WHERE ARE THE NEW HERBICIDES MODES OF ACTION

Hansjoerg Kraehmer, Arno Schulz, Bernd Laber

Bayer CropScience GmbH , Institute of Herbicide Research and Phytoregulators,
Industriepark Hoechst, H 872, D-65926 Frankfurt am Main, Germany

Summary

Three major reasons drive the demand of her¬bicides with new modes of action: weed resistance, gaps left over by existing standards and potential environmental risks with the existing chemistry. Ag-chem companies have established highly sophisticated tools to find new herbicide targets which could be successfully affected and which contribute to modern weed control. Weed resistance however, is not only caused by target site mutation. The HRAC classification of herbicides insinuates common characteristics of compounds within the same chemical family and the predictability of resistance risks. Some generalists assume that new modes of action automatically close gaps left by well established chemistry.

New ALS inhibitors may control ALS resistant weeds and weeds may demonstrate cross resistance against completely new compounds with a new mode of action. Farmers have always been forced to choose production tools which are cost efficient. Weed resistance management tools are only attractive when economic advantages over existing production systems become evident.

Keywords Herbicide modes of actions, weed control systems, weed resistance, weed spectrum of herbicides, target based screening, high throughput screening models

INTRODUCTION

Reasons for the demand of new modes of action

a) Weed resistance

Since the first observation of resistance to triazines in the late 60´s, further herbicide resistant biotypes with resistance to most of all herbicide classes have been identified worldwide in more than 154 dif¬ferent weed species (Vaughn). Herbicides do not induce resistance per se. The economic pressure on farmers has led to an ongoing reduction of diversity in the way crops are produced today. The diversity in crop rotations, cultural practices and chemical weed management strategies have been reduced in the last decades. A soil preparation by minimum tillage instead of using the plough is definitely promoting weed infestations and population shifts. A focus on a few crops only in a crop rotation minimizes the available cultural and chemical weed management options a farmer can utilize. The excessive use of one mode of action in a crop rotation definitely fosters shifts in weed populations and induces the development of herbicide resistance.

b) Similar chemistry is often characterized by characteristic performance weaknesses

The invention of a new interesting herbicide leads automatically to the synthesis of analogues and sometimes to a great number of very similar products with the same biochemical target. Tables 1a to 1c show an overview on registered ALS inhibitors.

Table 1a. Classification of ALS-Inhibitors according to Dollinger : imidazolinones and triazolopyrimidines

Chemical Family	Active Ingredient
Imidazolinones	imazapic imazamethabenz-methyl imazamox imazapyr imazaquin imazethapyr
Triazolopyrimidines	cloransulam-methyl diclosulam florasulam flumetsulam metosulam penoxsulam

Table 1b. Classification of ALS-Inhibitors according to Dollinger : Pyrimidinyl(thio)benzoates

Chemical Family	Active Ingredient
Pyrimidinyl(thio)-benzoates	bispyribac-Na pyribenzoxim *pyriftalid* pyrithiobac-Na *pyriminobac-methyl*

These families are chemically quite different. There¬fore, they target different crops and weeds. Their physicochemical and environmental behavior varies in a wide range. Some of them are even able to control ALS resistant weeds, e.g. TH-547 (Tanaka) or a new class of sulfonyureas claimed by DuPont (WO 02/062786 A1).

Table 1c. Classification of ALS-Inhibitors according to Dollinger : Sulfonylureas and Sulfonylaminocarbonyl-triazolinone

Chemical Family	Active Ingredient
Sulfonylureas	amidosulfuron azimsulfuron bensulfuron-methyl chlorimuron-ethyl chlorsulfuron cinosulfuron cyclosulfamuron ethametsulfuron-methyl ethoxysulfuron flazasulfuron flupyrsulfuron-methyl-Na foramsulfuron halosulfuron-methyl *imazosulfuron* iodosulfuron mesosulfuron metsulfuron-methyl nicosulfuron *oxasulfuron* primisulfuron-methyl prosulfuron pyrazosulfuron-ethyl rimsulfuron sulfometuron-methyl sulfosulfuron thifensulfuron-methyl triasulfuron tribenuron-methyl trifloxysulfuron triflusulfuron-methyl *tritosulfuron* TH-547
Sulfonylamino carbonyl-triazolinones	flucarbazone-Na propoxycarbazone-Na

Table 2. Characteristics of Sulfonylureas-, Fops- and PPO-Inhibitors

	Sulfonyl-ureas	FOPs	PPO-I.
Dose rates (g a.i./ha)	Very low <100g	Low < 500g	Variable 50-2000
Spectrum	Dicots + Monocots	Grasses only	Primarily dicots
Speed of action	Slow	Slow	Fast
Weak-nesses (e.g.)	Viola, Lamium, Veronica	Poa, Cynodon	Grasses
Environ-mental Risks	Carry over, soil mobility	Soil mobility	Phytoto-xicity after drift

Some compounds in the same mode of action group may have similar properties. Table 2 tries to list a few characteristics of ALS-, ACCase- and PPO-inhibitors.

c) Environmental risks

Old, high dose compounds often loose their re¬gistration due to high dose rates and persistence. Groundwater contamination risks are the basis of the withdrawal of registrations. Examples are urea herbicides such as diuron or triazines such as atrazine or simazine. New molecules often do not provide the same long lasting effect or are too expensive, however.

CAN THE HRAC CLASSIFICATION SERVE AS A CLASSIFICATION TOOL FOR RESISTANCE RISKS?

The HRAC classification is primarily based on modes of action but not on resistance phenomena

HRAC has classified all registered herbicides according to modes of action. This classification is often misleading as the association with an HRAC group does not necessarily define common resistance phenomena: some ALS inhibitors in the HRAC group B control ALS resistant weeds. Some weeds are resistant against all kinds of herbicides. The general discrimination of compounds of a chemical compound class is not justified on grounds of the HRAC system. HRAC makes clear statements about what the classification cannot provide: "The system itself is not based on resistance risk assessment ".

a) Target site resistance

Most herbicides bind to target enzymes. Some of these enzymes can be modified by nature without drastic effects on plant metabolism. The binding of herbicides, however, may be affected in a way that the mutated weeds become resistant. Most binding sites are well known for ALS inhibitors (e.g. Tan et al., Zheng et al.) and ACCase inhibitors (e.g. Délye&Michel). Mallory-Smith and Retzinger have proposed to classify herbicides by the site of action. The knowledge about the structure of a target site, however, does not guarantee the knowledge about the function of a resistance mecha¬nism. The expression of resistance genes e.g. is dependent on classical genetics: the fate of resistance alleles depends on their selective advantage in the presence of herbicides, as well as the dominance of the effects (Roux et al.).

b) Metabolic resistance

Metabolic resistance makes weeds resistant independent of modes of action. Degrading enzymes of plants and bacteria detoxify herbicides in nature. This process can be selective. It can be the reason for crop selectivity. Some weeds, however, take advantage of the mutation of degrading enzymes, e.g. cytochrome P450 oxidases or GST enzymes (Barrett ; Edwards and Dixon) . These enzymes can degrade all sorts of molecules independent of their mode of action. Cross resistance is often the consequence of such an adaptation of weeds.

Where does the HRAC classification lead to wrong conclusions in agriculture?

Subsidies in Europe and in the USA have a great impact on cropping and weed management de¬cisions. The European CAP reform was based on overproduction and budget crises, pollution, food scares and pressures arising from the expansion of the EU to countries highly dependent on agriculture.

New subsidy regulations are based on the reduction of agrochemicals and the sustainability of predefined environment values.

The Ger¬man BBA e.g. has developed the program Neptun to create crop protection indices which may be used to reduce the amount of pesticide application (Gutsche and Ross¬berg). The HRAC classification, however will not be suitable to attribute a resistance risk to a compound just because it belongs to a chemical family. Resistance management will therefore not be a logic argument for reducing herbicide applications.

NEW MODES OF ACTION CONTRIBUTED TO THE HIGH EFFICIENCY OF AGRICULTURE

The weed control systems of the past changed in waves

Auxins, PS-II and PS-I inhibitors dominated the 50's and 60's of the last century. They were followed by cell division inhibitors in the 60's and 70's. A great number of different modes of action entered the market in the 70's and 80's, e.g. glyphosate as an EPSP inhibitor, PPOs, carotenoid biosynthesis inhibitors, fatty acid biosynthesis inhibitors etc.. The 80's and 90's were characterized by ALS inhibitors.

Each mode of action allowed the control of new weeds in new crops. The industry could provide tools with low rates per acreage and with lower and lower costs. Advanced breeding technologies allowed the introduction of Herbicide Tolerance (HT) systems in the late 90's accompanied by a further decrease of herbicide costs. Many excellent herbicides are now out of patent and are produced by companies, which do not have to bear deve¬lopment risks nor the high costs of R&D.

No new mode of action for more than 20 years

On a first glance, our customers get the impression that scientists in the ag-chem industry are less creative and that patent busting is the only way of finding new molecules. Some believe that there are no new attractive modes of action left and that the chance of finding really new chemical structures is only low. The reasons for the innovation gap have indeed completely different reasons.

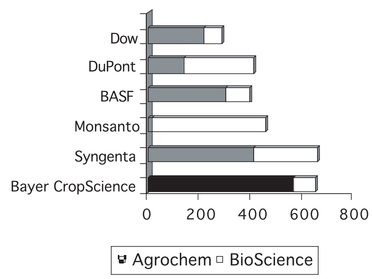
The technical standards and the costs for registration are very high

High efficiency and low cost for herbicides are the primary reasons for a lack of innovation. Costs for the development of new herbicides have increased drastically (Short). The regulatory hurdles are higher than ever. Consumers of agricultural goods regard agrochemicals as a threat to the environment rather than as tools, that have enabled agriculture to keep pace with the food demand of a logarithmic population growth. The global herbicide market exhibits all typical para¬meters of maturity: stagnating growth, price pressure and increasing competition, expiry of patents, establishment of regional generic industries, portfolio consolidation and concentration of the in¬dustry on a small number of global players. In¬creasing regulatory demands triggering high de¬velopment costs refrain the industry from serving smaller (niche) markets which remain without ad¬equate weed management solutions.

High hurdles are the reason for a reduced success rate in our industry

Many companies have changed their strategic focus. They have reacted to the above mentioned trends by shifting their research resources more and more into biotechnology activities (table 4)

Table 3. R&D expenses of selected companies in 2005 (Bayer CropScience in-house data, mio)



This is accompanied by a steep de¬cline in the number of patent applications for new active ingredients. Whereas in 1990 more than 250 her¬bicides patent applications were filed, this num¬ber dropped to less than 70 applications in 2003 (table 5).

Table 4. Number of herbicide patent applications between 1990 and 2005 (according to Stuebler 2006)

Table 5. Introduction of new herbicides and safeners between 2006 and 2012 according to Credit Suisse

Company	2006	Thereafter
BASF	0	2
Bayer CropScience	0	4
Syngenta	1	2

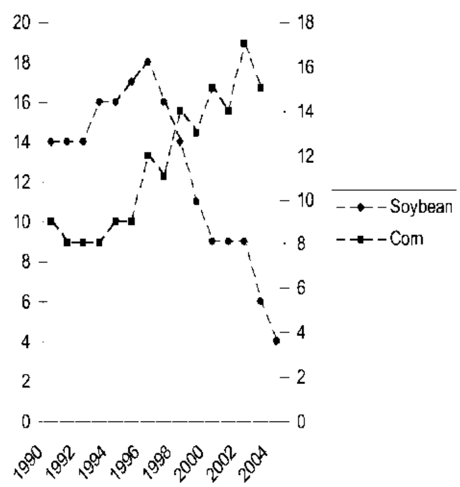
The average approval rate for novel herbicides has been 10 – 12 active ingredients per year over the last three decades. This figure has been significantly less in the recent years as a consequence of increasing performance demands in crop production as well as ever increasing regulatory hurdles.

THE REDUCTION OF COMPOUNDS IN THE MARKET WILL LEAD TO NEW PROBLEMS IN AGRICULTURE

Existing HT-programs will not solve all problems

The search for corn herbicides appeared unattractive in the 80s as atrazine dominated the market. Thereafter, new herbicides were needed as atrazine lost its registration in many countries. HT corn does not provide sufficient weed control tools. Corn differs from soybeans insofar as it is very susceptible to early weed competition. Wide row planting prevents sufficient dominance of corn over weeds between the rows. Single glyphosate treat¬ments will not be sufficient in most cases as weeds emerge over a long period after planting. Often, farmers cannot enter fields because of bad weather conditions or of workload conflicts at spraying time. Yield penalties are the consequences of late weed control. Therefore, pre-emergence herbicides are common practice in corn. The number of new molecules decreased in soybean during the last de¬cade but it increased in corn (table 8). A few herbi¬cides were quite successful, e.g. mesotrione of Syn¬genta (Annual Report 2005).

Table 6. Number of active ingredients applied on 5 or more % of treated corn and soybean acres in top producing US states (USDA, NASS data) according to VanGessel



European oilseed rape is used for the production of biodiesel. The acreage is supposed to increase. (Illing). HT-systems are used in Canada and in the USA but not in Europe. The low acreage in Europe did not allow the development of new herbicides yet. Increasing energy prices however will contri¬bute to the increasing importance of this crop. New herbicides are urgently requested.

Adaptation of weeds to new habitats

Apparently, some weed species in Brazil have adapted to cooler climates in the intercropping season, the safrinha. Weed control in the intercrops is not as intensive as in the main season. This leads to an increase of seedbanks and competition for the following crop (personal communication by Dio¬nisio Gazziero, EMBRAPA). Weed shifts can be attributable to ecological adaptation (Owen and Zelaya).

Several non-endemic weed species from southern Europe are penetrating into northern countries, e.g. *Abutilon theophrastii* Med. (Meinlschmidt), *Ambrosia artemisiifolia* L, (Bohren et al.), or *Setaria*-Species. These invasive weeds require new weed control tools.

AG-CHEM COMPANIES WILL DEFEND THEIR MARKET POSITION AND WILL TRY TO ADAPT THEIR PORTFOLIO TO NEW REQUIREMENTS

Many problems are to be solved

HT – systems have not gained a high proportion in a few major crops yet: cereals, rice, plantation crops, corn. Political, agronomy reasons and the lack of value capture systems for agrochemical companies are the reasons for this fact.

If we want to con¬trol the development of insensitive weed popu¬lations, we will have to alternate the use of herbi¬cides with dif¬ferent modes of action or to combine glyphosate with residual herbicides. Seve¬ral mixture partners can be used to control such weed popu¬lations (e.g. Krausz and Young).

The decrease in the number of soybean selective herbicides and the dominant position of glyphosate cause concerns about the availability of alternative herbicide solutions in the future. New soybean va¬rieties with stacked gly¬pho¬sate- and dicamba-tole¬rance traits are in de¬velopment. They will allow the control of some im¬portant glyphosate-resistant weeds in crop (Fraley). In the mid-term, however, glyphosate will stay available as an efficient weed control only if it is integrated in herbicide rotation pro¬grammes.

Unique Research Platforms Striving for Success

The successful conventional herbicide discovery process is based on the optimization of active che¬mical classes along with proven greenhouse scree¬ning technologies and will continue to play an im¬portant role in the future.

In order to increase efficiency, however, and to counteract the declining innovation rate (see above) the remaining global herbicide companies have revised their discovery strategies.

With the advent of miniaturization and automation in screening technologies and in chemical synthesis (combinatorial chemistry, automated synthesis) new dis¬covery platforms were established. In ad¬dition, pharma-like target-based discovery tech¬no¬logies were added to the platforms. The new screening platform builds a unique network con¬sisting of

1. Ultra-High-Throughput-in-Vivo-Screening (UHTVS) for the discovery of new compounds.
2. Target-based Ultra-High-Throughput-Bio¬che¬mi¬cal Screening (UHTBS).
3. Virtual-Target-Based-Screening (VTBS) as an exemplifying tool for rational design approaches.

The UHTVS opens a new dimension for discovery through rapid and reliable screening of whole plants. Several hundred thousand compounds can be tested annually for their herbicidal potential. The miniaturization makes it possible to test even compounds available only in minute amounts, thus potentially increasing chemical diversity.

In parallel, a target-based screen (UHTBS) is implemented for the directed discovery of compounds interacting with novel targets. These targets have been identified through either sys¬tematic genomic knock-out programmes (Höfgen et al.; Berg et al.) or by mode of action analysis of herbicidal hits from UHTVS.

These targets also provide the basis for elucidating the three-dimensional (3D) target protein structure. If we know the protein structure and especially the “active site” where its function is located, we will be in a position to use rational design approaches for chemical optimization. Once we know the structure binding to the active site, we are able to use what is known as “molecular modelling”. This technology (VTBS) offers direct proposals for optimized synthesis.

We are convinced that the new research platform will deliver high quality lead molecules which fulfil the demanding requirements to the invention of new herbicide standards.

WHAT ARE THE OBJECTIVES FOR NEW HERBICIDES IN AGROCHEMICAL COMPA¬NIES?

1. Broad spectrum efficacy against grass and dicotyledonous weeds
2. Flexibility for pre- and post-emergent use
3. Outstanding selectivity in respective crop production systems
4. Mode of action suitable to complement the herbicide rotation regimes (e.g. resistance management)
5. Low application rate
6. Favourable environmental behaviour
7. High level of safety

SCREENING AND PROFILING OF COMPOUNDS REQUIRE EXPERIENCE

Biological test systems are subject to a variation of results, especially when test conditions change from trial to trial. Glasshouse and field data for herbicides can vary considerably. The British Crop Protection Council dedicated this topic several conferences (e.g. Hewitt et al. 1994). Table 9 shows a number of factors playing a role when correlating glasshouse and field data.

Table 7. Factors influencing herbicide performance under glasshouse and field conditions and observed effects (Kraehmer, 1994).

Factors	Consequences
Genome	
– sensitivity varies within taxonomic order	– varying results due to vast number of closely related weed species – tolerant or resistant biotypes are sprayed by chance
– sensitivity depends on growth stage	– dormant seed or special stage of weed is not controlled – compound primarily controls ▪ growing plants or ▪ plants with enough biomass or ▪ germinating weeds
Environment	
– temperature, light, water, fertilizer, wind, soil, space – interaction with other plants and with pests – interaction with other chemicals	– variation of phenotype due to growing conditions: ▪ plant morphology ▪ plant sensitivity ▪ plant response
Crop-weed interaction	
– variation of weed density – variation of weed associations	– varying weed control due to different crop-weed interactions – weeds not affected take advantage

Many weed targets remained in screening test sets of our industry for several years. From time to time, however, species are exchanged according to new economic problems. ALS- and ACCase resistant weeds were included in the late 90s. Glyphosate resistant weeds, e.g. Lolium and Conyza biotypes may be added soon.

OUTLOOK

- Herbicides are and will remain an effective and economic input factor in the crop production globally. The demand of high quality crop commodities for food, feed, technical uses and bio-energy is significantly growing in view of a constantly declining availability of labor for crop production. In addition, the globally available land for crop production is limited. Numerous technology gaps in weed management offer substantial opportunities for novel and innovative herbicide solutions
- The number of innovative herbicide companies is still decreasing considerably
- There will be not more than 3 major players active in herbicide research
- It will become harder and harder to find new mode of actions
- The innovation rate will decrease

FarmTech Partners

at the show and on the farm.

FOR SUBSCRIPTIONS CALL:
1.800.665.1362

REFERENCES

Agricultural Statistics Board NASS, USDA

AgBioWorld (2006). Ten years after the first generation of genetically engineered (GE) varieties became commercially available, adoption of these varieties by U.S. farmers is widespread for major crops. AgBioWorld, 24 April 2006.

Barrett, M. (2000). The role of cytochrome P450 enzymes in herbicide metabolism- in Cobb, A.H. and R.C.Kirkwood : Herbicides and their mechanism of action, 25-34. CRC Press.

Beckie, H. J. et al. 2006. A decade of herbicide-resistant crops in Canada. Canadian Journal of Plant Science . In preparation.

Berg, D., K. Tietjen, D. Wollweber, R. Hain (1999). From genes to targets: imoact of functional genomics on herbicide discovery. Brighton Conference, BCPC, 491-500.

Burgos, N. (2006). Weed management systems in US rice and cotton. Visions 2020 – BayerCropScience Symposium in Frankfurt.

Bohren, C., Mermillod, G., Delabays (2006). Common ragweed in Switzerland: development of a nationwide concerted action. Journal of Plant Diseases and Protection, special issue XX, 497-503.

Credit Suisse (2006). Global Agrochemicals. Themes from 2006 Credit Suisse conference.
www.csfb.com/conferences/agchem2006/

Dollinger, M. (2005). Classification of Herbicides According to Mode of Action. www.plantprotection.org/hrac/Bindex.cfm?doc=moa2002.htm

Edwards, R. , D.P. Dixon (2000). The role of glutathione transferases in herbicide metabolism- in Cobb, A.H. and R.C.Kirkwood : Herbicides and their mechanism of action, 25-34. CRC Press.

E.I. Du Pont De Nemours and company (2001).
Herbicidal Sulfonylureas. WO 02/062786 A1

Fraley, R. (2006). Credit Suisse Agrochemical Conference Mar 10, 2006

Gutsche, V. and Rossberg, D. (2004). Crop protection indicators in Germany. OECD Expert meeting on farm management indicators and the environment, March 8-12, 2004.

Gerhards, R., M. Soekefeld, C. Timmermann, M.M. Williams. (2002) Site-Specific Weed Control in Maize, Sugar Beet, Winter Wheat and Winter Barley. Prec. Agricul. 3, 25-35.

Gerhards, R., M. Soekefeld, A. Nabout, R.-D. Therburg, W. Kühbauch. (2002). Online weed control using digital image analysis. Journal of Plant Diseases and Protection, special issue XVIII, 421-427.

Hager, A. (2003). The future of weed control in soybean: how many options will there be? http://www.cropsci.uiuc.edu/

Heap, I. (2006). International survey of herbicide resistant weeds at http://www.weedscience.com/

Hewitt, H. G., J. Caseley, L.G. Copping, B.T. Grayson, D. Tyson (1994). Comparing glasshouse and field pesticide performance II. BCPC Monograph 59, 1994.

Höfgen, R., J.Freitag, S.Maimann, F. Schmidt, H. Hesse (1999). Molecular approaches supporting the identification and validation of new herbicide targets. Brighton Conference, BCPC, 501-518.

Hurle, K., J. Petersen. (2000). Cultivation of herbicide resistant crops: weed management and environmental aspects. Plant Protection Science, Vol. 36, 112-116.

Kraehmer, H., P.E. Russell (1994). General problems in glasshouse to field transfer of pesticide performance. In BCPC Monograph 59, 3-16.

Krausz, R.F., Young, B.G. (2003). Sulfentrazone enhances weed control of glyphosate in glyphosate-resistant soybean (Glycine max). Weed Technology 17, 249-255.

Kudsk, P., J.C. Streibig. (2003). Herbicides – a two-edged sword. European Weed Research Society, Weed Research 43, 90 – 102.

Illing, C. (2005). European Agriculture- an economic factor. BASF Press Conference, August 30th, 2005.

Lein, W. F. Börnke, A. Reindl, T. Ehrhardt, M. Stitt, U Sonnewald. (2004) Target-based discovery of novel herbicides. Current Opinion in Plant Biology 7, 219-225 .

Mallory-Smith, C.A., E.J. Retzinger (2003): Revised classification of herbicides by site of action for weed resistance management strategies. Weed Technology 17, 605-619.

Meinlschmidt, E. (2006). Abutilon theophrastii Med. On arable land in Saxony-results of monitoring in the years 2002-2004 and management recommendations. Journal of Plant Diseases and Protection, special issue XX, 4871-492.

Michel, A., J. Wagner, H.U. Haas, K. Hurle. (2001) Characterization of resistance to ALS-inhibitors in three Amaranthus species. WSSA Abstracts, 2001 Meeting of the Weed Science Society of America, Greensboro, NC.Volume 41, 125.

Owen, M.D.K., Zelaya, I.A. (2005). Herbicide-resistant crops and weed resistance to herbicides.
Pest Management Science 61,301-311.

PlantTech (2006). Emerging News. March 2006, No.2

Powles, S.B., Lorraine-Colwill, D.F., Dellow, J.J. and Preston, C. (1998). Evolved resistance to glyphosate in rigid ryegrass (Lolium rigidum) in Australia. Weed Science 46,604-607.

Roux, F., A. Matéjicek, J. Gasquez and X. Reboud (2005). Dominance variation across six herbicides of the Arabidopsis thaliana csr1-1 and csr1-2 resistance allels.

P.L. Short (2006). Growing Agchem R&D. Chemical & Engineering News 19-22.

Sibony, M., A. Michel, H.U. Haas, B. Rubin, K. Hurle (2001) Sulfometuron-resistant Amaranthus retroflexus: cross-resistance to acetolactate synthase-inhibiting herbicides. Weed Research 41, 509-522.

Stuebler, H. (2006). How does Bayer CropScience herbicide Research respond to global market dynamics. Visions 2020 – BayerCropScience Symposium in Frankfurt.

Suszkiw, J. (2005). Clearfield sunflowers stand tall against herbicides. ARS National Program (#301). www.ars.usda.gov/is/AR/archive/jan05
05.htm Syngenta, (2006). Annual Review 2005. www.syngenta.com

Tan, S., R.R. Evans, M.L. Dahmer, B.K. Singh, D.L. Shaner (2005). Imidazolinone-tolerant crops: history, current status and future. Pest Management Science 61, 245-257.

Tanaka, Y., Y. Kajiwara, T. Kajiwara, M. Noguchi, N. Shimizu, K. Minami (2003): Sulfonylurea derivatives with fused heterocyclic moiety control sulfonylurea-resistant paddy weeds. J.Weed Sci.Tech. 48, 40-41

Timmermann, C., R. Gerhards, P. Krohmann, W. Kühbauch (2001). The economic and ecological impact of site-specific weed control. Proc. Of the 3rd International Conference on Precision Farming, Montpellier, France, 563-568.

USDA News Release 0106.06.

http://www.usda.gov/documents/ENVIRONMENTAL_QUALITY_INCENTIVES_PROGRAM.doc

http://www.usda.gov/documents/CONSERVATION_SECURITY_PROGRAM.doc

VanGessel, M. (2006). Weed Management Systems in US corn and soybean – Delmarva and Mid-West.

Visions 2020 – BayerCropScience Symposium in Frankfurt.

Vaughn, K. C. (2003). Herbicide resistance work in the United States Department of Agriculture-Agricultural Research Service. Pest Management Science 59,764-769.

Wagner, J., H.U. Haas, K. Hurle. (2002) Identification of ALS inhibitor-resistant Amaranthus biotypes using polymerase chain reaction amplification of specific alleles. Weed Research, 42, 280-286.

Wells, J. – Horizon Ag (2006), Personal Communication.

Zheng, D., W.L. Patzoldt, P.J. Tranel (2005). Association of the W574L ALS substitution with resistance to chloransulam and imazamox in common ragweed (Ambrosia artemisiifolia). Weed Science 53, 424-430.