Evolution of soybean weed management in the United States

by

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ABSTRACT

Weeds have been an unwanted nuisance since the beginning of agriculture. The processes and technologies utilized to manage this yield limiting problem have evolved over time. Soybean [*Glycine max* (L.) Merr.] production in the United States has experienced all of the major agriculture revolutions. This has included horse-drawn field implements, tractor power implementation, chemical era, and the most recent era of biotechnology. There has been a continuous gain in efficiencies with the discovery and introduction of new technologies to manage weeds in soybeans. A period of rapid discovery and introduction of new and novel herbicide sites of action (SOA) with improved efficacy on target weed populations was experienced. Some of the SOA utilized proved to be more prone to weed populations with herbicide-resistance. Introduction of new herbicide active ingredients, a few new SOA, and herbicide-tolerant crops has been the answer to herbicide-tolerant weed species issues as they have arisen in the past. Herbicide-tolerant weed species are on the rise and new SOA are at a standstill. Biotechnology has offered herbicide-tolerant crops to the industry allowing old chemistries to be utilized in new ways which has aided in the fight against weeds. Land managers must diversify weed management techniques encompassing all cultural, mechanical, and herbicidal methods of weed removal available to preserve the tools and technologies and manage weeds that are increasingly difficult to manage.

INTRODUCTION

The management of weeds in agriculture has been an obstacle since the beginning of agriculture. The tools and techniques used to restrain these invasive plants have evolved over the years. Weed populations have evolved in response to these management techniques (aka selection pressures). Weeds have proven themselves as a formidable competitor in this challenge. The purpose of this literature review is to gather a comprehensive review of all weed management techniques utilized in U.S. soybean [*Glycine max* (L.) Merr.] production since the beginning of soybean production until present day.

Soybeans have been grown as an agricultural crop in the U.S. since the middle of the 19th century (Shurtleff and Aoyagi, 2004). The first techniques utilized in the management of weeds were horse-drawn tillage implements (Shurtleff and Aoyagi, 2014). These were utilized in combination with crop rotations. During the first hundred years of U.S. soybean production, technology advancements were seen in mechanical management techniques. The invention of steam engines and eventually gasoline powered tractors offered more efficient methods of pulling tillage implements through the field (Timmons, 2005). As horses were removed from the farming operation, a shift was also seen in the crops being produced by the American farmer from small grains to more soybeans (Shurtleff and Aoyagi, 2004; Timmons, 2005). Advancements in the tillage equipment available for the management of yield robbing weeds has also been a part of the technology advancements (Cochrane, 1993).

The chemical era of agriculture is said to have begun in the 1940's with the introduction of synthetic auxin herbicides (Timmons, 2005). Since that time, there was a steady increase in herbicide use and in the introduction of new herbicide sites of action (SOA). This chemical technology was yet another more efficient method of managing weeds. Herbicides for weed management offered another tool that could be used to diversify weed management and reduce the time that was necessary for the process.

In 1996, the commercial introduction of genetically modified soybeans with herbicide-resistance to glyphosate {N-(phosphonomethyl)glycine} was the beginning of the biotechnology era (Beckie and Hall, 2014). This initial introduction proved to be revolutionary and has continued into present day agriculture. Further advancements have included the introduction of herbicide-tolerance to many other herbicide SOA and in some cases multiple herbicide-resistance stacked together. Plant biotechnology has allowed farmers to utilize old chemistries in new ways (Heap, 2014). Herbicide-tolerant crops have offered gains in physical efficiencies, economic benefits, and environmental advantages (Green and Owen, 2011).

With the introduction of new chemical and biotechnology products, there has often times been a tendency for overuse of these technologies. As it relates to soybean production, two examples of this are ALS (acetolactate synthase)-inhibitor herbicides and glyphosate-tolerant soybeans (Young, 2006; Heap, 2014). The ALS herbicides offered excellent weed control and a heavy reliance on these chemistries was experienced. The heavy selection pressure during the 1980's resulted in a high number of weed populations with resistance to ALS-inhibitor chemistry. The introduction of glyphosate-tolerant soybeans offered soybean producers an answer to this issue. Glyphosate applied to glyphosate-tolerant soybeans easily controlled all weeds that were present in soybean fields. This simplified weed management by giving farmers the option to control all weed issues with the application of one herbicide. A rapid adoption of this technology quickly followed and nearly all weed management was approached with this one dimensional tool for the during the years following the technology release (Young, 2006). Overreliance of glyphosate alone has proved to be a selection pressure that has yielded weed populations with resistance to glyphosate. Weed species with resistance to herbicides continues to grow and the number of sites of action with resistant weed populations continues to grow (Heap, 2014). The list of new herbicides with new sites of action available for commercial use has stopped growing. This leaves growers without new novel herbicides to battle weed populations that are increasingly less likely to be controlled with the herbicides of the past. The answer by the seed industry has been an increase in genetically-modified crops with resistance to a broader range of herbicides that have been in use for many years.

A diverse approach to weed management is necessary to reduce the advancement of herbicide-resistant weed species and loss of this valuable technology for future generations. This literature review will cover the history of weed management in U.S.

soybean production. The purpose of this review is to provide a better understanding of the weed management tools and technologies available to soybean producers in an effort to aid in maximizing the diversification of weed management.

THE BEGINNING OF SOYBEAN WEED MANAGEMENT

The first reported planting of soybeans in Iowa was in 1852 by J.J. Jackson in Davenport, Iowa (Hymowitz, 1987). Soybean production in the U.S. was first recognized in southern states at the end of the 19th century; grown for forage, cover crop, and hay/silage (Shurtleff and Aoyagi, 2004). The predominant growing region shifted to the Midwest in the 1920's, 30's, and 40's. Some reasons for this shift were; the high yielding environment, a shift away from oats as horse use declined, and an increasing demand for soy oil and meal.

Soybean Weed management in the early years:

> "1900 March – The use of horses for soy bean production is first mentioned. In Kansas, soy beans are cultivated, the same as corn, "using the two-horse cultivator..." (Cottrell et al., 1901)" (Shurtleff and Aoyagi, 2014).

Soil tillage has been an important part of agriculture since the beginning of human civilization (Lal et al., 2007). Tillage was initially utilized for seed bed preparation and also evolved into a method of post-emergent weed management. Many forms of hand tools were utilized in the initial years of civilization in Mesopotamia. The initial plow, known as an "ard", was developed during this time. The ard was initially constructed of wood and was manually maneuvered through fields by humans (Lal et al., 2007). Over the years, improvements were made and more durable materials were used for the cutting head; first stone and then transitioning to metal (Lal, 2009). The power used to pull this implement has varied; most commonly from people to oxen and horses. The ard also evolved from cutting and stirring soil into a tool for turning the soil over. The ard is considered the backbone of traditional farming and developed into the moldboard plow that is seen in agriculture today (Lal, 2009).

The United States was first introduced to the wooden moldboard plow around the year 1740 (Lal, 2009). Improvements made to the moldboard plow since its introduction in the United States can be attributed to multiple inventors and builders. In 1784, Thomas Jefferson designed an iron moldboard plow “moldboard of least resistance” (Lal et al., 2007; Lal, 2009). Charles Newbold patented the first all iron plow in 1796 (Cochrane, 1993; Lal et al., 2007; Lal, 2009). Other notable early plow inventors are the John Peacock patent of 1807 and the Jethro Wood patent of 1814 (Hurt, 2003). John Deere patented and began marketing the steel moldboard plow in 1837 (Cochrane, 1993; Hurt, 2003; Lal et al., 2007; Lal, 2009). John Deere’s “singing plow” handled the heavy and sticky soils of the Midwest like no other plows of the time (Cochrane, 1993). This walk behind moldboard plow was pulled by two horses and is said to be responsible for taming the West (Lal, 2009). Improvements continued to be made and by the 1870’s two-bottom riding, aka sulky, plows were being used in the United States (Hurt, 2003). With improvements to the plow came gains in efficiency and needs for additional horsepower. The sulky plow required four to five horses and the efficiency gained was an ability to plow five to seven acres per day compared to one acre per day with a walk-behind plow (Hurt, 2003).

In addition to the plow, many other mechanical tillage improvements became widely used in United States agriculture during the 1850’s. Harrows, cultivators, and disks are some examples of tillage improvements implemented during that time (Cochrane, 1993). The use of drag harrows began as early as 500 B.C. and is described as the dragging of tree limbs with the branches being utilized as the teeth. During the first century A.D. improvements were made to the harrow and the implement is depicted as an A-shaped log with wooden dowels placed through the log as teeth to be drug through the soil (Timmons, 2005; Olmstead and Rhode, 2014). In 1722, Jethro Tull, of Britain, invented a horse drawn hoe that resulted in a tool good for weed removal. The intended purpose of this hoe was not weed control but to breakup soil to make nutrients more easily available for plant uptake (Timmons, 2005; Olmstead and Rhode, 2014). Horse-drawn spike-toothed harrows were being utilized for field preparation in the United States beginning in the 1840’s (Cochrane, 1993). The spring-tooth harrow proved to be a good tool for removing small weeds when introduced to U.S. agriculture during the 1870’s (Olmstead and Rhode, 2014). Single-row cultivators and two-row sulky cultivators became available in the United States in the 1830’s and 40’s but did not reach the Midwest until the beginning of the Civil War (Cochrane, 1993). Cultivators were designed primarily for weed management within emerged crop rows. The rotary hoe was invented in 1890 and entered commercial production in 1912 (Gittins, 1950). The rotary hoe was utilized as a tool for early season cultivation to remove small weeds and break soil crust. The rotary hoe is an implement with a series of closely spaced wheels; each wheel containing multiple curved spokes (Bowman, 2001). The spokes on each wheel penetrate the soil and uproot small weeds. Increased travel speed across the field improves the uprooting action of weed seedlings.

Timmons (1970) mentions that weeds have long been recognized to reduce crop yields by Romans in the first century A.D. and possibly earlier in Chinese and Indian literature. In 1923, it was considered important to keep soybeans cultivated (Piper and Morse, 1923). Inadequate cultivation commonly resulted in excessive weed pressure that often times caused crop failure. The use of a harrow, rotary hoe or weeder was recommended after planting and before crop emergence to break soil crust and remove early emerging weeds. The “weeder” mentioned by Piper and Morse (1923) was likely a flex-tine weeder which is an implement with a series of coil spring wire tines pulled across the soil surface shallowly scratching and uprooting small weeds (Bowman, 2001). Soybeans were planted in rows and a common corn cultivator was used after emergence of the crops until the crop was ready to flower (Piper and Morse, 1923). An initial deep cultivation followed by frequent shallow cultivations to suppress weed pressure. In comparison to row planting soybeans, corn during this time was often planted in hills (also known as check planting) (Hurt, 2003; Olmstead and Rhode, 2014). This allowed for in-row cultivation to be completed in multiple directions across the field during the growing season. After the development of the check-row planter, in 1864, this technology became a standard planting method of crops (ex. corn) through the first half of the 20th century.

“Weed control is one of the youngest of sciences but a relatively old art” (Timmons, 2005). In the early years of agriculture, weeds were thought of as a curse with very little methods for removal. For many years much labor was required for the hand removal of weeds; which was the only method for managing weed infestations. Discovery and development advancements in mechanical methods of weed removal increased between 1901 and 1940 (Wills, 2003). This period of time was a commercial revolution for agriculture in the United States. Efficiency and productivity was increasing due to advancements in technology. The primary advancements of the times was a transitioning from horse power to gasoline powered tractors (Timmons, 2005). In the 1930's, it took approximately 30 minutes to plow one acre with a tractor. To complete this same work with a horse drawn plow would take four times that amount of time; approximately two hours. Tractors outnumbered horses on farms by the year 1955 (Hurt, 2003).

The steam engine was invented in the 1850's and peaked in use by the 1880's (Timmons, 2005). Steam engines in agriculture was rather brief and the main use was for belt driven operations. There were efforts to use traction steam engines for drawbar implements but there were many limitations (Gittins, 1950). The lighter gasoline engine tractors that emerged in the early 1900's proved to be more useful and maneuverable for field operations. Since the release of the original tractors continuous improvements have been made to the tractor to increase efficiencies. Two of the most significant advancements in tractor technology were the tricycle design of 1924 and rubber tires in 1932 (Gittins, 1950). The tricycle design allowed for tractor mounted implements that could be used for row crop work. This advancement in technology began the downward trend of horse use on farms. Low pressure rubber tires replaced steel wheels and increased the speed of many field functions by 25-50 percent. The increased efficiency was attributed to easier rolling that increased power and fuel efficiencies; both improved efficiency by approximately 25 percent. Other key advancements in the tractor were hydraulic lifting capabilities in the 1930's and the power take-off (PTO) in 1946. Improvements to the tractor and tillage implements allowed for more efficient methods of mechanical weed management during the first half of the 20th century. Herbicides for weed control began entering the picture in the early 1900's but cultural and mechanical practices remained the primary method of weed management in the early 20th century (Freed, 1980). The primary weed management practices during this time in the United States was crop rotation and frequent cultivations. Freed (1980) reminds us that mechanical and cultural practices did not provide farmers with ideal weed control and this shifted attention towards the discovery and development of more efficient tools like chemicals.

In a 1955-1957 study, by Lovely et al. (1958), of the rotary hoe as a tool to manage weeds in soybeans, it was mentioned that extensive mechanical weed control methods were being utilized in soybean production at that time (Lovely et al., 1958). Herbicide CDAA (N,N-diallyl-2-chloroacetamide) (WSSA 15) and NPA (N-1-naphthylphthalamic acid) (naptalam) (WSSA 19) were available in the 1950's but did not prove to be an economical option for soybean weed control in the Lovely study (Lovely et al., 1958; Timmons, 2005).

HERBICIDES

Sprayers have existed since the 1850's; beginning with handheld sprayers (Timmons, 2005). A sprayer on wheels was developed in 1887 (Gittins, 1950; Timmons, 2005). All sprayers during this era were used for disease and insect control. Sprayers for weed control did not start until after 1930 (Timmons, 2005). Timmons (1970) provides a good overview on the history of herbicides in Europe and the United States 1840-1940's used on a wide variety of crops. A summary of these early products can be found in Table 1. All herbicides covered in this literature review are identified with the Weed Science Society of America (WSSA) Site of Action (SOA) group number (ex. WSSA 1). Table 2 contains a complete listing the WSSA SOA group numbers and a description of each SOA. Herbicides interrupt plant life by binding to specific proteins (enzymes) and disrupting the function of that protein (Owen and Hartzler, 2017). The protein that is affected is the herbicide SOA. It is likely that soil sterilants (salts of acids) were the original herbicides in agriculture (Hildebrand, 1946). Beginning in 1900, the agriculture industry experienced a steady increase in the discovery of new herbicides (Timmons, 2005). The major development of the twentieth century was selective herbicides to manage weeds and not damage the crops growing in the same area (Plimmer, 2003). Until the discovery of the first organic chemistry herbicide, dinitros (DNOC) (4,6-dinitro-o-cresol) (WSSA 24) in 1932, all prior herbicides were inorganic compounds.

Dinitrophenols initially used as an insecticide since 1892 and was later discovered to have selective herbicidal properties (Copping and Hewitt, 1998).

Table 1. Herbicides 1840 - 1940's (Hilderbrand, 1946, Timmons, 1970).

Product	**Year**	**Location**	**Comments**
lime	1840	Germany	horsetail (*Equisetum sp.*)
sodium chloride	1854	Germany	soil sterilant, application rate 20 tons/A
boron	1876	NA	soil sterilant, phytotoxicity to plants was known
sodium chloride	1896	Vermont	soil sterilant, hawkweed (*Hieracium aurantiacium L.*)
sulfuric acid and iron sulfate	1855	Germany	weeds
copper sulfate	1896	France	weeds
copper sulfate	1905	United States	algaecide
copper sulfate, iron sulfate, sulfuric acid, and nitric acid	1899	US, Canada, Germany, and France	testing for control of annual forbs in cereals, CuSO4 and FeSO4 did not provide good weed control
sulfuric acid	1911	France	selective contact for control of annual forbs in cereals
sodium chloride	1915	Kansas	bindweed (*Convolvulus arvensis L.*)
sulfuric acid	1935	United States	selective contact for control of weeds in fields of onions and cereals
ammonium sulfamate (AMS)	1940		translocated poison to kill woody plants
sodium arsenite	1902 - 1937	United States	soil sterilant active on water hyacinth, aquatic weeds, and annual weeds
emulsified xylene-type aromatic solvents	1949	United States	aquatic weeds in flowing water
sodium chlorate	1923	France	translocated poison
carbon bisulfide	1906 - 1936	United States	soil fumigant
heating oil	1919 - 1940's	United States	nonselective contact for non-crop areas
sodium chlorate	1925 - 1930	United States	testing as translocated poison

sodium chlorate	1927 - 1940	United States	nonselective contact for perennials in non-crop areas and small patches within fields
salt of dinitrophenol (dinitros) (DNOC)	1933	France	annual forbs in cereals, first organic chemical herbicide; 4,6-dinitro-o-cresol in 1932
dinitros (DNOC)	1937 - 1945	United States and Canada	annual weeds in onion, legumes, cereals and flax; first organic chemical herbicide; 4,6-dinitro-o-cresol in 1932
sodium borates	1940's	United States	soil sterilant, St. Johnswort (*Hypericum perforatum L.*)
sodium pentachlorophenate	1940's		Brief testing as a herbicide
phenoxyacetic acid (2,4-D and MCPA)	**1942 - 1944**	**Britain and United States**	**Synthetic auxins for broadleaf weed control**
carbanilates	late 1940's		weedy grasses
aliphatic acids	late 1940's		weedy grasses

Table 2. WSSA Site of Action (SOA) Group Numbers (WSSA, 2013).

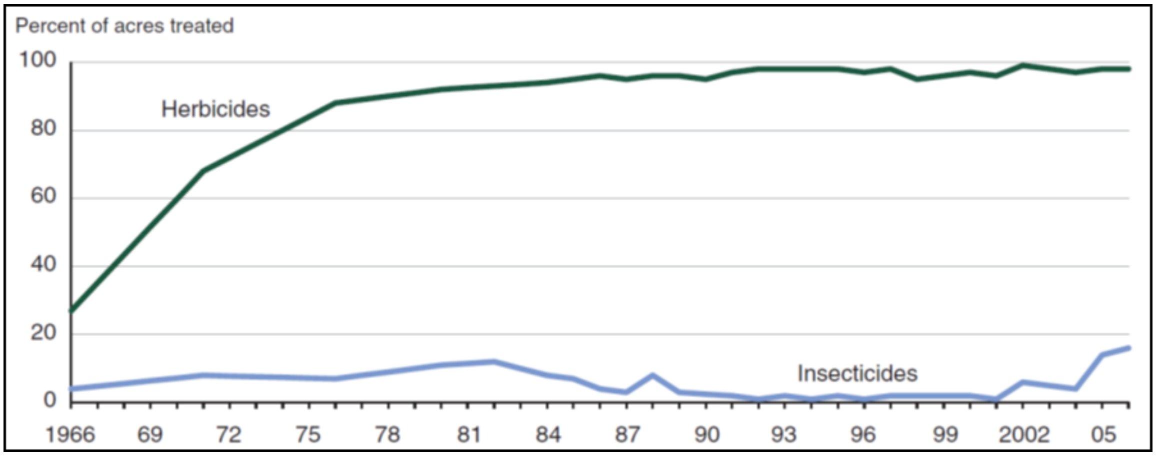
WSSA site of action (SOA) Group #	**Site of Action**
1	Acetyl CoA Carboxylase (ACCase) Inhibitors
2	Acetolactate Synthase (ALS) or Acetohydroxy Acid Synthase (AHAS) Inhibitors
3	Mitosis Inhibitors (Microtubule Inhibitors)
15	Mitosis Inhibitors (Long-chain Fatty Acid Inhibitor)
23	Mitosis Inhibitors (cell division inhibitors and microtubule organization/polymerization
4	Synthetic Auxins
5	Photosystem II Inhibitors
6	Photosystem II Inhibitors
7	Photosystem II Inhibitors
8	Fatty Acid and Lipid Biosynthesis Inhibitors
16	Fatty Acid and Lipid Biosynthesis Inhibitors
9	Enolpyruvyl Sheikimate-3-Phosphate (EPSP) Synthase Inhibitors
10	Glutamine Synthetase Inhibitors
11	Carotenaoid Biosynthesis Inhibitors (aka pigment inhibitors); chlorophyll and carotenoids accumulation inhibition
12	Carotenaoid Biosynthesis Inhibitors (aka pigment inhibitors); phytoene desaturase inhibitor
13	Carotenaoid Biosynthesis Inhibitors (aka pigment inhibitors); 1-deoxy-D-xyulose 5-phosphate synthase (DOXP) inhibitor
27	Carotenaoid Biosynthesis Inhibitors (aka pigment inhibitors); *p*-hyroxyphenyl pyruvate dioxygenase (HPPD) inhibitor
14	Protoporghyrinogen Oxidase Inhibitor (PPO)
17	Potential Nucleic Acid Inhibitors or Non-descript mode of action (organic arsenicals)
25	Potential Nucleic Acid Inhibitors or Non-descript mode of action (arylaminopropionic acids)
26	Potential Nucleic Acid Inhibitors or Non-descript mode of action (non-classified)
18	Dihydropteroate Synthetase Inhibitors
19	Auxin Transport Inhibitors
20	Cellulose Inhibitors (cell wall biosynthesis inhibitors)
21	Cellulose Inhibitors (cell wall biosynthesis inhibitors)
28	Cellulose Inhibitors (cell wall biosynthesis inhibitors)
29	Cellulose Inhibitors (cellulose biosynthesis inhibitors)
22	Photosystem I Inhibitors
24	Oxidative Phosphorylation Uncouplers
NC	Not Classified by WSSA or HRAC

Beginning in 1937, DNOC was used for annual weed control in crops of onions, legumes, cereals, and flax in the United States and Canada (Hildebrand, 1946). Dinitrophenols are very toxic to all living organism; including the operator (Copping and Hewitt, 1998). Uncoupling of oxidative phosphorylation is the process for mode of action and this causes a rapid death to any living organism contacted by the chemical. The Environmental Protection Agency (EPA) suspended this chemistry in 1986 and the products have been cancelled and are no longer available in the U.S. due to health risks and environmental concerns (EXTOEXNET, 1993). Hildebrand (1946) "War on Weeds" writing focused on the herbicides of the time; sulfuric acid, sinox (dinitro), ammonium sulfamate, oils, and 2,4-D {2-(2,4-dichlorophenoxy)acetic acid}.

Beginning in the 1940's, pesticides and herbicides were developed for use in World War II. These chemical developments were slowly integrated into civilian use during the years following World War II (Wills, 2003). 1942-1944 was the beginning of the "Chemical Era of Agriculture"; phenoxyacetic herbicides (WSSA 4) (ex. 2,4-D and MCPA{2-(4-chloro-2-methylphenoxy)acetic acid}) were discovered to have selective weed killing properties (Timmons, 2005). Other chemistries quickly followed the phenoxyacetic discovery; increasing the number of commercially available herbicides from fifteen in 1940 to twenty five by 1950 (Timmons, 2005). Plimmer (2003) summarizes the discovery of herbicide families following phenoxy acid as: 1951 ureas (WSSA 7) and uracils (WSSA 5), 1955 traizines (WSSA 5), 1960 bipyridiliums (WSSA 22), and 1963 dinitroanalines (WSSA 3). In continuation; 1967 alachlor [2- chloro-(2',6'-diethylphenyl)-N-(methoxymethyl)acetamide] (WSSA 15), 1971 glyphosate (WSSA 9), 1975 diphenyl ether (WSSA 14), 1975 aryloxyphenoxy propionate (WSSA 1), 1980 sulfonylurea (WSSA 2), 1981 imazaquin (2-[4,5-dihydro-4-methyl- 4-(1 -methylethyl)-5-oxo- lH-imidazol-2-yl]-3-quinoline- carboxylic acid) (WSSA 2), and 1982 isoxazolidinone (WSSA 13) (Plimmer, 2003; Appleby, 2005). Timmons (1970) writes that nitrile (bromoxynil) (WSSA 6) was first introduced in 1965. Within each of these herbicide families many active ingredients were discovered and introduced at different times over the years. Timmons (1970) and Appleby (2005) each provide a complete listing of commercial herbicides and the years of initial introduction; Timmons 1952-1969 and Appleby 1970-2005.

Herbicides are the main source of weed control for the majority of soybean growers (Buhler and Hartzler, 2004). The most widely used class of pesticides in the United States are herbicides (Plimmer, 2003). Prior to herbicides, weed management was achieved through cultivation and hand removal (Fernandez-Cornejo et al., 2014). In 1952, only 10 percent of corn acres were treated with herbicides. By 1976, 90 percent of the corn planted in the U.S. was being treated with herbicides. Soybeans experienced a similar expansion of herbicide use during the same time frame in the U.S. (Figure 1). United States soybean acres increased dramatically, between 1960 and 1981, from 24.4 million acres to 67.5 million acres. This is a more dramatic increase than any other U.S. row crop during that era. During this time (1960-80), an increase in herbicide use on soybean acres was documented as 0.1 lb/A of active ingredient being used in 1960 compared to 2.1 lbs/A of active ingredient applied in 1981. The source of these figures were from pesticide use surveys completed by United States Department of Agriculture (USDA), National Agricultural Statistics Service (NASS), and proprietary data from the Economic Research Service (ERS) (Fernandez-Cornejo et al., 2014).

Figure 1. Soybean herbicide use U.S. 1966 - 2006 (adopted from Fernandez-Cornejo and Vialou, 2014).



In 1968, the benzoic acid (WSSA 4), chloramben (3-amino-2,5-dichlorobenzoic acid), was the first herbicide to be of large presence in U.S. soybean production (Fernandez-Cornejo et al., 2014). The commercial name for chloramben was Amiben

(Timmons, 2005). Chloramben is a soil applied herbicide used for pre-emergence control of grasses and broadleaf weeds (Plimmer, 2003; Fernandez-Cornejo et al., 2014). The benzoic acid, dinoben (2,5-dichloro-3-nitrobenzoic acid), was discovered in 1956; shortly before the introduction of chloramben in 1958 (Plimmer, 2003). Both dinoben and chloramben provide selective weed control in soybeans but chloramben was more effective; resulting in it becoming a leading herbicide in the 1950's and 1960's. In 1968, over 30% of all pesticides applied to soybeans in the U.S. was chloramben (Fernandez-Cornejo et al., 2014). The benzoic acid chemical family also contains the commonly used broadleaf herbicide dicamba (3,6-dichloro-2-methoxybenzoic acid) (Plimmer, 2003). Dicamba was introduced as a broadleaf herbicide in the 1960's; commonly used in cereals and maize to control broadleaf weeds. The first benzoic acid herbicides introduced in the U.S. during the 1940's were TBA (2,3,6-trichlorobenzoic acid) and TIBA (2,3,5-triiodobenzoic acid). TBA was used as a broadleaf herbicide in cereals; with activity similar to dicamba. TIBA was used as a defoliant and growth regulator. Interestingly, unrelated to weed control, it is noted to have been used on soybeans to increase branching and stimulate flowering in an effort to increase yields. Other commonly used soybean herbicides in 1968 were trifluralin (α,α,α-trifluoro-2,6-dinitro-N,N-dipropyl-p- toluidine) (WSSA 3), linuron (3-(3,4-dichlorophenyl)-1-methoxy-l-methylurea) (WSSA 7), naptalam, and vernolate (S-propyl dipropylthiocarbamate) (WSSA 8) (Timmons, 2005; Fernandez-Cornejo et al., 2014).

As new and improved chemistries became available, the dominant presence of chloramben was reduced (Fernandez-Cornejo et al., 2014). Improved herbicides that became more commonly used on soybeans during the 1970's were alachlor [2-chloro-N-(2,6-diethylphenyl)-N-(methoxymethyl)acetamide] (WSSA 15), metribuzin [4-amino-6-(1,1-dimethylethyl)-3-(methylthio)-1,2,4-triazin-5(4H)-one] (WSSA 5), and trifluralin (Buhler et al., 1992; Timmons, 2005; Fernandez-Cornejo et al., 2014). One point of observation is that all herbicides applied to U.S. soybeans prior to the 1970's were pre-emergent soil applied products. Foliar applied herbicides increased in importance during the 1970's (Buhler and Hartzler, 2004). Foliar herbicides improve weed management by removing performance variability caused by herbicide interactions with soil and the weeds can be identified before application.

In 1974, it was noted that weeds in soybeans were chemically managed with pre-emergence herbicides (Wax et al., 1974). There were some broadleaf weed species not being controlled adequately; resulting in reduced crop yields from weed competition, harvesting loss, and reduced grain quality. The use of post-emergence herbicide applications on soybeans was not common practice in the Midwest at this time. Wax et al., 1974, noticed this problem and anticipated a demand for post-emergence applications of herbicides to remedy this issue. Studies were conducted over three years (1970, 1971, and 1972) to evaluate the response of commercial soybean cultivars to post-emergence herbicides bentazon [3-isopropyl-1H-2,1,3-benzothiadiazin-(4)3H-one 2,2-dioxide] (WSSA 6), bromoxynil [3,5-dibromo-4-hydroxybenzonitrile] (WSSA 6), chloroxuron [3-[p-(p-chlorophenoxy)phenyl]-1,1-dimethylurea] (WSSA 7), and 2,4-DB [4-(2,4-dichlorophenoxy) butyric acid] (WSSA 4). In this study, it was determined that all important commercial soybean cultivars in the U.S. and Canada were tolerant to post-emergence applications of bentazon.

Diclofop {methyl 2-[4-(2,4,dichlrorphenoxy)phenoxy]-propanoate} (WSSA 1) was the first of the acetyl CoA carboxylase (ACCase) herbicides to be introduced in the U.S. in 1975 (Wu and Santelmann, 1976; Appleby, 2005). Diclofop was a selective herbicide for grass control in broadleaf crops. Early post-emergence applications and pre-plant incorporated applications of diclofop showed the most phytotoxicity to weedy grass seedlings (Wu and Santelmann, 1976). Selective grass weed control was achieved with no injury to a soybean crop. There are two primary chemical families with ACCase site of action utilized in soybean production; Aryloxyphenoxypropionate (FOPs) and cyclohexanedione (DIMs) (Plimmer, 2003). Both chemical families interfere with the action site of enzyme Acetyl-CoA carboxylase preventing the synthesis of fatty acid in grass plants.

During the early 1970’s, there was a movement towards minimum-tillage (MT) and no-till (NT) corn and soybean production (Kapusta, 1979). In the U.S. weed management with reduced amounts of tillage was proving to be a hurdle. Changes in the herbicides that had been used was going to be necessary since soil incorporation with tillage was not going to be an option with NT and opportunities were reduced with MT. Many of the herbicides that had been used prior to this time required soil incorporation.

The opinion, at this time, was that weed management with herbicides was going to become more complex to remain effective. A full growing season may require a pre-plant burndown, 1-2 pre-emergence herbicides, and a post-emergence herbicide application. MT was being accepted and utilized quickly to decrease soil erosion and the cost associated with operations. In 1976-1978, Kapusta conducted Midwest soybean field studies to determine weed control, crop population, and grain yields with different herbicides and tillage systems. NT soybean yields in this study were consistently the lowest due to poor herbicide weed control and no cultivation to remove weeds. Another important observation was that available herbicides did not offer consistent weed control in all three tillage treatments (conventional tillage (CT), MT, and NT). A complete list of the herbicides used in the Kapusta (1979) studies are presented in Table 3.

Kapusta and Krausz continued evaluations of tillage and different combinations of herbicides in an eleven-year soybean field study (1979-1989). NT had been in practice for twenty years, but not on a wide scale (Kapusta and Krausz, 1993). Inconsistent weed control had consistently been a problem that prevented majority acceptance of NT by U.S. farmers. In 1985, a conservation compliance provision administered by the Food and Security Act was going to force a rapid increase of NT in future U.S. row crops. The rapid increase in NT practices was seen during 1987-1991 in U.S. soybean production fields. So the need to identify a more reliable herbicidal weed management program for NT was real.

Table 3. Herbicides used in the Kapusta study 1976-1978 (Kapusta, 1979).

Common Name	**Chemical Name**	**Application Timing**	**WSSA Group #**	**Comments**
Paraquat	1,1′-dimethyl-4,4'-bipyridinium salts	Pre-plant	22	
Alachlor	2-chloro-2',6' diethyl-N-(methoxymethyl)	Pre-emergence	15	
Metolachlor	2-chloro-N-(2-ethyl-6-methyl-phenyl)-N-(2-methoxy-1-methylethyl) acetimide	Pre-emergence	15	
Bifenox	methyl 5-(2,4-dichlorophenoxy)-2-	Pre-emergence	14	
Linuron	3-(3,4-dichlorophenyl)-1-methoxy-1-	Pre-emergence	7	
Metribuzin	4-amino-6-*tert*-butyl-3-(methylthio)-*as*-triazin-5(4H)-one	Pre-emergence	5	
Oryzalin	3,5-dinitro-N^4,N^4-dipropyl-sulfanilamide	Pre-emergence	3	soybean injury of 42 and 35%, MT and NT respectively in 1976
Pendimethalin	N-(1-ethylpropyl)-3,4-dimethyl-2,6-dinitrobenzenamine	Pre-emergence	3	
Naptalam	N-1-naphthylphthalamic acid	Pre and Post	19	
Bentazon	3-isopropyl-1H-2,1,3-benzo-thiadiazin-4(3H)-one 2,2-dioxide	Post	6	
Dinoseb	2-*sec*- butyl -4,6-dinitrophenol	Pre and Post	24	cancelled in US (no longer available)

During the 1980’s, new herbicides were introduced to the market that performed better under NT field conditions. Chlorimuron {2-[[[[(4-chloro-6-methoxy-2-pyrimidinyl) amino]carbonyl]amino]sulfonyl]benzoic acid} (WSSA 2), imazaquin (WSSA 2), and clomazone {2-[(2-chlorophenyl)methyl]-4,4-dimethyl-3-isoxazolidinone} (WSSA 13) were specifically mentioned in this literature as notable improved herbicides introduced during this era (Kapusta and Krausz, 1993). Chlorimuron (sulfonylurea) and imazaquin (imidazolinone) are both acetolactate synthase inhibitors (ALS) and clomazone is a pigment inhibitor (diterpene synthesis inhibitor). A list of the herbicides that were new and/or not included in the Kapusta 1976-1978 studies are presented in Table 4.

The design of this long-term experiment was to use the most effective pre-emergence and post-emergence herbicides of the time; even if that meant changing to new products over the course of the study (Kapusta and Krausz, 1993). Metribuzin and alachlor were the best performing pre-emergence herbicides at the beginning of this study. As the study progressed, it was recognized that pre-emergence metribuzin plus chlorimuron was more effective at controlling broadleaf weeds. Other new post-emergence herbicides utilized in this study were commercially introduced during the span of the study. Acifluorfen {5-[2-chloro-4-(trifluoromethyl)phenoxy]-2-nitrobenzoic acid} (WSSA 14) was one of the first protoporphyrinogen oxidase (PPO) inhibitors released in the U.S. and is a member of the diphenylether family (Kapusta and Krausz, 1993; Appleby, 2005). Sethoxydim (2-[1-(ethoxyimino)butyl]-5-[2-(ethylthio)propyl]-3-hydroxy-2-cyclohexen-1-one (WSSA 1) is an ACCase inhibitor and is the first active ingredient in the family of cyclohexanedione.

Table 4. The new herbicides incorporated into study since 1976-'78 studies (Kapusta and Krausz, 1993).

Common Name	**Chemical Name**	**Application Timing**	**WSSA Group #**	**Comments**
Glyphsate	N-(phosphonomethyl)glycine	Pre-plant	9	Broad-spectrum contact
Sethoxydim	(2-[1-(ethoxyimino)butyl]-5-[2-(ethylthio)propyl]-3-hydroxy-2-cyclohexen-1-one	Post-emergence	1	Selective for grass contact
Acifluorfen	{5-[2-chloro-4-(trifluoromethyl)phenoxy]-2-nitrobenzoic acid}	Post-emergence	14	Broad-spectrum contact
Clomazone	{2-[(2-chlorophenyl)methyl]-4,4-dimethyl-3-isoxazolidinone}	Pre-emergence	13	Broad-spectrum contact and residual
Imazaquin	{2-[4,5-dihydro-4-methyl- 4-(1 -methylethyl)-5-oxo- lH-imidazol-2-yl]-3-quinoline- carboxylic acid}	Pre-emergence	2	Broad-spectrum contact and residual
Chlorimuron	{2-[[[[(4-chloro-6-methoxy-2-pyrimidinyl) amino]carbonyl]amino]sulfonyl]benzoic	Pre-emergence	2	Contact

A combination of pre-emergence and post-emergence herbicides was recommended to achieve maximum weed control across the entire spectrum of all present weeds (Kapusta and Krausz, 1993). The study revealed that excellent weed control was possible with the available herbicides of the time. Due to the higher cost of using multiple herbicides, it was highly recommended to scout and identify the weeds before selecting the products to be applied. When weeds were adequately controlled the soybean yields and plant populations were equal across all tillage treatments. This data was consistent with other studies of similarity conducted during this time.

Imazethapyr {2-[4,5-dihydro- 4-methyl-4-(l-methylethyl)-5-oxo-lH-imidazol-2-yl]-5-ethyl-3-pyridinecarboxylic acid} (WSSA 2) offers weed control via soil residual and activity on emerged weeds (Lueschen and Hoverstad, 1991). Studies conducted by Lueschen and Hoverstad (1991) from 1987-1990, showed that imazethapyr had potential to adequately control weeds in no-till soybean production. Late April applications of early pre-plant imazethapyr showed excellent weed control and tank mixing with metribuzin improved weed control. Pre-plant applications of imazethapyr did not adequately control emerged weeds.

Imidazolinone and dinitroanaline herbicides dominated the soybean herbicide market from 1992-1996 (Young, 2006). Imazethapyr was at peak use on soybean acres in 1995 and was the most popular soybean herbicide at this time. Forty-four percent of soybeans were being treated with this herbicide in 1995. From 1992-1997, at least twenty percent of soybean acres were being treated with pre-emergent soil-applied herbicides; both trifluralin and pendimethalin {N-(1-ethylpropyl)-3,4-dimethyl-2,6-dinitrobenzenamine} (WSSA 3). Trifluralin and pendimethalin use on soybeans decreased to less than ten percent each after the introduction of glyphosate-tolerant crops 1997-2002 (Young, 2006).

Glyphosate became commercially available in 1974 (Heap, 2014). Initial applications were restricted to high value crops because of the high product cost. As the cost declined, use in row-crops increased as a product used for pre-plant burndown in no-till situations. The introduction of Roundup Ready® (RR) soybeans, in 1996, allowed for glyphosate to be used as a selective herbicide (post-planting) for the first time.

Glyphosate inhibits the biosynthesis of (aromatic acids) and is the only known herbicide with this SOA (Plimmer, 2003). Glyphosate inhibits the natural substrate, phosphoenolpyruvate (PEP), from binding with the enzyme 5-enolpyruvyl-shikimate-3-phosphate synthase (EPSPS). This results in an accumulation of shikimate in glyphosate treated plant tissues. This broad-spectrum, nonselective, foliar applied herbicide is labelled to control over 300 species of weeds (Green and Owen, 2011). The mode of action is considered slow and this allows herbicide translocation and accumulation at critical growing points before phytotoxicity begins and plant growth is terminated.

BIOTECHNOLOGY

The first genetically modified crops to improve weed management were those that were tolerant to herbicides (Plimmer, 2003). The first herbicide-tolerant soybean was achieved by traditional breeding and introduced in 1993 (Krämer and Schirmer, 2007). A naturally occurring allele, insensitive to ALS, was identified in the soybean genome and soybeans tolerant to sulfonylureas (STS®) became commercially available. STS® soybeans are planted on 2-4% of the total soybean production acres. In 2015, Dupont Pioneer introduced BOLT™ soybeans with an improved tolerance to sulfonylurea herbicides (Seed World, 2015). BOLT technology was achieved with a native soybean trait and was available in a stack with glyphosate tolerance. The technology was only available in group IV and V soybeans so the target market was for the Southern U.S.

The sulfonylurea herbicide family is by-far the largest of all herbicides; with a reported thirty-six active ingredients in 2007 (Krämer and Schirmer, 2007). The DuPont chemist George Levitt made the initial discovery of this chemical family in 1975. Sulfonylureas are the largest chemical family within the SOA AHAS/ALS (acetohydroxyacid synthase/acetolactate synthase) (Heap, 2014). More than one sixth of all registered herbicides are AHAS/ALS inhibitors. Popularity was due to low application rates, environmental friendliness, applicableness on a variety of crops, flexibility of application timing, and cost (Krämer and Schirmer, 2007). By 2007, sulfonylureas were commercially available in eighty countries and for use on all major crops and some specialty uses. AHAS/ALS inhibitors were labelled to control and have been used to control almost all major weed species (Heap, 2014). Synthetic auxins are the only herbicide to be applied to more acres than AHAS/ALS inhibitors.

The sulfonylurea SOA is interference of acetohydroxyacid synthase (AHAS) and acetolactate synthase (ALS); enzymes required for plant cell growth (Krämer and Schirmer, 2007). Branched chain amino acids valine, leucine, and isoleucine are synthesized by AHAS and ALS enzymes. This chemical interference of the AHAS and ALS enzymes prevents protein generation resulting in a stopping of cell division that causes plant death. Both ALS and AHAS have been used interchangeable and independent of each other to describe this SOA by many authors.

The *csr1-2* gene from *Arabidopsis thaliana* is imidazolinone-tolerant due to a gene point mutation (BASF, 2014a). The *csr1-2* gene encodes an AHAS enzyme that differs from the native *Arabidopsis* AHAS enzyme by one amino acid substitution. The only difference that results from this amino acid substitution is that the enzyme is tolerant to imidazolinone herbicides. Soybeans have a natural tolerance to some imidazolinone herbicides like imazaquin and imazethapyr due to rapid metabolism and degradation of the herbicide (Tecle et al., 1993). Multiple BASF sources report that soybeans are sensitive to the imidazolinone herbicides imazapyr {2-(4-methyl-5-oxo-4-propan-2-yl-1H-imidazol-2-yl)pyridine-3-carboxylic acid}and imazapic {5-methyl-2-(4-methyl-5-oxo-4-propan-2-yl-1H-imidazol-2-yl)pyridine-3-carboxylic acid} (BASF, 2014b). BASF capitalized on this discovery by genetically modifying soybean with the *csr1-2* gene via biolistics transformation; creating CV127 soybeans (Clearfield®) (BASF, 2014a). This technology was only intended for commercial production in Brazil and Argentina. Both growing regions have been granted approval by local governments and the technology has been available for a number of years for commercial production in those growing regions (ISAAA, 2018).

In 1995, a new era of weed management began with the introduction of genetically modified (GM) soybeans tolerant to the broad-spectrum herbicide glyphosate (Beckie and Hall, 2014). The U.S. is the top producer of GM crops and in 2014, 40% of the total world production area was located in the U.S. Of all GM crops grown during twenty years after introduction, 84% of the total was herbicide-resistance (HR). Over 90% of the U.S. planted soybean area, in 2014, was GM HR. The search for glyphosate-tolerant crops started within ten years of the herbicide introduction (Green and Owen, 2011). Green and Owen (2011) write from other sources that the glyphosate insensitive EPSP synthase gene (cp4 epsps) was isolated from soil bacterium (*Agrobacterium tumefaciens*) strain CP4. This bacterium surviving glyphosate was discovered in a glyphosate waste stream in the Luling, LA manufacturing plant. Green (2009) writes from other sources, glyphosate inhibits EPSPS, the sixth enzyme in the shikimate pathway that produces aromatic amino acids and the organic compounds synthesized by aromatic amino acids ex. phenylpropanoids (Green, 2009).

The first GT event commercially available in soybeans was GTS 40-3-2 (Roundup Ready®) (Green, 2009). From sources within (Green, 2009), the event was made of the enhanced cauliflower mosaic virus promoter e35S (CAMV e35S) and a chloroplast transit peptide from *Petunia hybrid*. Particle acceleration was the method of transformation. The initial GT event GTS 40-3-2 was reported to have yields 5-7% lower than conventional varieties; for unknown reasons (Elmore et al., 2001). Green (2009) from other sources, with GTS 40-3-2 the male reproductive parts of the soybean plant were strong sinks for residual glyphosate within the plant and susceptible to injury. In 2007, MON89788 (Roundup Ready2Yield®), a new GT trait for soybeans, was approved by the USDA. This trait was advertised as a higher yielding GT trait package. MON89788 has a different insertion site, stronger promoters, and elements that regulate trait expression more uniformly across male soybean vegetative and reproductive tissues. An *Agrobacterium*-mediated transformation was utilized. The promoter was e35S from the figwort mosaic virus and a promoter from *Tsf1* gene from *Arabodopsis thaliana* (FMV e35S/TSF1).

By 2004, 85% of all soybeans planted in the United States were resistant to glyphosate (Dill, 2005). The reason for the rapid acceptance and conversion to glyphosate-tolerant row crop production was due to affordability, simplicity, and conservation tillage. Due to the simplicity and effectiveness of applying a broad-spectrum herbicide that controlled all weeds in a row cropping system glyphosate became overused (Duke, 2011). Farmers went away from the diverse toolbox used before 1996 and converted over to a single weed management approach. Prior to the availability of herbicide-tolerant soybeans farmers had much more complicated and diverse weed management systems. These systems of managing weeds were time consuming, expensive, and less conservation friendly. The release of glyphosate tolerant soybeans turned out to be a revolutionary moment for the agriculture industry. This technology was accepted and utilized at unanticipated speeds. The adoption of GT crop technology was the most rapid ever seen in the history of agriculture. The number of active ingredients utilized for weed control on at least 10% of soybean acres decreased from 11 in 1995 to 1 by 2002 (Green and Owen, 2011).

A $10 reduction in maintenance cost resulted from the use of glyphosate-resistant crops compared to the pre-1996 traditional weed maintenance (Dill, 2005). This cost savings from 1996-2012 resulted in $45 billion in savings and a five percent increase in farm incomes (Duke, 2015). Thirty-eight percent of the economic savings was from increased crop yields from better control of weeds and sixty-two percent of the savings was from cheaper weed control. Other benefits were less reliance on tillage and in-season row cultivation. This makes it possible to grow row crops in narrower rows at higher populations and a faster canopy closure over the row was achieved (Dill, 2005). The carbon footprint of pest management was reduced from fewer trips across the field to control pests and complete tillage operations (Duke, 2011). The main advantages of glyphosate use on HT crops was effectiveness, simplicity, economical, and safeness (Green and Owen, 2011).

In 1998, glyphosate took the ranks as the most widely used herbicide on soybeans; the previous title holder was imazethapyr (Plimmer, 2003). Plimmer (2003) reported that 95% of soybean acres were being treated with herbicides. He reported that 46% of the soybeans were being treated with glyphosate; the previous year glyphosate was only applied to 28% of these acres. Before glyphosate-resistant soybeans were introduced in 1996, up to eleven herbicide active ingredients (7 SOA) were applied to soybeans in the United States (Young, 2006). By 2002, the number of active ingredients being applied to soybeans in the United States had decreased to just one (glyphosate). Young estimated 40% of U.S. soybean acres were being treated with only glyphosate in 2002. Glyphosate simplified and improved weed management in soybeans, but this revolutionary tool has come with some issues. Young stated most notably good agronomic practices are not always being utilized; there is a tendency to delay application and to solely rely on glyphosate. Both of these factors were resulting in extensive glyphosate-resistance weed selection pressure. In 2010, twenty-one weed species had been observed to have developed resistance to glyphosate (Duke, 2011). The widespread use of glyphosate partially resulted in less money being invested in new SOA discovery by chemical companies. Another contributing factor to less money being invested in new SOA research and discovery is a result of stricter rules and regulations (Green and Owen, 2011). In 2000, it was realized and written that glyphosate-tolerant crops would decrease the number of herbicides utilized, decrease the overall value of the herbicide market, and continuous use of glyphosate would shift the weed population to weeds difficult to control with glyphosate alone (Shaner, 2000). Shaner (2000) predicted a rapid shift, 3-5 years, of glyphosate-tolerance (GT) in the weed population if overreliance of glyphosate occurred. In 2003, the recommendation was for GT crops to be grown in rotation with conventional crops, while also utilizing non-chemical weed management approaches, and still utilizing other herbicides; to avoid future selection of GT weed species (Plimmer, 2003).

Glufosinate-resistant (LibertyLink®) corn and cotton were introduced commercially in the U.S. at the same time as glyphosate-tolerant soybeans (Green and Owen, 2011). Glufosinate-resistant soybeans (A2704-12) did not become commercially available until 2009. The U.S. approved multiple glufosinate-resistant soybean events in 1999 but commercial release was delayed by European regulatory agencies due to concerns about an antibiotic marker (Green, 2009). Glufosinate {2-amino-4-[hydroxy(methyl)phosphoryl]butanoic acid} (WSSA 10) is a broad-spectrum foliar applied herbicide that inhibits the enzyme glutamine synthetase (Green and Owen, 2011). Glutamine synthetase enzyme is needed for the conversion of glutamate + ammonium into glutamine in nitrogen metabolism. Glufosinate is a contact herbicide and much faster acting than glyphosate because it is not translocated through the plant. For the product to work well, it must be applied to small weeds and it is not effective on perennial weeds. Glufosinate has not been as popular as glyphosate due to higher application rates, higher costs, and more restrictive application timing. More than 120 broadleaf and grass weeds are labeled to be controlled and no weeds have been reported as resistant to glufosinate. It is very unlikely that future weed species populations will evolve resistance to this chemistry (Krämer and Schirmer, 2007). Attempts to generate target mutations and target overexpression have been unsuccessful. Weed populations that have been exposed to glufosinate selection for twenty years have not evolved resistance to this herbicide.

Glufosinate-resistance is gained by inactivating the metabolism of the chemical (Green and Owen, 2011). This inactivation has been achieved with either of two enzymes; phosphinothricin N-acetyltransferase (PAT) or basta N-acetyltransferase (BAR). PAT was isolated from the soil microorganism *Streptomyces viridochromogenes* and BAR from *Streptomyces hygroscopicus.* Glufosinate-resistant crops are commonly available because the trait has commonly been used as a marker for other GM traits i.e. insect resistance traits and do to the usefulness as an herbicide trait. Crops with stacked tolerance to both glyphosate and glufosinate were also reported to be commercially available in 2011.

The industries answer to the glyphosate-resistant weed pandemic has been to develop new HR traits for currently available herbicides (Green and Owen, 2011). These would be a combination of new traits in combination with the original glyphosate trait and new glyphosate traits. Green and Owen (2011) stressed that we must learn from our mistakes with glyphosate and realize that these new traits are temporary and must be used as a tool to diversify weed management. It will also be necessary to continue discovering new herbicide SOAs. They also reflected on glyphosate and noted that it should have been used as an herbicide to increase weed management diversity. It unfortunately resulted in the opposite; a one dimensional “silver bullet” weed management system that was not sustainable. Weed management became too simple and convenient. Green and Owen (2011) point out that glyphosate is still the most effective herbicide and it is not too late to diversify weed management while keeping glyphosate in the mix of a diversified approach. Crops with stacked herbicide-resistance to multiple herbicides and hopefully some new herbicide SOA will provide some relief to weed species resistant to herbicides (Heap, 2014).

A new stacked HT trait 356043 (Optimum® GAT®) for soybeans was identified by DuPont and being tested for a 2011 commercial release (Green, 2009). Expression of GAT4601 (glyphosate acetyltransferase) for glyphosate tolerance and a modified version of soybean acetolactate synthase (GM-HRA) for tolerance to ALS-inhibiting herbicides. Green (2009), sources within, the event was produced with particle acceleration transformation. The GAT4601 gene was sourced from soil bacterium *Bacillus licheniformis*. Processes of screening, gene shuffling, and site selected mutagenesis were used to identify the *gat* alleles with high levels of glyphosate-tolerance. Green (2009) explains from other sources, that the main promoter is synthetic-core promoter SCP1, with a portion of CaMV 35S promoter, and Rsyn7-Syn II (core synthetic consensus promoter). The selectable marker for the event in tissue culture was the *gm-hra* gene. DuPont announced in 2011, that it was giving up on commercializing this trait package (Pollack, 2012). A decision was made to stack the GAT trait with GTS 40-3-2, against patent rights, because the stack performed better. Stacking of the traits was not a legal option and a court appointed jury found DuPont guilty of patent infringement in 2012. The GTS 40-3-2 came off patent in 2014 so maybe we will see this stacking of two glyphosate-resistance traits and an ALS-resistance trait in commercial soybeans in the future.

Bayer CropScience was working to develop soybeans with resistance to HPPD (4-hydroxyphenylpyruvate dioxygenase) inhibitor isoxaflutole {(5-cyclopropylisoxazol-4-yl)(2-(methylsulfonyl)-4-(trifluoromethyl)phenyl)methanone} (WSSA 27) and to increase maize tolerance to this chemistry (Matringe et al., 2005). Strategies developed to achieve crop-resistance to HPPD inhibitors: 1) plant HPPD enzyme over-production, 2) synthesize homogentisate (2,5-dihydroxyphenylacetate) independent of HPPD, and 3) increase p-hydroxyphenylpyruvate (p-HPP) flux. Bayer in collaboration with MS technologies developed the soybean trait FG72 (LibertyLink®GT27™, Balance® Bean) (ISAAA, 2018; MS Technologies, 2018a). This is an approved soybean trait with herbicide-tolerance to glyphosate, glufosinate, and the isoxaflutole (ISAAA, 2018; MS Technologies, 2018b). LibertyLink®GT27™ soybeans became commercially available in the U.S. in 2017 (MS Technologies, 2018b).

Isoxaflutole is in the Isoxazole chemical family and was first patented in 1991 by Rhône-Poulenc Agriculture Limited; now Bayer Crop Science (Krämer and Schirmer, 2007). This was the first HPPD inhibitor herbicide for pre-emergence application in corn and first commercial availability was in South America in 1996. The most common trade name in the U.S. is Balance® and it is labelled to control broadleaf and grass weeds. There are currently no HPPD inhibitor herbicides registered for soybeans in the U.S. Isoxaflutole is rapidly converted into the herbicidal active compound diketonitrile (DKN) {3-cycloproyl-2-[2-(methylsulfonyl)-4-(trifluromethyl)benzoyl]-3-

oxopropanenitrile} in the soil and in plant tissue. Isoxaflutole is not very mobile in the soil and is more lipophilic than diketonitrile. These characteristics cause it to be more greatly absorbed by seeds, shoots, and root tissues. Diketonitrile is converted into benzoic acid with no herbicidal activity in the soil and in plants. Plants that are not susceptible (ex. maize) convert diketonitrile into benzoic acid at a faster rate than susceptible weeds. Proximity of the germinating seeds to the zone of herbicide also plays a factor in susceptibility. Maize is planted deeper than the germinating weed seeds that are in the zone of herbicide treated soil. HPPD-inhibitors control important weeds with foliar and/or soil residual activity (Green, 2012).

The plant enzyme HPPD is necessary for two processes in plants: 1) phenylalanine and tyrosine catabolism, and 2) prenylquinones biosynthesis (Matringe et al., 2005). Matringe et al. (2005) nicely displays both of these processes in Figure 1 of their publication. HPPD inhibitor herbicides cause bleaching in young leaves, increase tyrosine and phytoene levels, and deplete plastoquinone/vitamin E pools. Inhibition of HPPD by the herbicide is caused by a binding to the iron (Fe) on the active enzyme which is in competition with the p-HPP substrate. This chemical binding disrupts the reaction that is catalyzed by the HPPD enzyme.

The gene introduced was hppdPF W336 sourced from *Pseudomonas fluorescens* (strain A32) a modified HPPD enzyme that tolerates HPPD-inhibiting herbicides (i.e. isoxaflutole) due to an amino acid substitution that is less sensitive to DKN (Dreesen et al., 2018; ISAAA, 2018). The FG72 soybean trait was introduced by direct transfer of a chimeric construct into a wild type soybean containing a gene cassette with the W336 encoding sequence (Mason et al., 2017; Dreesen et al., 2018). Overexpression of HPPD resulted in a tenfold increase in soybean tolerance to isoxaflutole applied pre-emergence (Matringe et al., 2005). Glyphosate tolerance was achieved with the 2mepsps gene from *Zea mays* (double mutant version) (Mason et al., 2017; ISAAA, 2018). Binding affinity of glyphosate is decreased with the 2mepsps gene resulting in increased glyphosate herbicide-tolerance. The *pat* gene from *Streptomyces viridochromogenes* was used to obtain glufosinate herbicide-resistance. Biolistic transformation (particle acceleration) into soybeans was utilized to insert (EE-GM3) the gene containing both transgenes with glyphosate and HPPD inhibitor herbicide-tolerance (EFSA, 2015; Mason et al., 2017).

The transgenic soybean FG72 was then crossed, using conventional breeding methods, with transgenic soybeans resistant to glufosinate to achieve the final transgenic soybean with tolerance to all three herbicides; glufosinate, glyphosate, and isoxaflutole (Mason et al., 2017).

Syngenta developed a transgenic soybean tolerant to the HPPD-inhibitor herbicide mesotrione {2-(4-methylsulfonyl-2-nitrobenzoyl)cyclohexane-1,3-dione} (WSSA 27) (Kramer et al., 2014). The gene *avhppd-03* was sourced from oats (*Avena sativa* L.*)* and encodes an HPPD enzyme that is nearly identical to the HPPD enzyme in oats. The *avhppd-03* gene tolerates mesotrione herbicide with a reduced binding affinity of the herbicide to the enzyme. The promoter on this gene sequence causes avhppd-03 enzyme to be produced at a higher rate than the HPPD enzyme in wild type soybeans. This herbicide-tolerant soybean product is known as MGI-tolerant soybeans with tolerance to the three herbicides; mesotrione, glufosinate, and isoxaflutole (MGI) (Syngenta, 2013). The commercial product was to be released in collaboration with Bayer CropSciences at the end of this decade. Each company was also working to develop herbicide products and application programs to be utilized with this trait technology. The event code for this trait is SYN-00H2-5 and U.S. approval was granted in 2014 (ISAAA, 2018). Glufosinate-resistance was achieved by inserting the *pat* gene from *Streptomyces viridochromogenes.* Both genes were inserted into the soybean genome via agrobacterium-mediated transformation.

Dupont Pioneer has also reported discovery of HPPD-tolerance to be utilized in soybeans (Siehl et al., 2014). Tolerance to multiple HPPD inhibitor herbicides was accomplished with an optimized soybean promoter and an insensitive shuffled HPPD variant from *Zea mays.* The terminator in the gene sequence was ubiquitin3 from *Arabidopsis thaliana*. Accelerated particle bombardment was used to create the transgenic events in soybeans. The selectable marker used in this transformation was a chimeric gene with S-aldenosylmethionine synthase (SAMS) promoter and the ALS terminator region; both from soybean. Chlorsulfuron {1-(2-chlorophenyl)sulfonyl-3-(4-methoxy-6-methyl-1,3,5-triazin-2-yl)urea} (WSSA 2) was used for the initial in-vitro callus screening. In research conducted by Dupont Pioneer, transgenic soybean events showed tolerance to 4x labelled rates of mesotrione and isoxaflutole and 2x labelled rates of tembotrione {2-[2-chloro-4-methylsulfonyl-3-(2,2,2-trifluoroethoxymethyl) benzoyl]cyclohexane-1,3-dione} (WSSA 27).

Dow AgroSciences LLC has developed a herbicide-tolerant soybean event coded DAS-68416-4 with herbicide-tolerance to 2,4-D and glufosinate (Dow AgroSciences LLC, 2010). The *aad-12* gene from the gram-negative soil bacterium *Delftia acidovorans* expresses the protein aryloxyalkanoate dioxygenase (AAD-12). The AAD-12 enzyme has activity that results in metabolic inactivation of the 2,4-D herbicide. The AAD-12 enzyme degrades 2,4-D into 2,4-dichlorophenol a compound with no herbicidal activity. The *pat* gene has been utilized to acquire glufosinate-tolerance. A gene sequence containing both genes was inserted into the soybean genome with *Agrobacterium*-mediated transformation. The commercial name of the event DAS-68416-4 trait product is Enlist™ (ISAAA, 2018). Dow AgroSciences LLC in collaboration with MS Technologies LLC developed a triple stack herbicide-tolerant trait in soybeans with event code DAS-44406-6 (ISAAA, 2018). This event is the same as Enlist® with the addition of glyphosate tolerance. The glyphosate tolerance was obtained by adding the *2mepsps* gene from *Zea mays.* A gene sequence containing three genes (*aad-12, 2mepsps,* and *pat*) was inserted into the soybean genome with *Agrobacterium* generated transformation (Dow AgroSciences LLC, 2011). The commercial name for this triple stacked herbicide-tolerant transgenic soybean is Enlist E3™ (Dow AgroSciences, 2017).

It is believed that synthetic auxin growth regulator herbicides mimic the natural auxin plant growth regulator indole-acetic acid (Copping and Hewitt, 1998). The exact mode of action has not been determined. Naturally produced plant growth regulators in plants are maintained at a very specific concentration. It is theorized that plants sensitive to synthetic auxin herbicides are unable to reduce the high concentration of synthetic auxins when treated with the herbicide. The excessive concentration of synthetic auxins in the plant bind to auxin receptor sites and this continues until plant growth becomes abnormal or is suspended (Copping and Hewitt, 1998; Hartzler, 2017). There are three chemical families within the synthetic auxin mode of action; phenoxy, benzoic acid, and carboxylic acids/pyridines (Hartzler, 2017). 2,4-D belongs to the phenoxy family and is a selective herbicide for the control of a broad-spectrum of broadleaf weeds. Dow

Chemical Company has developed a new low-volatile form of 2,4-D to be used as the chemical component of the Enlist™ weed management system (Chahal et al., 2015). 2,4-D choline {2-(2,4-dichlorophenoxy)acetate;2-hydroxyethyl(trimethyl)azanium} is the 2,4-D formulation with reduced volatility and is manufactured with the Colex-D™ technology. Enlist Duo™ is the commercial name for the premixed 2,4-D choline and glyphosate herbicide that can be used with this trait package.

DowDupont Inc. has been awaiting China import approval of Enlist E3™ soybeans since 2013 (Polansek and Patton, 2018). They had originally planned for a full commercial U.S. launch of the product in 2015. While waiting to acquire additional import approvals, Dow and ADM have collaborated on a system to keep Enlist™ E3 grain and grain products in North America (Dow AgroSciences, 2017). A closed-loop system of production and processing has been put into place. Dow AgroSciences has protocols for the growers to follow to insure Enlist™ soybeans are not mixed with grain for exportation out of North America. There are four designated ADM processing facilities where the grain can be sold and processed into products for North America use only. The plants are in Mankato, MN; Frankfort, IN; Mexico, MO; and Deerfield, MO. This has obviously greatly reduced the availability of this technology to a very small segment of U.S. farming operations.

A University of Nebraska-Lincoln (UNL) scientist, Donald Weeks, and colleagues identified a gene to be utilized for dicamba-tolerance in crops like soybeans (Business Wire, 2005). The patent for this invention was originally filed in 1998 and patent No. US 7,022,896 B1 was issued on April 6, 2006 (Weeks et al., 2006). Monsanto signed a licensing agreement with the UNL to develop crops with dicamba-tolerance (Business Wire, 2005). Behrens et al. (2007) and sources within their text report on the gene function and plant transformation. Soil bacterium *Pseudomonas maltophilia* (strain DI-6) mineralizes dicamba converting it into non-herbicidal 3,6-dichlorosalicylic acid (DCSA) (Behrens et al., 2007). The gene responsible for this inactivation of dicamba is DMO (dicamba monooxygenase) which encodes the DMO enzyme. DMO enzyme prevents dicamba from building to toxic levels when in transgenic plants that have been treated with dicamba herbicide. A complete explanation of the enzyme reaction and the designed gene cassette for expression of DMO in transgenic plants can be found in

Behrens et al. (2007). *Agrobacterium*-mediated gene transfer was used to make the first transgenic plants with the DMO gene. The first plants to be transformed for gene validation were *Arabidopsis*, tomato [*Solanum lycopersicum* (L.)], and tobacco [*Nicotiana tabacum* (L.)]; all plants that are sensitive to dicamba. The initial herbicide screen of these plants transgenically modified with the DMO gene were a success. *Arabodopsis*, tomato, and tobacco plants expressing DMO all survived dicamba application rates 10-20 times above recommended application rates (5.6 kg/ha). Soybeans were transformed with the DMO gene and showed tolerance to repeated in-season dicamba applications (2.8 kg/ha) and no negative agronomic performance. The soybean field tests were conducted for three years with consistent results over the course of the multi-year study.

Monsanto event code MON87708 contains the DMO gene stacked with CP4 epsps (aroA:CP4) for tolerance to dicamba and glyphosate (ISAAA, 2018). *Agrobacterium*-mediated plant transformation was utilized for gene introduction. The gene source of DMO is reported to be from *Stenotrophomonas maltophilia* on the ISAAA website while Behrens et al. (2007) report the gene being sourced from *Pseudomonas maltophilia*. In 1993, *Pseudomonas maltophilia* was reclassified into a new genus *Stenotrophomonas, Strenotrophomonas maltophilia* is the only member; from sources within (Denton and Kerr, 1998). The commercial soybean trait package Genuity® Roundup Ready™ 2 Xtend™ was approved for U.S. cultivation in 2015 and all import approvals were obtained by 2016 (ISAAA, 2018). A commercial launch of the product in the U.S. was completed for the 2016 growing season (Monsanto, 2016). This product release was in advance of EPA approval of an approved dicamba herbicide formulation for post-emergence application to soybeans.

Dicamba herbicide has the same mode of action as 2,4-D (Hartzler, 2017). This family of herbicides is referred to as growth regulator herbicides, synthetic auxins, and/or WSSA group 4. Dicamba is from the benzoic acid family of chemistry within this mode of action. These are old chemistries and a Dicamba + 2,4-D mixture was a very common post-emergence application in Iowa corn production during the 1970’s and early 1980’s. Hartzler (2017) and sources within explain that there are risks associated with the use of synthetic auxins. Dicamba has a very high vapor pressure that can lead to volatilization and off-target movement. The risk of volatilization is higher when temperatures are above 85° F. Dicamba is also more susceptible to volatilization from crop vegetation than from soil. Another point of concern is that very low concentrations of dicamba can result in damage to off-target broadleaf plants. It was reported that concentrations of 0.005% of the dicamba rate can cause injury to soybeans without herbicide-tolerance. The source of non-target dicamba can come from inadequately cleaned spraying equipment, spray drift, and/or volatilization.

Monsanto, DuPont, and BASF have each commercialized dicamba herbicide products that are advertised to have reduced volatility. These products are the only three dicamba products registered for post-emergence use on dicamba-tolerant crops (US-EPA, 2017). Monsanto and DuPont have products using the same chemistry diglycolamine salt {3,6-dichloro-o-anisic acid) (DGA); XtendiMax® and FeXapan®, respectively, both with VaporGrip® technology. BASF has the dicamba herbicide product Enginia® {N,N-Bis-(3-aminopropyl)methylamine salt of 3,6-dichloro-0-anisic acid} (BAPMA). These herbicides were approved for commercial use during the winter of 2016/17 and the registration is only good for two years. The EPA will closely monitor the use of these products and trait technology to make a determination on future use after the 2018 growing season.

It has been reported that new formulations of dicamba do not prevent phytotoxic levels of dicamba acid moving out of treated soybean fields (Hartzler, 2017). In a 2016 field study on dicamba, secondary movement DGA moved 72 m further than BAPMA (Jones, 2018). The temperature during application was 31° C, RH 77%, and average wind speed of 8 km/hr (4.97 MPH). There are no third party or university studies on XtendiMax® with VaporGrip® technology available at this time. University of Tennessee weed scientist Tom Mueller was interviewed and stated “My field data shows dicamba emissions from Engenia® and XtendiMax® are lower compared to Clarity, but some dicamba still comes off the treated area.” (Smith, 2018).

XtendiMax® with VaporGrip® and FeXapan are both DGA dicamba salts which is the same as older dicamba chemistries ex. Clarity®. Clarity® available in 1992 was an improved chemistry over the Dimethylamine (DMA) salts, ex. Banvel®, that was commercialized in 1964 (BASF, 2017). BASF advertised that Clarity® had a 70%

reduction in volatility from Banvel®. VaporGrip® technology is advertised as reducing volatility by keeping dicamba in salt formation while in the spray tank (Monsanto, 2018). Protons separate dicamba from salt forming dicamba acid which is volatile. The VaporGrip technology is explained as removing protons from the solution which keeps dicamba in salt form that is not volatile. This technology is further explained in the U.S. patent as a polybasic polymer (Wright et al., 2012). Auxin salt forms an ionic bond with the polymer binding the auxin in solution. Auxin acid is said to be one hundred times more volatile than the bound dicamba. The BAPMA dicamba salt Engenia® is advertised as having 70% less volatility than the DGA Clarity® (BASF, 2017). University of Arkansas professor of weed science explains that volatility improvements have been achieved with the use of heavier salts (McGeeney, 2016). BASF reports that BAPMA has a heavier molecular weight and stronger bonds that reduce volatility (BASF, 2018).

HERBICIDE-RESISTANT WEEDS

A continual increase in the use of herbicides to manage weeds has been a benefit to agriculture but this has also resulted in an increase in herbicide-resistant weed populations (Buhler and Hartzler, 2004). The selection pressure placed on weed populations from agricultural practices naturally results in herbicide-resistant weed populations (Norsworthy et al., 2012). Weeds have a long history of adapting to many different crop management systems; not just herbicides. Examples of this adaptation presented by Buhler and Hartzler (2004) from other sources are weeds developing characteristics of the crop in response to hand weeding and weed seeds being selected for similar sizes as the crop in response to winnowing. Buhler and Hartzler (2004) give an overview of herbicide-resistance development in U.S. soybean production areas from a number of sources. The first weed populations to evolve herbicide-resistance in soybean producing areas was from repeated applications of triazine herbicides in corn. Weeds gained resistance to ALS inhibitors during the 1990’s from repeated use in soybean production. Selection pressure is considered the most crucial factor in the evolution of herbicide-resistance (Moss, 2002).

Weed populations often times gain herbicide-resistance by naturally occurring inherited traits from within the population gene pool (Moss, 2002). Most reported cases of herbicide-resistance are a result of altered biochemical functions, site of action, and metabolism. Altered site of action is the most common form of herbicide-resistance in weed populations and it is thought to be the fastest route of herbicide-resistance development.

Heap (2014) reports herbicide-resistance to be a normal result of natural selection and resistance is gained by five primary mechanisms. 1.) Target-site resistance occurs when the binding site enzyme is mutated in a way that prevents herbicide binding. Target-site resistance is commonly found within weed populations resistant to ALS inhibitor, ACCase inhibitor, dinitroanaline, and triazine herbicides. 2.) Enhanced metabolism is when a plant has an increased ability to metabolize a herbicide before typical plant death would occur. 3.) Decreased absorption/translocation allowing plant survival by reducing the movement of herbicides to the site of action. 4.) Sequestration of herbicide on cell walls and into vacuoles can reduce herbicide concentrations to below lethal doses. 5.) Gene amplification is when the target enzyme is over produced so that it would take higher rates of herbicide to inhibit the enzyme that results in plant death.

In 2014, Heap (2014) reported that 21 of the 25 herbicide sites of action had weed populations with evolved herbicide-resistance. This involved 220 unique weed species. The U.S. has the most herbicide-resistant weed species worldwide due to a long history of utilizing herbicides on a large scale. The occurrence of herbicide-resistance has steadily increased as the use of herbicides has increased (Heap, 2014).

A good source for current weed herbicide-resistance can be found at www.weedscience.org. This web site is the International Survey of Herbicide-Resistant Weeds tracking herbicide-resistant weeds worldwide. The website contains data and visuals for herbicide-resistance in a number of different categories.

Not all herbicide sites of action are equally susceptible to the selection of weed species herbicide-resistance (Heap, 2014). Characteristics of the weeds being treated with a herbicide have a great influence on the rate of selection for resistance. Examples of these characteristics include proliferation, breeding system, generations, seed viability, gene flow, etc. It also depends on the specific gene or genes tolerant to an herbicide in a plant species. Number of genes, occurrence, and strength of the genes within the population. The third component of selection is the actual selection pressure (herbicide application). Specifically, the number of individual plants being exposed to the herbicide selection pressure over the course of time.

Heap (2014) reported that the herbicide sites of action with the greatest number of resistant weed species were ALS inhibitors, photosystem II inhibitors (WSSA 5), ACCase inhibitors, synthetic auxins, bipyridilliums (WSSA 22), and EPSPS inhibitors; listed in the order of highest number of resistant weed species at the time. ALS and ACCase inhibitor resistant weed species have the highest economic impact.

One issue that has been encountered with the AHAS/ALS SOA is a large occurrence of weed species with evolved herbicide-resistance (Krämer and Schirmer, 2007). In 1998, the AHAS/ALS SOA was reported to have the highest number of weed species with populations that had gained resistance to this site of action; surpassing triazines. Approximately thirty-three percent of all herbicide-tolerance (HT) weed species have been selected by AHAS/ALS inhibitors (Heap, 2014). This is a result of herbicide use on a large area for many years (>30 years), a large number of susceptible weed species, and a high frequency of the initial gene mutations originating in the original weed species populations. Approximately seventeen percent of all registered herbicides are ALS inhibitors and this SOA is registered for all major crops. Heap (2018) International Survey of Herbicide Resistant Weeds reported 160 weed species worldwide with resistance to ALS inhibitors. In 2018, there were 52 weed species with resistance to ALS inhibitors in the U.S. alone.

Resistance to photosystem II inhibitors is more commonly associated with the popular use of atrazine (6-chloro-4-N-ethyl-2-N-propan-2-yl-1,3,5-triazine-2,4-diamine) on corn (Heap, 2014). Metribuzin was a commonly used pre-emergence herbicide in soybeans, as mentioned earlier in this document. Both, metribuzin (triazinone) and atrazine (triazine) have the same site of action (photosystem II). Preliminary research indicates that metribuzin may still effectively control triazine-resistant waterhemp (*Amaranthus tuerculatus*) (Owen and Hartzler, 2017). Heap (2018) reported that 74 weed species worldwide were resistant to photosystem II inhibitors and 26 in the U.S. alone. Heap (2014) and sources within report that primary forms of triazine herbicide-resistance are from gene mutation that reduces herbicide binding and metabolic resistance. Atrazine resistance is a result of many acres being treated over the course of many years and high initial frequency of the resistance genes.

Heap (2018) reports 48 monocot weed species worldwide with resistance to ACCase inhibitors and 15 weed species in the U.S. alone. This is a result of extended use on a large number of wheat (*Triticum aestivum* L.) production acres. Giant foxtail (*Setaria faberi* Herrm.) is the only species with resistance in Iowa and this is likely a result of extended ACCase utilization on soybean production acres. Heap (2014) reports from other sources that another contributing factor is 11 amino acid substitutions in the ACCase gene which generate an ACCase enzyme that is not sensitive to the herbicide. There are also some reported cases of weed species with metabolic resistance.

Heap (2018) reports that synthetic auxins in the U.S. alone have 9 weed species with resistance and worldwide there are 38 weed species with resistance. The majority of the weeds with resistance to synthetic auxins are not considered economically important because cases are not widespread (Heap, 2014). In the U.S., *Kochia scoparia* L. resistant to dicamba is the only weed species of notable concern but only on a limited basis.

PSI electron diverter herbicides had 32 weed species worldwide with reported resistance in 2018 (Heap, 2014). In the U.S., there was only 6 species with reported resistance. The first occurrence of resistance was discovered during the 1980's. It is somewhat unexpected to have this high of an occurrence of herbicide-resistance to PSI since the herbicides in this site of action are not easily metabolized and no target site resistance has ever been recognized. Primary forms of resistance are due to sequestration and reduced translocation. PSI resistance is considered to be of low economic concern.

Glyphosate-resistance continues to increase in importance and economical concern. Glyphosate-resistant weed species were reported to be wide spread across all of the U.S. soybean production regions and reports of new species are occurring more rapidly and gaining intensity as time progresses (Owen, 2011). Most cases of weed species resistant to glyphosate are due to nontarget-site resistance mechanisms, ex. sequestration and reduced translocation (Vencill et al., 2012). Glyphosate is considered low-risk for the development of weed resistance because there are only a few target-site mutations that allow resistance selection (Heap, 2014). Selection of glyphosate-resistant weeds is significant 1) because almost all weeds are susceptible to the herbicide, and 2) because there is such a large area planted to Roundup Ready (RR) crops and treated with glyphosate. In 2014, twenty-four weed species were reported to have evolved resistance to glyphosate worldwide; sixteen of these species were from RR cropping systems. The U.S. during this time had fourteen weed species reported to be tolerant to glyphosate in thirty-two states. Primary glyphosate-resistant weed species in the U.S. are listed in Table 5.

Table 5. Primary glyphosate-tolerant weed species in the U.S. (Heap, 2014).

Common Name	**Genus Species**	**Comment**
Horseweed	*Conyza canadensis*	Most widespread GR weed species. Easily controlled with affordable alternatives. Not a large threat at this time.
Palmeramaranth	*Amaranthus palmeri*	Greatest economic impact in the Southern U.S. Evolved resistance to other herbicides.
Water hemp	*Amaranthus tuberculatus*	Greatest economic impact in the Northern U.S. Evolved resistance to other herbicides.
Ragweed	*Ambrosia spp.*	
Kochia	*Kochia scoparia*	

Heap (2018) reported 17 cases of glyphosate resistance in the U.S. and 42 cases worldwide. This moves glyphosate into the top four for herbicide sites of action with the highest number of resistant weed species.

An increasing concern is the increasing occurrence of weeds that have evolved resistance to more than one herbicide site of action (Owen, 2011). This has been observed as both resistance to multiple modes of action and/or multiple herbicides within a family of herbicides (Heap, 2014). When a resistance mechanism provides a route of resistance to multiple herbicides it is known as cross-resistance. Altered target site enzymes can result in resistance to multiple herbicides that inhibit the same enzyme. The most common type of this is referred to as target-site cross-resistance. When a plant population has multiple herbicide-resistance mechanisms that result in resistance to multiple modes of action it is defined as multiple resistance.

In Iowa, there were three weed species with resistance to multiple herbicide sites of action reported to the International Survey of Herbicide Resistant Weeds (Heap, 2018). Owen (2017) reported a fourth weed species *Conyza canadensis* (L.) Cronquist (marestail or horseweed) with multiple herbicide-resistance to ALS inhibitors and PSII inhibitors; not yet reported to the International Survey of Herbicide Resistance. *Abrosia trifida* L. (giant ragweed) was reported to have evolved resistance in Iowa to HPPD inhibitors; not yet reported to the International Survey of Herbicide Resistance (Owen and Hartzler, 2017). A comprehensive list of weed species with evolved herbicide-resistance in Iowa (Table 6). In the U.S. there were 79 reported cases of weed species with multiple herbicide-resistance http://www.weedscience.org/Summary/MultibyCountry.aspx Accessed September 11, 2018.

The weed science department at Iowa State University conducted a sampling of waterhemp [*Amaranthus tuberculatus* (Moq.) Sauer] in 300 soybean fields across the state of Iowa during 2011 and 2012 and 400 soybean field during 2013 (Owen and Hartzler, 2017). The purpose of this study was to obtain a clearer picture of present herbicide-resistance conditions in the field at the request of the Iowa Soybean Association. Approximately 900 waterhemp populations were sampled in this study. Seeds were collected from in-field waterhemp plants to be grown in a greenhouse herbicide screening. Screening included treatments of ALS, PSII, EPSPS, PPO, and HPPD inhibitors. Treatments were selected due to popularity of use in Iowa agriculture.

Results of the screening showed that herbicide-resistance levels were very high for all sites of action tested. It was noted that waterhemp populations were typically scattered patches or single plants and populations were described as being low density. Waterhemp has the characteristic of yielding high amounts of seed and this could result in a rapid shift in herbicide-resistant population densities if weed management techniques are not adjusted. ALS resistance was found to be widespread and present in 100 percent of the waterhemp populations screened in 2013. PSII resistance was found to be widespread across the state and present in 97% of the waterhemp populations screened in 2013. Glyphosate resistant waterhemp was also widespread across the state of Iowa and present in 98% of the populations screened in 2013. PPO inhibitor herbicide-resistance was also found to be widespread across the state of Iowa and found in 83% of the population screened in 2013. PPO inhibitor herbicides use was increasing in use during this study for both pre-emergence and post-emergence applications. PPO inhibitor herbicide is thought to be the only herbicide option for selective post-emergence management of waterhemp. Due to increased use, there will be an increase in PPO resistant waterhemp populations.

Table 6. Iowa weed species with evolved herbicide-resistance as summarized by Owen and Hartzler (2017) from The International Survey of Herbicide Resistant Weeds (Heap, 2018). Accessed September 11, 2018.

Date reported	Weed species	Herbicide site of action (WSSA)	Multiple resistance reported
1985	Kochia (*Kochia scoparia*)	5	No
1989	Common lambsquarter (*Chenopodium album*)	5	No
1990	Pennsylvania smartweed (*Polygonum pensylvanicum*)	5	No
1992	Giant Foxtail (*Sertaria faberi*)	5	Yes
1994	Giant Foxtail (*Sertaria faberi*)	1	Yes
1993	Tall waterhemp (*Amaranthus tuberculatus*)	2	Yes
1996	Tall waterhemp (*Amaranthus tuberculatus*)	5	Yes
2009	Tall waterhemp (*Amaranthus tuberculatus*)	14, 9, and 27	Yes
1995	Common cocklebur (*Xanthium strumarium*)	2	No
1997	Common sunflower (*Helianthus annuus)*	2	No
1998	Shattercane (*Sorghum bicolor)*	2	No
2000	Giant ragweed *(Ambrosia trifia)*	2	Yes
2009	Giant ragweed (*Ambrosia trifia*)	9	Yes
2016	Giant ragweed *(Ambrosia trifia*)	27	Yes
2011	Marestail/horseweed (*Conyza canadensis*)	9	Yes
NA	Marestail/horseweed (*Conyza canadensis*)	2	Yes
NA	Marestail/horseweed (*Conyza canadensis*)	5	Yes

A wide distribution of HPPD resistant waterhemp populations was also found across the state of Iowa in 73% of the populations screened during 2013. A staggering 69% of the waterhemp populations screened revealed three-way herbicide resistance. This resistance was increasing during the course of this study. The three sites of action most commonly present in the three-way resistance were ALS, PSII, and EPSPS inhibitors. Future studies to include sampling and herbicide screening of giant ragweed and marestail were reported to be in planning stages.

FUTURE

What does the growing issue of weed populations evolving herbicide resistance mean for the future of farming? The resource of herbicides as a tool to manage weeds in agriculture are not invincible (Norsworthy et al., 2012). For this depletion of a very valuable tool to be reduced, action needs to be taken to diversify weed management approaches. The conventional methods of weed management are proving to be selection pressures that are conducive for rapid evolution of herbicide resistance. A single weed management practice used in repetition promotes the evolution of resistance to that practice. Best management practices will need to be implemented that include all cultural, mechanical, and herbicidal options. We cannot rely on new chemistries alone to alleviate the issue. Diverse weed management into the future will likely include a wide spectrum of pre-emergent and post-emergent herbicides, stacked herbicide-tolerant traits, and increased applications of tillage (Green, 2016). This need for more complex weed management practices will increase the cost and time needed to manage weeds. Diverse weed management systems of the future will need to include strategies for managing herbicide-resistant weed populations (Heap, 2014). Herbicide labels are now containing a section with suggestions on managing herbicide-resistant weed populations (Owen and Hartzler, 2017). Adoption of these management techniques are necessary for a sustainable future.

Tackling the issue of herbicide-resistant weeds is at a critical point (Heap, 2014). The trend for dealing with herbicide-resistant weeds has been answered in the past by the introduction of new chemistries and herbicide-resistant crops. Unfortunately, there are no new chemistries on the horizon and has not been any new SOA introduced commercially for over 30 years. Government regulations have made the process of discovering new herbicide SOA and trait tolerance packages very time consuming and expensive (Green, 2016). This complication will likely shift the industry to less restricted methods of herbicide-tolerance discovery like gene editing and possibly combating herbicide-tolerance in weed populations with RNAi technology.

Until the mid-2000s, after the introduction of glyphosate-tolerant crops it became increasingly common for glyphosate to be the only herbicide in the weed management program (Heap, 2014). As glyphosate-tolerant weeds became more prevalent, farmers began to diversify the herbicides being utilized to control weeds. This was seen primarily as an increased use of pre-emergent herbicides. There has been an increase in the use of old chemistries due to a lack of new SOA discovery and commercialization (Green, 2016). The staple herbicide for weed management will continue to be glyphosate due to continued effectiveness.

Herbicide-resistant crops will continue to be a part of diverse weed management programs (Heap, 2014). Stacked herbicide-tolerant traits will continue to provide an immediate short-term answer for the near future. These herbicide-tolerant trait packages will allow the use of old SOA in new ways in an effort to maximize the herbicide diversity that can be utilized. Heap (2014) predicts that herbicides will remain the primary weed management tool but will eventually be replaced by new technologies. Some examples of new technologies given were robotic weeders, nano-machines, and genetically engineered bioherbicides.

SUMMARY

Weeds have persistently remained a nuisance since the beginning of agriculture and that is not going to change anytime soon. The tools and methods of managing weeds will certainly continue to change into the future for all agricultural crops. This evolution of weed management has been apparent since the initial introduction of soybeans to Iowa in 1852.

U.S. soybean production has survived the era of horse drawn implements, tractor power integration, chemical era, and the most recent biotechnology era. Weeds have managed to survive through all of these tools and technologies that man has utilized to battle this yield limiting existence. Some tools have worked better than others and there has been a tendency of overreliance on the tools that work really well. The lesson that has been learned multiple times is that repeated use of one practice provides a selection pressure that will reveal weed populations immune to the management practice. The only method of reducing the occurrence of this rising issue is to diversify techniques utilized for the management of weed removal.

There have been a few chemical and biotechnology products that at first glance appeared to be "the silver bullet" and for short times they have been utilized and acted in that way with extremely good results. But when a single approach of weed management is utilized repeatedly, it is followed with the appearance of herbicide resistant weed populations. When the one-dimensional selection pressure is continued the resistance issue will continue to grow in diversity and density until the significance of that valuable tool is diminished in value. The take away message is that a diverse approach will need to be adopted to prevent the elimination of valuable herbicide products. It is likely that new technologies for weed management will be introduced in the future and it will be important to utilize these technologies in combination with existing methods to broaden the diversification of the management approach. If this approach of diversification would have been utilized with the introduction of glyphosate tolerant crops, we would very likely not be in the scenario of glyphosate tolerant weed species being the economical concern that they are at present.

The reality of weed management today is that we are managing herbicide-resistant weeds. All cultural, mechanical, and herbicidal options need to be considered for each unique situation encountered in the field. There are twelve best management practices recommended by Norsworthy et al. (2012) and endorsed by the WSSA:

1.) Understand the biology of the weeds present.
2.) Use a diversified approach toward weed management focused on preventing weed seed production and reducing the number of weed seed 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 weeds or those most prone to herbicide resistance.
7.) Apply the labeled herbicide rate at recommended weed sizes.
8.) Emphasize cultural practices that suppress weeds by using 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 after harvest to prevent a buildup of the weed seedbank.
12.) Prevent an influx of weeds into the field by managing field borders.

Weed management has seen an interesting cycle of tools and technologies. Weeds were initial managed with cultural practices and tillage. This was diversified with the introduction of herbicides and for many years the addition of new herbicide sites of action to the toolbox. With the introduction of glyphosate-tolerant soybeans, the diverse list of multiple sites of action utilized to manage weeds was rapidly converted to a one-dimensional herbicide tool. It has now been experienced firsthand that this miracle herbicide was not invincible if used repeatedly alone. There is still significant value there but diversification will need to be adopted to strengthen and manage herbicide resistance.

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