The Benefits of Herbicide-Resistant Crops

Running Title: Benefits of herbicide-resistant crops

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Abstract: Since 1996, genetically modified herbicide-resistant crops, primarily glyphosate-resistant soybeans, corn, cotton, and canola, helped revolutionize weed management and became an important tool in current crop production practices. Glyphosate-resistant crops enabled weed management practices that improved yield and profitability while better protecting the environment. Growers recognized their benefits and made glyphosate-resistant crops the most rapidly adopted technology in the history of agriculture. Weed management systems with glyphosate-resistant crops often relied only on glyphosate and were easy-to-use, effective, economical and more environmentally friendly than the systems that they replaced. Glyphosate worked extremely well controlling weeds in glyphosate-resistant crops for more than a decade, but some key weeds eventually evolved resistance and using glyphosate alone proved unsustainable. Now, growers need to renew their weed management practices and use

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glyphosate with other cultural, mechanical, and herbicide options in integrated systems. New multiple herbicide-resistant crops with resistance to glyphosate and other herbicides will expand the utility of existing herbicide technologies and be an important component of future weed management systems that help sustain the current benefits of high efficiency and high production agriculture.

Keywords: biotechnology, crop, weed, herbicide, glyphosate, resistance, tolerance, integrated weed management, best management practices

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"Over the next 50 years, the world's farmers and ranchers will be called upon to produce more food than has been produced in the past 10,000 years combined, and to do so in environmentally sustainable ways." - Norman Borlaug, Father of the Green Revolution and advocate for herbicide-resistant crops in a 2008 letter to then-Senator Barack Obama.

1 INTRODUCTION

The ability to use biotechnology to make glyphosate-resistant (GR) crops was a scientific breakthrough that helped revolutionize weed management[1] and provided much of the impetus to restructure the seed business.[2] For the last 16 years, the most effective choice to manage weeds for many growers has been to use glyphosate in GR crops. GR crops became available when weeds were becoming widely resistant to commonly used selective herbicides and farm size was increasing while the number of farm workers was decreasing.[3] Weed management was becoming too complicated, time consuming, and costly for the new agricultural systems. The ability to use glyphosate in GR crops made weed management easy, efficient, economical, and environmentally compatible – exactly what growers wanted.

The utility of glyphosate in high efficiency and high production agricultural systems drove the rapid adoption of GR crops.[4] Glyphosate provided great weed control for more than a decade, but it became a victim of its own success. Too many growers used glyphosate alone too often on too many hectares. In retrospect, glyphosate and GR crops were overused and 'lessons have been learnt'.[5] All experts now fully understand that weeds will adapt to any single highly effective weed management practice. Growers need to use diverse integrated weed management (IWM) systems – chemical and non-chemical.

Transgenic herbicide-resistant (HR) crops undergo extensive phenotypic, agronomic, morphological, and compositional analyses and must be found 'substantially equivalent' to their conventional counterparts before they can be approved for commercialization.[6] The herbicide resistance traits do not give any agronomic advantage or disadvantage to the crop until the herbicide is applied. Still, opponents often frame the technology as a threat to sustainable agriculture by objecting to potential unknown long-term effects on human health and the environment, the potential to create 'super weeds', and raise ethical questions about global agribusiness, the control of seed supplies, and scientists interfering with the natural order. In contrast, supporters claim HR crops allow growers to be more productive, are safe to eat, better for the environment, and enable better weed management options. HR crops have an impeccable history of safe commercial use and the United States National Academy of Sciences concluded without equivocation that GM crops do not pose any health risks that are not present in conventionally produced crops.[7] Still, a small but influential group of activists maintains that long-term uncertainty justifies extreme precaution and continues the debate.

Sustainable weed management is the foundation of sustainable agriculture. The debate over the sustainability of HR crops is primarily over the sustainability of the weed management systems in large-scale production agricultural systems and the evolution of resistant weeds.

Unlike insect-resistant crops that produce an insecticidal protein, HR crops do not put any selection pressure on the weeds to evolve resistance – only herbicides do. Thus, the benefits and the risks of HR crops with respect to sustainability relate to the benefits and risks of how the herbicides that they enable are used.

1.1 Discovery

For thousands of years, farmers have used selection and cross breeding to genetically modify crops. These methods are effective at getting desirable traits in and undesirable traits out of the crop but require intensive work and are slow. Recent breakthroughs in science and genetics have greatly expanded the toolbox that scientists can use to improve crops. For example, biotechnology can quickly isolate a desirable gene from one species and insert it into the DNA of another. Scientists can now change the biology of the crop to adapt to the herbicide. Still modifying crops enough so that they can tolerate broad-spectrum herbicides at a commercially acceptable level is always challenging.[8] By definition, herbicides must very effectively disrupt essential plant processes or otherwise they would not be able to kill weeds. Today, seed companies still use traditional breeding to produce HR crops, but the focus has shifted to using biotechnology.

The biotech HR crop revolution has been based on a remarkably few traits in a few crops so far (Table 1).[9] In fact, most of the impact is due to just one gene, the *cp4 epsps* that encodes for glyphosate-resistant 5-enolpyruvylshikimate-3-phosphate synthase (EPSPS, EC 2.5.1.19). The potential to expand HR crop technology to other herbicide traits is high. However, the ability to use biotechnology to make a crop resistant to a herbicide is not what will govern success. The attributes of the herbicide and its ability to bring benefits to growers and satisfy society's expectations for a safe, abundant and affordable food, fuel, and fiber supply in environmentally sustainable way will determine success.

1.2 Adoption

Growers have rapidly adopted GR crops - soybeans [*Glycine max* (L.) Merr.], corn (*Zea mays* L.), corn (*Zea mays* L.), cotton (*Gossypium hirsutum* L.), canola (*Brassica napa* L.), alfalfa (*Medicago sativa* L.) and sugarbeets (*Beta vulgaris* L.) - wherever they have become available .[10] Before GR crops, transgenic bromoxynil-resistant cotton and a wide array of non-transgenic HR crops were available (Table 2), but growers did not widely adopt them.[9] The key difference was the ability to use glyphosate, a relatively inexpensive and effective herbicide with an excellent environmental profile. Growers recognized the benefits of using glyphosate (Table 3) and made GR crops the most rapidly adopted technology in the history of agriculture (Figure 3).

In 2011, 126 million ha of the total 160 million ha of GM crops had herbicide resistance traits – 94 million had only herbicide resistance and 42 million had both herbicide and insect resistance traits.[10] Global adoption of HR crops continues to increase rapidly at about 10 percent per year. In the U.S., growers adopted GR soybeans on more than 80 percent of the soybean area just six years after commercialization. It only took eight years to reach 80 percent adoption in cotton, ten years in corn, and just three years in sugarbeets. In Argentina, growers adopted GR soybeans on more than 98 percent of their soybean area 5 years after commercialization.

Moreover, once growers adopted GR crops, they stayed with the technology. The unprecedented adoption rates in both developed and developing countries are a testimony to the value that millions of growers place in the technology.

2 BENEFITS OF HERBICIDE-RESISTANT CROPS

2.1 Efficacy

Selective herbicides have been a major contributor to improved crop production for the last 60 years, but nonselective herbicides could not be used in-crop before the advent of HR crops unless growers applied the herbicide in a way that it did not reach the crop, e.g., soil application before planting or directed spraying. The primary benefit of HR crops is to eliminate any injury from previously nonselective herbicides, but other benefits include better weed control resulting in higher yields and less need to till soil, lower costs, fewer application restrictions, and benefits from using a herbicide with a new mode-of-action and an improved environmental or toxicological profile.

Some of the first GR crop varieties were moved quickly to the market to meet high customer demand and had a 'yield drag'; or more appropriately a 'yield lag' because they were not fully adapted to local growing conditions.[1,11] Subsequent breeding into better-adapted lines returned yields to their expected levels, and GR crops have continued the linear trend for higher yields that has been constant for decades in corn, soybeans, and cotton.[12] In addition, some of the first GR crops did not give complete resistance to glyphosate under stress conditions[13] and the timing, rate, and number of glyphosate applications were restricted.[1] Glyphosate often injured the first GR cotton varieties and could even reduce yield,[14] but a second-generation trait eliminated this effect.[15]

2.2 Economics

2.2.1 Higher and more profitable yields. Weeds compete for water, nutrients and sunlight and are the most important pest complex in crop production. Deciding how to manage them is one of the most important agronomic decisions a grower makes.[16] GR crops have helped growers manage weeds and produce higher and more profitable yields (Table 4).[17] HR crops will help growers meet an ever-growing demand for food, feed, fiber, and fuel for the expected nine billion people in 2050. The yield benefit and higher quality seed is due to improved weed control, which is often better than the conventional weed management system it replaced. The amount of increase in yield generally depends on how effectively that grower previously controlled weeds. No transgenic HR crop directly increases yield, i.e., the traits *per se* do not enhance yield.

Critics of HR crops argue that the technology only benefits large-scale production agriculture. However, the yield increase from using GR crops has tended to be the greatest for small farmers in developing countries who benefit most from the improved weed control.[10] For example, the average yield increase for growers using GR soybeans in developed countries is seven percent versus 21 percent in developing countries.[18] HR crops have great potential to help small farmers in Africa where farmers rarely use herbicides and do not have the technology to apply them.[19] HR crops can allow the seed providers to apply the herbicide directly on the seed so the farmer only needs to plant the seed to get the benefit of the herbicide and does not need herbicide application equipment.

Small farmers in Africa are already using herbicide seed treatment to control parasitic weeds such as *Striga hermonthica* and *S. asiatica*, arguably the most difficult and most important weed problem. Selective herbicides and mechanical practices cannot control parasitic weeds, but some nonselective herbicides in HR crops can. In fact, small farmers are already using the nonselective imazapyr as a seed treatment in non-transgenic, HR corn. Other HR crop systems need to be commercialized so small farmers will have multiple options to help manage the evolution of resistance.[20]

Weeds that are closely related to the crop are often the most competitive and difficult to control with selective herbicides or mechanical practices. HR crops such as HR sorghum [*Sorghum bicolor* (L.) Moench] or HR rice (*Oryza sativa* L.) would allow growers to use a herbicide to control the related weed species while not injuring the crop. The main limitation of this approach is currently the likelihood of rapid gene transfer from the crop to the related weed populations. Biotechnology can help prevent this by tightly linking the herbicide resistance gene to genes for nonshattering, short stature, uniform flowering and germination that would be beneficial to the crop but significantly reduce weediness and thus the fitness of any feral escapes or weedy hybrids formed.[21] Another strategy would be to link the herbicide resistance gene to an RNA interference (RNAi) expression cassette that would selectively repress the detoxification of another herbicide that growers could then use to control any unwanted offspring .[22] Both strategies could help sustain HR crop technology when gene transfer to weeds is likely.

2.2.2 Lower production costs. HR crops became available when farm size and income were rising but the number of farm workers was decreasing. Weeds were also becoming widely resistant to selective herbicides and difficult to manage. Glyphosate was the ideal herbicides for HR crops.[5] When foliarly applied, glyphosate controlled essentially all weeds – 300 weed species - at a wide range of growth stages with no recropping restrictions. Growers could apply a single herbicide instead of many different ones to control their broadleaf and grass weeds.[1,23] The ability to use glyphosate in GR crops made weed management easy, effective and efficient. Even with the increased cost of seed associated with a technology fee, HR crops still reduced the cost to manage weeds and ultimately improved farm productivity.

2.2 Environmental benefits

The potential impact of HR crops on the environment has been controversial and generated heated debates, but the evidence clearly shows that GR crop systems have benefited the environment by reducing fuel use, soil erosion, and reliance on persistent herbicides with groundwater advisories. HR crops, especially GR crops, generally enable the use of more effective herbicides that reduce reliance on soil tillage for weed management and have improved toxicological and environmental profiles.[24,25,26]

2.2.1 Soil conservation. HR crops have enabled the widespread use of reduced tillage, also known as conservation tillage. Conservation tillage maintains a soil cover with crop residues which has many positive environmental benefits including reduced soil erosion and water pollution from nutrient and sediment runoff, protection from wind erosion, improved habitat for birds, mammals, and microorganisms as well as less consumption of fossil fuels and carbon dioxide emissions.[27,28] For example, conservation tillage can reduce soil loss more than 90 percent and movement of phosphorus more than 70 percent.[29] The crop residue builds organic matter, and there is less soil compaction because HR crop growers make fewer passes through the field with tractors than non-HR crop growers.[28]

The use of conservation tillage grew rapidly in the 1990s, driven by federal government programs requiring conservation efforts and the introduction of high-residue planting equipment. Improved weed control with the use of glyphosate in GR crops was also a major factor enabling the adoption of no tillage crop production to increase from 45 to 111 million ha between 1999 and 2009.[23,30] There is often a very close correlation of the use of GR crops and no-tillage crop production.[31] Of course, GR crops do not prohibit tillage; tillage is still an option if needed for an agronomic purpose.

2.2.1 Less herbicide. HR crops do not increase the use of herbicides. Even when a grower uses a HR crop-enabled herbicide, that herbicide usually replaces another herbicide.[32] In addition, the amount of herbicide used on HR crops, primarily GR crops, is often less. Since 1996, the amount of herbicide used on HR corn, soybeans, cotton and canola decreased by 204 million kg, a very similar amount to the amount insecticides have been reduced with transgenic, insect-resistant crops. In addition, the herbicides used in HR crops usually have less environmental impact, a more environmentally benign profile, than the herbicides used in conventional crops that they replaced (Table 5).[33]

HR crop seed is usually more expensive than non-HR seed, so growers that buy HR seed will likely use the herbicide the HR crop enables. However, HR crops do not inherently require the grower to use that herbicide. Herbicide use should still be a grower decision based on need. The impact of HR crops on herbicide use changes, depending on the crop and weed spectrum. For example, the use rate of glyphosate in sugarbeets is higher than the use rate of some of the herbicides it replaces, so switching to a GR crop system does not necessarily mean that less herbicide is used. Still, the environmental properties of glyphosate and associated practices such as conservation tillage make a strong case can be made that GR sugarbeets are better for the environment.[26,34]

2.2.1 Other benefits. Fuel savings with HR crops is both a cost and an environmental benefit. The reduction in fuel consumption is quite dramatic. For example, moldboard plowing typically uses 49.5 L/ha of fuel, whereas no tillage practices use only 13.1 L/ha.[27] Every liter of fuel saved reduces 0.44 kg of carbon dioxide emission. The cumulative permanent reduction in tillage fuel use in US soybeans from 1996 to 2009 amounted to a reduction in tillage fuel usage of 835 million liters, which equates to a reduction in carbon dioxide emission of 2,295.3 million kg.[33] An estimated one million tons of carbon is either sequestered or no longer released annually under land management practices facilitated by HR canola production, as compared to 1995, before the introduction of HR canola.[35]

HR crops often do not have the large profit or yield advantages expected for a technology that growers so rapidly adopted. Some studies have indicated that the grower decision to adopt was complex. For example, Fernandez-Cornejo et al.[36] found that GR soybeans were not associated with higher farm income, but rather higher off-farm and overall farm-household income. Farm workers could get a second job off the farm because of the flexibility and labor savings or the GR crop system.[37,38]

In another study, Hurley et al.[39] asked 1205 corn, soybean, and cotton growers that used GR crops what benefits they thought they were getting. The survey asked growers to rank the importance of 13 possible benefits other than profitability. Figure 2 shows what growers considered very important. More than 95 percent of corn, soybean and cotton growers ranked consistency and protection from yield loss as very important. In addition, more than 95 percent of growers ranked crop safety, a clean field, cost, application frequency, flexibility, family health, public health, and water quality as either very important or somewhat important. Some growers perceived benefits in all the 13 characteristics; more than 80 percent valued lowest ranking characteristic of wildlife quality as being very or somewhat important. These results suggest that unobservable health and environmental advantages as well as yield and herbicide application advantages were key reasons why growers rapidly adopted GR crops.

HR crops provide companies the benefit of intellectual property protection, particularly since the 1980 landmark U.S. Supreme Court decision that held that utility patents were valid on living organisms as altered by human beings.[40] The transgenic process to make HR crops creates a number of patentable invention opportunities to protect intellectual property and thus allows companies to recover their investment.[41] When technology is profitable, companies will invest more in research and development.

Another significant benefit for seed companies relates to the precision of gene insertion. As the number of transgenes increases, it becomes increasingly difficult for breeders to manage all the transgenic and nontransgenic characteristics. Many companies are developing stacked trait products. For example, more than two dozen transgenic crops with stacks of transgenes are currently commercial with one corn product having eight transgenes – two for herbicide resistance and six for insect resistance.[6] Researchers are also using biotechnology to insert multiple transgenes in a specific single locus. Any reduction in the number of loci will greatly help breeders manage transgenes and let them focus more on optimizing yield and other agronomic characteristics.[42]

3 EVOLUTION OF RESISTANT WEEDS

3.1 Overuse

With the introduction of GR crops, glyphosate became a new mode-of-action for in-crop use and could have increased the diversity of weed management practices. However, most growers only used glyphosate year after year over wide areas. Still, glyphosate alone initially worked extremely well and the use of other herbicides declined dramatically despite price reductions.[26] In fact, the number of herbicide active ingredients used on at least ten percent of U.S. soybeans declined from 11 in 1995 to just one in 2002 – glyphosate.[43]

The high effectiveness of glyphosate was not going to last forever, even in diverse weed management systems, but many did think the continuous use of glyphosate in GR crops would be sustainable when it was first introduced. However, this belief changed with the discovery of the first GR weed in a GR crop.[44] Today, at least 23 weed species have evolved resistance to glyphosate.[45] Applying glyphosate alone repeatedly across vast areas put unprecedented selection pressure on weeds and ultimately led to the widespread evolution of GR weeds.[46,47]

The greatest threat to the sustainability of current crop production systems is the rapid increase in weeds resistant to multiple herbicides, particularly weeds that are resistant to glyphosate and other herbicide modes-of-action. Currently, more than fifty weed species have resistance to multiple herbicide modes-of-action with at least eight GR weed species having resistance to four or more.[48] The news media has labeled the explosion of multiple HR populations of troublesome species such as Palmer amaranth (*Amaranthus palmeri* S. Wats.) and waterhemp [*Amaranthus tuberculatus* (Moq.) Sauer] as the "pigweed disaster".[49,50] Herbicide options to control these weeds are limited so growers are intensifying the use of tillage and even using expensive hand weeding in some situations.[51]

3.2 Lack of new herbicide technology

Growers need new weed management practices– practices other than herbicides and tillage. To date, the seed and agrichemical industries largely responded to the evolution of resistant weeds with existing tools in their toolbox – herbicide mixtures and multiple HR crops. HR crop research is focused on six modes-of-action that have been used extensively and currently represent 77 percent of the herbicide market. These herbicide technologies will incrementally help by enabling more herbicide options, but will not be total solutions (Table 6). Growers desperately need new herbicide technology.

The long drought of no new herbicide modes-of-action has been devastating for weed management .[52,53] Hopefully, this drought will end, and herbicides will be discovered in the near future that have new modes-of-action and control a broad-spectrum of monocotyledonous and dicotyledonous weeds. However, new herbicides are unlikely to be highly active against weeds with little or no effect on crops. HR crop technology will be essential to provide a high level of resistance in a broad-spectrum of crops. Ideally, industry will discover more than one broad-spectrum herbicide with a new mode-of-action and simultaneously commercialize them with their associated HR crops. This would make it much easier to implement the diverse weed management practices needed to sustain the technologies from the start.

3.3 Solutions

3.3.1 Future technologies. The days of crops being resistant to just glyphosate are ending.[9,54] The next wave of technology will combine glyphosate resistance with resistance to other herbicides. These multiple HR crops or 'stacks' will give growers more herbicide options to help reduce reliance on a single herbicide type. Companies carefully determine which herbicides have the best overall attributes before they invest resources to develop a HR crop. For example, glufosinate is a broad-spectrum herbicide with few resistant weeds. "Dual stack" crops with glufosinate and glyphosate resistance are already available to help control GR weeds in corn, soybeans, and cotton. Other multiple HR crops are expected in the next decade (Table 7).

Some of the new herbicide resistance traits for glyphosate, 4-hydroxyphenol pyruvate dioxygenase (HPPD)-inhibiting and auxin herbicides are based on metabolic inactivation, which has the advantage of making the active herbicide disappear within the plant (Table 8). For example, a dicamba trait uses an O-demethylase from bacteria to inactivate dicamba, providing crop safety.[55] Another technology is based on a family of *aad* genes that encode for aryloxyalkanoate dioxygenase enzymes to inactivate phenoxyacetate (e.g., 2,4-D) and pyridinyloxyacetate auxins (e.g., triclopyr and fluroxypyr).[56] Another trait is being developed for corn that inactivates both 2,4-D and acetyl coenzyme A carboxylase (ACCase)-inhibiting monocot herbicides known as FOPs (e.g., quizalofop).

Broadleaf crops resistant to synthetic auxin herbicides will likely be the next new HR crop technology. Auxin herbicides have been widely used for 60 years as selective herbicides in monocot crops and to control emerged broadleaf weeds prior to planting. Broadleaf plants are generally sensitive to auxin herbicides so auxin-resistant soybeans and cotton would be useful and enable new uses of a new mode-of-action in those crops. The impact of auxin-resistant crops could be very large if growers think they offer the best solution to control key weeds like Palmer amaranth and waterhemp. Relatively few weeds have evolved resistance to auxin herbicides so far despite their widespread use, and current plans are to always use auxin herbicides with other herbicide types to help minimize the evolution of resistant weeds.

Synthetic auxin herbicides are used very widely – on over 200 million ha globally. Auxin herbicides are already used in corn and soybeans, in the same areas that auxin-resistant crops will be used. The use of auxin herbicide will not be new, but auxin-resistant crops will increase the use of auxins in some situations. These situations need to be carefully evaluated so nearby sensitive plants are not injured because as little as 0.001 percent of the labeled rate can injure some very sensitive broadleaf crops.[57] New formulations with less volatile salts and drift control adjuvants will help reduce off-target movement and could even help reinvent auxin herbicide technology.[58,59] Fortunately, manufacturers, growers, and government regulators are actively working together to reduce this risk.[60] For this technology to be successful, growers will need to carefully follow label directions and make correct decisions on when and how to apply based on temperature, wind velocity, droplet size, release height, buffer zones, and drift reduction technologies.

Resistance to HPPD-inhibiting herbicides also could have a big impact in the next decade. HPPD-inhibiting herbicides control a number of important weed species with both foliar and soil residual activity. As with auxins, maize is naturally tolerant, but soybeans and cotton are sensitive to key HPPD herbicides. Two traits are under development in soybeans and cotton that would enable a new postemergence herbicide mode-of-action in those crops. Not many weed species are resistant to HPPD herbicides yet, but recent reports of HPPD-resistant waterhemp and Palmer amaranth will likely reduce the utility of these traits.[45]

Resistance traits for other herbicide types will also be useful. Herbicides that inhibit acetolactate synthase (ALS), protoporphyrinogen oxidase (PPO), and ACCase are widely used as selective herbicides and have high efficacy on key weeds, but the tendency of weeds to evolve resistance to these herbicides will limit their utility. Metabolic inactivation systems based on cytochrome P450 monooxygenases (P450) or glutathione transferase (GST) could have significant potential as traits for a range of herbicide types. For example, native P450 enzymes inactivate only certain auxin, PSII, cell division and ALS-inhibiting herbicides. Other options for HR crops are limited until new herbicides are available.

3.3.2 Best management practices. Weeds that have evolved resistance to glyphosate have not eliminated the ability of glyphosate to control other weeds. Glyphosate will almost certainly continue to be the largest selling herbicide in the world, but it is "not as good as it once was." Growers in areas that have not adopted GR crops yet can learn from the experience of growers who have. Herbicides alone cannot solve resistant weed problems. Multiple HR crops that allow the use of glufosinate, auxins, and HPPD-inhibiting herbicides will help growers manage resistant weeds and preserve conservation tillage and high yield, but will only be a component of the total solution. Growers need to use more diverse weed management practices to sustain the utility of HR crops and get out of the paradigm of needing a new technology each time nature adapts to the overuse of an old one.[61,62,63]

Multiple HR crop systems will help growers meet the most important principle of resistant weed management - to prevent the survival and spread of resistant populations.[64,65] However, experts now agree that weed management should not rely just on herbicides, especially not only one as what has happened in GR crops.[66] Because of the lack of new herbicide technologies (Duke 2012), new HR crops will be resistant to older herbicides with known limitations. Growers will need to use an array of cultural and mechanical practices in integrated weed management (IWM) systems (Table 9).[65] Unfortunately, growers do not currently perceive many of these practices to be as effective as herbicides and are reluctant to use multiple tactics until the most effective one is no longer effective. Better education and a reward system for using best management practices will help.

4 FUTURE OF HERBICIDE-RESISTANT CROPS

Glyphosate and GR crops performed well for more than a decade and helped revolutionize weed management practices, but now weed management technology needs to be renewed. Row crop growers adopted GR crops very rapidly because glyphosate gave superior efficacy and simplified weed management systems while providing economic and environmental benefits that continue to the present day. GR crops substantially decreased the use of herbicides and tillage, but the evolution of GR weeds is threatening these benefits. No weed management technology used alone is sustainable – weeds will adapt to any single tactic. Glyphosate is not as effective as it once was, but will continue to useful in diversified IWM systems.

Agriculture needs to take advantage of any technology that provides more food to a hungry world by enabling better control of weeds and does not hurt the environment or human health. HR crop systems are not perfect but are currently better than the alternatives in most situations. Growers also desperately need other weed management technologies. Unfortunately, no new technology for the foreseeable future will come close to matching the impact of using glyphosate in GR crops. New multiple HR crops will help by enabling new uses of existing herbicide technologies and thus be a major component of future IWM solutions that help sustain the current benefits of high efficiency and high production agriculture.

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Table 1. Currently available transgenic crop herbicide traits.

Crop	Herbicide	Primary Trait Gene(s)	Trait Designation	First Sales
Corn	Glyphosate	Multiple *zm-2mepsps*	GA21	1998
		Two *cp4 epsps cassettes*	NK603	2001
	Glufosinate	*Pat*	T14, T25	1996
Soybeans	Glyphosate	*cp4 epsps*	GTS 40-3-2	1996
			MON89788	2009
	Glufosinate	*Pat*	A2704-12	2009
Cotton	Glyphosate	*cp4 epsps*	MON1445/1698	1997
		Two *cp4 epsps*	MON88913	2006
		zm-2mepsps	GHB614	2009
	Glufosinate	*bar*	LLCotton25	2005
Canola	Glyphosate	*cp4 epsps, gox v247*	GT73	1996
	Glufosinate	*pat*	Topas 19/2	1995
Rice	Glufosinate	*bar*	LLRice601	2006
Sugarbeets	Glyphosate	*cp4 epsps*	KM-00071-4 (H7-1)	2007
Alfalfa	Glyphosate	Two *cp4 epsps*	MON00101-8, MON00163-7	2006[1]

[1]Glyphosate-resistant alfalfa had a five-year gap of no planting, pending legal clearances, until 2011.

Table 2. Summary of commercial nontransgenic herbicide-resistant crops.

Herbicide	**Crop**	**Year available**
ACCase inhibitor - sethoxydim	Corn	1996
Imidazolinones	Corn	1993
	Canola	1997
	Wheat	2002
	Rice	2002
	Sunflower	2003
Specific sulfonylureas	Soybeans	1994
	Sunflower	2006
	Sorghum	~2012
Photosystem II inhibitors	Soybeans	~1981
	Canola	1984

Table 3. Reasons often given for the rapid adoption of glyphosate-resistant crops.

Performance
Weed efficacy
Consistency
Crop safety
Higher yield
Lower production costs
Profitability
Simplicity
Convenience
Flexibility
Safety (occupational, family, environmental)
Saves time

Table 4. Income benefit from transgenic crops from 1996 to 2007.[17]

Crop	Income (USD$)	Yield (million tons)
Herbicide-resistant soybeans	21.8	67.8
Herbicide and insect-resistant corn	8.1	15.1
Herbicide and insect-resistant cotton	13.4	6.9
Herbicide-resistant canola	1.4	4.4

Table 5. Environmental impact of the change of herbicide use in herbicide-resistant (mostly glyphosate-resistant) crops globally from 1996 to 2009.[33] The environmental impact is determined by the Environmental Impact Quotient (EIQ), an indicator of a wide range of environmental impacts including the amount and toxicity of the pesticides used, leaching, run-off, and potential exposure to farm workers and consumers.

Crop	**Change in Herbicide Use (million kg)**	**Change in Herbicide Use on HR crops (%)**	**Change in Environmental Impact (%)**
HR soybeans	-40.9	-2.2	-16.0
HR corn	-140.3	-9.2	-10.5
HR cotton	-8.9	-4.0	-6.9
HR canola	-14.0	-16.2	-23.2

Table 6. Summary of weed efficacy and resistance status for key herbicide modes of action likely to be used with existing and future herbicide-resistant crops.[3]

	Glyphosate	Glufosinate	ALS inhibitors	Synthetic auxins	HPPD inhibitors	ACCase inhibitors
Weed Genus	**Control Rating (0-10) and Resistance status**[1,2]					
Dicotyledons						
Chenopodium	8R	8	7R	9R	9	0
Amaranthus	9R	8	9R	9R	9R	0
Abutilon	8	8	8-9	8	9	0
Xanthium	9	9	9R	9	8	0
Ambrosia	7-8R	8-9	7-8R	9	7-8	0
Conyza	7-8R	8	7R	8	8	0
Ipomoea	7	8	7	9	7	0
Kochia	9R	8	9R	9R	7	0
Monocotyledons						
Setaria	9-10	8-9	8-9R	0	4-8	9R
Sorghum	9-10R	6-9	8-10R	0	0-8	9R
Digitaria	9	8	9R	0	7	9R
Echinochloa	9	9	9R	0	7	9R
Panicum	9	8	8	0	5	9R
Lolium	9R	8R	8R	0	3	9R
Zea (feral crop)	9R	7R	8R	0	0	9R

[1] Weed control ratings are summarized from U.S. extension guides with 0 being lowest and 10 being the highest level of control and represent the highest observed for any herbicide in that class.

[2] An R next to herbicide efficacy rating indicates that the genus has evolved resistance to that herbicide class (Heap 2011).

Table 7. Publicly announced transgenic multiple herbicide-resistant crops.

Herbicide types	**Crops**
Glyphosate and glufosinate	Soybeans, corn and cotton
Glyphosate and ALS inhibitors	Soybeans and corn
Glyphosate, glufosinate and 2,4-D analogs	Soybeans and cotton
Glyphosate, glufosinate and dicamba	Soybeans and cotton
Glyphosate, glufosinate and HPPD inhibitors	Soybeans and cotton
Glyphosate, glufosinate, 2,4-D and ACCase inhibitors	Corn

Table 8. Publicly disclosed experimental herbicide resistance traits.

Herbicide/herbicide class	Characteristics
Glyphosate	Improved detoxification
	More resistant target site
Dicamba	Metabolic degradation
2,4-D	Metabolic degradation
ACCase inhibitors	Metabolic degradation
ALS inhibitors	Various resistant ALS target sites
HPPD inhibitors	Target site resistance, over-expression, alternate pathway, and/or pathway flux
PPO inhibitors	Resistant PPO target site
Multiple herbicide classes	GST-based metabolism
	P450-based metabolism

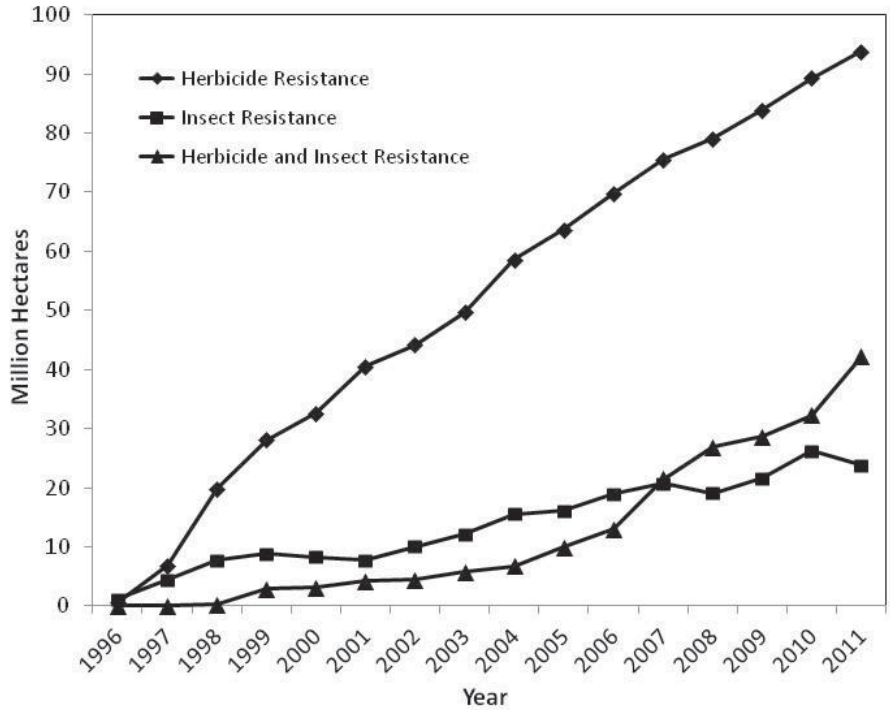
Table 9. Twelve best management practices endorsed by the Weed Science Society of America to reduce the threat of herbicide-resistant weeds to agricultural productivity.[65]

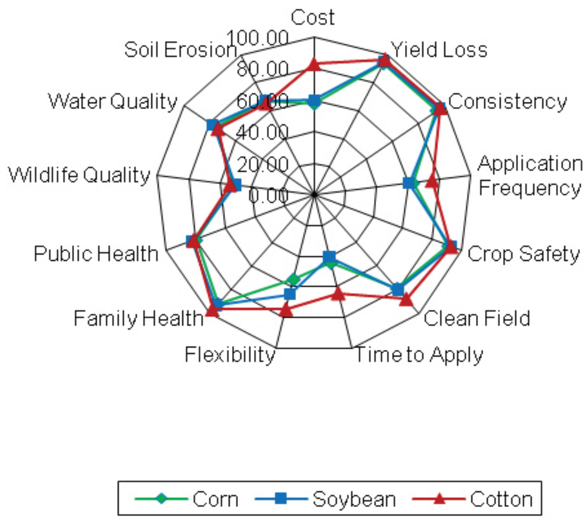
1. Understand the biology of the weeds present.
2. Use a diversified approach to weed management focused on preventing weed seed production and reducing the number of weed seeds in the soil seedbank.
3. Plant into weed-free fields and then keep fields as weed free as possible.
4. Plant weed-free crop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

FIGURE LEGENDS

Figure 1. Adoption of herbicide-resistant and insect-resistant crops globally (reproduced with permission).[10]

Figure 2. Percent of 1,176 corn, soybean and cotton growers reporting various glyphosate-resistant crop characteristics that are very important (used with permission).[39]


Herbicide Resistance
Insect Resistance
Herbicide and Insect Resistance
Million Hectares
Year
100
90
80
70
60
50
40
30
20
10
0
1996
1997
1998
1999
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011


Cost
Yield Loss
Consistency
Application Frequency
Crop Safety
Clean Field
Time to Apply
Flexibility
Family Health
Public Health
Wildlife Quality
Water Quality
Soil Erosion
100.00
80.00
60.00
40.00
20.00
0.00
Corn
Soybean
Cotton