The impact of glyphosate-tolerant crops on the use of other herbicides and on resistance management†

Dale L Shaner*
American Cyanamid Co, PO Box 400, Princeton, NJ, 08543-0400, USA

Abstract: Glyphosate can now be used for selective, post-emergence weed control in glyphosate-tolerant varieties of soybeans, cotton, canola and maize. It is estimated that glyphosate-tolerant soybeans in the US will account for 60–80% of the area planted by 2001. The rapid acceptance of this new technology is due to multiple factors including broad-spectrum weed control, low cost and simplicity. The use of glyphosate has resulted in a major reduction in the use of other herbicides including the ACCase inhibitors, ALS inhibitors, and Protox inhibitors. In the short term (three to five years) this change in herbicide use patterns will continue. In the long term (five to eight years), the primary reliance on glyphosate for weed control particularly in continuous cropping or in rotations of glyphosate-tolerant crops will result in a shift in the weed spectrum toward more tolerant weed species. As a result of this shift, other herbicides will be needed to fill these weed gaps. Continuous use of glyphosate may also lead to the selection of glyphosate-resistant weed populations, as has already occurred in Australia. However, shifts in the weed species' composition from highly susceptible toward more tolerant species will happen more rapidly than selection of resistance. New herbicides developed in the future will have to be extremely cost-effective to compete against glyphosate and may be geared towards controlling weeds tolerant to glyphosate. There will also be further development of new tolerant crops to other broad-spectrum, non-selective herbicides that will be able to compete directly with glyphosate.

Keywords: weed management; glyphosate; glyphosate-tolerant

1 INTRODUCTION

Glyphosate-tolerant crops will have a major impact on the weed management practices in many crops. Projections on the potential use of glyphosate-tolerant crops suggest that glyphosate will be the predominant herbicide used in cotton, soybeans and canola, and a major herbicide in maize (Table 1). The crop where this new technology has had one of the greatest effects to date on herbicide use patterns is soybeans. In 1998 approximately 40% of the soybeans planted in the US and 84% of the soybeans in Argentina were glyphosate-tolerant.[1] The rapid rise in the use of glyphosate, accompanied by a decrease in the use of other herbicides, is similar to what occurred in the late 1980s

Table 1. Projections on the planting of glyphosate-tolerant crops in North America[a]

	Year											
	1998		*1999*		*2000*		*2001*		*2002*		*2005*	
Crop	*Ha (×10⁶)*	*% of planted area*	*Ha (×10⁶)*	*% of planted area*	*Ha (×10⁶)*	*% of planted area*	*Ha (×10⁶)*	*% of planted area*	*Ha (×10⁶)*	*% of planted area*	*Ha (×10⁶)*	*% of planted area*
Soybeans	11.0	40	13.8	48	16.2	57	17.4	61	18.2	65	18.6	66
Cotton	1.6	32	1.6	32	1.6	40	2.4	47	2.4	49	2.8	50
Maize	0.4	1.5	1.2	4	2.4	8	4.0	12	4.9	15	6.5	20
Canola[b]	1.6	30	1.6	30	2.0	35	2.4	42	2.4	43	2.4	45

[a] Data from July 1998 Comtext Consulting Report 'Biotech Traits Commercialized 1997-1998'.
[b] Canadian Information based on internal Cyanamid estimates.

* Correspondence to: Dale L Shaner, American Cyanamid Co, PO Box 400, Princeton NJ, 08543-0400, USA
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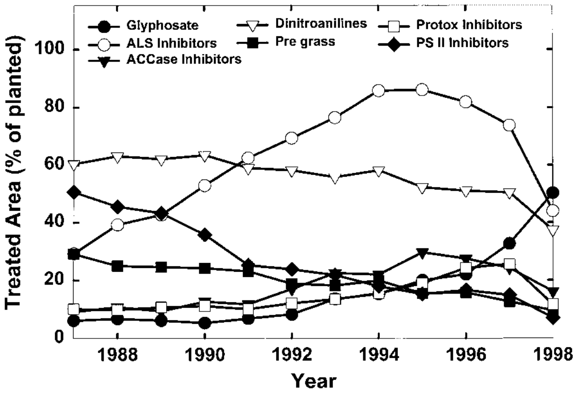

Figure 1. Herbicide use in US soybeans. Data derived from Doane's estimates based on survey data which approximate actual planted acres. By permission from Doane Marketing Research, Inc, St Louis, MO.

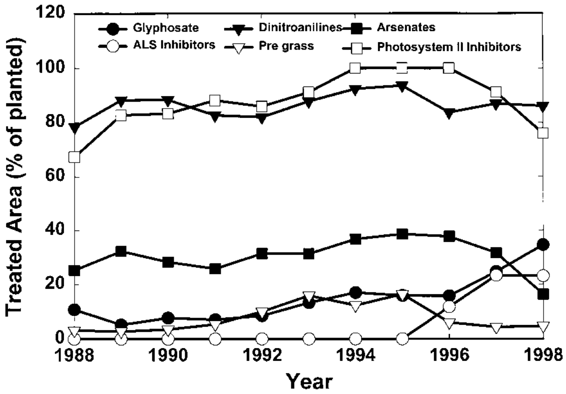

Figure 3. Herbicide use in US cotton. Data derived from Doane's estimates based on survey data which approximate actual planted acres. By permission from Doane Marketing Research, Inc, St Louis, MO.

and early 1990s with the advent of the acetolactate synthase (ALS) inhibitors in soybeans (Fig 1). By analyzing the history of the use of the ALS inhibitors, one might be able to predict how glyphosate-tolerant crops will affect the application of other herbicides as well as the effect of this technology on herbicide resistance management. In this paper I will analyze the effect that glyphosate-tolerant crops may have on the use and availability of other herbicides and the impact that the widespread adoption of this technology will have on herbicide resistance management.

2 SHORT-TERM IMPACT OF GLYPHOSATE-TOLERANT CROPS

Currently there are four major crops, canola, cotton, maize and soybean, for which glyphosate-tolerant varieties are available. The application of glyphosate has moved rapidly to a leading position in soybean, canola and cotton, with a concomitant decrease in the use of other herbicides (Figs 1–3). Since there have only been limited amounts of glyphosate-tolerant maize available, it is too early to tell if the use pattern of glyphosate in corn will follow the same pattern as in other crops (Fig 4). In soybeans, Monsanto recommends that farmers first prepare a weed-free seed bed either by cultivation or by using a pre-plant application of glyphosate followed by one or two applications of glyphosate before weeds are 30 cm in height. They discourage the use of pre-emergence herbicides in their programs.[2]

The herbicides affected by the increased use of glyphosate on tolerant varieties vary with the crop (Table 2). In soybeans there has been a dramatic decrease in the area treated with ALS inhibitors, falling from 86% of the treated area in 1993 to approximately 43% in 1998 (Fig 1). There has also been a decrease in the use of dinitroanilines, acetyl CoA carboxylase (ACCase) inhibitors and protoporphyrinogen oxidase (Protox) inhibitors.

In canola there has been a trend for decreased use of dinitroanilines (Fig 2) over the last three years. Part of this decrease may have been due to the spread of resistant *Setaria viridis* (L) Beaut,[3] and the introduction of imidazolinone-resistant and glufosinate-resistant canola varieties. There has also been a decrease in conventional tillage which means less herbicide incorporation (Kehler R, pers comm 1998.) The increase in glyphosate applications in 1998 was accompanied by the continued decline in the use of dinitroanilines and a decrease in the use of ACCase inhibitors. Glyphosate-tolerant varieties may have also slowed the

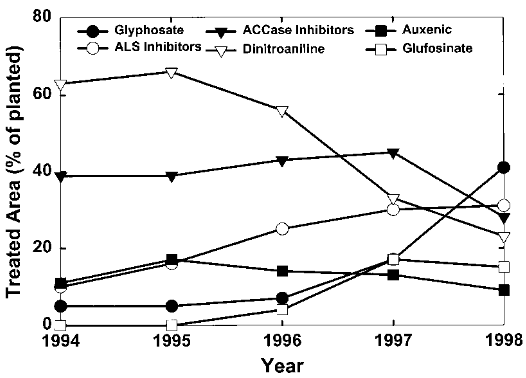

Figure 2. Herbicide use in Canadian canola. Data with permission from Criterion Research Corporation, Winnepeg, Mannitoba.

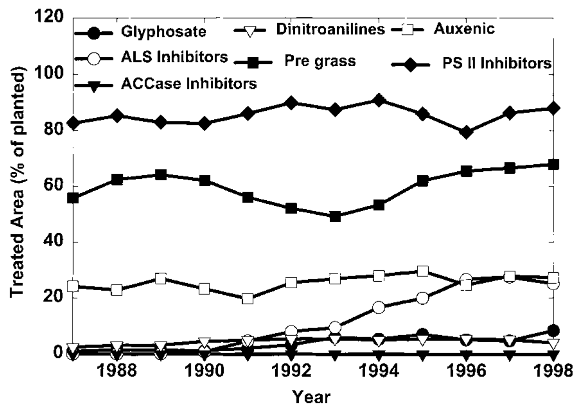

Figure 4. Herbicide use in US maize. Data derived from Doane's estimates based on survey data which approximate actual planted acres. By permission from Doane Marketing Research, Inc, St Louis, MO.

Table 2. Active ingredients used in crops, by herbicide category

Crop	*Class*	*Active ingredients*
Soybean	PS II Inhibitors	Metribuzin, linuron, bentazone
	ALS Inhibitors	Imazaquin, imazethapyr, imazamox, chlorimuron, thifensulfuron, flumetusulam, cloransulam
	ACCase Inhibitors	Fluazifop, diclofop, quizalofop, fenoxaprop, sethoxydim, clethodim
	PRE-Grass[a]	Alachlor, metolachlor, dimethanamid, fluthiamid
	Dinitroanilines	Pendimethalin, trifluralin
	PROTOX inhibitors	Acifluorfen, fomesafen, lactofen, flumiclorac, sulfentrazone
	CBI[b]	Clomazone
	Glyphosate	Glyphosate
Maize	PS II Inhibitors	Atrazine, simazine, metribuzin, linuron, bentazone, bromoxynil, pyridate
	ALS Inhibitors	Nicosulfuron, primisulfuron, prosulfuron, rimsulfuron, thifensulfuron, flumetsulam, halosulfuron, imazethapyr, imazapyr
	PRE-Grass[a]	Alachlor, metolachlor, acetochlor, dimethanamid, propachlor, butylate, EPTC
	Dinitroanilines	Pendimethalin, trifluralin, oryzalin
	Auxenic	2,4-D, 2,4-DB, MCPA, dicamba, clopyralid, triclopyr,
	Glyphosate	Glyphosate
	Glufosinate	Glufosinate
	Paraquat	Paraquat
Cotton	PS II Inhibitors	Atrazine, cyanazine, fluometuron, diuron, bromoxynil, dipropetryn, prometryn, bentazone
	ALS Inhibitors	Pyrthiobac
	ACCase Inhibitors	Fluazifop, fenoxaprop, diclofop, quizalofop, clethodim, sethoxydim
	PRE Grass[a]	Metolachlor
	Dinitroanilines	Pendimethalin, trifluralin, oryzalin, ethafluralin
	PROTOX Inhibitors	Oxyflurfen, acifluorfen, lactofen, fomesafen
	CBI[b]	Norflurazon, clomozone
	Arsenates	MSMA, DSMA
	Glyphosate	Glyphosate
Canola	ALS Inhibitors	Ethametsulfuron, imazethapyr, imazamox
	ACCase Inhibitors	Diclofop, fluazifop, fenoxaprop, quizalofop, sethoxydim, clethodim, tralkoxydim
	Dinitroanilines	Trifluralin,
	Auxenic Herbicides	Clopyralid
	Glyphosate	Glyphosate
	Glufosinate	Glufosinate

[a] Pre-emergence grass herbicides.
[b] CBI-Carotenoid Biosynthesis Inhibitors.

increase in the use of other herbicide-resistant varieties.

In cotton, the increased use of glyphosate may have resulted in the decreased use of the carotenoid biosynthesis inhibitors (CBI), photosynthesis inhibitors, and arsenates, with a minor reduction in dinitroanilines (Fig 3).

The rapid penetration of glyphosate-resistant varieties into the soybean, canola and cotton herbicide markets is due to several factors including (1) the ability to control most grasses and broadleaf weeds; (2) the simplicity of using only one herbicide; and (3) the lower cost of weed control.[4] Prior to the introduction of glyphosate-tolerant varieties, farmers used a combination of different herbicides in order to control the spectrum of weeds in their fields. With glyphosate, farmers rely on only one herbicide to control all the weeds. Delaying application of the herbicide to four to six weeks after planting and thus allowing crop competition to prevent further weed growth can compensate for the lack of residual activity of glyphosate. It has been estimated that 30% of the weed control in glyphosate-tolerant soybeans is due to crop competition.[5] It has also been shown in several studies that applying glyphosate too early in soybeans results in yield loss due to emergence of additional weeds after herbicide treatment.[6–9] Glyphosate treatments in soybeans have been less expensive than other herbicide treatments, saving up to US$22 per hectare over conventional treatments if only one application of glyphosate is used.[10] However, recent reductions in the price of other herbicides will shrink this cost advantage.[11]

3 LONG-TERM IMPACT OF GLYPHOSATE-RESISTANT CROPS

If the current trend continues, one would predict that in a short time there would be few, if any, other herbicides used in crops in which glyphosate-tolerant varieties are available. A similar conclusion could have been drawn with the introduction of the ALS inhibitors into soybeans in the 1980s. However, when a single herbicide is used to control weeds in a crop, the weed spectrum changes over time to more tolerant species that require the use of other weed management practices. Pike *et al*[12] have found that mixtures of herbicides provide much more reliable weed control than the use of a single product. This was the case for the ALS inhibitors, and the same will be true for glyphosate.

The use of ALS inhibitors rapidly increased in the soybean market in the late 1980s–early 1990s (Fig 1). At first, ALS inhibitors, either alone or in combination, were the only herbicides needed to control all of the major weeds in soybean. However, beginning in 1993, there was an increase in the use of Protox inhibitors. One reason for this rise was the shift in weed spectrum that occurred with the continued reliance on the ALS inhibitors. Weeds that were not well controlled by the ALS inhibitors began to increase. This was particularly evident in a major shift in the pigweed populations away from *Amaranthus retroflexus* L toward *A rudis* and *A palmerii* S Wats.[13,14] These latter two species are not well controlled by ALS inhibitors due either to natural tolerance or to the rapid selection of resistance.[15–19]

Glyphosate use in tolerant crops is at the very beginning of a growth curve (Figs 1–4). Current projections show that glyphosate-tolerant varieties will increase to 50–70% of the total area planted in certain crops (Table 1). However, reliance on glyphosate for weed control will undoubtedly cause a shift in the weed spectrum towards those species not well controlled by glyphosate similar to that which happened with the continuous use of ALS inhibitors. One would predict that, in the future, glyphosate will be a used on most of the hectares where glyphosate-tolerant crops are planted, but other herbicides will be combined with glyphosate to fill weed gaps. This aspect of the use of glyphosate is discussed more fully below.

4 OTHER IMPACTS OF GLYPHOSATE-TOLERANT CROPS

Another consequence of the widespread use of glyphosate-tolerant soybeans has been a decrease in the total value of the herbicide market for soybeans in the US. This decrease is due to the lower cost of the herbicide program for glyphosate. In response to this decrease, other major companies have also decreased the price of their herbicide programs to remain competitive with glyphosate. Thus, the value of the total soybean herbicide market in the US is projected to decrease 20–25% over the next few years.[1] This decrease in the value of the soybean herbicide market will affect the discovery of new herbicides for this market. Since it can cost up to $80–$100 million to develop a new herbicide,[20] companies may be reluctant to continue investing in a shrinking market. In addition, the low value of weed control in these markets will mean that any new product will have to be cost-effective in order to compete with existing products. The discovery of compounds that meet the new standards being set in the soybean herbicide market will become even rarer than it is today. Thus, farmers in the future may not have the broad choice of herbicides that they currently have. If some new weed problem develops, it may take additional time before a new herbicide will be discovered. In fact, new compounds may be targeted to fill the gaps in the spectrum of glyphosate rather than as a replacement for it.

Another response to the success of glyphosate-tolerant crops may be the development of other resistant crops that will allow the use of broad-spectrum herbicides. Such crops already exist with imidazolinone, sulfonylurea, and glufosinate. Rhone-Poulenc recently announced that they plan to develop and market isoxaflutole-resistant maize and possibly other crops.[21] The development of such crops will change the way in which companies search for and develop herbicides in the future by forcing them to look for potent, broad-spectrum compounds that will be used in genetically modified crop varieties.

5 GLYPHOSATE-RESISTANT CROPS AND RESISTANCE MANAGEMENT

One of the potential consequences of reliance on any single herbicide or on herbicides with the same mode of action to control weeds is the selection of resistant weed populations. This has been dramatically illustrated initially with the selection of triazine-resistant weeds and more recently in the selection of ACCase inhibitor- and ALS inhibitor-resistant weeds.[22] Currently there are over 200 documented cases of herbicide-resistant weed populations for almost all classes of herbicide, including glyphosate.[22]

The availability of glyphosate-tolerant crops provides a powerful tool for managing herbicide-resistant weeds. Farmers can now include a broad-spectrum, non-selective herbicide in their crop rotation pattern. With the proper integration of glyphosate-tolerant crops into a total weed management program, the selection of herbicide-resistant weeds could become a rare event. However, if glyphosate completely replaces other herbicides, then the value of this tool for resistance management could be diminished.

Bradshaw *et al*[23] argued that glyphosate is different from other widely used herbicides and will not readily select for resistance due to its mechanism of action and lack of plant metabolism. However, glyphosate-resistant *Lolium rigidum* Gaud populations have been found in Australia after continuous use of this herbicide over a number of years.[24,25] Although the mechanism of resistance has yet to be fully elucidated, it does not appear to be due to an altered target site or metabolism. It may be due to reduced uptake of glyphosate into the chloroplast.[26] Based on this preliminary information, while the arguments made by Bradshaw *et al*[23] are still valid, it appears there are other ways for plants to resist glyphosate than through alterations in the target site or metabolism. This means that one cannot predict *a priori* what the frequency of resistance to glyphosate will turn out to be.

The use recommendations made by Monsanto are going to increase the potential for the selection of naturally tolerant or resistant weed populations. In glyphosate-tolerant soybeans, cotton, and canola, the company's primary recommendation is to use glyphosate alone for weed control, and eliminate the use of pre-emergence herbicides or other post-emergence herbicides.[2,27,28] In soybeans the recommendation includes a pre-plant burndown application of glyphosate followed by one or two applications of glyphosate in the crop. Thus, a weed population could be treated up to three times within one season and the label allows up to 6.72 kg ha^{-1} to be applied during a season.[29]

If glyphosate-tolerant maize becomes as widely accepted as glyphosate-tolerant soybeans, then it is possible that glyphosate will be the primary herbicide used over a large area of the US for multiple years. The recommendation for glyphosate-resistant maize is to use a pre-emergence herbicide such as acetochlor or acetochlor plus atrazine along with glyphosate post-emergence.[30] The mixing of acetochlor and/or atrazine with glyphosate will help in delaying the selection of resistance to glyphosate, but this mixture will have limited activity on certain broadleaf weeds such as *Abutilon theophrasti* (L) Medic and *Ipomoea* spp. Although these weeds may be controlled by a post-emergence application of glyphosate, they will have escaped control by the pre-emergence herbicides. Hence, the use of acetochlor and/or atrazine with glyphosate may not alleviate the selective pressure of glyphosate on certain weed populations.

However, glyphosate resistance is probably not going to be the primary problem that the farmer will face. Weed shifts will probably occur much more rapidly than selection for resistance. It has already been demonstrated that control of *A rudis* by glyphosate can be difficult under the wrong environmental conditions. In 1998 in one field it took three applications of glyphosate before control of *A rudis* was achieved.[31] There are also certain species that are naturally tolerant to glyphosate, as mentioned above. It has been well documented that continuous use of a particular herbicide or herbicide class results in a change in the relative frequency of weed species.[32–36] Continuous use of glyphosate may also cause these weed shifts. In a study by Coble and Warren,[37] continuous use of glyphosate caused an increase in the infestation of *Ipomoea* spp over a three-year period compared to other herbicide programs.

Shifts in weed species composition has occurred already where glyphosate has been used in pre-plant no-till applications. Initially glyphosate was the only herbicide needed to control the weeds in no-till applications (L Wax, pers comm 1998), but with continued use of glyphosate, there was in increase in populations of *Conyza canadensis* Cronq, *Lactuca serriola* L, *Kochia scoparium* (L) Roth, *Xanthium strumarium* L, *Amaranthus* spp, *Chenopodium album* L and *Salsola iberica*. Now combinations of glyphosate with 2,4-D or dicamba are needed to give adequate control.[29] Similar shifts will probably occur in glyphosate-tolerant crops if glyphosate is the only herbicide used in those crops.

The weeds most likely to increase in frequency are those that either have natural tolerance to glyphosate or can avoid being treated due to germination and emergence patterns. Weeds that are more tolerant to glyphosate are listed in Table 3. Certain species, such as *Ipomoea* spp and *Sesbania exaltata* Rydb, have very high tolerance to glyphosate and are not controlled at the rates generally applied in tolerant varieties (0.84 kg AE ha^{-1}).[38] Other species such as *A theophrasti* can be controlled with glyphosate when the plants are small, but are not well controlled as the plants get larger.[38] This increased tolerance in larger plants will result in escapes under certain conditions.

The lack of control of certain weeds can result in very rapid increases of weed seed in the soil. Modeling work by Bauer and Mortensen[39] showed that control of *A theophrasti* has to be greater than 95% in order for the seed bank to be reduced or maintained. If control drops to 85% there can be a rapid increase in the soil seed bank and subsequent weed infestation (Fig 5). If a farmer rotates between glyphosate-tolerant soybeans and maize, there could be a rapid increase in *A. theophrasti* populations within three to five years.

Another potential problem with glyphosate-tolerant crops is controlling volunteer crops in subsequent years. One of the serious weed problems in soybeans is volunteer maize. If farmers plant glyphosate-tolerant maize followed by glyphosate-tolerant soybeans, they will not be able to control the glyphosate-tolerant, volunteer corn with glyphosate. This will necessitate the use of another herbicide with a different mode of action.

Table 3. Weed species with tolerance[a] to glyphosate

Crop	*Weed species*[b]
Soybean	*Abutilon theophrasti, Ipomoea* spp, *Amaranthus rudis, Solanum* spp, *Conyza* spp, *Sesbania exaltata*
Maize	*Abutilon theophrasti, Ipomoea* spp, *Amaranthus rudis, Solanum* spp, *Chenopodium album, Setaria faberi*
Cotton	*Commelina diffusa, Richardia scabra, Digitaria sanguinalis, Sesbania exaltata, Cyperus esculentus*
Canola	*Polygonum* spp, *Kochia scoparium, Stellaria media*

[a] Tolerance is defined as less than 70% control at 0.84 kg acid equivalent ha^{-1}.
[b] Based on published reports of weed control by glyphosate.[40–47]

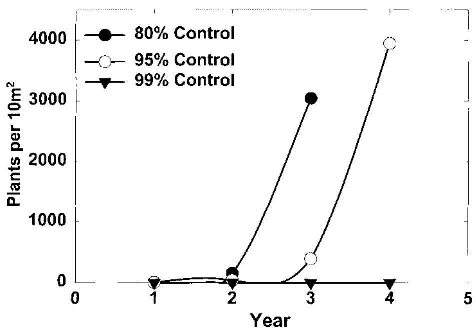

Figure 5. Modelling of the effect of level of weed control on *Abutilon theophrasti* plant populations. Model from Bauer and Mortensen.[39] (See paper for detail of model.) Assumptions for model: Initial seed population: 1000 $10\,m^{-2}$; Seed half-life: 15 years. Initial germination: 11.4%; seed mortality: 20% per year, seed production: 4300 seeds per plant.

6 CONCLUSIONS

Glyphosate-tolerant crops will have a major impact on the use of other herbicides. In the short term there will be decreased use of more narrow-spectrum products or tank mixtures. There will also be a decrease in the total value of the herbicide market. However, in the long term the continuous use of glyphosate will result in shifts in the weed spectrum toward more tolerant species and other weed management practices will have to be implemented to control these tolerant species. Herbicides in the future will either compete directly with glyphosate or will be used to fill the weed gaps of glyphosate. The reduction in the value of the herbicide market could result in a reduction in the search for new products and this may be detrimental in the future if unexpected problems arise. The success of glyphosate-tolerant crops may also lead to the development of crops resistant to other types of broad-spectrum herbicides.

Herbicide-resistant weed management will greatly benefit with the availability of glyphosate-tolerant crops if they are used in an integrated program. However, over-reliance on glyphosate could lead to problems. Herbicide resistance to glyphosate is not widespread, although two cases have already been documented. A more serious problem with reliance on glyphosate as the primary, if not sole, means of weed control will be a shift in the weed species. This shift will happen more rapidly than the selection of resistance, and will probably occur within the next three to five years if glyphosate is used alone.

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