(wileyonlinelibrary.com) DOI 10.1002/ps.3808

Global Herbicide Resistance Challenge

Agricultural productivity and sustainability, especially for the major field grain crops (wheat, rice, maize, soybean, canola) is essential to feed our exploding global human population. Only grains can be stored and globally transported at quantities that satisfy world food needs. Of the challenges to world food security, crop-infesting weeds are the biggest biotic threat. Crop weeds infest almost every crop field almost every year and they must be controlled to protect current and future harvests. For the past 50 years, chemical herbicides have made a major contribution to world food supply by reliably and economically controlling weeds in global crops. However, the many advantages of herbicides have resulted in over-reliance on herbicide technology in field crops and many other crops and situations. Herbicide selection persistently applied to huge weed populations over vast areas without diversity has inevitably resulted in the evolution of herbicide-resistant weed populations. Indeed, weed herbicide resistance evolution is a stark example of rapid evolution, with major negative consequences. Now, herbicide-resistant weeds, particularly in major field crops, are a widespread problem and a significant challenge to global food security.

To address the looming herbicide resistant weed issues the Global Herbicide Resistance Challenge Conference was held in Perth, Australia in February 2013. This conference considered many of the challenges we face in the fight against herbicide resistance in crops and weeds across the globe. Contributions ranged from understanding the exquisite details of the ways in which subtle single nucleotide mutations can endow herbicide resistance, through to practical field methods by which herbicide resistance can be managed and minimised. Key presentations delivered at this conference were video-recorded and can be accessed at www.ahri.uwa.edu.au

This special issue of Pest Management Science embraces reviews prepared by expert keynote speakers at the Global Herbicide Resistance Challenge Conference. These reviews distil the state-of-the-art herbicide resistance knowledge and understanding for the world's most important herbicides and crops/weeds. Reviews consider the underpinning genetics and dynamics of herbicide resistance evolution as well as modelling and techniques to mitigate, manage and minimise herbicide resistance. Collectively, these reviews provide a comprehensive and timely distillation of knowledge that is essential to tactics and techniques needed in winning the battle against herbicide resistance weed evolution and securing future global food supplies in a growing world. Finally, it is hoped that readers will be stimulated to take the lessons and messages presented in this special issue to help develop diverse crop and weed control systems that deliver sustained food and fibre production in the face of major herbicide resistance challenges.

Stephen Powles
University of Western Australia

Review

Received: 21 October 2013 Revised: 26 November 2013 Accepted article published: 2 December 2013 Published online in Wiley Online Library: 15 January 2014

(wileyonlinelibrary.com) DOI 10.1002/ps.3696

Global perspective of herbicide-resistant weeds

Ian Heap*

Abstract

Two hundred and twenty weed species have evolved resistance to one or more herbicides, and there are now 404 unique cases (species × site of action) of herbicide-resistant weeds globally. ALS inhibitor-resistant weeds account for about a third of all cases (133/404) and are particularly troublesome in rice and cereals. Although 71 weed species have been identified with triazine resistance, their importance has dwindled with the shift towards Roundup Ready® crops in the USA and the reduction of triazine usage in Europe. Forty-three grasses have evolved resistance to ACCase inhibitors, with the most serious cases being *Avena* spp., *Lolium* spp., *Phalaris* spp., *Setaria* spp. and *Alopecurus myosuroides*, infesting more than 25 million hectares of cereal production globally. Of the 24 weed species with glyphosate resistance, 16 have been found in Roundup Ready® cropping systems. Although *Conyza canadensis* is the most widespread glyphosate-resistant weed, *Amaranthus palmeri* and *Amaranthus tuberculartus* are the two most economically important glyphosate-resistant weeds because of the area they infest and the fact that these species have evolved resistance to numerous other herbicide sites of action, leaving growers with few herbicidal options for their control. The agricultural chemical industry has not brought any new herbicides with novel sites of action to market in over 30 years, making growers reliant on using existing herbicides in new ways. In addition, tougher registration and environmental regulations on herbicides have resulted in a loss of some herbicides, particularly in Europe. The lack of novel herbicide chemistries being brought to market combined with the rapid increase in multiple resistance in weeds threatens crop production worldwide.

Keywords: herbicide resistance; ALS inhibitors; ACCase inhibitors; glyphosate; survey; integrated weed management

1 INTRODUCTION

Herbicides have revolutionized weed control over the last 65 years, contributing significantly to increased crop yields over this period. Herbicides provide effective and economical weed control and are the primary method of weed control in agronomic crops, replacing manual labor, animals and mechanical weed control. As with all technologies, herbicides also face some challenges including safety and environmental issues, and the evolution of herbicide-resistant weeds. Insecticide resistance was first reported in 1908, and fungicide resistance in 1940, which led scientists to predict that herbicide-resistant weeds would appear shortly after their introduction in the mid-1940s.[1] However, weeds have much longer life cycles than insects or fungi and the first well-documented case of herbicide resistance, triazine-resistant *Senecio vulgaris*, did not appear until 1968.[2] Since then, there has been a steady increase in the occurrence and distribution of herbicide-resistant weeds; this review aims to document the current status of herbicide resistance globally.

2 DEFINITIONS

Herbicide resistance is a normal and predictable result of natural selection. Rare mutations that confer herbicide resistance to individuals within a weed population exist prior to herbicide treatment. They are enriched through repeated herbicide use to a point where the weed population is no longer controlled by the herbicide at the recommended rate under agricultural conditions.

There are five primary mechanisms of herbicide resistance.

1. Target-site resistance results from mutations that alter the herbicide binding site (often within an enzyme) preventing or reducing the ability of a herbicide to bind to the target site. Resistance to ALS inhibitor, ACCase inhibitor, dinitroanaline and triazine herbicides are often due to target-site resistance.
2. Enhanced metabolism is the increased ability of a plant to metabolize (degrade) a herbicide before it kills the plant.
3. Decreased absorption and/or translocation can result in sufficient restriction of herbicide movement to the site of action enabling the plant to survive.
4. Sequestration of a herbicide onto cell walls or into vacuoles reduces the concentration of herbicide that reaches the site of action and can result in resistance.
5. Gene amplification/overexpression increases the production of the target enzyme which necessitates a higher concentration of herbicide to reach the target site to inhibit the enzyme and cause death.

Cross-resistance occurs when a single resistance mechanism confers resistance to more than one herbicide. Target-site cross-resistance is the most common type, and is the result of an altered

* Correspondence to: Ian Heap, Director of the International Survey of Herbicide-Resistant Weeds, PO Box 1365, Corvallis, OR 97339, USA. E-mail: IanHeap@weedscience.org

Director of the International Survey of Herbicide-Resistant Weeds, PO Box 1365, Corvallis, OR 97339, USA

target site (enzyme) conferring resistance to other herbicides that inhibit the same enzyme.

Multiple resistance occurs when more than one resistance mechanism occurs within an individual plant. Multiple resistance is usually the result of sequential selection of resistance mechanisms by herbicides with different sites of action or through accumulation of resistance genes via pollen flow.[3]

3 WORLDWIDE OCCURRENCE OF HERBICIDE-RESISTANT WEEDS

The International Survey of Herbicide-Resistant Weeds (http://www.weedscience.org) records the occurrence and impact of herbicide-resistant weeds worldwide and is the source of the majority of data presented here.[4] The site has 1721 registered users and 413 scientists from 61 countries have contributed data to the website since it went live in 1993. Those regions/countries/researchers most vigilant in finding and reporting weed resistance to herbicides are well represented. But undoubtedly the survey under-represents the actual occurrence of herbicide-resistant weeds in many regions. There are currently 404 unique (weed species × herbicide site of action) cases of herbicide resistance recorded in the survey and ∼ 11 new cases are reported annually (Fig. 1). Resistance to one or more herbicide sites of action has been identified in 220 weed species (130 dicots and 90 monocots) and weeds have evolved resistance to 21 of the 25 known herbicide sites of action (Table 1 and Fig. 1).

Herbicide-resistant weeds have been reported in 66 crops in 61 countries. The USA has the greatest number of herbicide-resistant weeds (144) followed by Australia (62), Canada (59) and France (35) (Table 2). Up until the 1990s, herbicide resistance was primarily a problem of developed countries because they relied upon herbicides for weed control, whereas developing countries still relied upon hand-weeding as their primary method of weed control. In the last two decades, this has changed and now countries like China and Brazil rely primarily upon herbicides for weed control and are reporting a rapid increase in the incidence of herbicide resistance. China is ranked fifth in the world with 34 cases and Brazil is ranked eighth with 31 cases (Table 2). Figure 2 shows the number of weed species that have evolved resistance in various cropping and non-crop situations. Wheat and corn have selected 59 and 58 resistant weed species, respectively, followed by soybean (46) and rice (39). This is not surprising as these crops account for the highest herbicide usage over the largest area for the longest time. Next are roadsides (31 species) and orchards (27 species) where high selection pressure for resistance occurs because repeated applications (> 5) over a season are often used to achieve bare ground.

4 PROPENSITY OF HERBICIDES TO SELECT RESISTANCE

It is clear from Table 1 and Fig. 3 that some herbicide sites of action are more prone to resistance than others. There are several reasons for the different rates of selection of herbicide-resistant weeds by herbicides with different sites of action. Selection of resistance is primarily dependent on the characteristics of the weed species treated (fecundity, breeding system, generation time, fitness in the absence of herbicide, seed longevity, gene flow by pollen and seed, and seed dormancy), the frequency, number, dominance and fitness of genes that confer resistance to each herbicide

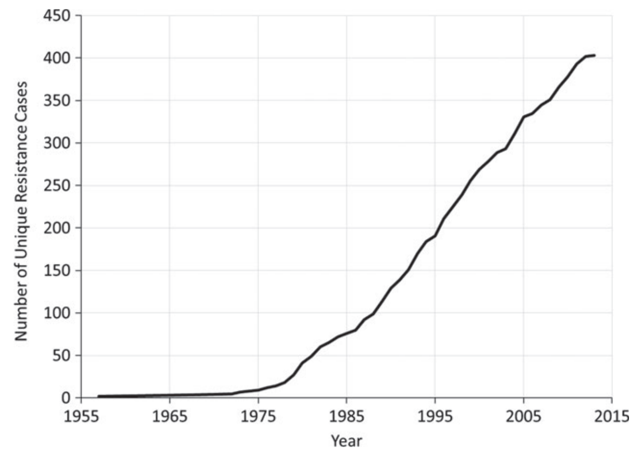

Figure 1. Chronological increase in the number of herbicide-resistant weeds worldwide. Reproduced from Heap IM, *International Survey of Herbicide-Resistant Weeds* (2013). http://www.weedscience.org.

site of action, and the number of individuals treated over time. Resistance is a numbers game, and the importance of the number of individuals treated over time should not be underestimated. If a herbicide is used infrequently on a small area, and only targets a few species it is unlikely to select many resistant weeds even if the initial mutation frequency was high (e.g. difenzoquat). Conversely, if the initial mutation frequency is very low for a herbicide, but it is used over a massive area, and targets most species, it is likely to select many resistant weeds (e.g. glyphosate). The worst case scenario happens when the initial mutation frequency is high, the herbicide is used on a massive area, and the herbicide targets many species (ALS inhibitors).

The herbicide groups that have selected the most herbicide-resistant weeds are ALS inhibitors (B/2), photosystem II inhibitors (C1/5), ACCase inhibitors (A/1), synthetic auxins (O/4), bipyridilliums (D/22) and glycines (G/9) (Table 1).

4.1 ALS inhibitors (B/2)

There are 54 registered ALS inhibitor herbicides globally, more than double the number of any other group, and they account for more than one sixth (54/302) of all registered herbicides (Fig. 4). ALS inhibitor herbicides have been used for over 30 years in all major crops and on most weed species. With the exception of synthetic auxins, more hectares have been treated with ALS inhibitors than any other herbicide group. In addition, the enzyme acetolactate synthase (the site of action of ALS inhibitor herbicides) is particularly vulnerable to gene point mutations that confer resistance to ALS inhibitor herbicides (Fig. 5). Given these facts, it is not surprising that ALS inhibitor herbicides have selected about a third of all herbicide-resistant weeds (133/404), more than any other herbicide group. The first reported case of ALS inhibitor-resistance was metabolic resistance to chlorsulfuron in *Lolium rigidum* in Australia in 1986,[5,6] followed by target site resistance in 1987 in *Lactuca serriola* in the USA.[7] The most important cases of ALS inhibitor-resistance are now in rice and wheat because many of the ALS inhibitor-resistant weeds in corn, soybean and cotton can be controlled by glyphosate in Roundup Ready® crops. Common ALS inhibitor-resistant weeds in rice are *Cyperus difformis*, *Echinochloa crus-galli*, *Sagittaria montevidensis* and *Alisma plantago-aquatica*, and common ALS inhibitor-resistant weeds in wheat are *Lolium* spp., *Kochia scoparia*, *Stellaria media*, *Avena fatua* and *Papaver rhoeas*.

Table 1. Occurrence of herbicide-resistant weed species to herbicide sites of action

Herbicide site of action	HRAC/WSSA[a]	Example herbicide	Dicots	Monocots	Total
ALS inhibitors	B/2	Chlorsulfuron	82	51	133
Photosystem II inhibitors	C1/5	Atrazine	49	22	71
ACCase inhibitors	A/1	Diclofop-methyl	0	43	43
Synthetic auxins	O/4	2,4-D	23	7	30
Bipyridiliums	D/22	Paraquat	18	10	28
Glycines	G/9	Glyphosate	11	13	24
Ureas and amides	C2/7	Chlorotoluron	8	15	23
Dinitroanilines and others	K1/3	Trifluralin	2	9	11
Thiocarbamates and others	N/8	Triallate	0	8	8
PPO inhibitors	E/14	Oxyfluorfen	6	0	6
Triazoles, ureas, isoxazolidiones	F3/11	Amitrole	1	4	5
Nitriles and others	C3/6	Bromoxynil	3	1	4
Chloroacetamides and others	K3/15	Butachlor	0	4	4
Carotenoid biosynthesis inhibitors	F1/12	Flurtamone	2	1	3
4-HPPD inhibitors	H/10	Isoxaflutole	2	0	2
Glutamine synthase inhibitors	Z/25	Glufosinate	0	2	2
Arylaminopropionic acids	Z/27	Flamprop-methyl	0	2	2
Unknown	F2/27	(chloro) - flurenol	0	2	2
Mitosis inhibitors	K2/23	Propham	0	1	1
Cellulose inhibitors	L/27	Dichlobenil	0	1	1
Organoarsenicals	Z/17	MSMA	1	0	1
Totals			208	196	404

Reproduced from Heap IM, *International Survey of Herbicide-Resistant Weeds* (2013). http://www.weedscience.org
[a] HRAC, herbicide grouping system developed by the Herbicide Resistance Action Committee; WSSA, Herbicide grouping system developed by the Weed Science Society of America.

Some cases of ALS inhibitor-resistant weeds in corn, soybean and cotton are becoming more important, particularly in *Amaranthus* spp. and *Ambrosia* spp., because these species now have glyphosate resistance in addition to ALS inhibitor- and other herbicide resistance.

4.2 Photosystem II inhibitors (C1/5)

There are 26 photosystem (PS)II inhibitor herbicides (triazines, triazinones, triazolinone, uracils, pyridazinones and phenyl-carbamates) that have been commercialized globally (Fig. 4), the most prominent being atrazine which provided the backbone of weed control in corn in the USA and Europe in the 1960s to 1990s. The discovery of simazine-resistant *Senecio vulgaris* in 1968 in a nursery in Washington State alerted weed scientists to the problem of herbicide resistance and sparked the discovery of triazine-resistant weeds in corn in the USA and Europe.[2] PSII inhibitor herbicides are prone to resistance because the initial frequency of resistant individuals is relatively high and they have been used over large areas for many years. Seventy-one species have evolved resistance to the PSII inhibitors, the majority of them discovered prior to the 1990s when alternative herbicides (ALS inhibitors, ACCase inhibitors and glyphosate) were introduced to control them. *Amaranthus*, *Chenopodium*, *Echinochloa* and *Solanum* spp. are particularly prone to the evolution of PSII inhibitor-resistance and infest many millions of hectares of corn in the USA and Europe. Most cases of PSII inhibitor-resistance are due to a mutation (Ser264 to Gly) in the *psbA* gene, which codes for the DI protein and reduces the binding of triazine herbicides to the thylakoid membrane in chloroplasts. However, some cases of enhanced metabolism have also been identified,[8] and metabolic resistance to triazine herbicides is widespread (up to 50% of triazine-resistant populations tested) in *Amaranthus tuberculatus* (Mike Owens, pers. commun.). Many PSII inhibitor-resistant weeds have been shown to have significantly reduced fitness compared with their susceptible counterparts in the absence of herbicide.

4.3 ACCase inhibitors (A/1)

Twenty ACCase inhibitor herbicides (Fig. 4) have been commercialized and they have been used in a variety of crops since their introduction in 1974. A total of 43 grasses have evolved resistance to ACCase inhibitors (Table 1). For many years, wheat production relied upon ACCase inhibitor herbicides (diclofop, fenoxaprop, clodinafop, etc.) for grass control over a massive area which resulted in the selection of 19 ACCase inhibitor-resistant grasses. There are now more than 25 million hectares of cereal crops infested with ACCase inhibitor grasses, the worst being *Avena*, *Lolium*, *Alopecurus*, *Phalaris* and *Setaria* species. There are 11 known target-site amino acid substitutions in the acetyl CoA carboxylase gene which result in an altered, insensitive form of the ACCase enzyme.[9–12] Metabolic resistance (via cytochrome P450) to ACCase inhibitors is also prevalent in *Lolium rigidum* and *Alopecurus myosuroides*.

4.4 Synthetic auxins (O/4)

Synthetic auxins were first introduced in the 1940s and are among the most widely used herbicides today. There are 22 commercialized synthetic auxin herbicides belonging to five chemical classes (Fig. 4). Thirty weed species have evolved resistance to synthetic auxins, however, few of these are widespread or of significant economic importance (Table 1). The four most widespread cases are not typical of synthetic auxin resistance as they are grasses with resistance to quinclorac (an unusual synthetic auxin with a novel mechanism of action on grasses). Only 2 of the other 26 cases, dicamba-resistant *Kochia scoparia* in the USA and 2,4-D-resistant *Raphanus raphanistrum* in Australia, infest more than 1000 ha. Compared with ALS inhibitor, PSII inhibitor, ACCase

Table 2. The number of herbicide-resistant weeds in each of 61 countries

No.	Country	No. of resistant weeds	No.	Country	No. of resistant weeds
1	United States	144	31	Yugoslavia	6
2	Australia	62	32	Austria	5
3	Canada	59	33	Costa Rica	5
4	France	35	34	Mexico	5
5	China	34	35	Norway	5
6	Germany	33	36	Thailand	5
7	Spain	33	37	Bulgaria	4
8	Brazil	31	38	India	3
9	Israel	29	39	Philippines	3
10	Italy	29	40	Portugal	3
11	United Kingdom	24	41	Cyprus	2
12	Belgium	18	42	Paraguay	2
13	Japan	18	43	Sri Lanka	2
14	Czech Republic	17	44	Sweden	2
15	Malaysia	17	45	Ecuador	1
16	Chile	16	46	Egypt	1
17	New Zealand	15	47	El Salvador	1
18	Turkey	15	48	Ethiopia	1
19	Poland	14	49	Fiji	1
20	South Africa	14	50	Guatemala	1
21	Switzerland	14	51	Honduras	1
22	South Korea	12	52	Hungary	1
23	Argentina	11	53	Indonesia	1
24	Iran	11	54	Ireland	1
25	Greece	10	55	Kenya	1
26	Venezuela	9	56	Nicaragua	1
27	Denmark	8	57	Panama	1
28	Bolivia	7	58	Saudi Arabia	1
29	Netherlands	7	59	Slovenia	1
30	Colombia	6	60	Taiwan	1
			61	Tunisia	1

Reproduced from Heap IM, *International Survey of Herbicide-Resistant Weeds* (2013). http://www.weedscience.org

inhibitor and glyphosate-resistant weeds, the synthetic auxins have very little economic impact and remain one of the least prone herbicide groups for the selection of resistance.

4.5 Bipyridilliums (D/22)

Paraquat and diquat have been used extensively since the 1960s and have selected 28 resistant weeds (Table 1). Paraquat and diquat are not readily metabolized, and no cases of target site resistance have been identified, so it is somewhat surprising that so many weeds have evolved resistance to the bipyridilliums. Reduced translocation and sequestration are the primary ways in which weeds have evolved resistance to the bipyridilliums. Bipyridillium-resistant weeds first appeared in the 1980s and intensive research was conducted on them at that time, however, they have not caused widespread economic damage and research on them has declined since then. *Conyza* spp. (*C. bonariensis*, *C. canadensis* and *C. sumatrensis*) and *Solanum* spp. (*S. americanum*, *S. nigrum* and *S. ptycanthum*) are particularly prone to evolving bipyridillium resistance.

4.6 Glyphosate-resistant weeds

Glyphosate has been commercially available since 1974 and is the most valuable herbicide ever discovered. Initially the cost of glyphosate restricted it to high-value situations, which included orchards, and non-crop sites. As the price decreased, glyphosate was used extensively in zero-tillage operations to control weeds prior to planting, and in fallow to kill weeds and preserve soil moisture. With the introduction of Roundup Ready® crops in 1996 (soybean), glyphosate usage increased dramatically and was being used selectively in agronomic crops for the first time. The first glyphosate-resistant weeds were found in orchards (*Lolium rigidum* in 1996 and *Eleusine indica* in 1997; Table 3 6) after repeated applications (5 to 10) per year for more than 15 years. Unlike the ALS inhibitors, ACCase inhibitors or triazines, there are few target-site mutations that confer resistance to glyphosate and it is considered a low-risk herbicide for selecting resistance. Despite this, the risk of selecting glyphosate-resistant weeds is significant for two reasons, the first being that glyphosate is effective on almost all weeds (most other herbicides control fewer than half of the weed species) which increases the likelihood of selecting resistance, and the second is the massive area treated with glyphosate in Roundup Ready® crops. Twenty-four weed species have evolved resistance to glyphosate in 21 countries (Table 3 and Fig.). Glyphosate-resistant weeds present the greatest problems in Roundup Ready® crops and to a lesser extent in orchards. Sixteen species have been identified with glyphosate resistance in Roundup Ready® cropping systems, twelve in orchards, nine in cereals, six on roadsides and industrial sites and one in turf. Many of the glyphosate-resistant weeds have been identified in several different situations, for instance glyphosate-resistant *Conyza canadensis* has been identified in alfalfa, corn, cotton, soybean, rice, wheat, fruit, grapes, nurseries, orchards, railways, roadsides and along fence lines (Table 3). Because *Conyza canadensis* has such an effective windborne dispersal mechanism it is likely that resistance has evolved under heavy glyphosate usage (Roundup Ready® crops, roadsides, orchards, railways) and spread to other situations. The USA reports 14 species that have evolved resistance to glyphosate in 32 of the 50 States. Although *Conyza canadensis* is the most widespread glyphosate-resistant weed it can be readily controlled with inexpensive alternatives so it does not present the greatest threat. Glyphosate-resistant *Amaranthus palmeri* in the southern USA and *Amaranthus tuberculatus* in the Mid-West have the greatest economic impact of all glyphosate-resistant weeds because they are widespread in Roundup Ready® crops and they have already evolved resistance to other herbicides. Other economically important glyphosate-resistant weeds include *Ambrosia* spp. and *Kochia scoparia* in the USA, *Digitaria insularis* and *Sorghum halepense* in South America and *Lolium rigidum* in Australia.

5 WORST HERBICIDE-RESISTANT WEEDS

Weed species from the genera *Lolium*, *Amaranthus*, *Conyza* and *Echinochloa* are some of the worst herbicide-resistant weeds globally. Weeds in these genera have a high degree of genetic diversity and have a proven capability to evolve resistance to a wide range of herbicide sites of action (Fig. 7). In the last 10 years, weed scientists have focused on glyphosate-resistant weeds, however, ALS inhibitor and ACCase inhibitor-resistant weeds still have a greater economic impact than glyphosate-resistant weeds. *Lolium rigidum* is the world's worst herbicide-resistant weed, having evolved resistance to 11 herbicide sites of action (Fig. 7), in 12 countries, and over more than 2 million hectares. *Lolium rigidum* has a high degree of genetic

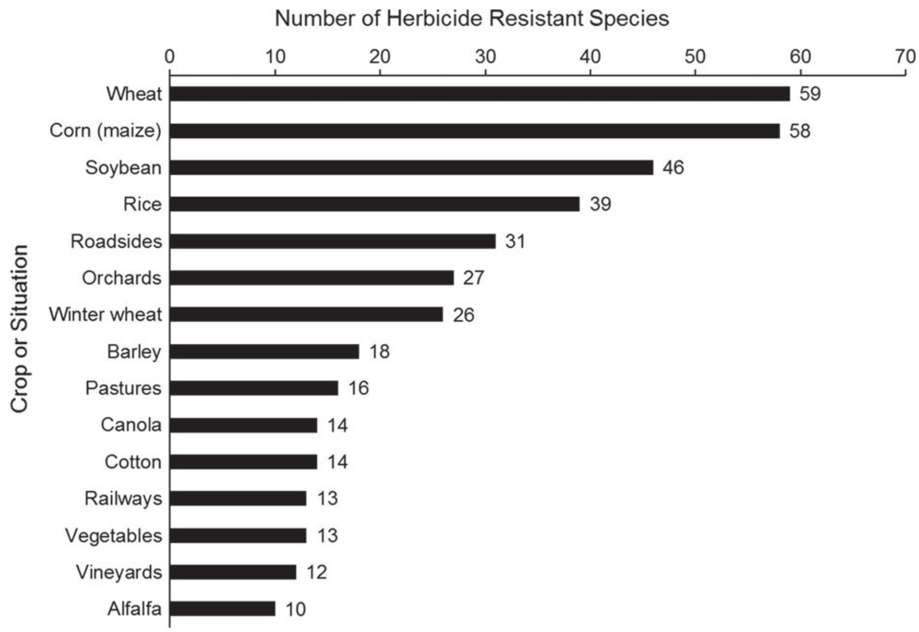

Figure 2. Number of herbicide-resistant species by crop or situation. Reproduced from Heap IM, *International Survey of Herbicide-Resistant Weeds* (2013). http://www.weedscience.org

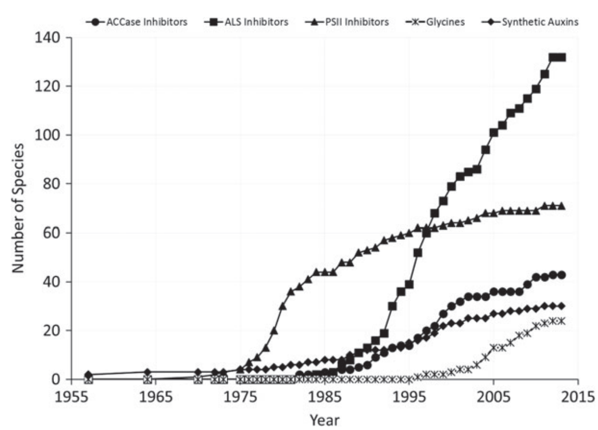

Figure 3. Chronological increase in the number of herbicide-resistant weeds for several herbicide classes. Reproduced from Heap IM, *International Survey of Herbicide-Resistant Weeds* (2013). http://www.weedscience.org

variability and rapidly evolves resistance to almost any herbicide that it is exposed to. It is particularly troublesome because it often develops cross-resistance (both target site and non-target site) and rapidly evolves multiple resistance to a wide array of herbicides through outcrossing. The closely related species *Lolium multiflorum* is also very prone to evolving multiple resistance. *Avena fatua* is the world's second worst herbicide-resistant weed because it is ubiquitous in cereal-growing regions and has evolved resistance to herbicides used in cereals (primarily to the ACCase inhibitor and ALS inhibitor herbicides, but also to three other sites of action) in 14 countries on more than 5 million hectares. *Avena fatua* does not evolve multiple resistance as quickly as *Lolium rigidum* because it is a predominately selfing species (∼5% outcrossing) and produces fewer seeds per plant than *Lolium rigidum*. However, it is more widespread in cereals around the world than *Lolium rigidum* and herbicide resistance in *Avena fatua* probably has a greater economic impact than any other herbicide-resistant weed. Other herbicide-resistant weeds that cause major economic damage are, *Echinochloa crus-galli* (19 countries, 8 sites of action), *Conyza canadensis* (15 countries, 5 sites of action), *Echinochloa colona* (11 countries, 6 sites of action), *Alopecurus myosuroides* (14 countries, 6 sites of action), *Eleusine indica* (8 countries, 7 sites of action), *Chenopodium album* (14 countries, 4 sites of action), *Kochia scoparia* (3 countries, 4 sites of action), *Amaranthus retroflexus* (15 countries, 4 sites of action), *Amaranthus tuberculatus* (2 countries, 6 sites of action) and *Amaranthus palmeri* (1 country, 6 sites of action).

6 DISCUSSION AND CONCLUSIONS

The fight against herbicide-resistant weeds is now at a critical point. For more than 40 years farmers have coped with herbicide-resistant weeds because the industry provided them with a relatively steady stream of new herbicides with novel herbicide sites of action. This is no longer the case. Industry has not brought a novel herbicide to market in over 30 years (Fig. 8), and the rapid rise of multiple resistance in weeds leaves many farmers with increasingly intractable weed control problems. Figure 9 presents the increase in multiple resistance in weed biotypes. Multiple resistance in weeds was not really an issue until the 1990s, but has rapidly increased since then. There are now 65 unique cases of multiple resistance in weeds, the majority (46) being populations that have resistance to two sites of action (Fig. 9). Twelve biotypes have resistance to three herbicide sites of action, three biotypes have resistance to four sites of action, and in one instance, a *Lolium rigidum* population was found to have resistance to seven herbicide sites of action. Multiple resistance in *Amaranthus palmeri* and *Amaranthus tubercultartus* is of particular concern in Roundup Ready® crops in the USA. Populations of *Amaranthus palmeri* with resistance to PSII inhibitors, ALS inhibitors, 4-HPPD inhibitors and glyphosate have been identified in southern states and populations of *Amaranthus tubercultartus* with resistance to PSII inhibitors, ALS inhibitors, PPO inhibitors, 4-HPPD inhibitors and glyphosate have been identified in the Mid-West. Globally, multiple resistance

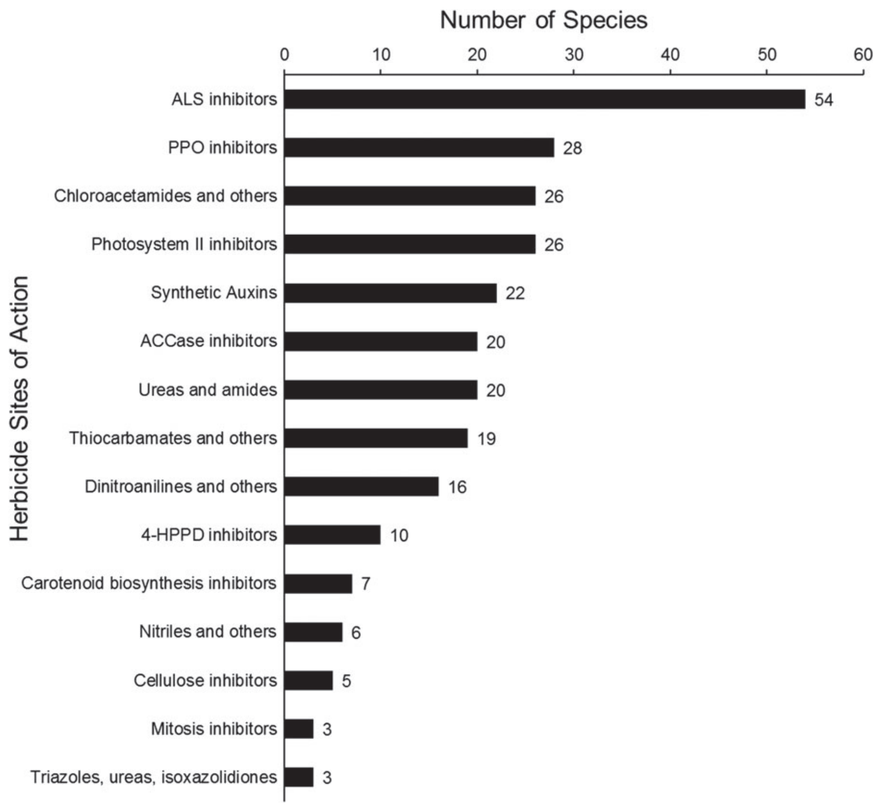

Figure 4. Number of registered herbicides for each of the major herbicide sites of action. Reproduced from Heap IM, *International Survey of Herbicide-Resistant Weeds* (2013). http://www.weedscience.org

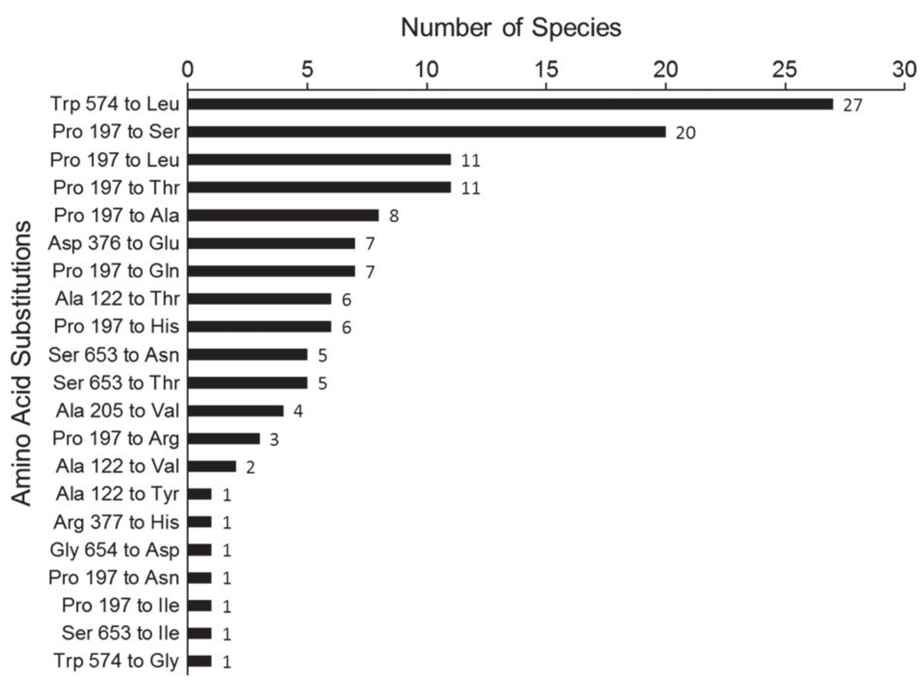

Figure 5. Number of ALS inhibitor-resistant species by amino acid substitution. Reproduced from Heap IM, *International Survey of Herbicide-Resistant Weeds* (2013). http://www.weedscience.org

Table 3. The occurrence of glyphosate-resistant weeds worldwide

No.	Species	First year	Situation(s)	Country and year[a]
1	*Amaranthus palmeri*	2005	Cotton, corn, soybean, alfalfa, orchards, roadsides, grapes, fence lines	USA (2005; GA, NC, AR, NM, AL, MS, MO, TN, IL, OH, KS, LA, MI, VA, AC, CA, DE)
2	*Amarnathus spinosus*	2012	Cotton	USA (MS)
3	*Amaranthus tuberculatus*	2005	Corn (maize), cotton, soybean, sugar beets	USA (2005; MO, IL, KS, MN, OH, IN, IA, MS, ND, SD, OK, TN, NE)
4	*Ambrosia artemisiifolia*	2004	Corn (maize), soybean	USA (2004; AR, MO, OH, IN, KS, ND, SD, MN), Canada (2012; ON)
5	*Ambrosia trifida*	2004	Corn (maize), cotton, Soybean	USA (2004; OH, AR, IN, KS, MN, TN, IA, MO, MS, NE, WI), Canada (2008; ON)
6	*Bromus diandrus*	2011	Fence lines	Australia (2011; SA)
7	*Chloris truncata*	2010	Crop land – cereals	Australia (2010; NSW)
8	*Conyza bonariensis*	2003	Coffee, corn, fruit, grapes, industrial sites, orchards, roadsides, soybean, wheat	South Africa (2003), Spain (2004), Brazil (2005), Israel (2005), Columbia (2006), USA (2007; CA), Greece (2010), Portugal (2010), Australia (2010; NSW, QLD, SA)
9	*Conyza canadensis*	2000	Alfalfa, corn, cotton, crop land, fence lines, fruit, grapes, nurseries, orchards, railways, rice, roadsides, soybean, wheat	USA (2000; DE, KY, TN, IN, MD, MO, NJ, OH, AR, MS, NC, PA, CA, IL, KS, VA, NE, MI, OK, SD, IA), Brazil (2005), China (2006), Spain (2006), Czech Republic (2007), Canada (2010; ON), Poland (2010), Italy (2011), Greece (2012)
10	*Conyza sumatrensis*	2009	Corn (maize), grapes, orchards, soybean	Spain (2009), Brazil (2010), Greece (2012)
11	*Cynodon hirsutus*	2008	Soybean	Argentina (2008)
12	*Digitaria insularis*	2005	Corn (maize), cotton, soybean, sunflower	Paraguay (2005), Brazil (2008)
13	*Echinochloa colona*	2007	Corn (maize), cropland, fence lines, grapes, orchards, roadsides, soybean	Australia (2007; NSW, QLD, WA), USA (2008; CA), Argentina (2009)
14	*Eleusine indica*	1997	Coffee, cotton, fallow, orchards, soybean	Malaysia (1997), Colombia (2006), China (2010), USA (2010; MS, TN)
15	*Kochia scoparia*	2007	Cereals, corn, cotton, crop land, soybean	USA (2007; KS, SD, NE, CO, MT, ND), Canada (2012; AB)
16	*Leptochloa virgata*	2010	Orchards	Mexico (2010)
17	*Lolium multiflorum*	2001	Barley, cereals, corn, cotton, crop land, fruit, grapes, lupins, orchards, roadsides, soybean, wheat	Chile (2001), Brazil (2003), USA (2004 - OR, MI, AR), Spain (2006), Argentina (2007)
18	*Lolium perenne*	2008	Barley, cropland, grapes, soybean, wheat	Argentina (2008), New Zealand (2012)
19	*Lolium rigidum*	1996	Apples, almonds, asparagus, canola, fence lines, grapes, orchards, railways, roadsides, wheat	Australia (1996; VIC, NSW, SA, WA) USA (1998; CA), South Africa (2001), France (2005), Spain (2006), Israel (2007), Italy (2007)
20	*Parthenium hysterophorus*	2004	Fruit	Colombia (2004)
21	*Plantago lanceolata*	2003	Grapes, orchards	South Africa (2003)
22	*Poa annua*	2010	Golf courses, turf	USA (2010; MO, TN)
23	*Sorghum halepense*	2005	Soybean	Argentina (2005), USA (2007; AR, MS, LA)
24	*Urochloa panicoides*	2008	Sorghum, wheat	Australia (2008 NSW)

Reproduced from Heap IM, *International Survey of Herbicide-Resistant Weeds* (2013). http://www.weedscience.org
[a] States are listed in order of the first recorded case.

caused by metabolic degradation of herbicides in grasses like *Lolium rigidum*, *Alopecurus myosuroides* and *Echinochloa* spp. have already resulted in massive economic damage and are likely to rival the impact of target site resistance in the future.

Herbicide resistance is the result of evolution and herbicide-resistance management strategies aim to destabilize evolution. Evolution thrives in a static environment, if growers control weeds using the same methods year after year then weeds will evolve strategies to circumvent the control methods, no matter what they are. The most common herbicide-resistance management strategy is to rotate herbicide sites of action. Certainly this may delay the evolution of herbicide resistance in many but not all cases (non-target site resistance may continue to evolve under this strategy), however, it is a first step in a comprehensive strategy to manage resistance. There is some evidence that herbicide mixtures may be a better resistance management strategy than rotation of herbicide sites of action.[13] Unfortunately, growers are less inclined to use herbicide mixtures as a resistance-management strategy because to be effective both herbicides must target the weeds at risk of becoming resistant, which can double the cost of weed control. Herbicide-resistant crops can be a part of resistance-management strategies because they enable growers to use old herbicide chemistries in new ways, increasing the diversity of herbicide sites of action that can be used. Stacking of herbicide-resistant traits can also allow growers to employ herbicide mixtures to delay resistance. Combinations of herbicide traits that include glyphosate, glufosinate, ALS inhibitors, 4-HPPD inhibitors and synthetic auxins are likely to become common in crop cultivars.[14,15] Although herbicides are often the backbone of weed management in crop production they should not be the

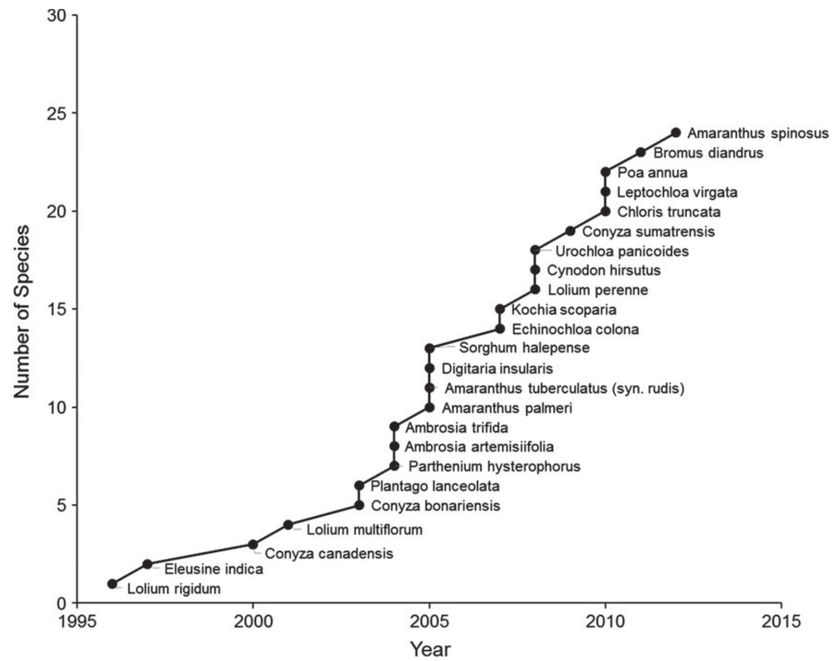

Figure 6. Chronological increase in glyphosate-resistant weeds worldwide. Reproduced from Heap IM, *International Survey of Herbicide-Resistant Weeds* (2013). http://www.weedscience.org

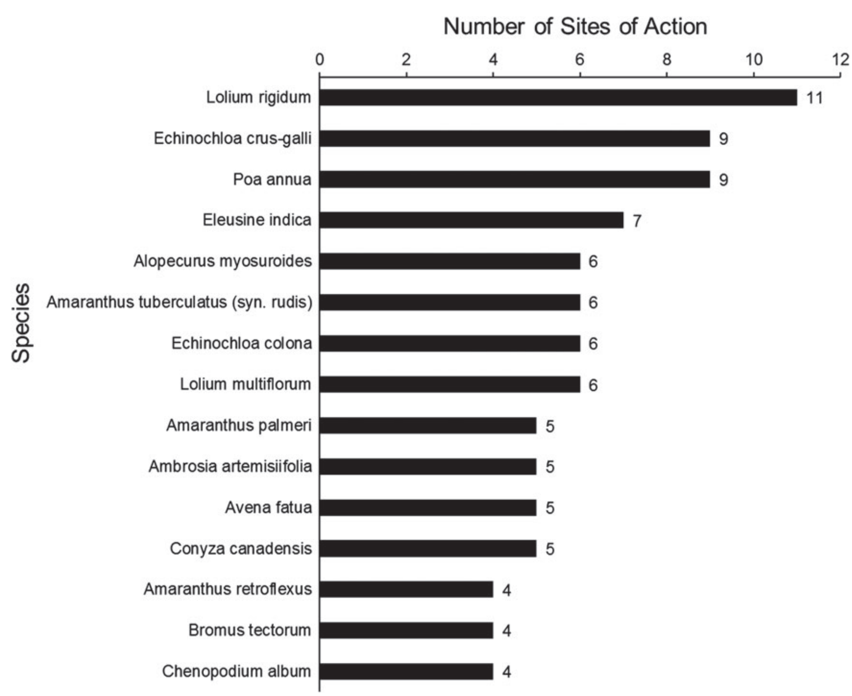

Figure 7. Top 15 weed species that have evolved resistance to multiple herbicide sites of action. Reproduced from Heap IM, *International Survey of Herbicide-Resistant Weeds* (2013). http://www.weedscience.org

only method of weed control. The best resistance-management strategies will involve the use of every available weed control tool (integrated weed management) in an effort to disrupt and destabilize weed populations to prevent them becoming a serious problem.

6.1 Weed control – past, present and future

Prior to the 1940s, farms were small, with diversified cropping systems integrated with livestock. Weed control was primarily through cultural practices, crop rotation, livestock, tillage and hand-weeding. Even so, there was significant loss to weeds. From the 1940s to mid-1990s the introduction of modern herbicides allowed growers to manage larger farms, with less diversity in cropping systems and livestock was decoupled from the cropping system. Herbicides also allowed growers to move to reduced- and no-till systems. This led to reduced erosion, better weed control, higher yields and greater profitability. Herbicide-resistant weeds appeared, but were relatively easy to control because companies

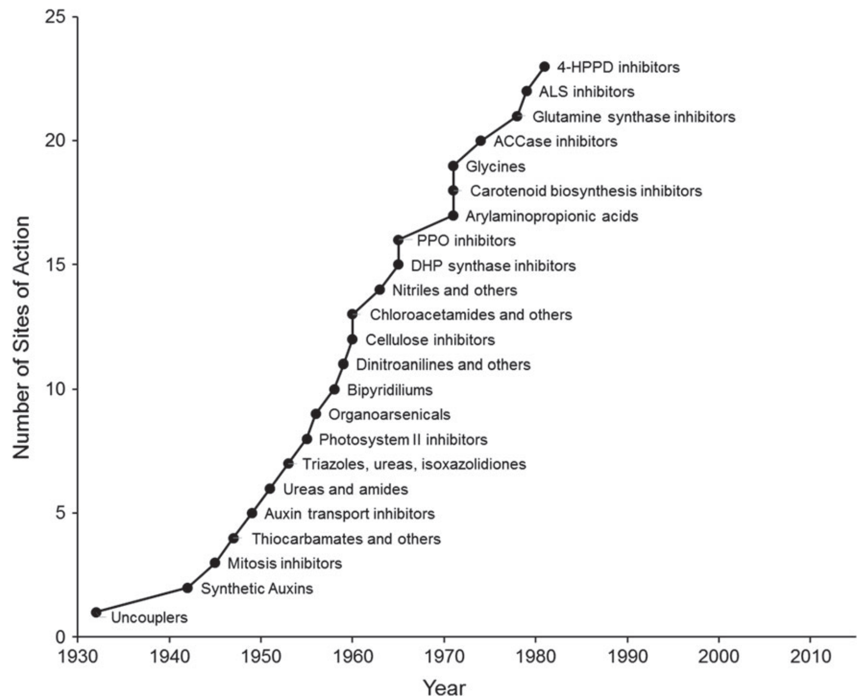

Figure 8. Chronological increase in the number of commercially available herbicide sites of action. Reproduced from Heap IM, *International Survey of Herbicide-Resistant Weeds* (2013). http://www.weedscience.org

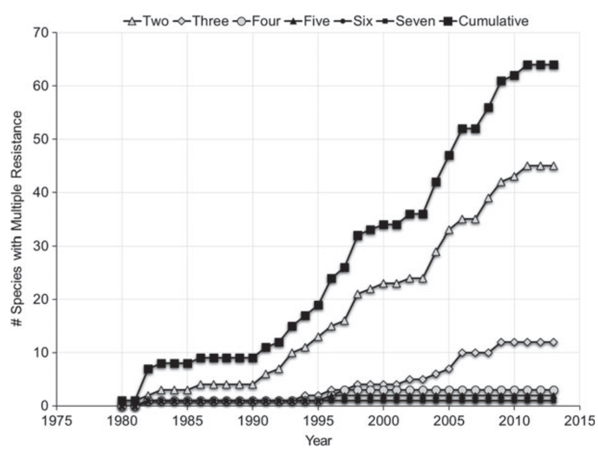

Figure 9. Number of weed populations that have multiple resistance to two or more sites of action. Reproduced from Heap IM, *International Survey of Herbicide-Resistant Weeds* (2013). http://www.weedscience.org

brought a succession of novel herbicide sites of action to market (Fig. 8). From the mid-1990s to the mid-2000s, there were less tillage and less diversity in weed control. Roundup Ready® crops were introduced and farmers began to rely upon two or three applications of glyphosate for weed control. The use of glyphosate in Roundup Ready® crops precipitated a decline in herbicide discovery, and also resulted in a generation of farmers with little knowledge of weeds and weed-control techniques. Weed control was good, yields were high and the farms were profitable. In the mid-2000s, the widespread appearance of glyphosate-resistant weeds, in particular *Conyza*, *Amaranthus* and *Ambrosia* species, in Roundup Ready® cropping systems forewarned growers that the use of glyphosate alone for weed control was not sustainable. Growers began adding more diversity in their herbicide program, primarily through the addition of pre-emergence herbicides. Multiple resistance became the biggest concern for sustained weed control in the USA. Between 2015 and 2025 multiple resistance in weeds will force changes in weed control programs. Herbicide-resistant crops with multiple stacked traits will provide some solutions, as will the introduction of a few new herbicide sites of action. Farmers will need reeducation in weed-control practices which may include diversification of cropping systems, increased tillage, cover crops, stale seed beds, zero tolerance for weed escapes in some crops, and most importantly, the adoption of herbicide-resistance management strategies. All of these are steps toward integrated weed management. Beyond 2025, there will be an increase in the discovery of new herbicide sites of action, possibly led by China, herbicide-resistant crop traits will continue to expand, there will be a greater diversity in cropping systems, and true integrated weed-management systems will develop. Herbicides will probably remain the backbone of weed-control programs for many years to come, however eventually they will be superseded by a new technology, possibly cheap robotic weeders, nano-machines or genetically engineered bioherbicides.

ACKNOWLEDGEMENTS

The International Survey of Herbicide-Resistant Weeds is funded and supported by the Herbicide Resistance Action Committee (HRAC). I would also like to thank all of the scientists that have contributed data to the survey.

REFERENCES

1 Harper JC, The evolution of weeds in relation to herbicides. *Proc Br Weed Control Conf* **3**:179–188 (1956).
2 Ryan GF, Resistance of common groundsel to simazine and atrazine. *Weed Sci* **18**:614–616 (1970).
3 Heap IM and LeBarron H, Introduction and overview of resistance, in *Herbicide Resistance and World Grains*, ed by Powles SB and Shaner DL. CRC Press, Boca Raton, FL (2001).

4 Heap IM, *International Survey of Herbicide-Resistant Weeds* (2013). http://www.weedscience.org
5 Heap I and Knight R, A population of ryegrass tolerant to the herbicide diclofop-methyl. *J Aust Inst Agric Sci* **48**:156–157 (1982).
6 Heap I and Knight R, The occurrence of herbicide cross-resistance in a population of annual ryegrass, *Lolium rigidum*, resistant to diclofop-methyl. *Aust J Agric Res* **37**:149–156 (1986).
7 Mallory-Smith CA, Thill DC and Dial MJ, Identification of sulfonylurea herbicide-resistant prickly lettuce (*Lactuca serriola*). *Weed Technol.* **4**:163–168 (1990).
8 Gronwald JW, Resistance to PSII inhibitor herbicides, in *Weed and Crop Resistance to Herbicides*, ed. by De Prado R, Jorrin J and Garcia-Torres L. Kluwer Academic, Dordrecht, the Netherlands (1997).
9 Brown AC, Moss S, Wilson ZA and Field LM, An isoleucine to leucine substitution in the ACCase of *Alopecurus myosuroides* (black-grass) is associated with resistance to the herbicide sethoxydim. *Pestic Biochem Physiol* **72**:160–168 (2002).
10 De´lye C, Zhang XQ, Michel S, Matejicek A and Powles SB, Molecular bases for sensitivity to acetyl-coenzyme-A-carboxylase inhibitors in black-grass. *Plant Physiol* **137**:794–806 (2005).
11 Liu WJ, Harrison DK and Chalupska D, Single-site mutations in the carboxyltransferase domain of plastid acetyl-CoA carboxylase confer resistance to grass-specific herbicides. *Proc Natl Acad Sci USA*, **104**:3627–2632 (2007).
12 Hochberg O, Sibony M and Rubin R, The response of ACCase-resistant *Phalaris paradoxa* populations involves two different target site mutations. *Weed Res* **49**:37–46 (2009).
13 Beckie HJ and Reboud X, Selecting for weed resistance: herbicide rotation and mixture. *Weed Technol* **23**:363–370 (2009).
14 Feng PCC, CaJacob CA, Martino-Catt SJ, Cerny RE, Elmore GA, Heck GR, *et al*, Glyphosate-resistant crops: developing the next generation products, in *Glyphosate Resistance in Crops and Weeds*, ed. by Nandula VK. Wiley, New York, NY, pp. 45–65 (2010).
15 Green JM and Castle LA, Transitioning from single to multiple herbicide resistant crops, in *Glyphosate Resistance in Crops and Weeds*, ed. by Nandula VK. Wiley, New York, NY, pp. 67–91 (2010).

