CROP INSIGHTS

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# Weed Management in the Era of Glyphosate Resistance

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## Summary


- The proliferation of glyphosate-resistant weeds is increasingly forcing growers to use additional or alternative management tools to achieve adequate weed control.
- For a small number of weed species, resistance to multiple herbicides now leaves growers with few viable options for control.
- No new herbicide modes of action have been commercialized in the last 20 years, and it is unlikely any will be coming in the near future.
- New herbicide-resistant crop technologies coming to market this decade will expand grower options for dealing with resistant weeds, but all rely on existing herbicide active ingredients with known weed resistance cases.
- Recent experience with glyphosate resistance indicates that all herbicides are susceptible to resistant weed evolution given enough time and repetition of use. Overreliance of any new weed management tool will eventually lead to its failure.
- Adopting best management practices for managing herbicide resistance will help prolong the useful life of current herbicides.


## Introduction

The development of glyphosate-resistant crops is one of the most important weed management innovations in the history of agriculture. The cost savings, broad-spectrum efficacy, crop safety, and ease of use of glyphosate-based weed management have driven rapid adoption of glyphosate-resistant products in multiple crops (Duke and Powles 2008). Herbicide-resistant hybrids and varieties have been planted on a majority of corn and soybean acres in the U.S. for many years (Figure 1). The vast majority of these hybrids and varieties are resistant to glyphosate.

The last 15 years can rightly be referred to as the "glyphosate era" of weed control. Glyphosate rapidly replaced other herbicides in soybean and by 2002 was used on 79% of soybean acres in the U.S. (Young 2006). A 2003 survey of Indiana soybean growers found that glyphosate was the only herbicide applied on 74% of glyphosate-resistant soybean acres (Johnson et al. 2007) and 65% of total soybean acres.

Giant ragweed is one of a few weed species with limited control options for corn and soybean growers due to resistance to multiple herbicides.

Adoption was slower in corn, but by 2010, glyphosate had become the most widely used herbicide in corn as well, with 66% of U.S. corn acres treated (USDA NASS 2011).

Many areas are now transitioning into a post-glyphosate era with glyphosate-resistant weeds now requiring additional or alternative management tools for satisfactory control. To date, glyphosate resistance has been confirmed in 24 weed species worldwide, including 14 in North America (Heap 2012). Glyphosate-resistant weed populations have been confirmed in 29 states and two Canadian provinces (Figure 2).

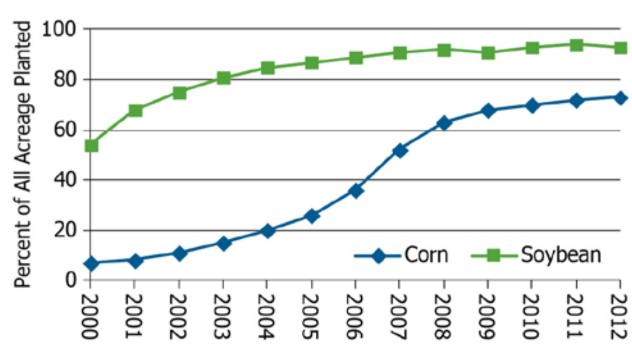


**Figure 1.** U.S. corn and soybean acres planted with genetically modified herbicide-resistant crops (USDA ERS).

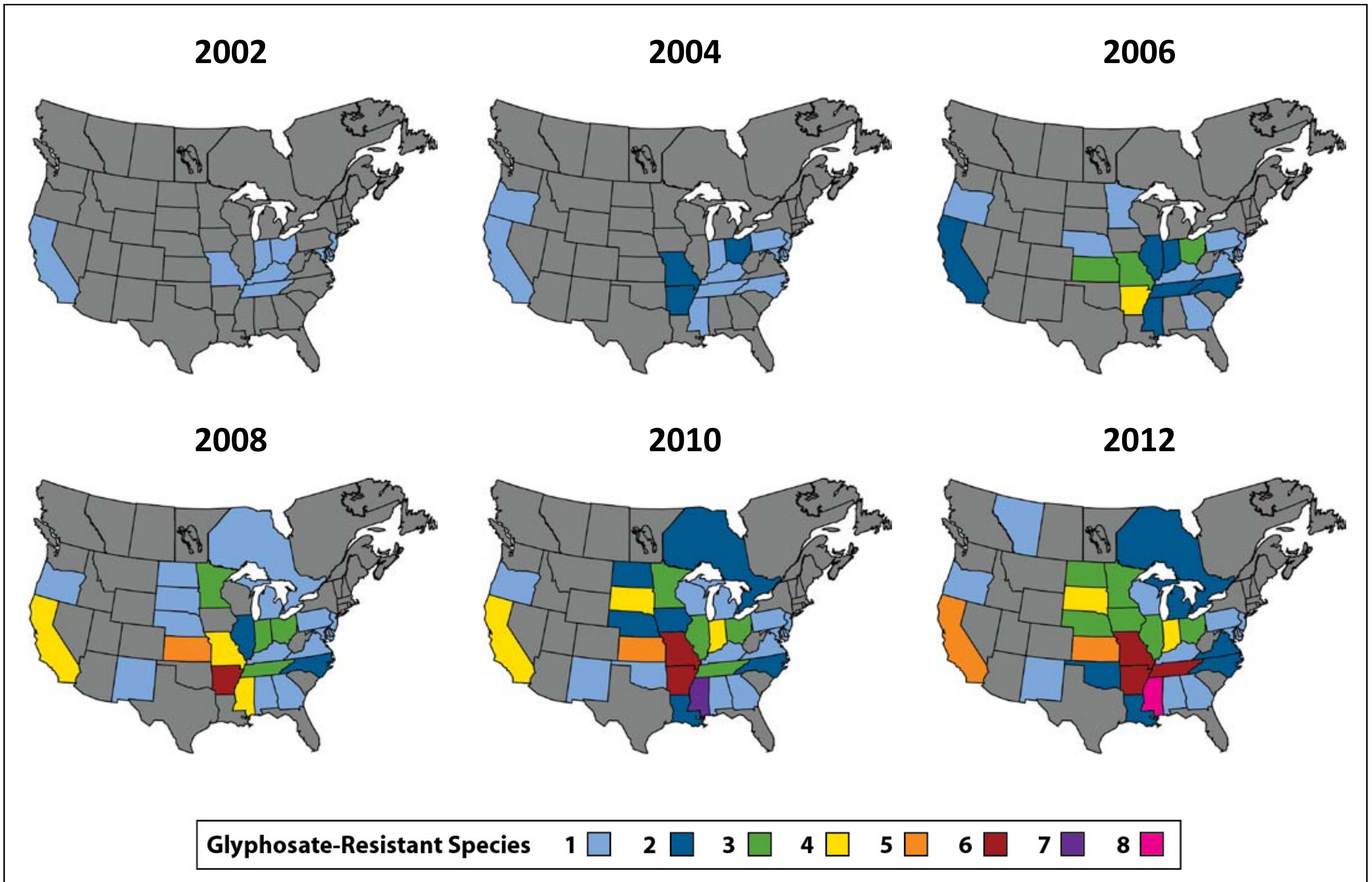


**Figure 2.** Confirmed glyphosate-resistant weed populations in North America, 2002-2012 (Heap 2012).

Problems with herbicide-resistant weed populations date back to well before the introduction of glyphosate-resistant crops in 1996. In fact, one of the reasons for the rapid adoption of glyphosate-resistant crops was as a solution to resistant weeds. At the time, glyphosate had been in use for over 20 years with no known cases of resistance evolution, which led some to doubt that resistance would ever develop. This doubt was reinforced by the relative scarcity of plant species expressing natural tolerance to glyphosate and the unlikelihood that the complex processes involved in creating glyphosate-resistant crops would be duplicated under field conditions. This outlook was short-lived, however, as cases of evolved resistance to glyphosate began to appear.

Despite the rapid increase in resistance cases over the last several years, glyphosate has a relatively low incidence of resistance evolution compared to many other herbicides. For example, the number of weed species with glyphosate resistance (24) is still relatively small compared to ALS inhibitor resistance (127) and triazine resistance (69). The total number of herbicide resistance cases worldwide has likely been reduced by the adoption of glyphosate-resistant crops because the herbicides replaced by glyphosate had a higher resistance risk in most cases. However, the unprecedented scale of glyphosate use increased its resistance issues. In addition, the high level of dependence upon glyphosate as a primary weed management tool across multiple crops makes the development and spread of resistant populations of particular concern.

Resistant weeds do not eliminate the usefulness of glyphosate as a herbicide. Glyphosate will continue to be an important and useful weed control tool for years to come, much like atrazine is still widely used in combination with other herbicides despite numerous cases of resistant populations (USDA NASS 2011). There are a small number of weed species, however, for which resistance to multiple herbicides now leaves growers with few viable options for control (Table 1).

**Multiple Herbicide Resistance - Definition**

Resistance to several herbicides resulting from two or more distinct resistance mechanisms occurring in the same plant.

**Table 1.** Weed populations with multiple resistance to glyphosate and one or more other herbicide modes of action in the U.S. and Canada.

| Species | State | Modes of Action |
|---|---|---|
| Common Waterhemp | MO, IL[1] | Glyphosate, ALS inhibitors, PPO inhibitors |
| | IL | Glyphosate, ALS inhibitors |
| | IL[2] | Glyphosate, ALS inhibitors, PPO inhibitors, photosystem II inhibitors |
| | IA | Glyphosate, ALS inhibitors, 4-HPPD inhibitors |
| Palmer Amaranth | GA, MS, TN | Glyphosate, ALS inhibitors |
| Giant Ragweed | OH, MN | Glyphosate, ALS inhibitors |
| Common Ragweed | OH | Glyphosate, ALS inhibitors |
| Horseweed | OH, ON | Glyphosate, ALS inhibitors |
| | MS | Glyphosate, paraquat |
| Kochia | AB | Glyphosate, ALS inhibitors |

[1] Hager 2011, [2] Bell et al. 2009, all others Heap 2012.

The most troublesome multiple-resistant weeds for North American crop production are two pigweed species, common waterhemp and Palmer amaranth. Like corn and sorghum, pigweeds are $C_4$ plants, making them very efficient at fixing carbon and well-adapted to high temperatures and intense sunlight. Pigweeds are also capable of producing greater than 500,000 seeds per plant and tend to germinate throughout the summer, making them difficult to manage in crops.

In contrast to other pigweed species, waterhemp and Palmer amaranth are dioecious (separate male and female plants). The resulting cross-pollination between plants can increase the genetic diversity of a population, which may favor development of herbicide resistance. Both species are very competitive with crops, particularly Palmer amaranth (Steckel 2007).

Common waterhemp resistant to glyphosate, ALS inhibitors, and PPO inhibitors is becoming increasingly common in Illinois (Hager 2011) and Missouri. A population resistant to these three modes of action plus photosystem II inhibitors (atrazine) has been documented in Illinois. In Iowa, a new type of resistance was added to common waterhemp's already impressive list when a population resistant to glyphosate, ALS inhibitors, and 4-HPPD inhibitors was discovered in 2011. Palmer amaranth resistant to glyphosate and ALS inhibitors has only been documented in three southern states so far, but will likely spread within the South as well as north into the Corn Belt (Hager 2005).

A soybean field infested with common waterhemp.

Following the amaranths on the list of troublesome multiple-resistant weed species are common and giant ragweed. Populations resistant to both glyphosate and ALS inhibitors have been confirmed for these two species. Much like the amaranths, the ragweed species are very competitive with crops due to their rapid growth rate (giant ragweed in particular will frequently overtop the crop canopy). The ragweeds do not produce nearly as much seed per plant as the amaranths (Johnson et al. 2007), which makes it more feasible to deal with resistant populations before they get completely out of control.

Other important multiple-resistant weed species are kochia and horseweed. Resistance to both glyphosate and ALS inhibitors has evolved in populations of these species. Horseweed resistant to glyphosate and paraquat has been documented in Mississippi.

With glyphosate no longer a viable control option for these weed species in an increasing number of cases, growers are often forced to turn to less effective and flexible herbicide options. These options frequently require more diligent management than growers have become accustomed to with glyphosate. Additionally, the increasing dependence on a dwindling number of viable chemical control options for the worst multiple-resistant weed species will accelerate the rate at which these options will fail. Glyphosate-resistant crops were themselves a solution to herbicide resistance issues at the time they were introduced–what new weed control options are on the horizon to help deal with herbicide resistance now?

## Outlook for New Weed Control Options

**Herbicide Discovery -** Since the introduction of glyphosate-resistant crops to the marketplace in 1996, no new herbicide modes of action have been commercialized (Table 2). New herbicide products have continued to come to market but in all cases have been either new premixes or formulations of existing active ingredients, or new active ingredients in existing herbicide classes.

**Table 2.** Approximate year of initial commercial introduction for herbicide modes of action.

| HRAC[1] | Site of Action | Year[2] |
|---|---|---|
| A | Inhibition of acetyl CoA carboxylase | 1975 |
| B | Inhibition of acetolactate synthase | 1980 |
| C1 | Inhibition of photosystem II (triazines) | 1953 |
| C2 | Inhibition of photosystem II (ureas and amides) | 1952 |
| C3 | Inhibition of photosystem II (nitriles and others) | 1964 |
| D | Photosystem-I-electron diversion | 1962 |
| E | Inhibition of protoporphyrinogen oxidase | 1966 |
| F1 | Inhibition of carotenoid biosynthesis at PDS step | 1976 |
| F2 | Inhibition of 4-HPPD | 1984 |
| F3 | Inhibition of carotenoid biosynthesis | 1955 |
| G | Inhibition of EPSP synthase | 1971 |
| H | Inhibition of glutamine synthetase | 1981 |
| I | Inhibition of DHP synthase | 1975 |
| K1 | Microtubule assembly inhibition | 1959 |
| K2 | Inhibition of mitosis | 1956 |
| K3 | Inhibition of VLCFAs | 1956 |
| L | Inhibition of cell wall (cellulose) synthesis | 1962 |
| M | Membrane disruption | 1930 |
| N | Inhibition of lipid synthesis | 1954 |
| O | Synthetic auxins | 1946 |
| P | Inhibition of auxin transport | 1955 |

[1] Herbicide Resistance Action Committee classification.

[2] Derived from Timmons 1970 and Appleby 2005.

Industry resources dedicated to developing new herbicide modes of action have sharply declined in recent years for a number of reasons (Duke 2011). The most obvious reason is the widespread adoption of glyphosate-resistant crops and glyphosate-based weed management programs. The effectiveness of glyphosate and its availability as a weed management tool in multiple crops reduced the demand for any new mode of action. This situation was exacerbated by price reductions following the glyphosate patent expiration and exacerbated even further as other active ingredients came off patent.

Another factor contributing to the lack of new herbicide modes of action coming to market is the extensive consolidation and downsizing in the crop protection industry in recent years (Figure 3). With fewer players in the market, the total amount of herbicide discovery research industry-wide has declined.

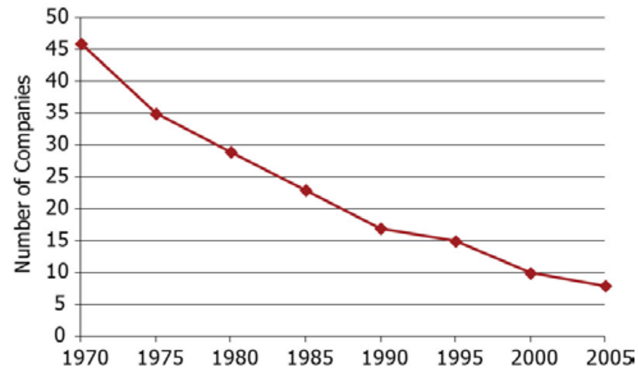


**Figure 3.** Approximate number of companies conducting herbicide discovery research 1970-2005 (Appleby 2005).

Finally, a further roadblock for developing new herbicide modes of action is the increased cost of bringing a new product to market. In 2008, an estimate of the combined costs of discovery and development of a new product put the total cost at $248 million (Bomgardner 2011). Products coming to market now face many more regulatory hurdles than existed when currently available modes of action were developed.

The increasing prevalence of glyphosate-resistant weeds has increased the demand and financial incentive for developing a new herbicide mode of action; however, the extensive process of bringing a new product to market means that any newly discovered active ingredient would not be available commercially for several years. It is not known what new herbicides may come to market well into the future, but for now it is clear that the next glyphosate is not waiting in the wings as a solution for resistant weeds.

**Expanded Options with Existing Herbicides -** Several new types of herbicide resistant crops coming to the market this decade will expand weed control options with existing herbicides. These crops will generally include resistance to multiple herbicides, increasing the available weed management options for growers. With new herbicide modes of action unlikely to appear anytime soon, multiple herbicide-resistant crops are the immediate future for weed control. These technologies will expand grower options for dealing with resistant weeds but in all cases rely on existing herbicide active ingredients that already have documented resistance issues of their own.

One alternative herbicide-resistant crop technology that is already available is glufosinate resistance (LibertyLink®). All hybrids with Herculex® insect protection also have the LibertyLink gene for glufosinate resistance. Growers have often not used glufosinate for weed control, despite their capability to do so, preferring to use glyphosate instead. Glufosinate-resistant soybeans have become increasingly available in recent years, primarily due to the need for additional tools to manage multiple-resistant pigweeds. The limited use of glufosinate for weed control has not created nearly the level of selection intensity that has been experienced with glyphosate; however, resistance has been documented in two weed species in the last few years. The first known case of resistance was goosegrass in Malyasia in 2009, a species with an extensive history of developing resistance to several different herbicides including glyphosate. Italian ryegrass resistant to both glufosinate and glyphosate was discovered in Oregon the following year.

Two upcoming technologies involve crops resistant to synthetic auxin herbicides, 2,4-D (Enlist™ Weed Control System) and dicamba (Roundup Ready® Xtend). Synthetic auxin herbicides have been widely used for many years and are known to have a relatively low risk for weed resistance (Gustafson 2008); however, multiple cases of weed resistance to 2,4-D, dicamba, or both have been documented over the course of their long histories.

Resistance to 2,4-D was first documented in 1957 and has since occurred in several weed species, although most are not important weeds in North America row-crop production. One notable exception is common waterhemp; a resistant population was discovered in 2009 in a grass seed production field in Nebraska that had received one or two 2,4-D applications annually for many years (Bernards et al. 2012).

Dicamba resistance has also been documented in multiple weed species including kochia in the western U.S. and Canada and common lambsquarters in New Zealand. Resistance in kochia is noteworthy due to the existence of several known glyphosate resistant populations in the same region. Any herbicide resistance issues in common lambsquarters take on an enhanced significance due to the fact that it is ubiquitous across much of the Corn Belt. Glyphosate resistance has not occurred to date in common lambsquarters, but variability in response has been documented (Sivesind et al. 2011).

Another forthcoming herbicide resistance technology is soybean resistant to 4-HPPD inhibitor herbicides (active ingredients in products such as such as Callisto®, Laudis®, and Balance® Flexx) being co-developed by Syngenta and Bayer. The 4-HPPD inhibitor herbicides are relatively new, which has limited the selection for resistant weeds to date. So far, the only weed species to evolve resistance to this mode of action is common waterhemp, with resistant populations first discovered in 2009. Resistant populations have now been documented in three Midwestern states, Illinois, Iowa, and Nebraska. Populations with multiple resistance to 4-HPPD inhibitors, ALS inhibitors, and PS II inhibitors have been confirmed in Illinois and Iowa, and a population resistant to 4-HPPD inhibitors, ALS inhibitors, and glyphosate was documented in Iowa.

**Weed Resistance to Herbicides Used with Current and Future Herbicide-Resistant Crops**

**Glufosinate**

- Resistant goosegrass in Malaysia in 2009; Italian ryegrass resistant to both glufosinate and glyphosate discovered in Oregon in 2010.
- Low use of glufosinate to date has limited the selection intensity for resistant weeds; if glufosinate use becomes more widespread, resistance cases will likely increase.

**Dicamba**

- Resistance documented in several weed species.
- Noteworthy cases include dicamba-resistant kochia in several western states and common lambsquarters in New Zealand.

**2,4-D**

- Resistance documented in numerous weed species, mostly outside of North America.
- 2,4-D-resistant waterhemp discovered in Nebraska in 2009.

**4-HPPD inhibitors (mesotrione, isoxaflutole)**

- Mesotrione-resistant waterhemp confirmed in Illinois, Iowa, and Nebraska. Iowa population resistant to both mesotrione and isoxaflutole.
- The relatively recent introduction of this mode of action has limited the selection intensity for resistant weeds. Resistance cases will likely increase.

## Lessons from Glyphosate Resistance

One lesson that glyphosate resistance in weeds has taught us is that all herbicides are susceptible to resistant weed evolution given enough time and repetition of use. The fact that glyphosate had been used for over twenty years prior to the introduction of glyphosate-resistant crops without any resistance issues led to some sentiment that this might not be the case for glyphosate. Resistant weeds did develop though, appearing first in areas where glyphosate had been applied multiple times per season for many years.

The lack of new herbicide modes of action coming to market means that relying on a steady stream of new products can no longer serve as a de facto solution for managing weed resistance. Forthcoming herbicide resistant crop technologies all rely on existing active ingredients with known cases of weed resistance. These new technologies will allow for expanded flexibility in using current herbicides for managing resistant weeds in the near term, but overuse of any of these new tools will lead to its failure. Once the efficacy of our current lineup of herbicides is exhausted, there is no guarantee that any new solutions will be coming to market very soon.

The most important way to prolong the usefulness of a herbicide is to not rely on it exclusively, instead using a variety of weed management tools as part of an overall program. Rotating or combining herbicide modes of action is an important step in this direction and can help reduce the selection intensity of any one active ingredient. Multiple resistant weeds can make achieving this a challenge, however.

A weed species needs to be controlled by more than one herbicide in the program, which can be difficult with a very limited range of effective herbicide options. Multiple herbicide resistant crops will expand these options; however, using a broader range of herbicides does not, in itself, constitute an integrated weed management strategy. A truly integrated strategy should incorporate non-chemical control tactics as well. Mechanical weed control and crop rotation are examples of two such tactics available to growers, but the feasibility of their implementation will vary depending on the characteristics of a cropping system. The following list includes several strategies for mitigating the evolution and spread of herbicide resistance in weeds.

**Best Management Practices for Managing Herbicide Resistance (Norsworthy et al. 2012)**

- Understand the biology of the weeds present.
- Use a diversified approach toward weed management focused on preventing weed seed production and reducing the number of weed seed in the soil seedbank.
- Plant into weed-free fields, and then keep fields as weed free as possible.
- Plant weed-free crop seed.
- Scout fields routinely.
- Use multiple herbicide mechanisms of action that are effective against the most troublesome weeds or those most prone to herbicide resistance.
- Apply the labeled herbicide rate at recommended weed sizes.
- Emphasize cultural practices that suppress weeds by using crop competitiveness.
- Use mechanical and biological management practices where appropriate.
- Prevent field-to-field and within-field movement of weed seed or vegetative propagules.
- Manage weed seed at harvest and after harvest to prevent a buildup of the weed seedbank.
- Prevent an influx of weeds into the field by managing field borders.

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