herbicide use with introduction and widespread adoption of synthetic auxin-resistant soybeans, which includes both MON 87708 soybean and Dow's 2,4-D-resistant soybeans (Mortensen et al. 2012).[10] Figure 4 and its caption from that publication are reproduced below; the caption provides an explanation of the assumptions used in their projection.

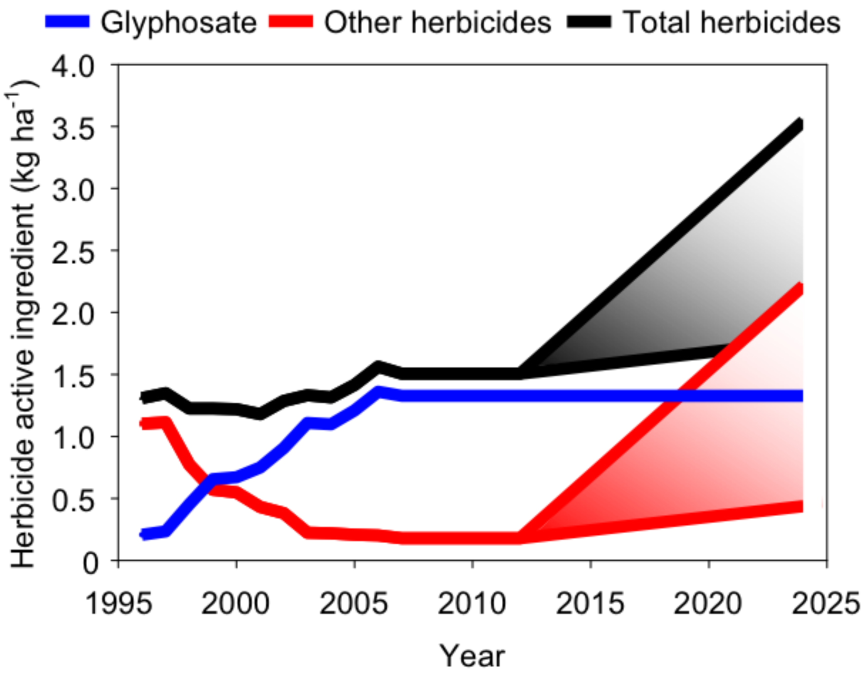

Figure 4. Total herbicide active ingredient applied to soybean in the United States. The data from 1996 to 2007 are adapted from Figure 2-1 in NRC (2010), and the projected data are based on herbicide programs described by Arnevik (2010) and Olson and Peterson (2011). To forecast herbicide rates from 2008 to 2013 we assumed that the applications of glyphosate and other herbicides will remain constant at 2007 levels until 2013, when new resistant soybean varieties are likely to become available. We estimated yearly increases in synthetic auxin herbicides (assumed to drive increases in other herbicides) by assuming that the adoption of stacked synthetic auxin–resistant cultivars mirrors the adoption of glyphosate-resistant cultivars, such that 91% of soybean hectares are resistant to synthetic auxin herbicides within 12 years. We further assumed that all soybean hectares with stacked resistance to glyphosate and synthetic auxin herbicides will receive an annual application of glyphosate and dicamba or 2,4-D. We assumed that the use rates of glyphosate will remain at current levels, and our estimates for dicamba and 2,4-D encompass lower (0.28 kilograms [kg] per hectare [ha]) and higher (2.24 kg per ha) use rates, which are in line with the rates currently used on tolerant crops (i.e., corn and wheat) and with rates being researched and promoted by Dow and Monsanto.

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[10] 2,4-D and dicamba are closely related members of the synthetic auxin class of herbicides, and are used at similar rates. Mortensen et al address these two HR soybean varieties together for purposes of the projection because they present many of the same risks.

Mortensen et al.'s Figure 4 shows annual baseline herbicide use of roughly 1.5 kg/ha (= 1.34 lbs/acre) on soybeans from 2007 to 2012. The first auxin-resistant soybean is assumed to be introduced in 2013. The rate of adoption of auxin-resistant crops is projected to mirror that of Roundup Ready crops: from 0 to 91% over 12 years. A broad range of possible auxin usage is projected on auxin-resistant soybean acres: from 0.28 kg/ha/year (0.25 lbs/acre/year) to 2.24 kg/ha/year (2 lbs/acre/year).

The low-end auxin projection of 0.28 kg/ha (0.25 lbs/acre) is based on current auxin usage on crops, such as corn and wheat, that have natural tolerance to auxin herbicides. The high-end auxin projection of 2.24 kg/ha (2 lbs./acre) is based on herbicide programs for auxin-resistant crops being promoted by Monsanto and Dow. Soybean acreage has averaged 74.1 million acres (30 million ha) from 2007 to 2011. If one assumes unchanged soybean acreage in 2025, then the projection estimates that 67.4 million acres (91% of 74.1 million) or 27.3 million ha would be planted to auxin-resistant varieties in 2025.

Based on the low-end projection, auxin use on soybeans in 2025 would be 7.6 million kg (16.9 million lbs). With the high-end projection, auxin usage on soybeans would be 61.2 million kg or 134.8 million lbs. The lower-end projection is clearly a substantial underestimate, since 0.25 lb/acre matches the average annual rate of dicamba currently applied by those few soybean growers who apply it preemergence (USDA NASS AgChem 2006).

Farmers who grow MON 87708 soybeans would likely make some combination of pre- and post-emergence applications of dicamba, weighted to POST applications. High preemergence rates of 0.5 to the maximum permitted 1 lb./acre would likely provide significant residual control of emerging, early-season weeds. This is suggested by the increased waiting interval presently required for 0.5 lb./acre (28 days) versus 0.125-0.25 lb./acre (14 days) preemergence applications. Postemergence use would be still more likely to approach the maximum permitted in the proposed registration (1 lb./acre in two 0.5 lb./acre applictions). Both the average POST application rate and the average number of POST applications would gradually climb from 2013 to 2025 as weed shifts occur to more dicamba-tolerant species, and dicamba-resistant weeds evolve. This development will mirror the rising rate and number of applications of glyphosate with increasing adoption of RR crops and emergence of GR weeds. Annual use of glyphosate on soybeans and cotton doubled and tripled, respectively, in the period when RR versions of these crops were widely adopted (Benbrook 2009a, p. 29). While rates used initially would probably be lower, by 2025, growers of MON 87708 soybeans would likely apply dicamba at annual rates of 1.5 to 2 lbs./acre, 75% to 100% of the maximum proposed seasonal use.

Mortensen et al.'s estimate for aggregate adoption of 2,4-D/dicamba-resistant soybeans is based on the rate of adoption of glyphosate-resistant soybeans, or 0 to 91% of soybean acreage over 12 years. Ninety-one percent of land planted to soybeans is roughly 67 million acres. Is this a realistic adoption scenario?

Monsanto and Dow are both targeting growers who have glyphosate-resistant and ALS-inhibitor-resistant weeds as their most likely market. It is estimated that one or more glyphosate-resistant weeds now infest 30 (Heap 2012) to 60 million (Bomgardner 2012) acres of U.S. cropland, with acreage infested growing rapidly (see discussion below). This doesn't take into account U.S. acreage infested with ALS inhibitor-resistant weeds, which CFS estimates at over 20 million acres based on reports listed in the International Survey of Herbicide-Resistant Weeds. If Monsanto's and Dow's assumption that soybean growers with resistant weeds are likely adopters of their respective products, then Mortensen et al.'s projection of 91% adoption of auxin-resistant soybeans by 2025 appears to be justified.

However, even if one doubts that resistant weeds will expand so dramatically, there are additional factors at play that will likely increase adoption beyond what would be expected purely from resistant weed-infested acreage. For instance, Mortensen et al. describe several important "agronomic drivers" that would boost adoption, including "defensive use" by farmers who wish only to protect their soybeans from injury by auxin drift emanating from the fields of neighbors who grow the corresponding auxin-resistant soybeans.[11] Such "defensive" reasons for HR crop adoption have been noted for Roundup Ready corn, for instance in Arkansas (Baldwin 2010).

Marketing decisions by Monsanto and Dow will also be important. Monsanto has pursued an aggressive "trait penetration" strategy with its Roundup Ready crops, which is most evident with Roundup Ready corn. By incorporating the Roundup Ready trait in the most desirable corn hybrids, and withdrawing non-RR versions of those same hybrids, farmers who have little or no use for the RR trait nevertheless purchase hybrids containing it (Hubbard 2009, pp. 29-33). Some then go on to make use of the trait (for which they have paid a premium) even though they originally did not want it. Monsanto will likely pursue the same strategy with MON 87708, increasing farmer adoption beyond what it would otherwise be. Having purchased soybeans with the dicamba-resistant trait, whether for defensive reasons or from lack of suitable non-dicamba-resistant varieties, farmers are then more likely to utilize it through application of dicamba.

If the 67.4 million acres of auxin-resistant soybeans projected by 2025 were equally divided between 2,4-D and dicamba-resistant varieties, and assuming farmers utilize 75% of the dicamba permitted by the proposed label, one would expect over 50 million additional lbs. of dicamba to be sprayed on soybeans (1.5 lbs./acre x ½ of 67.4 million acres). Under this projection, total dicamba use could significantly exceed 50 million lbs. (to a maximum of 100 million lbs.) if MON 87708 were to prove more popular than Dow's product,[12] or Dow's 2,4-D-resistant soybeans are for some reason not introduced.

It is more difficult to project the impact of the proposed registration in spurring greater dicamba use on other crops, such as corn and wheat. If one assumes dicamba use on corn expands from the current 6.8% to 50% of corn acres due to progressively waning concern

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[11] Defensive adoption would be spurred still more with the anticipated introduction and adoption of dicamba-resistant corn and cotton.

[12] An Iowa farmer consulted by CFS, George Naylor, believes dicamba's greater residual activity vs. 2,4-D would make MON 87708 more popular than Dow's 2,4-D-resistant soybeans.

over drift damage to soybeans with increasing MON 87708 adoption, then total dicamba use on corn would rise from the current 1.075 million lbs./year to 7.9 million lbs./year, based on 2010 corn acreage of 88.2 million acres and assuming current 2,4-D use rates on corn.

Further substantial increases in dicamba use on corn would occur with Monsanto's anticipated introduction of dicamba-resistant corn in several years, because dicamba-resistant corn would eliminate the crop injury concerns that currently limit the application window and use rates of dicamba on corn. Monsanto also plans introduction of dicamba-resistant cotton, which if widely adopted would directly increase dicamba use on cotton, and further erode the drift injury-related concerns of other farmers using dicamba, for instance on MON 87708 under the proposed registration, near cotton fields. Soybeans are widely grown in southern cotton-growing states, such as Arkansas and Tennessee.

It is important that EPA carefully consider the broader issues raised above as it evaluates the proposed registration. The agricultural landscape is not comprised of discrete and disconnected bits of land growing certain crops. The phenomenon of herbicide drift injury is a concrete manifestation of the interrelationships in the agricultural landscape that farmers do and must consider in making decisions as to which crops and crop varieties to grow and which agricultural practices to use, including decisions on herbicide use. A broader assessment approach as here recommended is also urgently needed to properly assess the threat of herbicide-resistant weeds entailed by the proposed registration, as discussed further below.

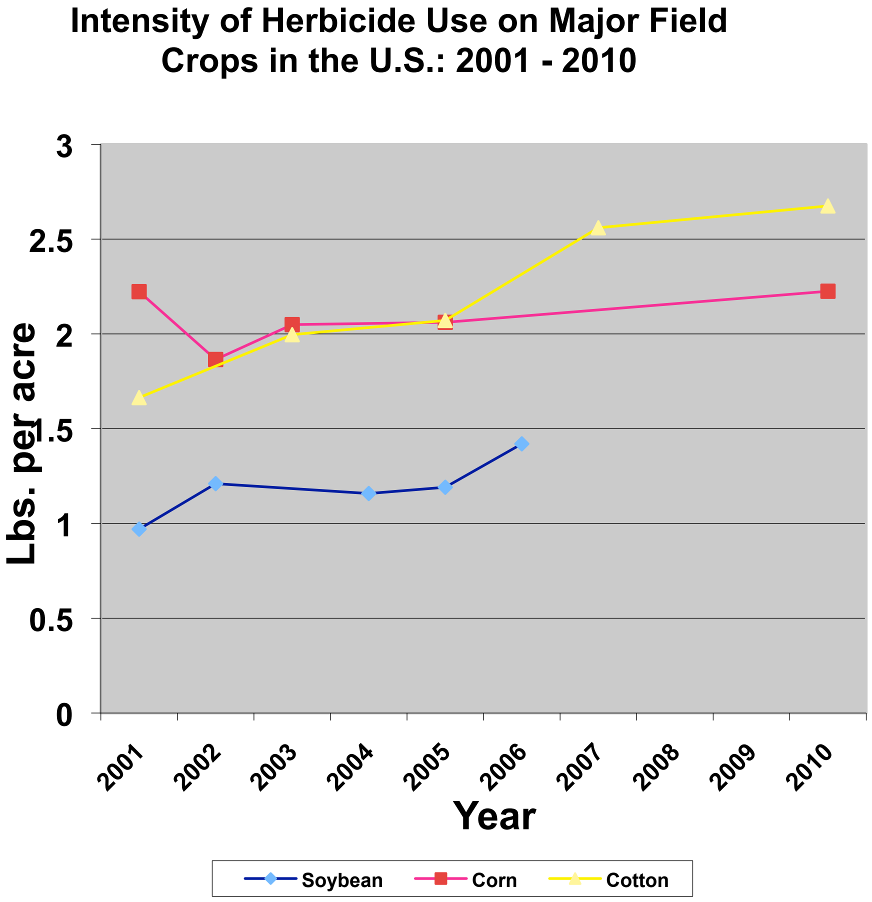
Granting the proposed registration would thus likely entail a 50 million lb. increase in dicamba use on soybeans, assuming a realistic adoption scenario, by 2025; and an additional, conservatively estimated 8 million lb. increase in use on non-dicamba-resistant corn, for 58 million lbs. of dicamba applied annually. This projection ignores the clear potential for greater dicamba use in wheat in areas where it is grown near soybeans. Further increases to be expected with introduction of dicamba-resistant corn and cotton would easily drive this figure to well over 100 million lbs. per year. 58 million lbs. would represent a more than 20-fold increase over current agricultural use of dicamba herbicides.

MON 87708 will sharply increase overall herbicide use on soybeans

Monsanto envisions and will promote dual use of dicamba and glyphosate with MON 87708 stacked with Roundup Ready as a normal feature of this crop system (Monsanto 2010 at 601). Mortensen et al (2010) project continuing use of glyphosate at current rates with adoption of 2,4-D and dicamba-resistant soybeans (see caption to figure above). Thus, they see little or no potential for dicamba to displace use of glyphosate with MON 87708 soybeans stacked with Roundup Ready.

Combined use of both herbicides will be necessary to control both glyphosate-resistant weed biotypes (dicamba) and troublesome grass weeds of soybeans (glyphosate) that dicamba, as a broadleaf herbicide, does not kill. Troublesome grass weeds in soybeans that dicamba does not control include foxtail, crabgrass, barnyardgrass, volunteer corn, wild oat, woolly cupgrass, shattercane, fall panicum, Johnsongrass and quackgrass.

Widespread adoption of RR versions of soybeans and cotton triggered substantial 50% and more increases in herbicide intensity on these crops, as displayed in the figure below. MON 88708 stacked with the RR trait would increase herbicide intensity to much higher levels.



Notes: Average annual per acre herbicide use on soybean, soybeans and cotton from 2002-2010. **Source:** "Agricultural Chemical Usage: Field Crops Summary," USDA National Agricultural Statistics Service, for the respective years. USDA does not collect data every year for each crop. For instance, no soybean data has been collected since 2006, and no corn data was collected from 2006 to 2009. 2010 corn and cotton data in USDA-NASS AgChem (2010). http://usda.mannlib.soybeanell.edu/MannUsda/viewDocumentInfo.do?documentID=1560

The impact of the proposed registration on evolution of herbicide-resistant weeds

Summary

U.S. agriculture's undue reliance on single-tactic, chemical-intensive weed control generates huge costs in the form of herbicide-resistant weeds – costs that could be avoided or greatly lessened with sustainable integrated weed management techniques that emphasize non-herbicidal tactics. Herbicide-resistant crop systems promote more rapid evolution of resistant weeds than do other (non HR crop) uses of the pertinent herbicide(s). This is clearly demonstrated by the history of glyphosate-resistant weeds, which have emerged almost exclusively in the Roundup Ready crop era. Weeds resistant to synthetic auxin herbicides, the class to which dicamba belongs, are already numerous, indicating that auxin-resistance is prevalent in the plant world. The proposed registration would facilitate greatly increased dicamba use on weeds already resistant to glyphosate and other herbicides, leading to still more intractable, multiple herbicide-resistant weeds. Clear evidence of cross-resistance and/or tolerance to auxin herbicides among weed species exacerbates the threat. Multiple herbicide-resistant weeds lead to increased selection pressure for resistance to evolve to the ever fewer remaining effective herbicidal control options. In light of these considerations, weed scientists have recently called for mandatory stewardship practices to address the likely emergence of auxin-resistant weeds with auxin-resistant crop systems. Volunteer HR soybeans with resistance to multiple herbicides may become ever more problematic weeds. Monsanto's stewardship recommendations for MON 88708 are entirely inadequate. Because herbicide-resistant weeds, once evolved, can spread their resistance traits via cross-pollination and seed dispersal, stewardship recommendations that focus on persuading individual growers to "do the right thing" are ineffective, and risk undermining the utility of valuable herbicides for non HR crop uses. Regulation is a rational response to this "tragedy of the commons" dilemma, in which the susceptibility to weeds is the common resource rapidly being squandered.

Weed management vs. weed eradication

Weeds can compete with crop plants for nutrients, water and sunlight, and thereby inhibit crop growth and potentially reduce yield. While less dramatic than the ravages of insect pests or disease agents, weeds nevertheless present farmers with a more consistent challenge from year to year. However, properly managed weeds need not interfere with crop growth. For instance, organically managed corn has been shown to yield as well as conventionally grown varieties despite several-fold higher weed densities (Ryan et al. 2010). Long-term cropping trials at the Rodale Institute reveal that average yields of organically grown soybean were equivalent to those of conventionally grown soybean, despite six times greater weed biomass in the organic system (Ryan et al. 2009). Weeds can even benefit crops – by providing ground cover that inhibits soil erosion and attendant loss of soil nutrients, habitat for beneficial organisms such as ground beetles that consume weed seeds, and organic matter that when returned to the soil increases fertility and soil tilth (Liebman 1993). These complex interrelationships between crops and weeds would seem to call for an approach characterized by careful management rather than indiscriminate eradication of weeds.

Farmers have developed many non-chemical weed management techniques, techniques that often provide multiple benefits, and which might not be utilized specifically or primarily for weed control (see generally Liebman & Davis 2009). For instance, crop rotation has been shown to significantly reduce weed densities versus monoculture situations where the same crop is grown each year (Liebman 1993). Cover crops – plants other than the main cash crop that are usually seeded in the fall and killed off in the spring – provide weed suppression benefits through exudation of allelopathic compounds into the soil that inhibit weed germination, and when terminated in the spring provide a weed-suppressive mat for the follow-on main crop. Common cover crops include cereals (rye, oats, wheat, barley), grasses (ryegrass, sudangrass), and legumes (hairy vetch and various clovers. Intercropping – seeding an additional crop amidst the main crop – suppresses weeds by acting as a living mulch that competes with and crowds out weeds, and can provide additional income as well (Liebman 1993). One common example is intercropping oats with alfalfa. Higher planting densities results in more rapid closure of the crop "canopy," which shades out and so inhibits the growth of weeds. Fertilization practices that favor crop over weeds include injection of manure below the soil surface rather than broadcast application over the surface. Techniques that conserve weed seed predators, such as ground beetles, can reduce the "weed seed bank" and so lower weed pressure. In addition, judicious use of tillage in a manner that does not contribute to soil erosion is also a useful means to control weeds.

Unfortunately, with the exception of crop rotation and tillage, such techniques are little used in mainstream agriculture. This is in no way inevitable. Education and outreach by extension officers, financial incentives to adopt improved practices, and regulatory requirements are just a few of the mechanisms that could be utilized to encourage adoption of more integrated weed management systems (IWM) that prioritize non-chemical tactics (Mortensen et al. 2012). Meanwhile, the problems generated by the prevailing chemical-intensive approach to weed control, exacerbated by the widespread adoption of herbicide-resistant crops, are becoming ever more serious.

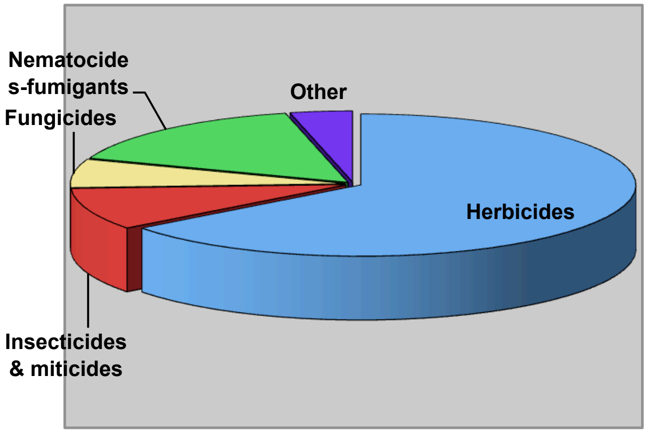
The high costs of herbicide-only weed control

In 2007, U.S. farmers spent $4.2 billion dollars to apply 442 million lbs of herbicide, and uncounted billions more on technology fees for herbicide-resistance traits in major crops. Overall, the U.S. accounts for one-quarter of world herbicide use (EPA Pesticide Use 2011, Tables 3.1, 5.2, 5.6). Surely this intensive herbicidal onslaught should make American fields among the most weed-free in the world. But such is not the case. As farmers gradually came to rely more on herbicides as the preferred and then often the sole means to control weeds, herbicide-resistant weeds have become increasingly severe and costly.

The first major wave of herbicide-resistance came in the 1970s and 1980s as weeds evolved resistance to the heavily used triazines, such as atrazine (see Benbrook 2009a for this discussion). The next major wave of resistance comprised weeds resistant to ALS inhibiting herbicides in the 1980s and 1990s. Just five years intervened between introduction of the first ALS inhibitor herbicide in 1982 and the first resistant weed population (1987). One of the major factors persuading farmers to adopt Roundup Ready, glyphosate-resistant crops was the prevalence of weeds resistant to ALS inhibitors. Weeds have evolved resistance at least 21 "modes of action," or herbicide classes, in the world (ISHRW HR Weed Ranking 9/20/12).

According to the USDA's Agricultural Research Service, up to 25% of pest (including weed) control expenditures are spent to manage pesticide (including herbicide) resistance in the target pest (USDA ARS Action Plan 2008-13-App. II). With an estimated $7 billion spent each year on chemical-intensive weed control (USDA ARS IWMU-1), herbicide-resistant weeds thus cost U.S. growers roughly $1.7 billion (0.25 x $7 billion) annually. These expenditures to manage resistance equate to tens and perhaps over 100 million lbs of the over 400 million lbs of agricultural herbicide active ingredient applied to American crops each year (see figure below), as growers increase rates and make additional applications to kill expanding populations of resistant weeds

Agricultural Pesticide Use in the U.S. by Type: 2007



Herbicides comprise by far the largest category of pesticides, defined as any chemical used to kill plant, insect or disease-causing pests. In 2007, the last year for which the Environmental Protection Agency has published comprehensive data, weedkillers (herbicides) accounted for 442 million lbs of the 684 million lbs of chemical pesticides used in U.S. agriculture, nearly seven-fold more than the insecticides that many associate with the term "pesticide." Source: "Pesticides

Industry Sales and Usage: 2006 and 2007 Market Estimates," U.S. Environmental Protection Agency, 2011, Table 3.4 (EPA Pesticide Use 2011 in supporting materials).

Increasing the rate and number of applications, however, rapidly leads to further resistance, followed by adding additional herbicides into the mix, beginning the resistance cycle all over again, just as overused antibiotics breed resistant and then multiple-drug resistant bacteria. This process, dubbed the pesticide treadmill, has afflicted most major families of herbicides, and will only accelerate as U.S. agriculture becomes increasingly dependent on crops engineered for resistance to one or more members of this by far largest class of pesticides (Kilman 2010).

Besides costing farmers economically via herbicide-resistant weeds, the chemical-intensive pest control regime of HR crop systems also has serious public health and environmental consequences. Various pesticides are known or suspected to elevate one's risk for cancer, neurological disorders, or endocrine and immune system dysfunction. Epidemiological studies of cancer demonstrate that farmers in many countries, including the U.S., have higher rates of immune system and other cancers (USDA ERS AREI 2000). Little is known about the chronic, long-term effects of exposure to low doses of many pesticides, especially in combinations. Pesticides deemed relatively safe and widely used for decades (e.g. cyanazine) have had to be banned in light of scientific studies demonstrating harm to human health or the environment. Pesticides also pollute surface and ground water, harming amphibians, fish and other wildlife.

Herbicide-resistant weeds thus lead directly to adverse impacts on farmers, the environment and public health. Adverse impacts include the increased costs incurred by growers for additional herbicides to control them, greater farmer exposure to herbicides and consumer exposure to herbicide residues in food and water, soil erosion and greater fuel use and emissions from increased use of mechanical tillage to control resistant weeds, environmental impacts from herbicide runoff, and in some cases substantial labor costs for manual weed control. These are some of the costs of unsustainable weed control practices, the clearest manifestation of which is evolution of herbicide-resistant weeds.

Why herbicide-resistant crop systems promote rapid evolution of resistant weeds

Herbicide-resistant (HR) crop systems such as MON 87708 soybeans involve post-emergence application of one or more herbicides to a crop that has been bred or genetically engineered to survive application of the herbicide(s). These HR crop systems promote more rapid evolution of herbicide-resistant weeds than non-HR crop uses of the associated herbicides. This is explained by several characteristic features of these crop systems.

HR crops foster more ***frequent*** use of and ***overreliance*** on the herbicide(s) they are engineered to resist. When widely adopted, they also lead to more ***extensive*** use of HR crop-associated herbicide(s). Herbicide use on HR crops also tends to occur ***later in the season***, when weeds are larger. Each of these factors contributes to rapid evolution of resistant weeds by favoring the survival and propagation of initially rare individuals that have genetic mutations lending them resistance. Over time, as their susceptible brethren are killed off, these rare individuals become more numerous, and eventually dominate the weed population.

High frequency of use means frequent suppression of susceptible weeds, offering (at frequent intervals) a competition-free environment for any resistant individuals to thrive. Overreliance on the HR crop-associated herbicide(s) means little opportunity for resistant individuals to be killed off by alternative weed control methods, thus increasing the likelihood they will survive to propagate and dominate the local weed population. Widespread use of the HR crop system increases the number of individual weeds exposed to the associated herbicide(s), thus increasing the likelihood that there exists among them those individuals with the rare genetic predisposition that confers resistance. The delay in application fostered by HR crop systems means more weeds become larger and more difficult to kill; thus, a greater proportion of weeds survive to sexual maturity, and any resistant individuals among them are more likely to propagate resistance via cross-pollination of susceptible individuals or through deposition of resistant seeds in the seed bank; in short, a higher likelihood of resistance evolution.

Below, we discuss these resistant weed-promoting features of HR crop systems in more detail, with particular reference to systems involving glyphosate-resistance (Roundup Ready) and auxin-resistance.

GE seeds in general, including HR seeds, are substantially more expensive than conventional seeds (Benbrook 2009b). Their higher cost is attributable to a substantial premium (often called a technology fee) for the herbicide-resistance trait. This premium constitutes a financial incentive for the grower to fully exploit the trait through frequent and often exclusive use of the associated herbicide(s), and a disincentive to incur additional costs by purchasing other, often more expensive herbicides.

> The cost of RR [Roundup Ready] alfalfa seed, including the technology fee, is generally twice or more than that of conventional alfalfa seed. Naturally, growers will want to recoup their investment as quickly as possible. Therefore, considerable economic incentive exists for the producer to rely solely on repeated glyphosate applications alone as a weed control program. (Orloff et al. 2009, p. 9).

To our knowledge, Monsanto has not revealed its pricing for MON 87708 seed, but it is likely to be considerably more expensive than currently available GE varieties.

Overreliance is especially favored when the associated herbicide(s) are effective at killing a broad range of weeds, which tends to make other weed control practices less needed, at least until weed resistance emerges. Glyphosate is such a broad-spectrum herbicide; dicamba provides control of most broadleaf weeds. Applied together or sequentially, glyphosate and dicamba would initially provide broad-spectrum control of soybean weeds, making use of other weed control measures unnecessary until the inevitable rapid evolution of auxin resistance, often in populations already resistant to glyphosate and/or other herbicides. Greater use of non-chemical weed control tactics is the only way to avoid the evolution of increasingly intractable, multiple HR weeds.

Frequent use and overreliance are also fostered when the HR crop-associated herbicide(s) are inexpensive relative to other herbicides. Monsanto lowered the price of Roundup herbicide (active ingredient: glyphosate) in the late 1990s to encourage farmers to adopt Roundup Ready crop systems and rely exclusively on glyphosate for weed control (Barboza 2001),[13] and the price has fallen further since then. Dicamba is even cheaper than glyphosate, and in fact is one of the least inexpensive herbicides on the market (U of Tenn 2011, p. 94). As suggested by Orloff et al. (2009), quoted above, overreliance on HR crop-associated herbicide(s) is particularly favored when the HR trait premium is high and the price of the associated herbicide(s) is low, the likely scenario with MON 87708 soybeans. Any price premium for a dicamba product registered for use on MON 87708 would encourage farmers to use cheaper and more drift-prone formulations.

One of the key changes wrought by herbicide-resistant crop systems is a strong shift to post-emergence herbicide application, which generally occurs later in the season on larger weeds, versus early-season use on smaller weeds or prior to weed emergence that is more characteristic of conventional crops. It is important to understand that facilitation of post-emergence herbicide use as the sole or primary means of weed control is the *sine qua non* of HR crop systems, not an incidental feature. Early-season uses include soil-applied herbicides put down around the time of planting; these herbicides have residual activity to kill emerging weeds for weeks after application. The Roundup Ready soybean system has practically eliminated use of soil-applied, or indeed of any herbicide other than glyphosate.

Weed scientist Paul Neve has simulated the rate at which weeds evolve resistance to glyphosate under various application regimes (Neve 2008). His results show unambiguously that the post-emergence use of glyphosate unique to glyphosate-resistant crop systems fosters resistant weeds much more readily than traditional uses ("prior to crop emergence") typical of conventional crops. This is consistent with the massive emergence of glyphosate-resistant weeds only after glyphosate-resistant crops were introduced (see below):

> Glyphosate use for weed control prior to crop emergence is associated with low risks of resistance. These low risks can be further reduced by applying glyphosate in sequence with other broad-spectrum herbicides prior to crop seeding. Post-emergence glyphosate use, associated with glyphosate-resistant crops, very significantly increases risks of resistance evolution. (Neve 2008)

Glyphosate-resistant crop systems have fostered later post-emergence applications than many agronomists anticipated, which increases the potential for resistant weed evolution.

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[13] Monsanto has greatly increased the price of RR seed to compensate for reduced income from sale of Roundup.

> Growers rapidly adopted glyphosate-resistant crops and, at least initially, did not have to rely on preventive soil-applied herbicides. Growers could wait to treat weeds until they emerged and still be certain to get control. ***Many growers waited until the weeds were large in the hope that all the weeds had emerged and only one application would be needed. Today, experts are challenging this practice from both an economic and a sustainability perspective.*** (Green et al. 2007, emphasis added)

> Following the widespread adoption of glyphosate-resistant soybean, ***there has been a subtle trend toward delaying the initial postemergence application longer than was once common***. Because glyphosate provides no residual weed control and application rates can be adjusted to match weed size, ***producers hope that delaying the initial postemergence application will allow enough additional weeds to emerge so that a second application will not be necessary.*** (Hagar 2004, emphasis added)

University of Minnesota weed scientist Jeff Gunsolus notes that: "Larger weeds are more apt to survive a postemergence application and develop resistance." (as quoted in Pocock 2012). University of Arkansas weed scientist Ken Smith notes that application of Ignite (glufosinate) to cotton plants with dual resistance to glyphosate and glufosinate (Widestrike varieties) in order to control large glyphosate-resistant weeds risks generating still more intractable weeds resistant to both herbicides (as quoted in Barnes 2011, emphasis added):

> Many growers who use Ignite on WideStrike varieties do so after they discover they have glyphosate-resistant weeds, according to Smith. To combat this, ***growers will make an application of Ignite on weeds that, on occasion, have grown too big to be controlled by the chemistry. This creates a dangerous scenario which could possibly encourage weeds to develop resistance to glufosinate***, the key chemistry in Ignite. ***The end-result, according to Smith, would be disastrous***.

It should be noted that Dr. Smith's concern is that weeds will evolve resistance to the same two herbicides to which the HR crop is resistant, which both undermines the utility of the crop and creates a potentially noxious HR weed that becomes extremely difficult to control. As discussed further below, this tendency for weeds to mimic the herbicide resistances in the crop is a general feature of HR crop systems, and sets up a futile and costly chemical arms race between HR crops and weeds.

Overview of glyphosate-resistant crops and weeds

A discussion of glyphosate-resistant (GR) crops and weeds is important for two reasons. First, the rapid emergence of GR weeds in RR crop systems is evidence of the resistant weed-promoting effect of HR crop systems in general, as discussed above, and provides insight into the risks of resistant weed evolution in the context of the MON 87708 soybean system. Second, the prevalence of glyphosate-resistant weeds is the motivating factor in Monsanto's introduction and farmers' potential adoption of MON 87708 under the proposed registration.

Glyphosate-resistant crops represent by far the major HR crop system in American and world agriculture, and provide an exemplary lesson in how HR crop systems trigger HR weeds (see Benbrook 2009a for following discussion). Glyphosate was first introduced in 1974. Despite considerable use of the herbicide, for the next 22 years there were no confirmed reports of glyphosate-resistant weeds. A few small and isolated populations of resistant weeds – mainly rigid and Italian ryegrass and goosegrass – emerged in the late 1990s, attributable to intensive glyphosate use in orchards (e.g. Malaysia, Chile, California) or in wheat production (Australia).

Significant populations of glyphosate-resistant weeds have only emerged since the year 2000, four years after the first Roundup Ready (RR) crop system (RR soybeans) was introduced in 1996, followed by RR cotton & canola in 1997 and RR soybean in 1998. According to the International Survey of Herbicide-Resistant Weeds (ISHRW), multiple populations of 23 weed species are resistant to glyphosate in one or more countries today; of these, 26 populations of ten species are also resistant to herbicides in one to three other families of chemistry in addition to glyphosate (ISHRW GR Weeds 4/22/12).[14] Based on acreage infested, GR weeds have emerged overwhelmingly in soybeans, cotton and soybean in countries, primarily the U.S., where RR crop systems predominate (see CFS RRSB 2010, which has further analysis of GR weeds).

The first glyphosate-resistant (GR) weed population confirmed in the U.S., reported in 1998, was rigid ryegrass, infesting several thousand acres in California almond orchards (ISHRW GR Weeds 4/22/12). Beginning in the year 2000 in Delaware, glyphosate-resistant horseweed rapidly emerged in Roundup Ready soybeans and cotton in the East and South. Just twelve years later, glyphosate-resistant biotypes of 13 species are now found in the U.S., and they infest millions of acres of cropland in at least 27 states (ISHRW GR Weeds 4/22/12).[15]

Based on Center for Food Safety's periodic compilation of data from the ISHRW website over the past four years, glyphosate-resistant weeds in the U.S. have evolved at an accelerated rate in recent years. As of November 2007, ISHRW recorded eight weed species resistant to glyphosate, covering up to 3,200 sites on up to 2.4 million acres. By Sept. of 2012, as many as 440,000 sites on up to 18,700,000 acres were documented to be

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[14] A population of one additional weed species (for 24 total) has evolved resistance to glyphosate since the cited 4/22/12 list was compiled, spiny amaranth in Mississippi. See http://www.weedscience.org/Case/Case.asp?ResistID=5682.

[15] Now 14 weed species, in at least 30 states. GR weeds have been documented in three additional states since this 4/22/12 list was compiled. For South Dakota and Wisconsin, see list at http://www.weedscience.org/Summary/UspeciesMOA.asp?lstMOAID=12&FmHRACGroup=Go. For Montana, see AgNews (2012). Thus, all 10 major soybean growing states how have GR weeds.

infested by glyphosate-resistant weeds (CFS GR Weed List – 9/20/12). This astonishing proliferation of resistant weeds – an over 130-fold increase in number of sites and 8-fold increase in acreage – is portrayed in the figure at the end of this section.

However, the true extent of GR weeds is much greater than even the maximum figures shown in the graph, because "...the voluntary basis of the contributions [to ISHRW] likely results in underestimation of the extent of resistance to herbicides, including glyphosate" (NRC 2010, p. 2-12). Many examples could be cited to illustrate to what extent ISHRW underestimates the extent of GR weed populations, but one will suffice. Illinois weed scientist Bryan Young recently reported 5-6 million acres of Illinois cropland infested with glyphosate-resistant waterhemp (as quoted in Lawton 2012, confirmed with Dr. Young, personal communication). Yet ISHRW lists GR waterhemp as infesting just 100 acres in Illinois (ISHRW Illinois Waterhemp). Inclusion of this single updated report in the ISHRW system would raise the GR weed infested acreage by one-third. It appears that much or all of this waterhemp is resistant to ALS inhibitors as well, with a significant portion also resistant to PPO inhibitors and/or triazine herbicides (Tranel 2010).

Dr. Ian Heap, who manages the ISHRW website cited above, confirms that: "The survey is definitely too low because researchers report the first cases and enter in the area infested. Often they don't return in subsequent years to keep updating the survey." Dr. Heap estimates that "there are about 40 million acres affected by glyphosate-resistant weeds," but notes that if one accounts for "overlapping acres" infested with more than one GR weed, "the estimate probably comes down to about 30 million actual acres" (Heap 2012). Dow has an even higher estimate of GR weed-infested acreage of 60 million acres (Bomgardner 2012). Thus, actual acreage infested with glyphosate-resistant weeds is double to triple the 18.7 million acres reported by ISHRW and shown in the figure below. However, the figure can be assumed to accurately capture the extremely rapid pace of GR weed emergence.

Early on, most resistant weed populations were driven by intensive glyphosate use associated with RR soybeans and RR cotton. However, adoption of corn with the Roundup Ready trait has increased sharply in recent years, from 20% to 72% of national corn acres from just 2004 to 2011. The increasing reliance on glyphosate associated with the growing use of RR soybean/RR corn rotations is the major factor driving the rapid emergence of resistant weeds in the Midwest and Northern Plain states. In general, more GR weeds are emerging on agricultural land planted to several crops that are predominantly Roundup Ready in the U.S., which since 2008 includes sugar beets. The most recent example is the emergence of GR common waterhemp on land planted to soybeans, corn and sugar beets in North Dakota (ISHRW GR Weeds 4/22/12).

Populations of some glyphosate-resistant weeds, such as GR Palmer amaranth, GR horseweed, GR kochia, and GR common waterhemp, are properly regarded as noxious weeds. The increased use of herbicides and increased use of soil-eroding tillage operations to control them cause harm to the environment and natural resources (e.g. loss of soil and increased runoff of agricultural chemicals). When not properly managed due to the difficulty of controlling them, these noxious weeds can sharply reduce yields, while successful control efforts often involve a several-fold increase in weed control costs, in either case harms to the interests of agriculture. A brief, documented overview of these harms is provided in Benbrook (2009a, Chapter 4).

Synthetic auxin-resistant crops and weeds

Synthetic auxin herbicides like dicamba act by mimicking plant growth hormones such as indole acetic acid. Monsanto maintains that "there is a low potential for dicamba-resistant broadleaf weed populations to arise from the use of dicamba applied to MON 87708 integrated into the Roundup Ready soybean system," and gives the following reasons for this opinion (Monsanto 2010, p. 601).

1) Dicamba will be used together with glyphosate, with recommended use of a soil residual herbicide, and such use of multiple modes of action "is a primary way to delay the development of resistance;"
2) Resistance to auxin herbicides has developed slowly, hypothetically due to multiple sites of action within plants, suggesting that resistance is determined by multiple genes as a quantitative trait;
3) Only four broadleaf weeds have confirmed as resistant to dicamba in the U.S., while relatively low numbers of weed species have confirmed resistance to synthetic auxin herbicides in general; and
4) Confirmed dicamba- and auxin-resistant weeds are found primarily in the West rather than in major soybean production regions, and weeds with known dicamba resistance are not major soybean weeds.

There are several serious flaws in these arguments, which were persuasively rebutted by Mortensen et al. (2012). First, Monsanto's two points regarding past history of auxin- and dicamba-resistant weed emergence have little bearing on the future course of resistance with introduction of MON 87708 under the proposed registration. As explained above, use of an herbicide in the context of an HR crop system very significantly elevates the risk of resistant weed emergence relative to non-HR crop uses of the same herbicide. Monsanto officers cannot fail to understand this, given the history of glyphosate-resistant weeds with their RR crops, but apparently prefer to ignore the lesson.

However, even to the limited extent that past resistance is relevant, Monsanto is in error. The ISHRW website lists 50 biotypes[16] of 30 different weed species with resistance to synthetic auxin herbicides internationally (ISHRW SynAux Weeds 9/20/12). Of the 21 herbicide modes of action to which weeds have evolved resistance, synthetic auxin-resistant weeds rank fourth in terms of number of resistant species, in the top quintile (ISHRW HR Weed Ranking 9/20/12). Contrary to Monsanto, this is a quite high number of resistant species relative to other modes of action. While this is in no way determinative of which weed species will evolve resistance in the future, it does indicate that the genetic

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[16] We use the term "biotype" to refer to a single listing on the ISHRW website. For instance, four biotypes of the single species kochia have evolved auxin resistance in four different states.

predisposition to survive auxin treatment is quite prevalent in the plant world. Moreover, five new auxin-resistant biotypes and 1 new species have been recorded by ISHRW over just the past five months,[17] indicative of continuing and perhaps accelerated emergence of auxin-resistant weeds.

Nine biotypes of five different weed species have confirmed resistance to dicamba: lambsquarters (1), common hempnettle (1), kochia (4), prickly lettuce (1) and wild mustard (2) (see ISHRW SynAux Weeds Table 9/20/12 for following discussion). One other biotype highly resistant to 2,4-D also exhibits reduced sensitivity to dicamba (common waterhemp in Nebraska, discussed further below). Interestingly, four biotypes of four species have confirmed resistance to dicamba and other auxin herbicides, while one other population has multiple resistance to dicamba and several ALS inhibitors. The cross-resistance of dicamba-resistant weeds to other auxin herbicides is troubling, because it removes alternative weed control options, and could undermine the utility of both auxin-resistant soybean varieties. Many auxin-resistant weeds have not been tested for dicamba resistance, so there could be considerably more weed species and biotypes that are immune to the herbicide.

The argument that auxin-resistant weeds have developed slowly due to multiple sites of action in the plant is also specious. In most cases, scientists have not elucidated the precise mechanisms by which weeds evolve resistance, making predictions about the likelihood of weed resistance on this basis extremely hazardous. This is particularly true of auxin resistance, the precise mechanisms of which have yet to be elucidated. Monsanto scientists likewise predicted very little chance of glyphosate-resistant weed evolution in the 1990s (Bradshaw et al. 1997), and for much the same reasons: dearth of resistance from past use of glyphosate, and the molecular nuances of glyphosate's mode of action.[18] These predictions were of course disastrously wrong, but they did help quell concerns about GR weed evolution and forestall efforts to establish mandatory weed resistance management programs as Monsanto was introducing its Roundup Ready crops. Interestingly, only one GR weed had been identified by the time the first RR crop was introduced in 1996 (ISHRW GR Weeds 4/22/12), in contrast to the 30 weed species with biotypes resistant to auxins today.

The experience with glyphosate-resistant weeds demonstrates that neither a narrow focus on the biochemical nuances of resistance mechanisms, nor the frequency of resistance evolution in the past, provide an accurate basis for forecasting what will happen when the herbicide in question is used in the context of an herbicide-resistant crop system. What it does demonstrate is that the characteristic ways in which HR crop systems are used in the field, as discussed above, make them far more likely to trigger evolution of resistant weeds than non-HR crop uses of those same herbicides.

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[17] 45 biotypes and 29 species when CFS last recorded these data (compare ISHRW SynAux Weeds 4/22/12 to ISHRW SynAux Weeds 9/20/12).

[18] Interestingly, another reason put forward by Monsanto scientists Bradshaw and colleagues for the unlikelihood of GR weed evolution was Monsanto's past failures in multiple attempts to engineer glyphosate-resistant plants, the arrogant presumption being that Nature could certainly not accomplish what had proven so difficult for Monsanto's scientists.

Monsanto's third argument, that use of both dicamba and glyphosate on MON 87708 soybean stacked with glyphosate resistance will hinder evolution of weeds resistant to either one, also lacks merit. This argument ignores the obvious fact that the huge extent of existing GR weed populations – with many billions of individual weeds on 30 to 60 million infested acres – make it near certain that some among them will have the rare genetic mutations conferring resistance to dicamba ***as well***. Mortensen et al. (2012) provide the mathematical exposition (emphasis added):

> First, when an herbicide with a new mode of action is introduced into a region or cropping system in which weeds resistant to an older mode of action are already widespread and problematic, the probability of selecting for multiple target-site resistance is not the product of two independent, low-probability mutations. In fact, the value is closer to the simple probability of finding a resistance mutation to the new mode of action within a population already extensively resistant to the old mode of action. For instance, in Tennessee, an estimated 0.8–2 million ha of soybean crops are infested with glyphosate-resistant horseweed (C. canadensis) (Heap 2011). Assuming seedling densities of 100 per m^2 or 10^6 per ha (Dauer et al. 2007) and a mutation frequency for synthetic auxin resistance of 10^{-9}, ***this implies that next spring, there will be 800–2000 horseweed seedlings in the infested area that possess combined resistance to glyphosate and a synthetic auxin herbicide*** ((2×10^6 ha infested with glyphosate resistance) x (10^6 seedlings per ha) x (1 synthetic auxin–resistant seedling per 10^9 seedlings) = 2000 multiple-resistant seedlings). In this example, these seedlings would be located in the very fields where farmers would most likely want to plant the new stacked glyphosate- and synthetic auxin–resistant soybean varieties (the fields where glyphosate-resistant horseweed problems are already acute). Once glyphosate and synthetic auxin herbicides have been applied to these fields and have killed the large number of susceptible genotypes, these few resistant individuals would have a strong competitive advantage and would be able to spread and multiply rapidly in the presence of the herbicide combination.

The upshot is that dicamba-resistant crop systems like MON 87708 soybean will very likely foster rapid evolution of weeds resistant to dicamba and glyphosate. In those cases where the GR weed populations in dicamba-treated crop fields already have resistance to one or more additional modes of action, the result will be evolution of still more intractable weeds with multiple-herbicide resistance, including to dicamba and glyphosate.

Multiple herbicide-resistant crops and weeds

Mortensen et al. (2012) note that there are currently 108 biotypes of 38 weed species possessing simultaneous resistance to two more classes of herbicide, and that 44% of them have appeared since 2005. Since herbicide-resistant weeds began to emerge in a significant way around 1970 (triazine-resistant weeds),[19] this means that nearly half of multiple HR weed biotypes have emerged in just the past seven years of our 40-year history of significant weed resistance. This global trend is also occurring in the U.S., where acreage infested with multiple HR weeds has increased by 400% over just the three years from November 2007 to November 2010 (Freese 2010, p. 15). There are at least 12 biotypes of weeds resistant to glyphosate and one or more other herbicide families in the U.S. (11) and Canada (1) that are attributable to RR crop systems, all but one having emerged since 2005 (CFS GR Weed List 9/20/12).

The progressive acquisition of resistances to different herbicide classes has the insidious effect of accelerating evolution of resistance to those ever fewer herbicides that remain effective. This is well-expressed by Bernards et al. (2012) with reference to multiple-herbicide-resistant waterhemp, though it applies more generally:

> The accumulation of multiple-resistance genes within populations and even within individual plants is of particular concern. This resistance stacking limits chemical options for managing waterhemp and, where weed management depends primarily on chemical weed control, results in additional selection pressure for the evolution of resistance to the few herbicides that are still effective.

There is already evidence that the scenario of dicamba resistance evolving in weeds already resistant to one or more herbicide classes, as depicted by Mortensen et al. (2012), will occur with four especially problematic species of weeds: horseweed, Palmer amaranth, waterhemp and kochia. These are the four weed species deemed most likely to evolve problematic populations of dicamba-resistant weeds by weed scientists (Crespo 2011).

i. Horseweed

Horseweed, or marestail, is the most prevalent GR weed. First discovered in 2000 in Delaware, GR horseweed has emerged in just over a decade to infest up to 8.4 million acres in 20 states (CFS GR Weed List 9/20/12[20]), up from 3.3 million acres in 16 states in February 2009 (Benbrook 2009a, p. 35). It is particularly prevalent in Tennessee, Kansas and Illinois, with populations infesting up to 5 million, 2 million and 1 million acres, respectively. GR horseweed in Mississippi is also resistant to paraquat, the first time multiple resistance to these two herbicides has been documented, while in California a population of horseweed's Conyza relative, hairy fleabane, with dual resistance to glyphosate and paraquat was recently reported to infest up to 1 million acres. Ohio has glyphosate/ALS inhibitor-resistant[21] horseweed.

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[19] A few auxin-resistant biotypes emerged in the 1950s and 1960s.

[20] Consult this chart for data in the following discussion. It should also be noted that these acreage-infested estimates are highly conservative, in view of the underreporting in the ISHRW system, as discussed above.

[21] CFS suspects that GR weeds that are also resistant to ALS inhibitor herbicides are greatly underreported by ISHRW; this is certainly the case with waterhemp (see discussion below).

Weed scientists regard GR horseweed as a "worst-case scenario" in RR cropping systems because this weed is well adapted to no-tillage planting systems popular among GR crop growers. It also produces up to 200,000 seeds per plant, and its seeds can disperse extremely long distances in the wind (Owen 2008), which may partly explain the prevalence of GR horseweed.

GR horseweed can reduce cotton yields by 40 to 70% (Laws 2006), and is also problematic in soybeans. In 2003, Arkansas weed scientist Ken Smith estimated that Arkansas growers would have to spend as much as $9 million to combat glyphosate-resistant horseweed in 2004 (AP 2003). An uncontrolled outbreak of GR horseweed in Arkansas could reduce the income of cotton and soybean farmers by nearly $500 million, based on projected loss in yield of 50% in 900,000 acres of cotton and a 25% yield loss in the over three million acres of soybeans (James 2005). Tennessee is especially hard hit, with up to 5 million acres of both cotton and soybeans infested with GR horseweed.

Because GR horseweed is often controlled with tillage, it has led to abandonment of conservation tillage practices on substantial cotton acreage in Tennessee and Arkansas, with similar trends reported in Mississippi and Missouri (Laws 2006) and perhaps other states. This in turn increases soil erosion. An NRC committee reported that increased tillage and increased herbicide use are common responses to glyphosate-resistant weeds (NRC 2010). Evolution of multiple herbicide-resistance reduces options for chemical control and so increases the chances for still more soil-eroding tillage.

The many farmers with GR and multiple-HR horseweed would be prime candidates for MON 87708. Yet Purdue University weed scientists have flagged horseweed as a plant with the genetic "plasticity" to readily evolve resistance to multiple herbicides:

> Multiple-resistant and cross-resistant horseweed populations have evolved to various combinations of the previous herbicide modes of action in Israel, Michigan, and Ohio (Heap 2009), providing evidence for the plasticity of this weed. (Kruger et al. 2010a).[22]

These same scientists have already founded increased tolerance to dicamba and 2,4-D in several horseweed populations, demonstrating the high potential for horseweed to evolve additional resistance to dicamba in the context of heavy postemergence use enabled by the proposed registration:

> "Population 66 expressed almost twofold greater tolerance to 2,4-D ester and approximately three- to fourfold greater tolerance to diglycolamine salt of dicamba than populations 3 and 34 (Table 1). Population 43 was more

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[22] As noted above, horseweed has also evolved dual resistance to glyphosate and paraquat in Mississippi; in California, a glyphosate/paraquat-resistant biotype of the closely related *Conyza* weed hairy fleabane was recently reported to infest up to 100,000 fields on as much as 1 million acres. See http://www.weedscience.org/Case/Case.asp?ResistID=5250.

> sensitive to growth regulators than population 66 but expressed slightly higher levels of tolerance to 2,4-D ester and diglycolamine salt of dicamba than populations 3 and 34 based on dry weight measurements." (Kruger et al 2010b)

It is significant that these two populations each exhibit increased tolerance to both dicamba and 2,4-D, indicating the potential for evolution of resistance to both herbicides if either one is used. In addition, the increased tolerance to dicamba of both populations was found only with the diglycolamine, but not the dimethylamine salt of dicamba, suggesting that the proposed registration might more readily lead to auxin-resistant horseweed than would other forms of dicamba.

Kruger et al also predict that auxin herbicides will be applied later to larger horseweed plants in the context of auxin-resistant crop systems (Kruger et al 2010a). In follow-up research, they found that larger plants are much more difficult to control with auxin herbicides:

> ***While it is realistic to expect growers to spray horseweed plants after they start to bolt,*** the results show that timely applications to [small] horseweed rosettes are the best approach for controlling these weeds with growth regulator herbicides [dicamba and 2,4-D]. ***Growers should be advised to control horseweed plants before they reach 30 cm in height because after that the plants became much more difficult to control***. (Kruger et al. 2010b, emphasis added)

As discussed above, increased survival of larger weeds means a greater likelihood of resistant individuals among them surviving to propagate resistance via cross-pollination or seed production. And as the authors acknowledge, it is "realistic" to expect late application of dicamba with MON 87708, because that is precisely how growers use these crop systems, as demonstrated with the history of RR crops.

This tendency to delay application to kill larger weeds will be greatly facilitated by the high-level dicamba resistance of MON 87708, since larger weeds require higher rates to control. The proposed label permits 2 post-emergence applications of up to 0.5 lb./acre each, up through the time when soybeans are in full bloom (R2). But much higher rates could be used without risk of crop injury. In fact, the developers of dicamba-resistant soybeans report resistance to dicamba at rates 5 to 10-fold higher than the maximum proposed single application rate (2.5 to 5 lbs./acre):

> "Most transgenic soybean events showed resistance to treatment with dicamba at 2.8 kg/ha and 5.6 kg/ ha under greenhouse conditions (fig. S9) and complete resistance to dicamba at 2.8 kg/ha (the highest level tested in field trials) (Fig. 3)" (Behrens et al 2007).

As discussed above in relation to RR crops, farmers delay application in order to avoid the trouble and expense of a second application, whether this is a wise tactic or not. Thus, advising growers to spray weeds when they are small will likely not be any more effective with MON 87708 than were similar recommendations made for glyphosate with Roundup Ready crops.

Cultivation of MON 87708 under the proposed registration is quite likely to promote rapid evolution of horseweed resistant to dicamba and perhaps 2,4-D as well, often in combination with glyphosate-resistance. As noted above, tillage is a frequent response to glyphosate-resistant horseweed, and will be a still more frequent response to dicamba/glyphosate-resistant horseweed, since dicamba will be eliminated as an alternative control option. This would lead to further reductions in conservation tillage and increased soil erosion.

ii. Waterhemp

Waterhemp is regarded as one of the worst weeds in the Corn Belt. It grows to a height of 2-3 meters, and emerges late into the growing season. Controlled trials in Illinois demonstrated that late-season waterhemp reduced corn yields in Illinois by 13-59%, while waterhemp emerging throughout the season cut yields by up to 74% (Steckel & Sprague 2004).

ISHRW lists 12 biotypes of GR waterhemp, all of which have emerged since 2005 in corn, soybeans, cotton and/or sugar beets, almost certainly all in RR crop systems (CFS GR Weed List 9/20/12). While ISHRW records up to 1.1 million acres infested with GR waterhemp, this is a vast underestimate. As noted above, Illinois weed scientist Bryan Young estimates a substantial 5-6 million acres infested with GR waterhemp in his state.

Waterhemp has an astounding ability to evolve resistance to herbicides. Biotypes resistant to one to four herbicide families have been identified in several Midwest and Southern states, from North Dakota to Tennessee (see CFS GR Weed List 9/20/12 for those resistant to glyphosate). Triple herbicide-resistant waterhemp infests up to one million acres in Missouri, while populations resistant to four herbicide classes, sardonically called "QuadStack Waterhemp" (Tranel 2010), have arisen in Illinois. Tranel's investigations suggest that the 5-6 million acres of GR waterhemp in Illinois noted above are all resistant to ALS inhibitors, with some additionally resistant to PPO inhibitors and/or triazines.

Tranel states that multiple herbicide-resistant waterhemp "appears to be on the threshold of becoming an unmanageable problem in soybean," and is quite concerned that if already multiple herbicide-resistant waterhemp evolves resistance to additional herbicides, "soybean production may not be practical in many Midwest fields" (Tranel et al 2010). Corn is often rotated with soybeans, and so could be similarly affected.

In early 2011, waterhemp was identified as the first weed with resistance to a relatively new class of herbicides, HPPD inhibitors, the fifth mode of action to which waterhemp has evolved resistance (Science Daily 2011), prompting weed scientist Aaron Hagar to comment that "we are running out of options" to control this weed. Populations of waterhemp in Iowa and Illinois are resistant to HPPD inhibitors and two other modes of action (ISHRW Waterhemp 2012).

Just months later, a waterhemp population highly resistant to 2,4-D and with significantly reduced sensitivity to dicamba was discovered (Bernards et al 2012), and it is potentially resistant to the popular corn herbicides atrazine and metolachlor as well, which would make it particularly difficult to manage (UNL 2011). The weed scientists who discovered this resistant weed population clearly understand the likelihood that auxin-resistant crops – "if used as the primary tool to manage weeds already resistant to other herbicides," the hallmark of these systems – will lead to still more intractable, multiple herbicide-resistant weeds:

> New technologies that confer resistance to 2,4-D and dicamba (both synthetic auxins) are being developed to provide additional herbicide options for postemergence weed control in soybean and cotton. The development of 2,4-D resistant waterhemp in this field is a reminder and a caution that these new technologies, if used as the primary tool to manage weeds already resistant to other herbicides such as glyphosate, atrazine or ALS-inhibitors, will eventually result in new herbicide resistant populations evolving. (UNL 2011)

In a peer-reviewed publication about this same waterhemp population, these scientists call for mandatory weed resistance prevention measures for MON 87708 soybean and other auxin-resistant crops:

> ***The commercialization of soybean, cotton and corn resistant to 2,4-D and dicamba should be accompanied by mandatory stewardship practices*** that will minimize the selection pressure imposed on other waterhemp populations to evolve resistance to the synthetic auxin herbicides. (Bernards et al. 2012, emphasis added)

A close reading of this paper helps explain their concerns. First, the 2,4-D-resistant waterhemp population is resistant to extremely high rates of 2,4-D, with some plants surviving application of 35,840 grams/hectare of 2,4-D, equivalent to 32 lbs/acre, or 32 times the maximum single 2,4-D application rate in the proposed label for 2,4-D use on MON 87708 soybean. Second, this population also has significantly reduced sensitivity to dicamba. This is important because it suggests that waterhemp has the capacity to evolve simultaneous resistance to both 2,4-D and dicamba, even without application of dicamba (no dicamba use was reported on the field where this weed evolved 2,4-D resistance); and because the elimination of 2,4-D as an effective control option is compounded by the elimination or at least erosion of the efficacy of a second important control tool, dicamba. Third, as noted above, waterhemp is one of the most damaging weeds in the Corn Belt, and multiple herbicide-resistance makes it still more damaging and expensive to control.

It is interesting to note that the field where this waterhemp evolved resistance to 2,4-D and tolerance to dicamba had also been regularly treated with atrazine and metolachlor: "Since

1996, atrazine, metolachlor, and 2,4-D were applied annually to control annual grasses and broadleaf weeds" (Bernards et al. 2012). This suggests the possibility of resistance to atrazine and/or metolachlor as well: "Research is underway at UNL to determine whether this waterhemp population has developed resistance to additional herbicide mechanisms-of-action" (UNL 2011).

Use of multiple herbicides is supposed to forestall evolution of resistance to any single herbicide. At least in the case of this waterhemp population, this strategy apparently did not work. Atrazine-resistant waterhemp has been reported in Nebraska and other states, and is particularly prevalent in Kansas, with up to 1 million infested acres reported.[23] Thus, it is possible that this population had previously evolved resistance to atrazine, demonstrating the potential for "resistance-stacking." However, there is only one report of a confirmed metolachlor-resistant weed population in the entire world, rigid ryegrass in Australia, and just seven reports of resistance to the chloracetamide class of herbicides to which it belongs.[24] Monsanto's recommendation that farmers use a soil residual herbicide in addition to dicamba and glyphosate with MON 87708 will most likely not be followed, as explained above. However, this waterhemp population suggests that the herbicidal onslaught approach may not always be successful even if utilized. In addition, Bernards and colleagues' call for mandatory stewardship practices suggests that HR crops, as explained above, are particularly prone to foster rapid evolution of weed resistance.

iii. Palmer amaranth

Perhaps the most destructive and feared weed in all of U.S. agriculture is glyphosate-resistant Palmer amaranth (see Benbrook 2009a, Chapter 4). Second only to GR horseweed in prevalence, GR Palmer amaranth is estimated to infest 112,000 to over 220,000 fields covering up to 7.0 million acres in 12 states, all but one in corn, cotton and/or soybeans (CFS GR Weed List 9/20/12). Best known for plaguing cotton and soybean growers in Southern states, this weed is rapidly emerging in Corn Belt states like Illinois and Missouri; populations have recently been reported in Michigan (ISHRW GR Weed List 4/22/12) and Ohio (Ohio Farmer 2012). In California, a population of GR Palmer amaranth has just been reported infesting three predominantly Roundup Ready crops (alfalfa, corn, cotton) as well as orchards, vineyards, roadways and fencelines.[25] Palmer amaranth is feared especially because of its extremely rapid growth – several inches per day – which means it can literally outgrow a busy farmer's best attempts to control it while still small enough to be killed. It also produces a huge number of seeds, so just one mature weed can ensure continuing problems in future years by pouring hundreds of thousands of resistant weed seeds into the "weed seed bank." Left unchecked, its stem can become baseball bat breadth, and is tough enough to damage cotton pickers. Glyphosate-resistant Palmer amaranth can dramatically cut yields by a third or more, and occasionally causes

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[23] See entries for "photosystem II inhibitors," the class of herbicides to which atrazine belongs, at http://www.weedscience.org/Summary/USpeciesCountry.asp?lstWeedID=219&FmCommonName=Go.

[24] http://www.weedscience.org/Summary/UspeciesMOA.asp?lstMOAID=18&FmHRACGroup=Go

[25] http://www.weedscience.org/Case/Case.asp?ResistID=5690.

abandonment of cropland too weedy to salvage. In Georgia, Arkansas and other states, farmers have resorted to hiring weeding crews to manually hoe this weed on hundreds of thousands of acres, tripling weed control costs (Haire 2010). Herbicide regimes of six to eight different chemicals, including toxic organic arsenical herbicides such as MSMA otherwise being phased out (EPA 2009, p. 3), are recommended to control it (Culpepper and Kichler 2009).

At least three states (Mississippi, Georgia and Tennessee) have Palmer amaranth resistant to both glyphosate and ALS inhibitors; the most recent one, reported in 2011, infests over 100,000 sites covering up to 2 million acres in Tennessee (CFS GR Weed List 9/20/12). Palmer amaranth belongs to the same genus as common waterhemp (*Amaranthus*), and to some extent can interbreed with it. Both have considerable genetic diversity. The demonstrated ability of waterhemp to evolve resistance to auxin herbicides suggests that a similar potential likely exists in Palmer amaranth. Growers with GR and multiple HR Palmer amaranth would be prime candidates to adopt MON 87708, and utilize them under the proposed registration. Palmer amaranth must be judged a high-risk weed for evolution of resistance to dicamba and other auxin herbicides, which would undermine the efficacy of existing, pre-emergence use of dicamba in battling this serious weed threat.

iv. Kochia

Kochia is a fourth serious weed, described further at CFS (2010). It has evolved widespread resistance to many different herbicides, and is on the ISHRW's list of the top ten most important herbicide-resistant weed species (ISHRW Worst HR Weeds). Limited populations of glyphosate-resistant kochia first emerged in Kansas in 2007, but recent reports suggest that it is now likely prevalent in the entire western third of Kansas, as well as parts of Colorado (Stahlman et al. 2011). A second population identified in Nebraska (2009) was first listed on ISHRW in December of 2011; a third in South Dakota (2011) infests up to 10,000 acres and was first listed in May of 2012; while a fourth infesting up to 1,000 acres in North Dakota was first listed in August of 2012. Kochia resistant to both glyphosate and ALS inhibitors was recently identified in Alberta, Canada (2012).[26] All of the US populations emerged in corn, soybeans and/or cotton (almost certainly RR versions), while the Canadian population emerged in cereals and "cropland" that may also include RR crops.

Stahlman et al. (2011) state that the original four populations in Kansas likely evolved glyphosate-resistance independently, but the rapid emergence across such a broad swath of the state suggests the potential for spread of the original populations, perhaps by resistant seed dispersal, as kochia "tumbleweed" can disperse seeds at considerable distances (see CFS 2010). CFS (2010) also documents that kochia is a serious weed of both alfalfa and sugarbeets, Roundup Ready versions of which have been recently introduced and are widely grown. GR kochia infesting these RR crops would seriously impair the efficacy of the RR trait; likewise, selection pressure from glyphosate use with these crop

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[26] See entries under Kochia at http://www.weedscience.org/Summary/UspeciesMOA.asp?lstMOAID=12&FmHRACGroup=Go.

systems (especially in rotation with other RR crops, as seen particularly with RR sugar beets, which are frequently rotated with RR corn and/or RR soybeans) could rapidly lead to still more extensive emergence of GR kochia.

Four biotypes of kochia have also evolved resistance to dicamba in Montana, Idaho, North Dakota, and most recently Nebraska. The Nebraska population first emerged in corn in 2010, and Nebraska is a major soybean producing state. Nearly half of all confirmed dicamba-resistant weed populations in the world are kochia biotypes, which may suggest a genetic proclivity in this species to evolve resistance to this herbicide. The extremely rapid emergence of GR biotypes in RR crop systems may induce growers to adopt MON 87708 to control it; and kochia's demonstrated propensity to evolve resistance to dicamba make it a prime candidate to evolve multiple resistance to dicamba, glyphosate and other herbicides.

Stewardship

It is highly doubtful whether Monsanto's stewardship plan for MON 87708 soybean will be effective in forestalling weed resistance to 2,4-D. For at least 15 years, companies and weed scientists have touted voluntary stewardship guidelines and best management practices as the chief bulwark against evolution of resistant weeds in the context of HR crop systems. These programs and exhortations have demonstrably failed with Roundup Ready crops, or there would not be an epidemic of glyphosate-resistant weeds. A critical assessment of Monsanto's failed stewardship messages, practices and actions with Roundup Ready crops is essential to inform its current plans with respect to the use of MON 87708 under the proposed registration.

Monsanto insisted that weeds would not evolve glyphosate resistance to any serious extent when RR crops were first being introduced, based mostly on assumptions concerning the presumed rarity of glyphosate-resistance mutations, the lack of glyphosate-resistant weed evolution up to that time, and nuances of the herbicide's mode of action (Bradshaw et al. 1997). Many weed scientists were not convinced, and called for serious measures to forestall evolution of GR weeds (Freese 2010, question 1). Monsanto introduced its RR crops as "RR crop systems" designed for sole reliance on glyphosate for weed control. Even several years after GR weeds first emerged in RR soybeans and then cotton, Monsanto promoted "glyphosate-only" weed control programs in farm press advertisements dating to 2003 and 2004, ads that leading weed scientists castigated as irresponsible for promoting weed resistance (Hartzler et al. 2004). Interestingly, this ad campaign was designed to encourage farmers to adopt Roundup Ready corn, in which farmers had shown little interest up to that time, in contrast to Roundup Ready soybeans and cotton, which had been readily adopted. The effect of Monsanto's glyphosate-only, RR corn ad campaign was to promote glyphosate-only weed control programs in RR corn/RR soybean rotations. (Up to that time, most corn/soybean farmers had rotated RR soybeans with conventional corn, utilizing primarily non-glyphosate herbicides with the latter.) The subsequent rapid rise of RR corn in combination with existing RR soybeans led directly to emergence of GR weeds in Midwest and Northern Plains states beginning in 2005. Thus, Monsanto not only failed to promote proper stewardship practices to forestall GR weed emergence; it actively promoted practices that led directly to the expanding GR weed epidemic in corn/soybean country.

As discussed above, dicamba use on non-dicamba-resistant corn will likely increase considerably with significant adoption of MON 87708 under the proposed registration. This will result in more acres treated every year with dicamba in popular corn/soybean rotations. Monsanto's planned introduction of dicamba-resistant corn in a few years would greatly exacerbate matters, since the elimination of corn injury concerns will make dicamba-resistant corn a more attractive option for farmers.

Monsanto's recommendation to use a soil residual herbicide in addition to dicamba and glyphosate with MON 87708 will not be followed by the majority of growers, and as discussed above in relation to waterhemp is of questionable value for those who do. If Monsanto were a responsible steward of dicamba-resistant technology, the company would strongly advise growers of MON 87708 to abstain from dicamba use when rotating to corn (or small grains crops like wheat); and it would not have developed dicamba-resistant corn at all, which if introduced will almost surely lead to tens of millions of acres treated with dicamba each year in rotations of dicamba-resistant corn and soybeans, and thus to massive evolution of dicamba-resistant weeds.

Dow's introduction of competing 2,4-D resistant crops may not offer much help in terms of diversifying selection pressure, due to clear emerging evidence that resistance to either auxin herbicide may often confer resistance or at least increased tolerance to the other. Two weed populations have confirmed resistance to both dicamba and 2,4-D (prickly lettuce in Washington, and wild mustard in Canada, see ISHRW SynAux Weeds Table 9/20/12). The recently discovered 2,4-D-resistant waterhemp in Nebraska has significantly decreased sensitivity to dicamba as well. And preliminary research strongly suggests that horseweed populations with increased tolerance to 2,4-D also have increased tolerance to dicamba. Finally, it is interesting to note that MON 87708 itself possesses increased tolerance to three tested phenoxy herbicides – 2,4-D, MCPA and 2,4-DB (Monsanto 2010 at 76-77). While the precise mechanisms of auxin resistance in weeds have not been fully elucidated, the evidence presented above suggests strongly that cross-resistance among auxin herbicides is a frequent occurrence.

This suggests the need to consider the cumulative impacts of all auxin-resistant crops together for purposes of assessing their potential for fostering auxin-resistant weeds. This is surely the reasoning that prompted Bernards et al. (2012) to call for "mandatory stewardship practices" for "soybean, cotton and corn resistant to 2,4-D and dicamba." Furthermore, the demand for "mandatory" practices is an implicit acknowledgement of the failure of voluntary programs such as Monsanto's.

Spread of weed resistance and tragedy of the commons

Weeds evolve resistance through strong selection pressure from frequent and late application as well as overreliance on particular herbicides, as fostered especially by HR crop systems. However, once resistant populations of out-crossing weeds emerge, even small ones, they can propagate resistance via cross-pollinating their susceptible counterparts (Webster & Sosnoskie 2010). It is estimated that common waterhemp pollen can travel for one-half mile in windy conditions, and so spread resistance to neighbors' fields via cross-pollination (Nordby et al. 2007). A recent study was undertaken to measure waterhemp pollen flow because "[p]ollen dispersal in annual weed species may pose a considerable threat to weed management, especially for out-crossing species, because it efficiently spreads herbicide resistance genes long distances," because the "severe infestations and frequent incidence [of waterhemp] arise from its rapid evolution of resistance to many herbicides," and because "there is high potential that resistance genes can be transferred among populations [of waterhemp] at a landscape scale through pollen migration" (Liu et al. (2012). The study found that ALS inhibitor-resistant waterhemp pollen could travel 800 meters (the greatest distance tested) to successfully pollinate susceptible waterhemp; and that waterhemp pollen can remain viable for up to 120 hours, increasing the potential for spread of resistance traits.

A second recent study made similar findings with respect to pollen flow from glyphosate-resistant to glyphosate-susceptible Palmer amaranth (Sosnoskie et al. 2012). In this study, susceptible sentinel plants were planted at distances up to 250-300 meters from GR Palmer amaranth. From 20-40% of the progeny of the sentinel plants at the furthest distances proved resistant to glyphosate, demonstrating that glyphosate resistance can be spread considerable distances by pollen flow in Palmer amaranth.

Whether out-crossing or inbreeding, those resistant individuals with lightweight seeds can disperse at great distances. Dauer et al. (2009) found that the lightweight, airborne seeds of horseweed, the most prevalent GR weed (CFS GR Weed List 2012), can travel for tens to hundreds of kilometers in the wind, which is likely an important factor in its prevalence. Hybridization among related weeds is another potential means by which resistance could be spread, for instance by weeds in the problematic *Amaranthus* genus (Gaines et al. 2012). Movement of resistant seed via waterways when excessive rainfall leads to flooding has been suggested as one explanation for the epidemic spread of glyphosate-resistant and multiple herbicide-resistant waterhemp[27] in the sugarbeet production region of Minnesota and North Dakota (Stachler et al 2012).

Thus, even farmers who employ sound practices to prevent emergence of herbicide-resistant weeds themselves can have their fields infested with resistant weeds from those of other farmers. With reference to GR weeds, Webster & Sosnoskie (2010) present this as a tragedy of the commons dilemma, in which weed susceptibility to glyphosate is the common resource being squandered. Since responsible practices by individual farmers to prevent evolution of weed resistance in their fields cannot prevent weed resistance from spreading to their fields as indicated above, there is less incentive for any farmer to even try to undertake such prevention measures.

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[27] For the recent confirmation of multiple HR waterhemp, see http://www.ag.ndsu.edu/homemoisture/cpr/weeds/herbicide-resistance-in-waterhemp-in-mn-and-nd-and-management-in-sugarbeet-corn-and-soybean-5-24-12.

The weed science community as a whole has only begun to grapple with the implications of the ***spread*** of resistance, particularly as it relates to the efficacy of weed resistance management recommendations based solely on individual farmers reducing selection pressure. It may not be effective or rational for farmers to commit resources to resistance management in the absence some assurance that other farmers in their area will do likewise. This suggests the need for a wholly different approach that is capable of ensuring a high degree of area-wide adoption of sound weed resistance management practices. This represents still another reason to implement mandatory stewardship practices to forestall emergence of dicamba -resistant weeds in the context of MON 87708 soybean and similar auxin-resistant crops.

Volunteer MON 87708 soybean

Volunteer soybeans are not normally considered problematic weeds, but with the advent of RR soybeans there are some reports that glyphosate-resistance makes them more difficult to control. For instance, York et al. (2005) report that volunteer glyphosate-resistant soybean can be a problematic weed in glyphosate-resistant cotton planted the next season. They note in general that: "Volunteer crop plants are considered to be weeds because they can reduce crop yield and quality and reduce harvesting efficiency." York and colleagues tested several herbicidal options to control GR soybean volunteers, including pyrithiobac, trifloxysulfuron, and each herbicide mixed with MSMA, an arsenic-based herbicide that EPA is in the process of phasing out due to its toxicity, though an exemption has been made for continued use in cotton to control GR Palmer amaranth (EPA 2009). They also note that paraquat can be used to control GR soybean volunteers prior to emergence of cotton. Some farmers have also reported problematic volunteer RR soybean in the following year's corn, and sought advice from extension agents on how to deal with it (Gunsolus 2010). Recommendations include use of 2,4-D, dicamba, atrazine and/or other herbicides. In both cases, it is glyphosate-resistance that has made volunteer soybean a control problem for farmers, and necessitated the use of more toxic herbicides for control.

MON 87708 soybean volunteers (stacked with Roundup Ready) would possess resistance to dicamba as well glyphosate, eliminating dicamba and glyphosate and reducing the efficacy of 2,4-D as herbicidal control options. These volunteer soybeans weeds would thus be still more of a management challenge than RR soybean volunteers, and lead to use of more toxic herbicides (e.g. MSMA, paraquat, atrazine) or tillage to control.

Soybean is primarily a self-pollinating crop, but the potential for perhaps considerable cross-pollination is suggested by the frequency with which pollinators – bees (honeybees and wild bees), wasps and flies – visit soybean fields (Anonymous 2012, O'Neal & Gill 2012). Insect pollinators are known to effect pollination at considerable distances from the source plants, including from primarily self-pollinating crops (e.g. Pasquet et al. 2008).

In addition to MON 87708, three other HR soybean events are presently pending deregulation by USDA: Dow's 2,4-D- and glufosinate-resistant soy, BASF's isoxaflutoleresistant soy, and Bayer's imidazolinone-resistant variety.[28] While multiple HR soybean volunteers via cross-pollination would likely be an infrequent occurrence, it could trigger serious weed management challenges where it does occur.

As a general matter, such "resistance stacking" speeds evolution to those herbicides that remain effective. It limits chemical options for managing weeds, and "where weed management depends primarily on chemical weed control, results in additional selection pressure for the evolution of resistance to the few herbicides that are still effective" (Bernards et al. 2012). While this statement was made with reference to HR waterhemp, it applies more generally to multiple HR weeds, including HR soybean volunteers.

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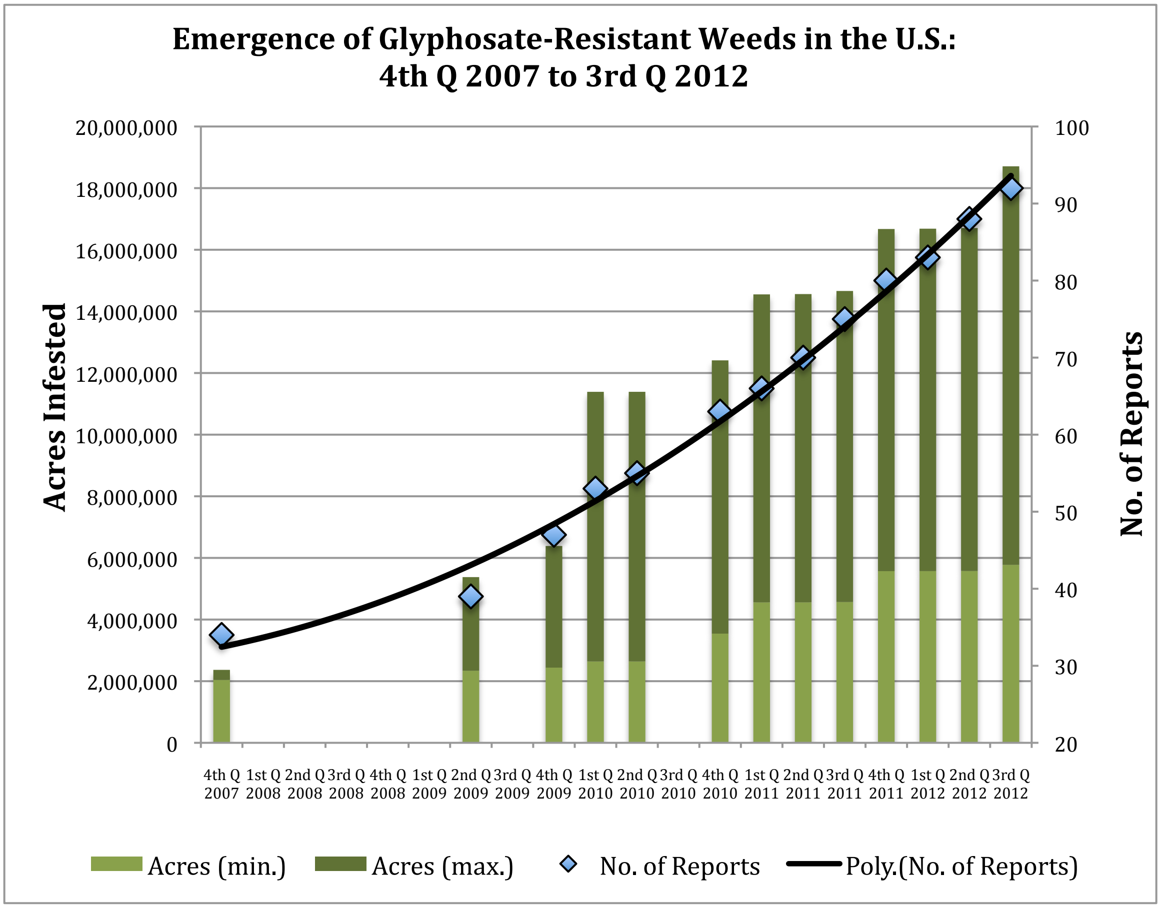
[28] See entries at http://www.aphis.usda.gov/biotechnology/not_reg.html, last visited 8/22/12.



Legend: This chart plots data on glyphosate-resistant weeds in the U.S. compiled from the International Survey of Herbicide-Resistant Weeds (ISHRW) as of September 20, 2012. See CFS GR Weed List (2012) for the data upon which this chart is based. The ISHRW lists reports of confirmed herbicide-resistant weeds submitted by weed scientists.[29] Each report normally contains the year of discovery, the number of sites and acreage infested by the resistant weed population, the crop or non-crop setting where the weed was found, whether or not the population is expanding, and date the report was last updated. Note that months to several years can elapse before a putative resistant weed population is confirmed as resistant and listed on the website. ISHRW reports sites and acreage infested in ranges due to the difficulty of making precise point estimates. CFS aggregated ISHRW data for all glyphosate-resistant weed reports on 13 dates – 11/21/07, 2/2/09, 11/19/09, 2/25/10, 5/18/10, 11/30/10, 1/6/11, 7/5/11, 9/28/11, 12/31/11, 3/28/12, 7/2/12 and 9/20/12 – corresponding to the 13 bars in the graph above. The bars were assigned to the appropriate quarterly period on the x-axis. The minimum and maximum acreage values represent the aggregate lower- and upper-bound acreage infested by all glyphosate-resistant weeds listed by ISHRW on the given date. The number of reports is plotted on the secondary y-axis. The figures shown here are very conservative, because ISHRW is a voluntary reporting system and many GR weed populations are never reported, or if reported are often not updated to account for expansion. ISHRW organizer Dr. Ian Heap concedes that these figures are "way too low," and in August 2012 estimated that 40 million acres were infested with a GR weed (30 million if overlapping acres infested with more than one GR weed are counted just once) (see Heap 2012). As noted in the text, Dow estimates 60 million GR weed-infested acres. This suggests that GR weed prevalence is roughly

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[29] Each report may be accessed by (and corresponds to) a link at: http://www.weedscience.org/Summary/UspeciesMOA.asp?lstMOAID=12&FmHRACGroup=Go.

twice to three times the upper-bound estimates shown here. Even so, this graph provides a sense of the rapid course of GR weed emergence in the U.S.

The proposed registration would sharply increase non-target crop and plant injury from dicamba drift episodes

Dicamba use under the proposed registration would likely lead to a considerable increase in injury to non-target crops and wild plants, for reasons related to features of HR crop systems in general and to the properties of dicamba in particular. As discussed above, HR crop systems facilitate postemergence weed control programs in which the herbicide is generally applied much later in the season, when neighboring crops have leafed out and are more susceptible to drift injury. High-level resistance to the herbicide facilitates use of higher rates without risk of crop injury, increasing the drift "dose" that non-target crops and plants receive, as well as the range of drift at levels that can damage plants. With widespread adoption of an HR crop, there is much greater use of the associated herbicide(s), and farmers become less cautious in drift prevention measures, on the assumption that most of their neighbors are growing crops with the same herbicide-resistance trait.

Roundup Ready crops illustrate the problem. Although glyphosate is not a drift-prone or volatile herbicide, two surveys of state pesticide regulators have found that glyphosate consistently ranked second, behind only 2,4-D, in drift-related crop injury episodes (AAPCO 1999, 2005). These surveys were conducted from 1996-1998 and 2002-2004 during the years of rapid Roundup Ready crop adoption and associated sharp rise in postemergence glyphosate use. In Arkansas, an important factor encouraging Roundup Ready corn adoption was to defend against drift from glyphosate use on Roundup Ready soybeans and cotton. According to Ford L. Baldwin, of Arkansas-based Practical Weed Consultants, Inc.:

> "A lot of growers planted Roundup Ready corn in the beginning out of self defense. I looked at enough glyphosate drift on conventional corn to understand why." (Baldwin 2010)

Steve Smith, Director of Agriculture for Red Gold, an Indiana-based tomato processor, reports that tomato farmers based in Indiana, Ohio and Michigan who supply his firm experienced over $1 million in losses over a four-year period from glyphosate drift emanating from Roundup Ready crop fields (Smith 2010). In controlled experiments, Kruger et al (2012) have confirmed that glyphosate causes substantial yield reductions to tomatoes at low, drift-level doses.

Properties of dicamba make it a much greater threat than glyphosate. Like most auxin herbicides, dicamba has very broad-spectrum activity on broadleaf plants, which include soybeans and cotton as well as nearly all vegetables and fruits. Auxin herbicides are also very potent, dicamba more so than 2,4-D, such that very low drift-level doses can cause considerable damage. Finally, while most herbicides pose a drift threat only during their initial application, dicamba is extremely volatile, and is known to volatilize from plant surfaces days after the initial application to move off-target and cause damage to crops and wild plants at considerable distances.

Behrens and Lueschen (1979) report that post-emergence dicamba sprays used on 250,000 ha of corn in Minnesota in 1974 resulted in 68 reports of dicamba drift effects on soybeans. In contrast, post-emergence use of 2,4-D on 800,000 ha hectares of corn yielded just seven reports. This suggests that pound for pound, dicamba is much more prone to cause drift-related crop damage than 2,4-D. This finding is supported by the AAPCO surveys referenced above. In these surveys, dicamba consistently ranked third among all herbicides in drift-related crop injury episodes, behind only 2,4-D and glyphosate, despite its extremely limited use. In the latter survey period (2002-2004), just 4-5 million lbs./year of dicamba were used agriculturally in the entire country (Monsanto 2010 at 198). In the same period (2003), roughly 30 million lbs. of 2,4-D and 130 million lbs. of glyphosate were applied annually (EPA Pesticide Use 2011), 7-fold to 30-fold more, respectively.

In a series of field and glasshouse experiments, Behrens and Lueschen (1979) established that dicamba, volatilizing after application to corn, caused symptoms on soybean plants placed up to 60 meters downwind of the treated corn; that dicamba volatilizing from treated corn could be detected via effects on soybeans for three days after the application; and that dicamba volatilization was enhanced by higher temperatures and lower humidity, and extinguished by rainfall.

Interestingly, this team determined that dicamba acid and various salt forms had widely varying volatilization rates from glass surfaces, and that the vapors of more volatile salts (after application to corn) caused much greater damage to nearby soybeans in closed jars than did the less volatile salts. However, in field experiments, these differences largely disappeared. That is, less volatile salts applied to corn vaporized to damage downwind soybeans almost as much as the highly volatile (e.g. dimethylamine) salts. The diglycolamine salt being proposed for registration is apparently less volatile than the widely used dimethylamine salt. However, this may not translate into lesser injury to crops from volatilization.

In tests involving the diglycolamine salt of dicamba, Andersen et al (2004) simulated dicamba drift injury by directly treating soybeans with 5.6 to 56 g a.e./ha dicamba (1% to 10% of the label rate for corn). These treatments reduced soybean yields by 14% to 93%. Andersen et al found greater soybean injury in the drier of the two years of their experiment, in line with the findings of Behren and Lueschen that lower humidity enhanced volatilization, and rainfall extinguished it. Finally, it was found that dicamba applied in a mixture with crop oil concentrate, which enhances absorption of the active ingredient by crop tissues, resulted in slightly higher levels of injury. This highlights the importance of considering dicamba's activity in the forms in which it is actually used by farmers.

Kelly et al (2005) examined the impact of low-level dicamba in combination with other post-emergent herbicides on soybeans, to simulate the effect of dicamba vapor drift in a realistic soybean production setting. Similar to Andersen et al, this team found yield reductions from application of 5.6 g a.e./ha dicamba (1% the label rate for corn) either alone or in combination with each of several post-emergent soybean herbicides (glyphosate, imazethapyr, imazamox, or fomesafen) of from 7% to 41%, with the dicamba/fomesafen combination lowering soybean yield more than any of the other combinations. This study is important in establishing yield losses from soybean exposure to realistic volatilization drift rates (e.g. 1%) under field conditions where such exposure is accompanied by application of common post-emergent soybean herbicides.

Tomatoes are even more sensitive to dicamba than soybeans. Recent experiments have established that a dose of dicamba of just 1.5 g/ha caused 5% flower loss at the early bloom stage of development, while 2.4 g/ha caused 5% flower loss at the early vegetative stage (Kruger et al 2012). These rates are extremely low, representing roughly 1/300th to 1/200th of a typical application rate, respectively, and are well within levels that would result from drift and volatilization under field conditions. Only slightly higher levels were found to trigger a 10% loss in marketable fruit.

Potential impacts of the proposed registration on human health

Dicamba is a chlorinated benzoic acid herbicide similar in structure and mode of action to 2,4-D, and is used in both agriculture (e.g. corn, wheat) and on lawns. In 1992, epidemiologists with the National Cancer Institute (NCI) found that farmers exposed to dicamba were twice as likely to contract non-Hodgkin's lymphoma (Cantor 1992). A subsequent study by NCI scientists reported associations between dicamba exposure and higher incidence of lung and colon cancer in pesticide applicators (Samanic et al 2006).

Researchers have also found a 20% inhibition of the nervous system enzyme acetylcholinesterase in a group of certified pesticide applicators whose only common pesticide used was dicamba (Potter et al 1993). Acetylcholinesterase is an enzyme critical to neurological function. Children exposed to residues of organophosphate insecticides (which kill insects by disrupting acetylcholinesterase function) in foods have higher rates of attention deficit hyperactivity disorder (Bourchard et al 2010), a condition afflicting 4.5 million children in the U.S. (Monday 2010). Exposure to dicamba may have similar effects.

Dicamba is moderately persistent in soil and water, and is frequently found contaminating ground and suface waters, for instance in 28% of rivers sampled in the U.S. (Thurman et al 2003). Pregnant mice that ingested drinking water spiked with low doses of a commercial herbicide product containing dicamba, 2,4-D and mecoprop had reduced litter size, suggesting that this herbicide mixture has developmental toxicity (Cavieres et al 2002). A study of the frequency of sister chromatid exchanges (SCEs) and cell-cycle progression assays revealed that high doses of dicamba can damage DNA, leading the study authors to warn that dicamba is a "potentially hazardous compound to humans" (Gonzalez et al 2006). Another study that examined dicamba after its activation by plant (dicamba–treated corn) or animal (liver microsomes) found it to be mutagenic in standard bacteria and yeast assays (Plewa et al 1984). A fuller description of the potential health impacts of dicamba may be found in Cox (1994).

Given the clear potential for serious health impacts from exposure to dicamba, the vastly increased use that would be facilitated by the proposed registration is clearly contrary to the interests of farmers and the general public.

Environmental impacts of dicamba use with MON 87708 soybean

Overview of environmental impacts

Herbicide resistant crops are not the ultimate cause of increased conservation tillage, nor are they required to maintain conservation tillage. EPA should not succumb to the arguments that use purported benefits of conservation tillage to counterbalance harms of increased dicamba use. First we analyze the relationship of conservation tillage to herbicide use with HR crops, and then environmental impacts of dicamba use on MON 87708.

Herbicide resistant crops not responsible for increased conservation tillage

Contrary to prevalent misconceptions, herbicide-resistant crop systems have not driven any meaningful increase in the use of conservation tillage. The following discussion may be summarized as follows.

First, there is considerable doubt concerning whether HR soybean cultivation is even correlated with conservation tillage practices.

Second, to the extent there is such a correlation, the causation is from prior adoption of conservation tillage to subsequent adoption of HR soybeans. In contrast, the adoption of HR crops does not predispose to greater use of conservation tillage.

Third, steeply declining soil erosion rates in the 1980s and the first half of the 1990s leveled out in the following decade of Roundup Ready crop adoption. These data are irreconcilable with the proposition that HR crops drive greater use of soil-saving cultivation regimes.

Fourth, soil-saving federal farm policies, not HR crops, were primarily responsible for increased use of conservation tillage and reduced soil erosion in American agriculture.

Fifth, HR crops in fact promote ***greater*** use of soil-eroding tillage to remove herbicide-resistant weeds, which the use of these crop systems fosters.

Finally, we show that some purported benefits often attributed to conservation tillage are disputed in the scientific community, while in other cases this form of tillage appears to have adverse impacts.

i. Correlation in question

One often sees reference to a ***correlation*** between adoption of RR soybeans and greater use of conservation tillage practices. However, much of the data upon which this purported correlation is based come from suspect sources, such as the American Soybean Association, a lobby group that represents Monsanto and other large agrichemical-seed firms. In a widely cited assessment of the environmental impacts of glyphosate-resistant crops, Cerdeira and Duke (2006) note that:

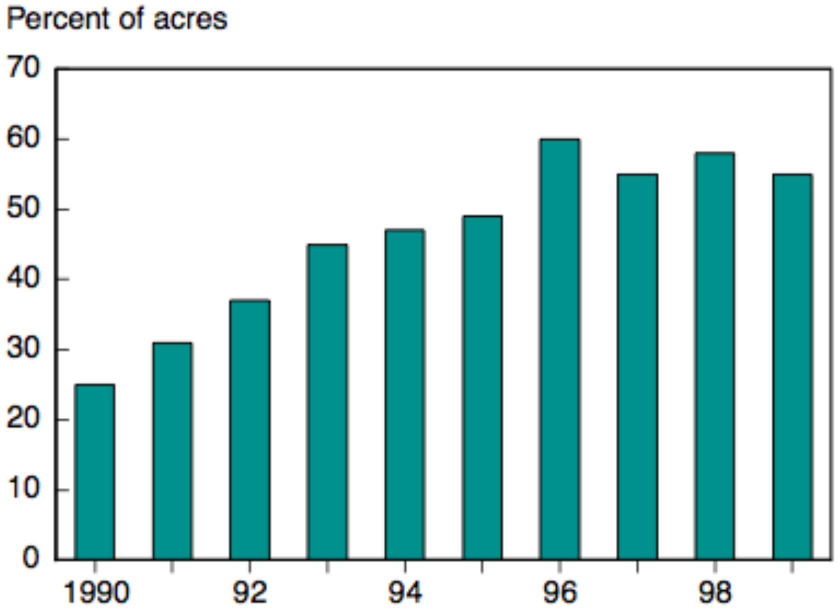
> Considering the relatively high level of potential environmental improvement that can be gained by reducing tillage, there is a remarkable paucity of refereed publications on the influence of GRCs [glyphosate-resistant crops] on tillage practices and associated environmental effects. (p. 1638).

Despite this caution, the authors proceed to base their discussion of purported reductions in soil loss and compaction from GR crop systems almost entirely on a survey conducted by the American Soybean Association (ASA) in 2001, a survey that was not subject to peer review or published in any "refereed publication." These ASA survey results are extremely difficult to reconcile with an assessment conducted the following year by USDA agricultural economists Jorge Fernandez-Cornejo and William McBride. These authors have shown that adoption of conservation tillage in soybean production rose sharply in the years ***prior to*** introduction of RR soybeans, then stagnated in at least the first four years of their cultivation (1996-1999).

> Adoption of conservation tillage for soybeans grew (at a decreasing rate) from about 25 percent of the soybean acreage in 1990 to 48 percent in 1995 (Fig. 11), the 5-year period previous to the introduction of herbicide-tolerant soybeans. Growth of conservation tillage increased further in 1996, but then appears to have stagnated between 50 and 60 percent in the following years (Fernandez-Cornejo & McBride 2002, p. 29).

Figure 11

Use of conservation tillage - soybeans



Source: Fernandez-Cornejo (2000) based on USDA data (USDA, 1997a updated from ARMS).

From: Fernandez-Cornejo & McBride (2002), p. 29.

Roundup Ready soybeans were introduced in 1996, and were adopted extremely rapidly. They comprised 7.4%, 17%, 44.2% and 55.8% of total soybean acreage in the years from 1996 to 1999, respectively. This represents 4.75, 11.90, 31.84 and 41.14 million acres of Roundup Ready soybeans in the corresponding years (see table below). Yet Figure 11 above shows clearly that soybean growers overall practiced conservation tillage to a considerably greater extent in 1996, when under 5 million acres were Roundup Ready, than in 1999, when RR soybean acreage had increased over eight-fold, to 41.14 million acres, to comprise over half of all soybeans grown. These data, at the very least, cast great doubt on a purported correlation between RR soybeans and use of conservation tillage.

Yet in the same publication, Fernandez-Cornejo & McBride (2002) present an “estimate,” based on the same USDA Agricultural Resources Management Survey (ARMS) that served as the source of Figure 11 above, to the effect that 60% of Roundup Ready soybean acres were under conservation tillage, versus just 40% of conventional soybean acres.

> A larger portion of the acreage planted with herbicide-tolerant soybeans was under conservation tillage than was acreage growing conventional soybeans. According to estimates based on USDA’s ARMS data, about 60 percent of the area planted with herbicide-tolerant soybeans was under conservation tillage in 1997 (fig. 12). In comparison, only about 40 percent of the acres

> planted with conventional soybeans were under conservation tillage the same year.(Fernandez-Cornejo and McBride 2002, p. 29)

These estimates are irreconcilable with the data portrayed in Figure 11, as shown in the table below.

	1996	**1997**	**1998**	**1999**
Total soybean acres (thousands)	64195	70005	72025	73730
Percent HR soybeans	7.4%	17.0%	44.2%	55.8%
HR soybean acres	4750	11901	31835	41141
Conventional soybean acres	59445	58104	40190	32589
Percent of total soybeans under conservation tillage (from Fernandez-Cornejo & McBride 2002, Figure 11)		54%		
Acres of soybeans under conservation tillage		37803		
Scenario assuming that HR soy cultivation correlates with conservation tillage (1997)				
60% HR soy under con-till		7141		
40% conv'l soy under con-till		23242		
Predicted soy acres under con-till		30382		
Scenario's deviation from reality				
Deficit in con-till acres		7421		
Amount by which actual con-till soy acres exceeds prediction (in percent)		24%		
Scenario assuming equal (54%) adoption of con-till on HR and conventional soybean acres		37803		

The estimate (scenario) according to which 60% of RR and just 40% of conventional soybeans were under conservation tillage in 1997 yields just 30.4 million acres of conservation-tilled (con-till) soybeans, when the true figure is 37.8 million acres, or 24% more. Clearly, the estimate linking RR soybeans to con-till soybeans is in error. Since the great majority (83%) of soybeans in 1997 were conventionally tilled, the most likely explanation for the deficit is that conventional soybean growers used conservation tillage (con-till) to a greater extent than presumed in the estimate. The scenario assuming equal adoption of con-till by the two groups gives the expected, and correct, result. The latter scenario of equal adoption of con-till is supported by the following finding.

ii. Conservation tillage leads to HR seeds, not vice versa

After noting the "correlation" between RR soybeans and conservation tillage that is critiqued above, Ferndandez-Cornejo and McBride conducted an econometric analysis to determine causation, which reached the following conclusion with respect to no-till, one form of conservation tillage:

> According to the econometric model results, using 1997 ARMS survey data, farmers using no-till for soybeans were found to have a higher probability of adopting herbicide-tolerant seed, but using herbicide-tolerant seed did not significantly affect no-till adoption. This result seems to suggest that farmers already using no-till found herbicide-tolerant seeds to be an effective weed control mechanism that could be easily incorporated into their weed management program. On the other hand, the commercialization of herbicide-tolerant soybeans did not seem to have encouraged adoption of no-till, at least [in] the year of the survey, 1997. (p. 29)

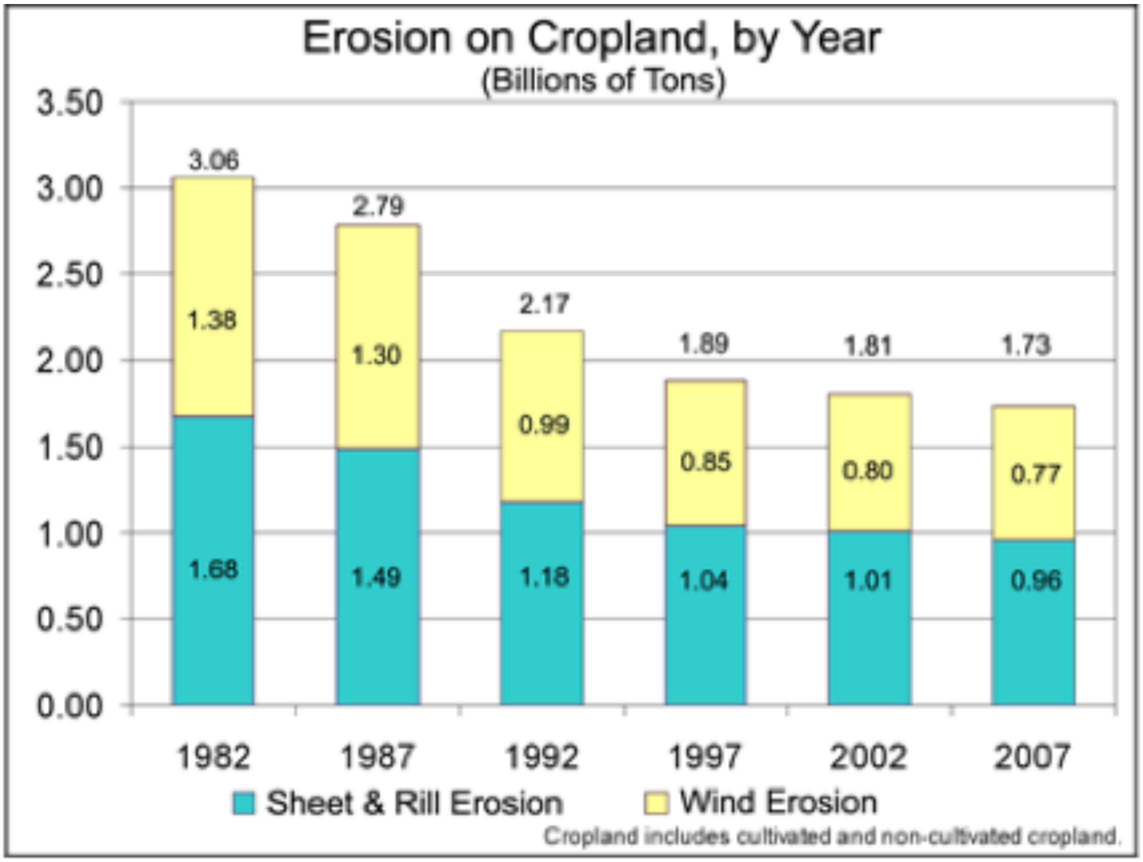
Thus, even if one were to posit a correlation, the causation flows from prior adoption of conservation tillage to subsequent adoption of HR soybeans, not the reverse. In short, HR soybeans do not increase adoption of conservation tillage.

It is unclear why these trained agricultural economists did not detect this serious and obvious discrepancy in the data they presented, but it is indisputable that they did. It is also quite striking that Fernandez-Cornejo and McBride (2002) offer absolutely no explanation for the rapid rise in conservation-tilled soybeans in the 5 years leading up to introduction of RR soybeans (1990-1995, see Figure 11). We offer an explanation below.

iii. Reductions in soil erosion come to an end during the decade of herbicide-resistant crop adoption

Conservation tillage is widely credited with bringing about large reductions in soil erosion rates. Thus, if HR soybeans, corn and cotton did in fact promote greater use of conservation tillage, one would clearly expect to see sharply falling soil erosion rates over the period of their widespread adoption, in the areas where these crops are widely grown. However, gold-standard data from USDA's soil conservation experts, the Natural Resources Conservation Service (NRCS), show that this is not the case.

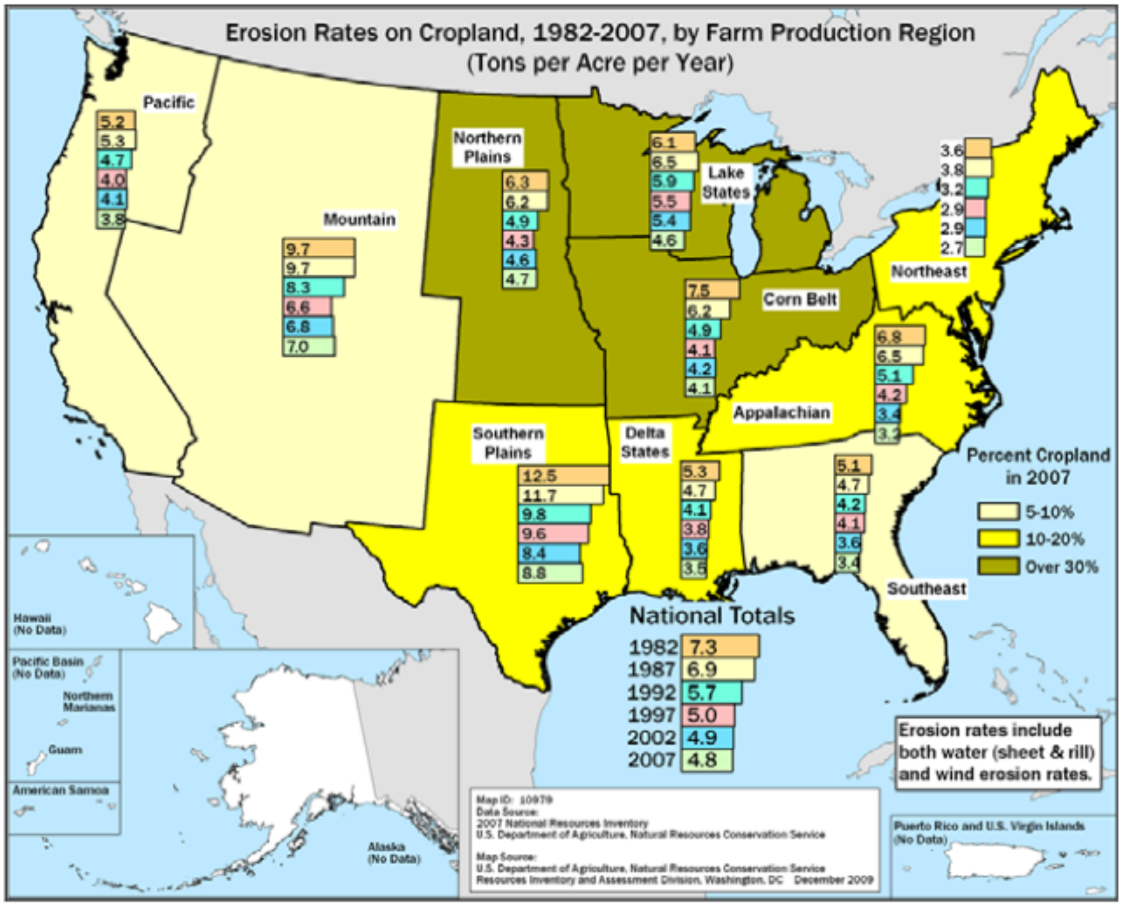
Below, we reproduce a chart from page 2 of NRCS's 2010 report: "2007 National Resources Inventory: Soil Erosion on Cropland" (USDA NRCS 2010, in supporting materials). The chart represents NRCS' best estimate of cropland erosion from 1987 to 2007. According to NRCS: "[E]rosion rates computed from NRI data are estimates of average annual (or expected) rates based upon long-term climate data, inherent soil and site characteristics, and cropping and management practices." Tillage regimes are the primary component of "cropping and management practices," and thus play a large role in determining soil erosion rates. It is well established that soil erosion increases with the intensity of tillage, and decreases as farmers adopt regimes that leave more plant residue on the soil (USDA ERS AREI 2002). Thus, the chart below reflects in large degree the tillage regimes used by farmers.



From: NRCS (2010), p. 2.

On a national basis, water and wind erosion on cropland declined sharply by 38% from 1982 to 1997, from 3.06 to 1.89 billion tons. In the following decade, however, soil erosion almost leveled out, declining by just 8%, from 1.89 to 1.73 billion tons. Herbicide-resistant crops were first introduced in 1996, and the area planted to them (HR soybeans, corn and cotton) increased steadily from 16.0 million acres in 1997 to 117.2 million acres in 2007 (Benbrook Supplemental 2009, Table 5). If HR crops promoted adoption of conservation tillage in any significant way, one would surely expect a much stronger decline in soil erosion over a period when their adoption increased by 100 million acres.

However, NRCS' survey offers still more compelling evidence at the regional level. The following map (from p. 3) breaks down average annual soil erosion rates, in tons per acre per year, by farm production region. For each region, rates for the six survey periods (1982, 1987, 1992, 1997, 2002 and 2007) are shown stacked from top (1982) to bottom (2007). The rates in this map are also listed in Table 36 of the report (pp. 12-16).



Erosion Rates on Cropland, 1982-2007, by Farm Production Region
(Tons per Acre per Year)

Erosion rates include both water (sheet & rill) and wind erosion rates.

Map ID: 10979
Data Source:
2007 National Resources Inventory
U.S. Department of Agriculture, Natural Resources Conservation Service

Map Source:
U.S. Department of Agriculture, Natural Resources Conservation Service
Resources Inventory and Assessment Division, Washington, DC December 2009

The Corn Belt states (Iowa, Illinois, Indiana, Missouri and Ohio) and the Northern Plains states (Kansas, Nebraska, North and South Dakota) comprise two-thirds of the nation's corn and soybean acreage, and all of these states have high adoption rates of GE herbicide-resistant soybeans and corn. If the supposition that HR crops and HR soybeans in particular promote conservation tillage were correct, one would certainly expect to see an appreciable decline in soil erosion in these two regions over the 1997 to 2007 period when HR versions of these crops were widely adopted; and that decline should be far more pronounced than the national average. However, this is not the case at all.

In the Corn Belt states, the annual erosion rate remained constant at 4.1 tons per acre from 1997 to 2007, while ***erosion actually increased in the Northern Plains states*** over this same period, from 4.3 to 4.7 tons per acre, in both cases bucking the national trend of modest decline. Of the eight other farm production regions, all but two (Mountain and Lake States) had declining erosion rates. Clearly, the massive adoption of HR corn and soybeans from 1997 to 2007 did not foster increased adoption of soil-conserving practices; if it had, it would have been reflected in declining rather than stable or increasing erosion rates.

iv. Federal farm policy triggered sharp declines in soil erosion prior to HR crop adoption

The other question raised by NRCS' report is this: what explains the sharp declines in soil erosion in ALL farm production regions, including Corn Belt and Northern Plains states, in the 1982 to 1997 period before any appreciable adoption of HR crops? The decline in soil erosion over this period is also consistent with increased use of conservation tillage in soybeans from 1990 to 1995, as displayed in Figure 11 above. The answer is clear. Strong financial incentives to adopt soil-saving farming practices contained in the 1985 and 1990 Farm Bills were chiefly responsible for increased use of conservation tillage. According to Coughenour and Chamala (2000), authors of a book examining the history of conservation tillage in the U.S. and Australia:

> There is little mystery about what brought ***a sea change in farmers' tillage*** decisions as the 1990s unfolded. The compliance provisions of the 1985 Farm Bill and the 1990 amendments dramatically altered the effective policy and institutional environment. ***Farmers who wanted governmental support payments had to begin implementing their farm conservation plans (FCPs) by 1995, and their plans often included provision for conservation tillage.*** The balance of factors favoring use of no-tillage systems has also been strengthened by the progressive change in the cultural climate favoring farmers' acceptance of program requirements and changes in farming practice. (p. 286, emphases added)

v. Weakening enforcement of farm conservation plans brings soil erosion reductions to an end

Soon after the 1995 deadline for implementation of farm conservation plans had passed, however, enforcement of these plans dramatically weakened, and further progress in preventing soil erosion was stymied. As explained by the Environmental Working Group:

> In 1997, after a decade of historic progress cutting soil erosion and polluted runoff from farmers' fields, America's soil, streams, lakes and rivers were improving.
>
> That historic achievement was driven by a 1985 federal law that required farmers to put conservation practices in place on their most vulnerable cropland in return for the billions of dollars of income and insurance subsidies they were getting from taxpayers. The "Highly Erodible Land Conservation" provisions of the 1985 Food Security Act required farmers to fully implement an approved soil conservation plan by 1995 on cropland that was determined to be "highly erodible." USDA's Economic Research Service (ERS) completed a comprehensive evaluation of those so-called conservation compliance provisions in 2004. ERS concluded that conservation compliance reduced soil erosion on highly erodible cropland by 331 million tons a year — a 40 percent reduction between 1982 and 1997 (USDA ERS 2004).
>
> ***Unfortunately, those gains were short-lived. Enforcement of conservation requirements weakened and in 1996 went off the rails altogether when Congress made an abortive push to phase out farm subsidies — and with***

> ***them the conservation requirements.*** The phase-out of farm subsidies turned out to be a mirage, and Congress immediately returned to its old habits — plowing billions into farmers' hands through ad hoc disaster payments and bringing all the farm subsidies back with a vengeance in the 2002 farm bill.
>
> ***The only thing that turned out to be real was the phase-out of enforcement of conservation requirements. The result has been a decade of lost progress and mounting problems.*** (EWG 2011, p. 28, emphases added).

In short, sharp reductions in soil erosion from the mid-1980s to the mid-1990s were driven by federal farm policy that made subsidies to farmers contingent on implementation of soil conservation plans on erodible land. Dramatic weakening of USDA enforcement of those plans in the mid-1990s explains the leveling off of soil erosion rates from 1997 to 2007. HR crops, adopted during this same decade, had essentially no influence on farmers' use of conservation tillage practices.

USDA's Natural Resources Conservation Service also credits federal farm policy as being "largely responsible" for increased use of soil-conserving cultivation practices:

> Total acres of conservation tillage systems rose steadily in the late 1980s to 37.2% of all planted acres in 1998 (Figure 2b). The implementation of Farm Bill Compliance standards containing residue management practices was largely responsible for much of this increased adoption (USDA-NRCS 2006a, p. 3).

"Residue management practices" refer to conservation tillage practices.

Environmental impacts of conservation tillage

Even if using dicamba with MON 87708 soybean is part of a conservation tillage program for some growers, the environmental benefits attributed to reduced tillage are not well substantiated, other than slowing soil loss.

Soil and water

Although herbicide-facilitated no-till methods may decrease soil erosion, they do not always increase soil quality or reduce water pollution, and under some conditions actually increase agrichemical runoff, degrading water quality.

No-till and other conservation-tillage systems discourage the disturbance of the soil, which can lead to over-compaction (Fabrizzi et al. 2005, Tebrugge 1999). In the absence of soil disturbance, some studies have shown that fertilizers broadcast on the soil surface are washed off the field by rain, thus polluting waterways as well as lowering nutrient-use efficiency (Malhi et al. 1996). Pesticides also can end up at higher concentrations in runoff from fields in conservation tillage. Crop residues are left on the surface in these systems, and surface residues intercept sprayed pesticides that are then washed off during rain (Baker and Shiers 1989, Martin et al. 1978). "If this washoff water becomes a part of surface runoff, herbicide concentrations can be quite high." (Mickelson et al. 2001). Research conducted on corn herbicides confirmed these conclusions. While no---till systems had the lowest volume of runoff, the concentrations of atrazine and cyanazine in runoff water were always greater (statistically significant in most cases) in no---till systems than for the other tillage regimes (Mickelson et al. 2001).

Fertilizer and pesticides can also run off more rapidly from no-till fields into drainage ditches, then into the watershed via more extensive pores, including earthworm burrows (Shipitalo et al. 2004, Comis 2005).

There is thus no guarantee that use of herbicide-dependent conservation tillage systems will result in overall benefits to soil and water quality, even if use of dicamba with MON 87708 soybean were to increase use of conservation tillage in the short term.

Climate change

It is often claimed that continued use of conservation tillage associated with GE crops will reduce GHG emissions as a result of increased carbon sequestration in soils, decreased fuel consumption, and the reduction of nitrogen soil amendments. These benefits for climate change of a purported preservation of no-till sobyean acreage are generally unsubstantiated. Recent work by Blanco-Canqui and Lal (2008) and a careful review of the literature by USDA researchers Baker et al. (2007) cast doubt on the claim that no-till results in more carbon sequestration than tillage in most conditions. Other gases that contribute to global warming– such as nitrous oxide (N2O), methane (CH4), and ammonia (NH3) – are reported to be generally higher in no-till fields, as well.

Scientists from the USDA's Agricultural Research Service and Department of Soil, Water & Climate at the University of Minnesota (Baker et al. 2007) reviewed the literature on the effects of tillage on carbon sequestration in agricultural soils and concluded that in order to accurately determine how much carbon is sequestered, it is necessary to sample the soil to a depth that the roots grow. This is because much of the carbon fixed in photosynthesis is translocated to the roots and some is exuded into the soil where it stimulates the growth of various microorganisms. The deeper roots and microorganisms may also store carbon for a longer period of time than the more shallow roots.

The vast majority of tillage-soil carbon sequestration studies have sampled no deeper than the top 30 cm (roughly 1 foot) of soil. When studies of carbon sequestration are limited to the top 30 cm of soil, more carbon is stored in no-till than tilled fields, on average. However, when the sampling includes more of the root zone (below 30 cm; corn roots can go down more than 200 cm), tilled fields have as much stored carbon as their no-till counterparts (Baker et al. 2007). In some cases, tillage results in more carbon storage.

Thus, the claim that conservation tillage results in more carbon sequestration than conventional tillage seems to be a result of sampling bias.

Blanco-Canqui and Lal (2008) published a study questioning carbon sequestration in no-till fields, as well. This study covered a large geographic area, looking at farmers' fields rather than small research plots, and sampling throughout the root zone. Not only did the plowed plots store as much carbon as the no-till plots when sampled below 10 cm, three of the plowed areas sequestered more carbon.

They come to a similar conclusion about using no-till to sequester carbon as Baker and colleagues:

> This regional study shows that NT [no-till] farming impacts on SOC [soil organic carbon] and N [nitrogen] are highly variable and soil specific. In MLRAs [Major Land Resource Areas] where NT soils have greater SOC than tilled soils, the gains in SOC are limited solely to the surface soil layers (<10 cm). The net effect of NT on SOC sequestration for the whole soil profile (0-60 cm) is not significantly different from that of plow tillage…
>
> Based on the data on soil profile C distribution from previous reports and this regional study, the view that NT farming would increase SOC over PT [plow tillage] is questionable... (Blanco-Canqui and Lal 2008, p. 701)

Other greenhouse gases may also be affected by tillage systems:

- Fertilizers in no-till fields are generally more vulnerable to volatilization. Fertilizers are often applied to the surface in no-till fields (Rochette et al. 2009), which can result in up to 50% of urea being volatized as ammonia (NH3) (Sommer et al. 2004). Some studies showed that cumulative NH3 volatilization was three times greater in no-till than in plowed fields, attributed to the reduced ability of nitrogen to infiltrate soils in the presence of crop residues on the surface of untilled soils (Al-Kanani et al. 1992).

- Ammonia can be oxidized and transformed into the greenhouse gas N2O. Once emitted, ammonia can also be rapidly converted to the aerosol ammonium (NH4+) that contributes to ecosystem fertilization, acidification, and eutrophication. These processes increase methane emissions and decrease carbon sequestration through photosynthesis, thereby exacerbating climate change.

- Globally, most N2O emissions are the result of microbial processes in soil, both aerobic nitrification and anaerobic denitrification (Smith and Conen 2004). No-till soils have demonstrated elevated levels of water-filled pore space (WFPS), determined by water content and total porosity (Mosier et al. 2006). WFPS appears to be closely related to soil microbial activity. One study demonstrated that WFPS in no-till systems to be 62% compared to 44% for plowed soils (Linn et al. 1984). Other studies have implicated no-- till in greater N2O releases, as well (Ball et al. 1999, Rice and Smith 1982).

The point of citing these studies that show exacerbation of greenhouse gas emissions and degradation of soil and water quality with no-till methods is not to discount environmental benefits of conservation tillage in specific situations, particularly when it is used with other techniques of sustainable agriculture (Davis 2010). Using sustainable methods to decrease tillage for soil conservation is indeed important. However, relying on conservation tillage as an argument for a whole range of environmental benefits HR crops and herbicides without critical analysis of the best science available.

In fact, overall environmental benefits and harms from use of dicamba with MON 87708 soybean are likely to have more to do with changes in herbicide use that accompany the this cropping system than with tillage methods that may or may not be different.

Environmental effects of increased dicamba use with MON 87708 soybean

Injury to plants and other non-target organisms from exposure to dicamba

Dicamba is a particularly potent poison for many species of plants, especially dicotyledons (dicots, or broadleaf plants) that are sensitive to very low drift levels and to dicamba-contaminated water in semi-aquatic areas (US EPA 2006) p. 18 - 19, as also discussed in our comments on injury to crop plants above. Dicot species vary in their sensitivity to dicamba, e.g. (Johnson et al. 2012). Even monocots such as members of the grass and lily families can be killed by off-site movement from labeled doses of dicamba, and suffer sub-lethal injuries from drift levels at certain times in their life cycles (US EPA 2005, 2006).

Injury from dicamba in water

In reregistering dicamba, EPA said: "Based on fate characteristics, dicamba and DCSA would be somewhat persistent in aerobic and anaerobic conditions and would be expected to be persistent in groundwater" (US EPA 2006) p. 14. Dicamba has in fact been detected in ground water, although the quality of sampling is considered unreliable because measurements were not necessarily taken in areas where dicamba was in use, and detection levels were often unknown and probably high (US EPA 2005) p. 39, which would tend to underestimate the extent of contamination.

Dicamba is more frequently detected in surface waters, however. Water sampling in rivers by USGS bears out the propensity of dicamba to enter and persist in water bodies, even in numbers of samples that are disproportionately high compared to the extent of dicamba use (Thurman et al. 2001). In this 2001 study, USGS researchers developed a more sensitive and less laborious method to detect dicamba and 2,4-D in water, saying that previous methods made it difficult to conduct reliable extensive sampling. They applied their better method to river water samples from 14 areas across the US taken as part of the US Geological Survey's National Water Quality Assessment (NAWQA) program, and selected to represent different leaching and runoff scenarios, after rains during the peak herbicide application season. Surprisingly, although 5 times more 2,4-D than dicamba was used agriculturally, dicamba was detected in more samples – 28% of samples for dicamba vs. 16% of samples for 2,4-D. The highest percentage dicamba samples came from corn and soybean region of the White River of Indiana, whereas the 2,4-D samples were most common in the wheat-growing region of the Red River.

Plants can take up dicamba via water through their roots or from exposure of above ground plant parts to the contaminated water, putting sensitive terrestrial plants in riparian areas and semi-aquatic wetland areas at particular risk from increased use of dicamba with MON 87708 soybean (US EPA 2005).

Aquatic animals may also be at increased risk after applications of dicamba formulations to MON 87708 soybean. In reregistering dicamba, EPA examined databases where ecological incidents were reported, and there were some aquatic cases:

> Approximately, 100 incidents have been reported associated with dicamba usage. Incidents reported include impacts to terrestrial and aquatic non-target plants and animals. The majority of reported incidents are damage to plants including a wide range of crops (corn, sorghum, soybeans, sugar beets and wheat) as well as impacts to non-crop plants. The specific impacts varied from browning and plant damage to mortality of all plants within the treated area. Aquatic impacts reported consist of three fish kill incidents associated with pasture and residential turf application. (US EPA 2005) p. 6.

Looking at the more complete description of incidents, one fish-kill occurred after an agricultural application. Fish kills were also reported from turf and pasture applications. The reasons for the fish-kills are not discussed. Dicamba is reported to have only slight acute toxicity to fish (US EPA 2006) p. 16, so perhaps surfactants were the toxic agent (Cox 1994). Chronic and sub-lethal toxicity of dicamba to aquatic organisms have not been studied (US EPA 2006) p. 16.

These results indicate that more frequent and extensive use of dicamba with MON 87708 soybean will have an impact on levels of dicamba found in diverse water bodies in watersheds where soybeans are grown, and that these new impacts need to be assessed for their potential to injure non-target species of both plants and animals.

Injury to plants from spray drift and volatilization of dicamba

Reports of injury to non-target crops from dicamba spray drift and volatilization are common, even from registered existing uses of dicamba, as discussed in our comments on this topic, above.

If dicamba is moving off-site far enough to cause injury to crops, it is undoubtedly also causing injury to wild plants. Drift of dicamba is most likely to impact vegetation near the site where it is applied, so borders of fields and adjacent fencerows, wetlands, woodlands, riparian areas, and old-fields are vulnerable. These areas provide most of the biodiversity found in agricultural landscapes (e.g., Boutin and Jobin 1998). But with a volatile herbicide such as dicamba, injury has also occurred at locations distant from the application site, putting organisms in a variety of natural areas at risk.

Note that EPA only models spray drift when determining risks, because volatilization is too difficult to model (US EPA 2005), although it is an acknowledged hazard. In fact, the European Food Safety Authority has this as a "Critical area of concern" for dicamba use: "[d]icamba has the potential for long-range transport through the atmosphere." (EFSA 2011) p. 14.

It is likely that even crop injury from pesticide moving off-site is significantly under-reported:

> When crops are damaged by off-target movement of herbicides, the affected growers may settle their differences without the intervention of government enforcement agencies or courts. However, in the absence of a damage report to a state agency or court settlement, there are no records of their occurrence, due to lack of a centralized herbicide incident reporting system in the United States. For incidents that are more contentious or serious, a likely sequence of events arising from herbicide damage to non-target crops may include: 1) a complaint to a state agency over damage cause[d] by an herbicide, 2) an ensuing investigation that may uncover a violation (but which may not resolve the economic loss by the farmer whose crop is affected), and 3) lawsuits that use the investigation as evidence of harm…However, the majority of lawsuits are settled out of court with the stipulation that the plaintiffs not divulge the contents of the settlement to anyone including the government. (Olszyk et al. 2004, p. 225)

When only wild plants are harmed, injury may not be noticed or reported at all. Therefore, most information about risks of herbicide exposure for wild plants and ecosystems comes from experimental studies and comparative surveys rather than from incident reports. It is clear that non-target organisms do risk injury from dicamba used in agriculture, and that use dicamba with MON 87708 soybean is likely to increase that risk to the extent that the crop system involves increased use and changes in patterns of use of dicamba.

Injury from the effects of off-site pesticide movement on pests and pathogens

Herbicides can also have direct effects on plant pathogens, either stimulating or suppressing the growth of particular bacteria and fungi (Duke et al. 2007; Sanyal and Shrestha 2008). Indirect effects on plant diseases are also common, and involve a variety of mechanisms: “Another potential indirect effect is alteration of plant metabolism or physiology in a way that makes it more susceptible or resistant to plant pathogens. For example, induction of higher levels of root exudate (e.g., Liu et al., 1997) or altered mineral nutrition (proposed by Neumann et al., 2006).” (Duke et al. 2007).

Herbicide dosage is important for the effects, and sometimes drift levels can stimulate the growth of pathogens, whereas full application rates suppress the same pathogens. Thus non-target plants may be at higher risk for diseases than the treated crop itself from herbicide applications: “It is not unusual for low rates of herbicides to stimulate in vitro pathogen growth (e.g., Yu et al., 1988). Hormesis (the stimulatory effect of a subtoxic level of a toxin) is common with both fungicide effects on fungi and herbicide effects on plants (Duke et al., 2006). Thus, dose rates are likely to be highly important in both direct and indirect effects of herbicides on plant disease”(Duke et al. 2007).

EPA thus needs to assess the impact of increased use of dicamba with MON 87708 soybean on the pests and pathogens of non-target plants.

Injury to terrestrial wild animals from off-site movement of dicamba

Of the herbicides considered for invasive species control by the US Forest Service in the Pacific Northwest, dicamba is of special concern (USDA Forest Service 2005):

> Dicamba, triclopyr, and 2,4-D have the highest potential to adversely affect wildlife. Dicamba has a relatively low acute toxicity to adult animals, in terms of direct lethal doses, but adverse effects on reproduction and nervous systems occur at much lower doses. Dicamba shows a consistent pattern of increased toxicity to larger sized animals, across several species and animal types (i.e. birds and mammals). Dicamba exposures exceed the toxicity indices for five scenarios at the typical application rate, and nine scenarios at the highest application rate. (Bautista 2005)p. 22.

Based on this analysis, in their Record of Decision for the invasive plant control program the Forest Service decided not to use dicamba or 2,4-D:

> I recognize the cost-effectiveness of 2,4-D and dicamba. It has been commonly and widely used on both private and public lands for the last several decades. At the Regional scale, however, no situations were found where these herbicides would be absolutely necessary.
> These herbicides are inherently more risky than the ten I am approving for use. Forest Service risk assessments consistently place these two herbicides in higher risk categories for human beings, large mammal and birds (see FEIS Chapter 4.4 and 4.5). (USDA Forest Service 2005) p 25.

These concerns about dicamba impacts on wild animals will only be amplified by the increased use of dicamba with MON 87708.

Injury to animals from ingestion of dicamba residues and metabolites from use of dicamba with MON 87708

New types of metabolites and different ratios of residues and metabolites are present dicamba-treated MON 87708

Dicamba applications with MON 87708 soybean will also leave dicamba residues and metabolites in the MON 87708 soybean tissues, including some metabolites that may be unique compared to those in non-MON 87708 soybean. Also, there may be more wild food plants that take dicamba and metabolites from contaminated water and soil at higher levels with use of dicamba on MON 87708 soybean.

In order to determine how applications of dicamba to MON 87708 will affect the kinds and amounts of residues and metabolites, it is essential to have data on the kinds and amounts of dicamba residue and metabolites in non-dicamba resistant soybean treated with dicamba for comparison. Monsanto did not supply these control data in their MON 88708 Soybean Deregulation Petition (Monsanto 2010) or in their Magnitude of Residue studies (Moran and Foster 2010) - a serious omission. Nor was CFS able to find this information in primary published reports. However, detailed data from industry studies on dicamba residues and metabolites in non-dicamba-resistant soybeans and other plants (Butz and Atallah 1982, as cited in Yamada 2010) is available from the FAO (Yamada 2010), along with summaries of these data (FAO 2011).

Plants – both those that are sensitive to dicamba, such as soybean, and those with natural tolerance, such as corn and wheat – take up dicamba from leaves, stems and roots, and then translocate it to growing regions, such as seeds and other reproductive parts. But most of the dicamba that enters the plant remains as the parent herbicide. Metabolism results in a variety of compounds:

> Despite some differences in the rate of metabolism and translocation, there seems to be a common metabolic pathway of dicamba after its foliar application to these four plant species. The metabolism of dicamba appear to follow: hydroxylation of dicamba at the 5-position to form 5-OH dicamba; O-demethylation of 5-OH dicamba to form DCGA; O-demethylation of dicamba to form DCSA; O-demethylation of dicamba and hydroxylation to form DCGA; and conjugation of 5-OH dicamba and DCSA with glucose to form the ß-D-glucosides. (FAO 2011) p. 181.

Below is a diagram of the proposed pathway of dicamba metabolism in plants:

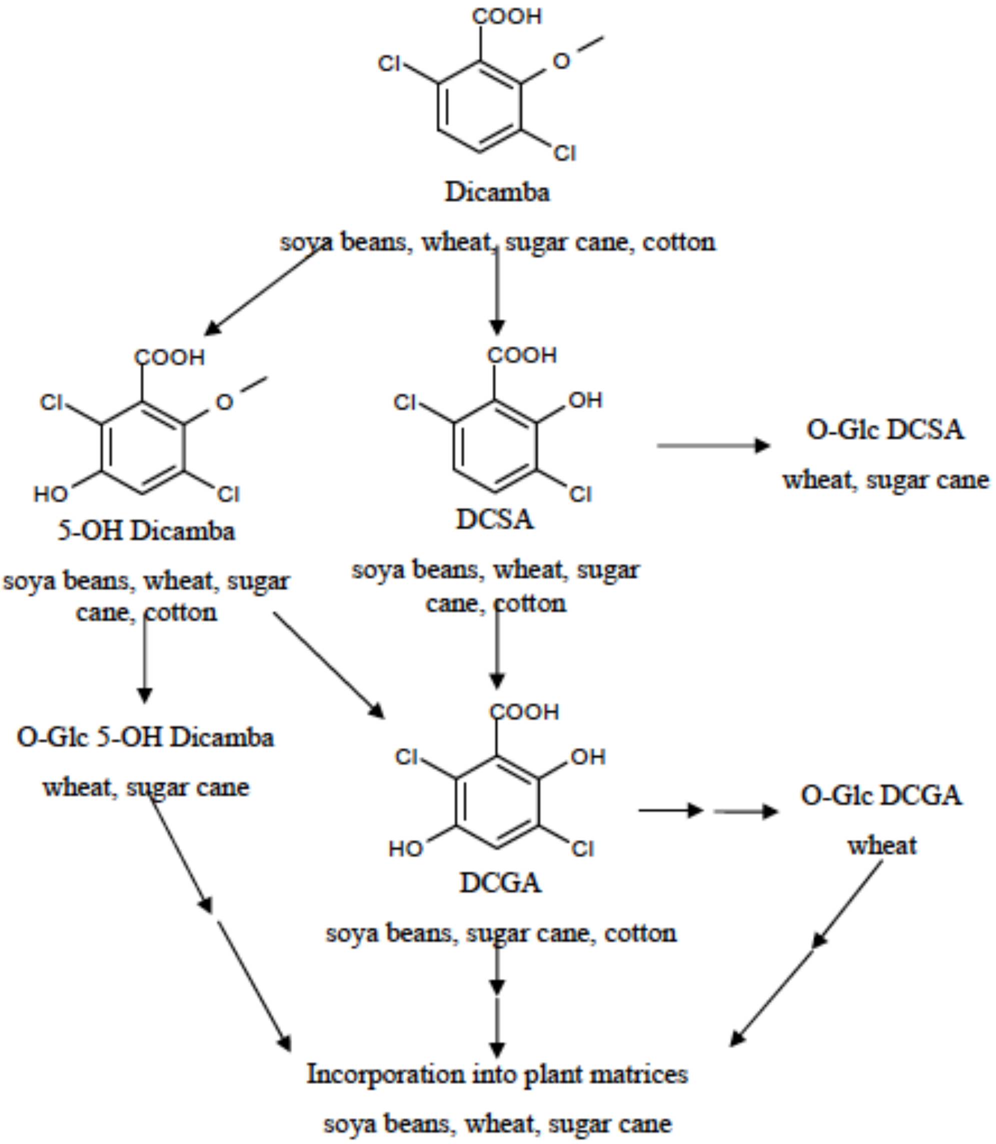


Figure 2 Proposed metabolic pathway of dicamba in plants

For studies of dicamba metabolism in soybean, radiolabeled dicamba was applied at a low rate that allowed plant development to continue. Residues and metabolites were measured at different times after the applications, and in different plant tissues. In summary, most of the recovered radioactivity was in parent dicamba, with small amounts in DCSA. Low levels of the metabolite DCSA were measured at the earlier application timings, and both DCSA and DCGA were measured at very low levels at later applications. Conjugates of DCSA and DCGA were not detected. The data presented in full (Yamada 2010) p. 954 – 957, and are summarized in the final report:

> [14C]-Dicamba was applied at a sub-toxic rate of 5.17 μg/plant to soya bean plants (foliar application) grown on untreated soil at two different timings.
>
> With the early podfill growth stage application, radioactivity rapidly decreased from 85% to 4.6% of the total applied radioactivity (TAR) in treated leaves in the first seven days after application. After 14 days, the total recovered radioactivity averaged 42% of the TAR, about a half of which was found in immature beans. This indicates rapid and significant incorporation and translocation from leaf to beans.
>
> Over 64% and 94% of respective TRR were attributed to unchanged dicamba in treated leaves and immature beans 14 days after treatment. About 17% of the TRR in the leaf samples collected 14 days after treatment (DAT) was attributed to DCSA while **only 0.6% of the TRR in the 14-DAT immature bean samples was DCSA.** No di-hydroxylated metabolites were observed.
>
> The result indicates that dicamba is translocated without metabolization or conjugation while at the site of application, dicamba goes through gradual O-demethylation.
>
> With late senescent growth stage application, also rapid decline of radioactivity from 77% to 11% of TRR was observed in treated leaves 6 days after application. Only 63% of the TAR was recovered in the plant 6 days after treatment, among which 26% was found in the intact plant while another 24% was recovered from abscised leaves.
>
> Untreated leaves, stems, roots, pods and immature beans 6 days after treatment contained similar radioactivity. Their radioactivity levels were similar also to those of the same tissues after early podfill stage application except immature beans. With late senescent growth stage application, there was far less translocation of dicamba to beans compared to early podfill stage application. Only 2.1% of TAR or 8% of the TRR remained in immature beans 6 days after treatment. (FAO 2011) p. 179 – 180.
>
> About 64% and 44% of respective TRR were attributed to unchanged dicamba in treated leaves (not abscised) and beans 6 days after treatment. **Only 0.3% and 0.7% of the respective TRR were attributed to DCSA** in 6-DAT bean sample and treated leaves (not abscised**). Similarly small amounts of 5-OH dicamba and DCGA were also found in treated leaves and immature beans but neither exceeded 1.0% of TRR** (p. 179).

These data on kinds and relative amounts of residues and metabolites in non-dicamba-resistant soybean should be the baseline for comparison with MON 87708 soybean. CFS was unable to obtain Monsanto's Nature of Residue study, but a summary of the findings was included in the Magnitude of Residue study (Moran and Foster 2010):

> The study of the nature of the residue (Miller and Mierkowski, 2010) demonstrated that, in dicamba-tolerant soybean**, dicamba is metabolized mainly to a glucose conjugate of 3,6-dichloro-2-hydroxybenzoic acid (DCSA), with smaller amounts of conjugates of 2,5- dichloro-3,6-dihydroxybenzoic acid (DCGA) and another glucose conjugate of DCSA.** Dicamba was present at very low levels. Another metabolite, 2,5-dichloro-3-hydroxy-6-methoxybenzoic acid (5-hydroxydicamba), which is observed in corn, was not found as a metabolite of dicamba in dicamba-tolerant soybean. The conjugates are very complex molecules which are not readily synthesized to produce analytical reference standards. (Moran and Foster 2010) p. 30.

From this summary, it appears that there are metabolites of dicamba present in MON 87708 soybean that are not found in the metabolism studies of non-dicamba-resistant soybean, namely glucose conjugates of DCSA and DCGA. These conjugates are present in other crop plants that were studied, but at very low levels, rather than being the major products, as here. And, although the toxicity of DCSA and DCGA has been studied, apparently the toxicity of the conjugates has not been studied.

Note that in the Magnitude of Residue studies, the DCSA and DCGA conjugates are converted to DCSA and DCGA for measurements, so the levels of the unique and untested conjugates are not discernable in the results (Moran and Foster 2010).

Besides these qualitative differences, the relative levels of parent dicamba to its metabolites is "flipped" in MON 87708, with dicamba being low and metabolites high, instead of the other way around.

Of course, given how little dicamba is used in soybeans today, and then only pre-plant or just before harvest, little dicamba or metabolites are ever detected (Yamada 2010).

Another concern is whether the formaldehyde produced in the breakdown of dicamba by the engineered DMO enzyme in MON 87708 soybean when dicamba is applied results in formaldehyde levels over and above those that naturally occur in soybean, and that may be injurious to animals that eat the plant parts, since there can be health effects from ingestion of formaldehyde (http://www.atsdr.cdc.gov/phs/phs.asp?id=218&tid=39). Formaldehyde levels in dicamba treated MON 87708 soybean tissues should be tested after applications to see if they fall below or above safe limits.

EPA must assess the impacts of these substantial differences in kinds and amounts of dicamba residues and metabolites when dicamba is used with MON 87708 soybean compared to control soybean plants, for both human health and for wildlife.

Wild animals, including pollinators, are at particular risk from dicamba residues and metabolites

Food safety assessments based on residue and metabolite studies for humans are not appropriate for wildlife. Humans eat the seeds and processed products from seeds of soybean, whereas wild animals may eat any part of the plant, including pollen and nectar (pollinators). Herbicide residues and metabolites in seeds are almost always lower than in vegetative tissues, partly because applications are made so much earlier than seed development; and also because seeds are not contacted directly by herbicides, being covered by the pod. Feed for livestock, such as hay and forage, is likely to have higher herbicide residues than do seeds, but it is assessed for feed safety after the approved waiting time post-application, whereas wild animals may eat the these vegetative tissues immediately after applications and thus receive a much higher dose. Residues and metabolites in pollen and nectar used by pollinators – organisms beneficial to agriculture – are not taken into account in food and feed assessments, either.

Monsanto did not report levels of transgene expression in pollen or nectar of MON 87708 (Monsanto 2010, p. 79 - 80). However, it is safe to assume that the engineered DMO enzyme is active reproductive parts including pollen because Monsanto is recommending authorization for post-emergence applications through the early reproductive stages of development (Monsanto 2010, p. 208). If so, it is possible that metabolites will be present in pollen and nectar as a result of dicamba applications. Metabolites could also be translocated into floral parts from elsewhere in the plant. Residues and metabolites of dicamba were not measured in floral parts.

There is precedence for looking at gene expression in pollen as part of environmental risk assessments. Levels of gene expression in pollen have been of great interest for Bt crops, for example. Corn pollen expressing cry proteins is toxic to some insects should they happen to ingest the pollen in sufficient quantities (Malone and Pham-Delègue 2001). Expression levels in pollen of different corn Bt events have been compared, and there is a wide range of cry protein levels and specificities, and thus potential for harm to butterflies, for example (e.g., Mattila et al. 2005). The potential risk of exposure to Bt via pollen has been investigated for the endangered Karner Blue butterfly (Peterson et al. 2006), identifying counties where butterfly sites are located near cornfields and thus need further study.

Potential harmful effects dicamba and its metabolites in MON 87708 soybeans on honeybees and the honey produced from their collection of pollen and nectar are of particular concern. Soybeans are visited by honeybees that are located near soybean fields, and honeybees gather both nectar and pollen (Chiari et al. 2005, see references cited in introduction). Surprisingly, very recent research in Iowa has shown that many species of wild pollinators also frequent soybean fields (Anonymous 2011, O'Neal and Dill 2012).

Many honeybees do live near soybean fields during pollination season. According to Krupke and Hunt (2012) "…[m]ost commercial pollinator honeybees in the US spend May through October in the Upper Midwest where these crops [e.g., corn and soybeans] dominate the landscape."

If dicamba is used on MON 87708 soybean during flower development, or if dicamba or metabolites are redistributed in the plant - from earlier applications - during growth, presence of dicamba and metabolites in pollen and nectar would be expected. Other phloem-translocated herbicides, such as glyphosate, do accumulate in pollen along with nutrients, because developing anthers and pollen are strong "sinks." There is evidence that 2,4-D and other herbicides also travel to anthers because it causes male-sterility (Hsu and Kleier 1990), similar to the action of glyphosate (Yasuor et al. 2006). Other systemic pesticides are common contaminants of corn pollen (Mullin et al. 2010, Burlew 2010).

Pollen and the nectar producing cells of MON 87708 soybean may be protected from the toxic effects of dicamba because of the expression of DMO, and so may accumulate more dicamba and metabolites than non- MON 87708 soybean flowers would: if the pollen and nectar-producing cells remains viable, they will be a stronger sinks for a longer period of time (Geiger and Bestman 1990, Chen et al. 2006).

Surprisingly, the DMO enzyme itself may retain its activity in honey, even during digestion by immature bees, able to degrade herbicides brought in from sources other than MON 87708 soybean (and dicamba-treated resistant corn) into metabolites (Grogan and Hunt 1979).

Finally, one of the only studies to examine changes in nectar after introducing a defense compound via genetically engineering is relevant here (Sala Junior et al. 2008). Monsanto asserts that formaldehyde (a metabolite of dicamba in MON 87708 soybean) and salicylic acid (similar to DSCA, also a metabolite of dicamba in MON 87708) may trigger plant defense (Monsanto 2010, p. 250). EPA thus needs to consider the toxicity to beneficial organisms of defense compounds made in nectar of MON 87708 flowers in response to dicamba applications, as Sala Junior and colleagues did in citrus.

Sweet orange trees were genetically engineered to express an antibacterial peptide, sarcotoxin IA, to see if this peptide protected the orange trees against bacterial citrus canker. Because orange blossoms attract a variety of pollinators, and nectar composition is important to the health of pollinators, these researchers wanted to know if there were differences in nectar constituents:

> Nectar varies in chemical composition and these characteristics reflect the type of pollinator (Baker and Baker 1983). Also, the nectar is not sterile. Insects or avian pollinators certainly transfer microorganisms from flower to flower and, for this reason, a chemical variation in the nectar composition could alter the microflora present in the nectar… Results so far suggest that transgenic plant impacts on pollinators will depend on a case-by-case analysis of the gene concerned and its expression in the parts of the plant ingested by insects (Malone and Pham-Dele`gue 2001). Considering this aspect, studies of the nectar chemical composition are

> important to access environmental impacts of transgenic plants. (Sala Junior et al. 2008) p. 2.

And they did, in fact, find difference that could impact pollinators:

> In summary, the floral nectar components of the conventional and transformed STX IA sweet orange trees were analyzed to study possible quantitative and qualitative modifications. The results showed that there are significant differences in the primary and secondary metabolites contents. These data suggest that the introduction of the gene responsible for the production of the antibacterial peptide sarcotoxin IA could modify the amino acids, triacylglycerides and purine alkaloids contents present in the sweet orange nectar. Such nectar with altered composition may affect floral visitors, such as nectar robbers, generalist pollinators and specialized pollinators. This work shows that deeper investigations are required to enlarge our understanding of multispecies interactions, as plant–pollinator, plant–herbivore and plant–microorganisms and to evaluate the impact of gene insertions on the nectar composition of genetically modified plants. (Sala Junior et al. 2008) p. 6.

In summary, EPA needs to reconsider potential increased risks to wild animals of various types from eating MON 87708 soybean tissues after applications of dicamba, or drinking runoff, in light of herbicide use projections, taking into account the difference between human or livestock exposure vs. wild animal exposure.

In particular, to properly consider any unreasonable adverse effects of using dicamba with MON 87708 soybean, EPA must consider how such use may have an unreasonable adverse effect on pollinators, which are organisms beneficial to agriculture. Taken together, the fact that honeybees are likely to collect pollen and nectar of MON 87708 soybean after it has been sprayed with dicamba, that resulting residues and metabolites are likely to be different from those in conventional soybeans since such soybeans are not treated with dicamba during growth, and that some of these metabolites may trigger defense responses that have impacts, we request that the EPA consider the impacts to honeybees and other pollinators, as in the guidelines for analyzing impacts of transgene products on bees set out by Malone and Pham-Delègue, for example (2001, p. 299 – 300).

Impacts to non-target species of dicamba use patterns with MON 87708 soybean

When dicamba is used during the season is also an important factor in determining risk of injury to non-target organisms. Simply, the amount of injury that non-target organisms will sustain is determined by how sensitive they are to the dicamba formulation and by the dose they receive. Plants are more sensitive to dicamba at some stages of development than at others. Because MON 87708 soybean has been engineered to withstand dicamba, thus removing biological constraints, this herbicide can be used during the main growing season for the first time.

Timing of dicamba applications in the growing season

Herbicide applications are more likely to coincide with life-stages of plants that are the most sensitive to injury because the MON 87708 soybean itself is less sensitive to injury during spring and summer than is non- MON 87708 soybean. This is a general outcome of herbicide-resistant crop systems: “The role of total postemergence programs to control grass and broadleaf weeds has expanded with the development of herbicide-resistant crops…Postemeregence application of a herbicide to a genetically-modified (GM) crop often occurs when non-GM plants are in the early reproductive growth stage and most susceptible to damage from herbicide drift….Consequently, most drift complaints occur in spring and summer as the use of postemergence herbicide applications increase.” (Lee et al. 2005, p. 15) Plants – both crop and wild species –are often most sensitive to herbicide injury as pollen is forming (Olszyk et al. 2004). This has been clearly shown with dicamba and injury to tomato plants (Kruger et al. 2012).

Total use of dicamba at the landscape level

Another way that dicamba use will increase with MON 87708 is by increasing the total number of soybean acres that are treated with this herbicide. Within a given year, many more soybeans acres will be sprayed, as we show in our comments on herbicide use. Also, since corn and soybeans are often rotated on the same acreage within a region, it is likely that both dicamba-resistant soybeans and corn being treated with dicamba will be grown in proximity, greatly increasing the total acres exposed to dicamba in a given year. And because of the corn-soybean rotation, the likelihood that dicamba will be used on the same acreage one year after the next is greater as well.

At a landscape level this change in dicamba use pattern will result in a larger number of individuals of a wider array of species in proximity to MON 87708 soybean fields and thus to dicamba, with attendant impacts.

Also, levels of dicamba in water bodies within particular watersheds are likely to increase with more extensive use, as dicamba loads from different fields run off and mix together in creeks and rivers draining the watershed (Thurman et al. 2001).

These impacts of more extensive use of dicamba with MON 87708 soybean need to be assessed by EPA, in addition to other impacts.

Impacts to biodiversity of dicamba use with MON 87708 soybean

EPA needs to fully consider the impacts to biodiversity of the substantial changes in herbicide use amounts and patterns that are part of the MON 87708 soybean system, based on the full rates and maximum number of applications allowed by label, and extent of use in a given year and across years.

Biodiversity in soybean fields

An example of harm to biodiversity in corn fields from an herbicide-resistant crop system is the recent decline in milkweed populations in Midwestern fields with probable impacts on monarch butterflies, as described in a series of studies (Hartzler and Buhler 2000, Hartzler 2010, Brower et al. 2011, Pleasants and Oberhauser 2012). The basic conclusions are well stated in the abstract of the most recent publication by Pleasants and Oberhauser (2012):

> Abstract. 1. The size of the Mexican overwintering population of monarch butterflies has decreased over the last decade. Approximately half of these butterflies come from the U.S. Midwest where larvae feed on common milkweed. There has been a large decline in milkweed in agricultural fields in the Midwest over the last decade. This loss is coincident with the increased use of glyphosate herbicide in conjunction with increased planting of genetically modified (GM) glyphosate-tolerant corn (maize) and soybeans (soya).
>
> 2. We investigate whether the decline in the size of the overwintering population can be attributed to a decline in monarch production owing to a loss of milkweeds in agricultural fields in the Midwest. We estimate Midwest annual monarch production using data on the number of monarch eggs per milkweed plant for milkweeds in different habitats, the density of milkweeds in different habitats, and the area occupied by those habitats on the landscape.
>
> 3. We estimate that there has been a 58% decline in milkweeds on the Midwest landscape and an 81% decline in monarch production in the Midwest from 1999 to 2010. Monarch production in the Midwest each year was positively correlated with the size of the subsequent overwintering population in Mexico. Taken together, these results strongly suggest that a loss of agricultural milkweeds is a major contributor to the decline in the monarch population.
>
> 4. The smaller monarch population size that has become the norm will make the species more vulnerable to other conservation threats.

Here, 16 years after the introduction of Roundup Ready soybeans, major impacts of associated herbicide use are just now surfacing, with only a handful of researchers doing this kind of “post-market” ecological research. EPA needs to consider these kinds of harms, and how to prevent them, before rather than after registering dicamba for new use with MON 87708 soybean.

The use of dicamba with MON 87708 soybean will result in more applications per season of dicamba, also a systemic herbicide, and likely to be used in addition to full rates of glyphosate. It is also reasonably foreseeable that in the future MON 87708 soybean will be treated with dicamba and glyphosate, in rotation with dicamba-resistant corn similarly treated, as we have commented. Weed biodiversity, such as small populations of milkweed, within these fields won't have a chance to survive. Tolerant and resistant weeds will come to dominate, simplifying the number of plant species in the fields, and this by definition is a decrease in biodiversity. Also, with specialist herbivores, such as the monarch butterfly that rely completely on particular plant species, other kinds of plants will not substitute for their requirements.

Besides the direct toxicity of the increased herbicides used with MON 87708 soybean to plant population diversity within soybean fields and ramifications for animals from changes in plant diversity, there will also be an increase in herbicide exposure from residues and their metabolites in MON 87708 soybean tissues. A wide variety of animals feed on soybean leaves, flower parts, and seeds, including many beneficial organisms such as honeybees and other pollinators.

Also, some animals may be over-sprayed during applications of dicamba, and others may brush against newly sprayed foliage, receiving higher dicamba doses in MON 87708 soybean with possible toxic impacts (US-EPA 2009, Freemark and Boutin 1995). Animals at particular risk are discussed in our comments on listed species, below.

EPA needs to assess potential impacts to animals in fields of MON 87708 soybean in light of the foreseeable increase in exposure to dicamba and metabolites based on realistic use scenarios and a wide range of relevant independent scientific studies.

Biodiversity around soybean fields

Increased spray drift, volatilization and runoff from use of dicamba with the MON 87708 soybean is likely to alter the very habitats important for biodiversity in agroecosytems, such as hedgerows, riparian areas, unmanaged field margins, and other areas where wild organisms live near fields (Freemark and Boutin 1995, Boutin and Jobin 1998, Olszyk et al. 2004). Based on experiences with dicamba sensitive crops, natural areas miles from agricultural applications of dicamba may also be at increased risk from the use of greater amounts of the herbicide in MON 87708 soybean, since it can volatilize under certain conditions, as we have discussed earlier in these comments.

Particular species of plants are more or less sensitive to dicamba, and at different times of the year, so that a specific off-target dicamba event is likely to change the population dynamics in affected areas. For example, dicamba movement in mid-spring may kill sensitive dicotyledonous wildflowers at seedling stages, cause male sterility in less sensitive grasses about to flower, and have little effect on younger grasses or still-dormant perennials (Olszyk et al. 2004). These impacts may result in long-term changes in the mix of plant species, favoring annual weeds over native plants, for example (Boutin and Jobin 1998, Boutin et al. 2008). And if there are dicamba resistant plants in these habitats, they will of course be better able to withstand drift and may become more abundant (Watrud et al. 2011).

These herbicide-induced changes in plant populations can then indirectly impact "microbial communities, occurrence of plant pathogens, or diminished insect populations. Both direct and indirect effects could lead to numerous negative impacts on ecosystem services including wildlife habitat, nutrient cycling, control of soil erosion, recreation, timber or pulp production, livestock grazing, control of noxious plant species and aesthetics…." (Olszyk et al. 2004).

There are studies of species composition in field margins (Kleijn and Snoeijing 1997) and hedgerows that border conventional fields compared with fields managed organically without herbicides (Boutin et al. 2008) showing differences in plant populations that indicate just these sorts of species shifts from herbicide exposure. Also, "[i]n controlled experiments with plant communities, Pfleeger and Zobel (1995) demonstrated that variable species responses to herbicide exposure [including 2,4-D] may alter the competitive interactions within a community. Such shifts in a community could result in changes in frequency and production and even extinction of desired species…" (Olszyk et al. 2004).

Recent experiments have shown that drift levels of the broad-spectrum herbicide glyphosate alter population structures of plants that include some herbicide-resistant individuals, favoring an increase in those with the glyphosate-resistance trait. Differences in the populations persist years after the last "drift" incident, affecting the kinds of beneficial soil fungi present and growth of subsequently planted species, for example (Watrud et al. 2011).

Animals depend on plant biodiversity for most of their needs, so it would be surprising if herbicide induced changes in plant populations had no effects on animal biodiversity around soybean fields. Freemark and Boutin (1995) reviewed the literature on how herbicide use has affected wildlife, and found that, as expected, biodiversity has been affected in areas adjacent to sprayed crop fields, including types and abundance of small mammals and birds. An example of how drift levels of dicamba may impact animals has to do with the ability of dicamba to cause sterility in grasses that are in early stages of reproduction, and "…reproduction is critical for the ability of non-crop native plants to pass along their traits. Furthermore, many wildlife species depend upon seed production of non-crop plants for their food source." (Olszyk et al. 2004). Many insects depend on abundant pollen, as well.

Herbicides such as dicamba that selectively kill dicots may be particularly injurious to butterflies, often considered an indicator of ecosystem health. If these herbicides are applied frequently and over a broad area – as will happen with dicamba use on MON 87708

– negative impacts on butterflies are particularly strong. A study of pesticide effects on butterflies in agricultural areas of England makes this point:

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

Researchers implemented experimental mitigation measures to determine whether changes in pesticide use would result in more butterflies in the landscape. One of these measure involved limiting the use of "persistent broadleaf herbicides" near field edges, and instead using herbicides that were more specifically targeted against grasses:

> The outer section of a tractor-mounted spray boom (approximately 6 m) is switched off when spraying the outer edge of a crop, avoiding the use of certain chemicals (persistent broadleaf herbicides and all insecticides other than those used for controlling the spread of Barley Yellow Dwarf Virus). Whilst the rest of the field is sprayed with the usual compliment of pesticides, more selective chemicals (e.g. graminicides rather than broad-spectrum herbicides) are sprayed on the edges (Boatman and Sotherton, 1988). (Longley and Sotherton 1997) p. 8.

They found that there were indeed more butterflies after taking these measures, and also that there were more dicots, the main source of nectar, as well as more biodiversity in general:

> In addition, as a result of selective herbicide use, Conservation Headlands are rich in broadleaved plants, thereby increasing the availability of nectar resources for butterfly species. (Longley and Sotherton 1997) p. 8.
>
> The unsprayed headlands have also been shown to benefit the survival of rare weeds (Schumacher, 1987; Wilson, 1994), small mammals (Tew, 1988), beneficial invertebrates (Chiverton and Sotherton, 1991; Cowgill et al., 1993) and gamebird chicks (Rands, 1985; Rands, 1986). However, to be of long-term value for butterfly conservation, unsprayed headlands need to be maintained over consecutive years to allow the survival of those species which are univoltine and have poor powers of dispersal. (Longley and Sotherton 1997) p. 9.

In conclusion, these researchers emphasize the need for research on impacts of pesticide use over time:

> In addition to short-term studies, covering single cropping seasons, information is also needed on the effects of different spray and cropping regimes over several seasons on butterfly communities in exposed areas. Only then will it be possible to make reliable predictions and recommendations for butterfly conservation on arable farmland. P. 12(Longley and Sotherton 1997)

Implications of this butterfly study in England are clear for use of dicamba with MON 87708: dicamba is an herbicide that selectively kills broadleaved plants (dicots), the main nectar source for adult butterflies, even those species whose larvae feed on grasses. Dicamba is also likely to be used more often during a season, more extensively in an area, and from year to year with MON 87708 soybean than it is currently used on soybean or in agriculture. This is exactly the opposite use pattern than that recommended for mitigation of pesticide impacts on butterflies, that were also shown to be protective of biodiversity in general.

These studies with butterflies are likely to indicate broader impacts. EPA provides a summary of dicamba impacts to plants with cascading effects for biodiversity:

> The guideline terrestrial plant studies indicate that dicamba negatively impacts seed germination (radicle length), seedling emergence (shoot length), and vegetative vigor (shoot weight) in monocots and dicots. Non-lethal effects included brown leaf tips, necrosis, decrease in size, leaf curling, chlorosis, and stem tumors. Dicamba acid and its'salts in formulated TEPs are readily absorbed through the foliage and roots of plants; consequently, it could be injurious to non-target plant species by drift, runoff, or leaching to roots. Damage to non-target plants may be sufficient to prevent the plant from competing successfully with other plants for resources and water. Listed plant species may be especially impacted by exposure to dicamba because of the impact of the loss of a few individuals to the population. Consequently, there is a potential concern for listed species with either broad or narrow dependencies on impacted plan species/populations/communities for habitat, feeding or cover requirements. In terrestrial and shallow-water aquatic communities, plants are the primary producers upon which the succeeding trophic levels depend. If the available plant material is impacted due to the effects of dicamba and the salts of dicamba, this may have negative effects not only on the herbivores, but throughout the food chain. Also, depending on the severity of impacts to the plant communities [i.e., forests, wetlands, ecotones (edge and riparian habitats)], community assemblages and ecosystem stability may be altered (i.e. reduced bird populations in edge habitats; reduced riparian vegetation resulting in increased light penetration and temperature in aquatic habitats, loss of cover and food for fish). (US EPA 2005) p 75.

It is clear, then, that increased use of dicamba with the MON 87708 soybean is likely to have negative impacts on biodiversity around soybean fields, perhaps at some distance.

Impacts to threatened and endangered species of dicamba use with MON 87708 soybean

EPA needs to assess how the new use of dicamba with MON 87708 will impact threatened and endangered species, based on the full rates and schedule that will be allowed by label, and extent of use.

All of the harms from increased use of dicamba, and applications later in the season, with MON 87708 soybean to plants, animals, and other organisms, and to their habitats, discussed above, apply to species that are at risk of extinction. Endangered species near fields where dicamba is applied to MON 87708 soybean will be at increased risk from exposure to dicamba via drift of particles and vapor, runoff, accidental over-spraying, and recently sprayed plant parts and soil. Their habitats will be at higher risk of being altered from changes in plant populations with attendant impacts.

However, the stakes of dicamba exposure are higher for listed species, especially for plants: "Determination of herbicide effects to threatened and endangered plant species in native plant communities is especially critical. In the US, the federal government has listed over 500 plant species as threatened and endangered and the Nature Conservancy considers 5,000 of the 16,000 native species to be at risk. Almost 50% of these species are annuals that are dependent on seed production or the seed bank for survival, thus any reproductive effects of herbicides could affect their survival." (Olszyk et al. 2004).

EPA has determined in a preliminary risk assessment for listed species that "dicamba exceeds LOCs" fon the following taxonomic groups, at all application rates considered (lowest rate 0.75 lb a.e./acre):

- small birds (20 and 100 g) feeding on short grasses, tall grasses, and broadleaf forage/small insects at all application rates and maximum and mean predicted residue levels

- small birds (20 g) feeding on fruit, pods, seeds/large insects at all application rates and maximum predicted residue levels

- large birds (1000 g) feeding on short grasses, tall grasses, and broadleaf forage/small insects at all application rates and maximum predicted residue levels

- non-target terrestrial plants - monocots and dicots adjacent to treated areas and in semiaquatic areas at all application rates (all uses modeled) by ground and aerial spray application; dicots in spray drift at all application rates (all uses modeled) by ground and aerial spray application (US EPA 2005) p. 73, excerpts for "all application rates" only.

Critical habitat is also clearly at risk from dicamba use given the potential for indirect effects via plants which constitute the base of ecosystems. (US EPA 2005) p 75.

Summarizing these findings, EPA concludes:

> 4. Risk to Endangered Species
> The Agency's screening level ecological risk assessment for endangered species results in the determination that dicamba will have no direct acute effects on threatened and endangered freshwater fish, estuarine fish, and aquatic invertebrates. However, the assessment indicates that dicamba has the potential for causing risk to endangered birds, mammals, and non-target plants. Further, potential indirect effect to any species dependent upon a species that experiences effects cannot be precluded from use of dicamba. These findings are based solely on EPA's screening level assessment and do not constitute "may effect" findings under the Endangered Species Act. Chronic RQs exceeded LOCs for endangered mammals at all application rates modeled. Acute LOCs were exceeded for endangered birds at all application rates. LOCs were exceeded for terrestrial plants adjacent to treated areas and in semi-aquatic areas at all application rates. (US EPA 2006) p. 20.

EPA enacted environmental risk mitigation measures because of these non-target risks, lowering the maximum single application rate to 1.0 lb ae/acre, and the yearly rate to 2.0 lb ae/acre per year, but states that these measure will not eliminate risks: "This will result in lowering the potential risks of concern to aquatic plants. This rate reduction will also lower acute risks to all animals (except small herbivorous birds), as well as chronic risk to mammals. Assessed risks to terrestrial plants will be lowered, but not eliminated" (US EPA 2006) p.23. In particular, risks to specific listed species from dicamba need to be addressed, and have not been to date, as far as CFS can determine.

However, 2,4-D – another auxin herbicide – was recently subjected to a Pesticide Effects Determination by EPA (US-EPA 2009) and Biological Opinion from the National Marine Fisheries Service (NMFS 2011), both finding adverse impacts of agricultural uses of 2,4-D to several specific endangered species. The detailed information in these reports can be extrapolated to mean that almost all threatened and endangered species would be similarly impacted by dicamba with MON 87708 soybean.

Specifically, the EPA evaluated the risks of 2,4-D use to the threatened California red-legged frog (CRLF) and Alameda whipsnake (AW) and their critical habitats. This frog lives in both coastal and interior mountain ranges, using both water bodies and riparian and upland sites; and eats wide variety of plant and animal foods during its aquatic and terrestrial phases, including insects, other amphibians and an occasional small mammal. The Alameda whipsnake is found in scrub and chaparral, as well as riparian areas, grasslands and savannas; also has a varied diet that includes insects, amphibians, other reptiles, small mammals and birds (US-EPA 2009, p. 55).

Just about all of these habitats and prey types are potentially impacted by use of 2,4-D at agricultural rates, either directly or indirectly (US-EPA, summary of effects p. 11 – 25). Looking at specific use of 2,4-D applied with ground equipment on field corn or popcorn, for example, the "level of concern" is exceeded for direct effects on the terrestrial habitat of CRLF and with aerial applications for AW. "Level of concern" is exceeded for indirect effects on prey, including terrestrial invertebrates and plants, frogs, small mammals (CRLF and AW), and also for birds (AW). Small mammals were also likely to be directly impacted, based on incident reports. After going through the whole assessment process, EPA concluded that use of 2,4-D in a variety of scenarios, including on corn, was "likely to adversely affect" both the CRLF and AW via indirect effects on prey, and was likely to modify critical habitat (US-EPA 2009, p. 175 – 179). They initiated a formal consultation with FWS based on these conclusions.

Many threatened and endangered animals share the basic food and habitat requirement of CRLF and AW, including other amphibians and reptiles, but also mammals and birds. This leads to the reasonable expectation that EPA would find that use of dicamba on MON 87708 soybean would similarly be "likely to adversely affect" prey and habitats of threatened and endangered animals found near these fields, given the similarities between 2,4-D and dicamba in many respects. In particular, the ability of 2,4-D to alter habitat by injuring plants, and thus changing plant populations is relevant to the potential for dicamba to do the same.

The only EPA consultation over 2,4-D impacts on threatened and endangered species that has proceeded to the "biological opinion" stage is for Pacific salmonid fishes (NMFS 2011). These are fish species that spawn in the floodplains of the Pacific coast, and then go to sea for a few years before returning up rivers and creeks to their original spawning ground to begin again. Here the NMFS concluded that agricultural uses of 2,4-D were "likely to adversely modify" critical habitat because of injury to plants. They expressed concern about toxicity to plants from agricultural applications near riparian zones in the floodplains, for example (NMFS 2011, p, 540 – 543). Riparian vegetation "provides shade, bank stabilization, sediment, chemical and nutrient filtering, and provides a niche for the terrestrial invertebrates that are also salmon prey items…We believe the a.i. [2,4-D] will have a detrimental effect on riparian vegetation…" (NMFS 2011, p. 627 – 628).

Although soybeans are not grown to any extent in the Pacific Northwest, many threatened and endangered aquatic species will have similar habitat requirements for water quality and prey as do Pacific salmonids, including some that are in habitats near soybean cultivation and thus could be impacted by the increased use of dicamba on MON 87708 soybean.

EPA did produce a brief "no effect determination" for dicamba and the Pacific salmonids in 2003 (US EPA 2003), but it only considers direct toxicity impacts of dicamba on aquatic organisms, including the fish themselves. It does not consider any of the kinds of impacts from dicamba injury to plants or to habitat. Given the results of NMFS' biological opinion where these habitat effects were found to be significant, EPA needs to reconsider their limited "no effect determination" for dicamba.

In fact, because of the determinations regarding 2,4-D and CRLF, AW and Pacific salmonids, combined with scientific studies on impacts of herbicides on biodiversity, and the information on risks to listed species in dicamba RED, EPA should initiate consultations with FWS and NMFS concerning the use of dicamba with MON 87708 soybean. EPA's consultation duties under the ESA on the direct and indirect impacts of its approval action in no way vitiates the ESA duties of any other agencies (such as USDA/APHIS) for the impacts of their own approval action.

Conclusion

Clearly, the proposed registration for use of dicamba on MON 87708 would have numerous serious and adverse impacts, as discussed in detail above.

CFS would be happy to discuss the issues raised in these comments with EPA staff in the interests of a full, rigorous and scientifically credible assessment of the proposed registration for use of dicamba on MON 87708 soybean.

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