CAST

Management of Pest Resistance:

Strategies Using Crop Management, Biotechnology, and Pesticides

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Management of Pest Resistance: Strategies Using Crop Management, Biotechnology, and Pesticides

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The Steering Committee recognizes the outstanding efforts of two persons who provided leadership and assistance at many stages of the project: Cindy Lynn Richard, CIH, Program Coordinator at CAST, for extensive symposium planning; and Sharlene R. Matten, Ph.D., U.S. Environmental Protection Agency, on loan to CAST at the time of the symposium, for assiduous coordination work on the symposium and the proceedings as well as drafting key sections of the publication.

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Foreword

Following a recommendation by the CAST National Concerns Committee, the CAST Board of Directors authorized development of a symposium to address issues regarding pest resistance management. An eminent group of experts was chosen as a Steering Committee, under the leadership of Dr. Barry J. Jacobsen. The committee planned and conducted the symposium, which was held on April 10–11, 2003 in Indianapolis, Indiana in conjunction with the Fourth National Integrated Pest Management Symposium that took place on April 8–10. After the CAST symposium, Dr. Sharlene R. Matten chaired the development of this Special Publication.

Symposium authors submitted drafts of their presentations that were edited by the CAST editorial staff. The CAST Executive Committee and Editorial and Publications Committee reviewed the final draft, and the authors reviewed the proofs. The CAST staff published the document as an online Special Publication. The symposium authors are responsible for the document's scientific content.

On behalf of CAST, we thank the Steering Committee members, the symposium and proceedings chairpersons, and the contributing authors who gave of their time and expertise to conduct the symposium and prepare the Special Publication as a contribution by the scientific community for public understanding of the issues. We also thank the employers of the scientists, who permitted participation of these individuals at no cost to CAST. CAST thanks all members who made additional contributions to assist in the preparation of this document. The members of CAST deserve special recognition because their unrestricted contributions in support of CAST financed the preparation and online presentation of this Special Publication.

CAST is providing electronic access to this document to a broad range of government officials including Members of Congress, the White House, the U.S. Department of Agriculture, the Food and Drug Administration, the Environmental Protection Agency, and the Congressional Research Service. Additional recipients include media personnel and institutional members of CAST. Individual members of CAST may access the document free of charge through the CAST website at <www.cast-science.org>. The document may be reproduced in its entirety without permission. If copied in any manner, however, credit to CAST and to the authors would be appreciated.

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Interpretive Summary

These proceedings reflect presentations and discussions from the two-day national symposium held April 10–11, 2003 in Indianapolis, Indiana, entitled "Management of Pest Resistance: Strategies Using Crop Management, Biotechnology, and Pesticides." The symposium, convened by the Council for Agricultural Science and Technology (CAST), was the first U.S.-based multidisciplinary stakeholder meeting on pest resistance management (PRM) since the 1995 American Chemical Society meeting on mechanisms of pest resistance and the 1984 National Research Council meeting on pest resistance. The symposium provided the opportunity for stakeholders involved in insect, weed, and pathogen pest management to come together in a fruitful discussion of issues, laying the foundation for future collaborations addressing PRM.

The overall goal of the symposium was to provide a collective framework in which more effective and preventative pest resistance management could be developed. The major objectives of the symposium were to (1) identify the common issues related to PRM across disciplines; (2) identify ways to remove barriers that hinder more effective and preventive resistance management (RM); (3) provide opportunities for further discussions on PRM; (4) identify research activities in RM; and (5) provide this information to lawmakers, federal agencies—especially the U.S. Environmental Protection Agency (EPA) and the U.S. Department of Agriculture (USDA)—academia, extension, industry, consultants, and the public.

The agenda was developed by a steering committee composed of representatives from the EPA, the USDA, industry (Resistance Action Committees), academia, public interest groups, and grower organizations. Forty-seven speakers gave a total of 55 presentations, 52 of which are compiled in this publication. Most of the eight sessions included an opportunity for public comment and discussion. Approximately 120 stakeholders from industry, academia, extension, consultancies, federal and state governments, grower organizations, and public interest groups participated in the symposium.

The organization of these proceedings reflects the eight sessions of the symposium agenda.

1. **Scope of North American Pest Resistance Problems in 2003.** The first session presented assessments of the scope and magnitude of pest/pesticide resistance problems in North America among insects, weeds, and pathogens by respective experts in the field.
2. **Issues in Pest Resistance Management.** Speakers addressed pest resistance issues for major North American crops, looking at what has been and is being done to protect against resistance and assessing barriers to PRM. The discussion included fruits and vegetables, cotton, potato, small grains, corn/soybean, turf/ornamental crops, and organic agriculture.
3. **Lessons Learned I: Balance between Industry, Academia, Users, and Regulators.** Case studies were presented to examine how the pest/pesticide resistance concerns raised in the previous two sessions actually have been addressed in the field. The studies included glyphosate and acetolactate synthase herbicide resistance, fungicide resistance in fruit and vegetable crops, insecticide resistance in pests of cotton and crucifers, and insect RM in *Bacillus thuringiensis (Bt)* crops.
4. **Lessons Learned II: Have Models Helped?** Speakers addressed the predictive and descriptive roles modeling plays in RM. Issues discussed included how models have been used to identify data gaps/needs, the uncertainty associated with input parameters, and, ultimately, the validity and applicability of modeling as an effective assessment tool.
5. **Role of Stakeholders.** Speakers from various stakeholder groups addressed their own roles and the roles of others in PRM, as well as barriers and challenges in RM.
6. **Lessons Learned III: How Can We Work to Remove Barriers to Comprehensive Resistance Management Implementation? How Can We Work Together Better?** This two-part session examined the opportunities for consumers, pesticide distributors and producers, federal and state regulators, researchers, and educators to overcome common obstacles to effective RM.

7. **Pest Resistance Management Goals.** This session focused on specific strategies for PRM. Speakers outlined the reasons for proactive rather than reactive RM, assessed the role of monitoring and agricultural information technology, and highlighted practical measures to limit selection pressure. The role of education and communication in long-term PRM also was discussed.
8. **Symposium Conclusions and Recommendations.** The last section of these proceedings is a compilation of conclusions and recommendations that were reached during the presentations and discussions throughout the symposium.

Keys to Effective Resistance Management

The coverage of different classes of pesticides (herbicides, fungicides, and insecticides) made evident the important differences among and within these classes in terms of RM needs and highlighted the necessity of addressing these needs on a case-by-case basis. The overall conclusion of the symposium was that PRM is very important to the sustainability of agricultural production systems. Achieving proactive or preventive RM is a desirable goal, but how to achieve it is a complex process that requires extensive input and commitment by all stakeholders. The keys to effective RM are strong science; environmentally benign, feasible, and cost-effective strategies; and education about the benefits of implementation. In addition, multiple pest control tactics including cultural practices, biological control, transgenic plants producing pesticidal substances (such as *Bt* insecticidal toxins), and chemical pesticides (with different modes of action) can help decrease the selection pressure for the evolution of pest resistance. Further research into the development, implementation, and adoption of RM is necessary.

Symposium Conclusions

- Understanding of the scientific basis for why a strategy works is fundamental to the success of effective, preventative RM strategies.
- Formulating RM plans before commercialization of a new chemical active ingredient is desirable.
- Education and training are fundamental to the implementation and adoption of RM strategies.
- Resistance management benefits must be demonstrated to growers.
- Successful RM should be profitable, sustainable, and environmentally beneficial.
- Federally funded RM research is important to the successful development and implementation of effective RM strategies and should be a component of federally funded IPM grant programs.
- The USDA and the EPA play important roles in PRM and pesticide regulation.
- Central and permanent databases of pest and pesticide resistance information are important and need continued funding.
- Agricultural information technology provides a mechanism for disseminating forecast tools to know where and when to use a pest control technology.
- Barriers exist that impede the development of effective RM strategies. These barriers include (1) limited understanding of the factors affecting resistance evolution, (2) limited product availability, (3) economic factors, (4) short-term solutions, (5) focus on individual crops/pests rather than a holistic systems approach for the agroecosystems, (6) lack of clear goals and objectives, (7) lack of clear RM regulatory policy, (8) limited federally funded and industrial funded RM research, and (9) competitive marketing practices within industry that discourage proactive/preventative RM.
- Predictive models are useful for comparing RM options and identifying key data gaps, but they offer a simplified reality.
- Resistance monitoring plays an important role in surveillance and detection of resistance before field failure when suitable tools are available.
- Plant breeding can be an important component in successful implementation of effective RM and should be encouraged in this context.
- In organic production of short-term annuals, pest resistance has been a big issue because of the extensive focus on crop rotation and other cultural management practices, soil management, and the use of biological pesticides.

Symposium Recommendations

Participants made several RM recommendations and suggestions in a discussion held at the end of the symposium. These recommendations focused on four areas: (1) Science, (2) Research and Extension, (3) Education, and (4) Policy.

Science Recommendations

- Resistance management strategies should be developed on a case-by-case basis, considering characteristics of the chemistry, the target pests, and the management system using certain guiding principles.
- Guidance and direction are needed in developing resistance monitoring programs for new technologies including establishment of baseline susceptibility, detection techniques, and sampling strategies.
- Resistance management strategies should be flexible to allow changes over time due to the temporal and spatial variation in the pest/crop/pesticide situation. Databases can be used to measure the extent of resistance both temporally and spatially. Further funding of resistance databases is recommended.
- Standard definitions should exist for resistance for pest/pesticide combinations and methods of documentation and validation.
- Economic benefits and costs of effective RM should be clearly developed and articulated.

Research and Extension Recommendations

- There should be explicit RM priorities within the federal government, e.g., create a new competitive grants program to focus on RM, strengthen existing USDA competitive grants research programs to provide more explicit priorities to fund RM research, strengthen RM research for minor crops and Regional Integrated Pest Management Centers.
- Create an RM research initiative supported jointly by funds from a user fee associated with pesticide sales and funds from the federal government.

Education Recommendations

- Resistance management education programs should continue to be developed and implemented as part of ongoing pesticide education programs.
- Consumer education programs should include the cost of producing "blemish-free" food in the marketplace and the use of reduced-risk pesticides.
- The USDA grading standards and the marketing of food internationally should be examined for their impact on RM.

Policy Recommendations

- Although all stakeholders noted the EPA's role in RM as being important, there was disagreement about the scope and regulatory nature of this role. Some participants recommended a mandatory role for the EPA in RM, but consensus was not achieved in the limited time available.
- Several suggestions were made that Farm Bill priorities should be changed to provide better funding of RM research and education, e.g., the Natural Resources Conservation Service should recognize RM as a conservation practice.

Introduction

Pesticide resistance[1] can be defined as a heritable and significant decrease in the sensitivity of a pest population to a pesticide. Pests are found in groups as diverse as insects, mites, fungi, bacteria, viruses, weeds, nematodes, and certain mammalian species such as rodents. Worldwide, more than 540 insect and mite species (MSU–CIPS 2000), more than 100 plant pathogen species, and more than 270 weed biotypes (WeedScience 2003) are reported to have evolved *resistance* to pesticides (Hart and Pimentel 2002). Virtually every chemical pest suppression tactic known has elicited some form of adaptive biochemical response in the target pest. Behavioral adaptation to pest management practices also is known. For example, certain corn rootworm populations no longer are controlled by rotating soybean with corn. Pesticide resistance can lead to unsatisfactory pest control, increased crop losses, increased control costs, and increased use of pesticides, especially in the absence of viable alternatives. Pest resistance management is a very important component of *integrated pest management* (IPM) because it can help to ensure sustainable production-scale agriculture, uninterrupted food safety, and continued environmental protection.

The United Nations Environmental Program listed pest resistance to pesticides as the third most serious threat to global agriculture behind soil erosion and water pollution. Crop losses due to pesticide resistance are estimated to be approximately $1.4 billion annually in the United States (Hart and Pimentel 2002). Pest resistance is an issue for all types of pest suppression tactics—chemical as well as biological. Tactics may include *transgenic crops* engineered to produce crop protectants such as insecticidal proteins from *Bacillus thuringiensis (Bt).*

Because of the impact that pest resistance can have on the sustainability of agriculture and environmental protection, the Council for Agricultural Science and Technology (CAST) convened a 2-day national symposium entitled "Management of Pest Resistance: Strategies Using Crop Management, Biotechnology, and Pesticides" to encourage a cross-disciplinary dialogue among different stakeholders working on pest resistance management issues involving insects, pathogens, and weeds. The overall goal of the symposium was to provide a collective framework in which more effective and preventative resistance management could be developed. The major objectives of the symposium were to (1) identify the common issues related to pest resistance management across disciplines; (2) identify ways to remove barriers that hinder more effective and preventative resistance management; (3) provide opportunities for further discussions on pest resistance management; (4) identify research activities in resistance management; and (5) provide this information to lawmakers, federal agencies—especially the U.S. Environmental Protection Agency (EPA) and the U.S. Department of Agriculture (USDA)—academia, extension, industry, consultants, and the public.

The symposium was held April 10–11, 2003 in Indianapolis, Indiana. The agenda was developed by a steering committee consisting of representatives from the USDA, the EPA, industry (Resistance Action Committees), academia, public interest groups, and grower organizations. Forty-seven speakers gave a total of 55 presentations. (After the symposium the talks were posted on the CAST website, <http://www.cast-science.org>). Most of the eight sessions included an opportunity for public comment and discussion. Approximately 120 stakeholders from industry, academia, extension, consultancies, federal and state governments, grower organizations, and public interest groups participated in the symposium.

These proceedings have been compiled at the direction of the CAST Board of Directors, to capture the discussions and make them publicly available. The organization of the proceedings reflects the eight sessions of the symposium agenda:

1. **Scope of North American Pest Resistance Problems in 2003.** The first session presented assessments of the scope and magnitude of pest/pesticide resistance problems in North America

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[1] Italicized terms (other than scientific names) are defined in Appendix B: Glossary.

among insects, weeds, and pathogens by respective experts in the field.

2. **Issues in Pest Resistance Management.** In the second session, speakers addressed pest resistance issues for major North American crops, looking at what has been and is being done to protect against resistance and assessing barriers to pest resistance management. The discussion included fruits and vegetables, cotton, potato, small grains, corn/soybean, turf/ornamental crops, and organic agriculture.
3. **Lessons Learned I: Balance between Industry, Academia, Users, and Regulators.** This session used case studies to examine how the pest/pesticide resistance concerns raised in the previous two sessions actually have been addressed in the field. Case studies included glyphosate and acetolactate synthase (ALS) *herbicide resistance*, *fungicide resistance* in fruit and vegetable crops, *insecticide resistance* in pests of cotton and crucifers, and insect resistance management in *Bt crops*.
4. **Lessons Learned II: Have Models Helped?** Speakers addressed the predictive and descriptive roles modeling plays in resistance management. The following issues were discussed: how models have been used to identify data gaps/needs, the uncertainty associated with input parameters, and ultimately, the validity and applicability of modeling as an effective assessment tool.
5. **Role of Stakeholders.** Speakers from industry, academia, public interest groups, federal and state governments, and crop consultancies addressed their roles in pesticide resistance management, barriers and challenges in resistance management, and the roles of others in resistance management.
6. **Lessons Learned III: How Can We Work to Remove Barriers to Comprehensive Resistance Management Implementation? How Can We Work Together Better?** This two-part session examined the opportunities for consumers, pesticide distributors and producers, federal and state regulators, researchers, and educators to overcome common obstacles to effective resistance management.
7. **Pest Resistance Management Goals.** This session focused on specific strategies for pest resistance management. Speakers outlined the reasons for proactive rather than reactive resistance management, assessed the role of monitoring and agricultural information technology, and highlighted practical measures to limit selection pressure. In addition, the role of education and communication in long-term pest resistance management was discussed.
8. **Symposium Recommendations for Pest Resistance Management—Where to Now?** The final session was a moderated discussion on the important messages from the symposium.

The last section of these proceedings is a compilation of conclusions and recommendations. The conclusions are those that were reached during the presentations and discussions throughout the symposium. The recommendations emerged from Session 8 and focus on four topics: science, research and extension, education, and policy.

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1.1 Scope of North American Pest Resistance Problems in 2003: An Overview

Mark E. Whalon and Robert Hollingworth

Introduction

In 2001 the world's pesticide market exceeded $34 billion, while in the United States it exceeded $11 billion. It has been estimated by Hart and Pimentel (2002) that pesticide resistance surpasses $1.4 billion in environmental, ecological, and human impact costs. What are some of the features driving resistance development in North American societies? Consumerism certainly drives much of the globalization and free-market decisions in North America today. Bilateral trade agreements and falling tariffs have opened the way to new markets and products. Both pesticide regulations and the enactment of the Food Quality Protection Act (FQPA 1996) are seen by some as emergent properties of consumerism (Kramer 1990) and the environmental movement (Stroshane 1999). Consumers demand inexpensive blemish-free fruits and vegetables. Federal and state regulations require wholesome and labeled products as well as numerous other quality-related characteristics. Thus, consumerism in its myriad forms swiftly has overtaken outdated forms of production, marketing, and sales of agricultural products. Consumers have power in the marketplace today, and their power is partially translated into increased pressure toward “perfect” product quality that only can be delivered through increasingly intense pest management systems.

Environmentalism and Consumerism

The environmental movement also has fostered new awareness and a drive toward new legislation and regulations targeting pesticides in agriculture and health protection. Environmental concern also has been linked to the consumer movement (Burger 1990) in Western societies, and together they are global in scope (Gilley 2001), extending even into Third World countries. *Environmentalism* transects the demographics of Western societies and strongly affects the regulatory policies in the United States, Canada, and Mexico.

Environmentalism and consumerism together have several pest management and resistance management impacts. First, North American societies source products globally and transport these goods rapidly into the country. Second, more than 60% of North American pests historically have been introduced, with new introductions occurring almost weekly. At this rate, will North American societies eventually import most of the ecologically compatible global pest species despite our phytosanitary barriers? Emerging with consumerism on a global scale, market access through nontariff phytosanitation barriers has become a gauntlet that every entrepreneur must run. Both the introduction of invasive species and phytosanitation requirements dictate additional pesticide applications and potentially accelerate resistance selection.

Within this context is resistance, in which the genetic-based adaptation of pests to man's effort to control them has become more and more important as globalism, consumerism, and market access concerns drive pesticide use. From this point of view, it is not difficult to believe that resistance problems will plague agriculture and human and animal health protection for the foreseeable future.

As authors, we represent applied ecology and insect toxicology. In our view, it is difficult to look past the inference that resistance is a symptom of a dysfunctional ecosystem. That is, agricultural production systems often are defined as disrupted ecosystems (Southwood 1973). Resistance can be viewed logically as a symptom or indicator of an ecosystem that has been disrupted beyond its natural equilibrium, resulting in an ecologically negative outcome. Therefore, resistance is a consequence of pesticide overuse in a utilitarian and reductionist sense.

This perspective also could be adopted in human and animal health protection where the problem with antimicrobial resistance has surfaced repeatedly in the popular media. It is somewhat ironic that media would focus on antibiotic resistance and human health while resistance issues with insecticides, herbicides, and fungicides in food production rarely surface. Insecticide, acaracide, and filaricide resistance also is a critical issue for human health protection in North America, but the media surprisingly overlooks it, too, and ignores efforts by the U.S. Centers for Disease Control and the World Health Organization to track various disease-vector resistance development in the Americas, Asia, and Africa. With the recent media attention in North America on the introduction of the mosquito-vectored West Nile virus into suburban and urban population centers, one might expect a somewhat broader articulation of the fragile nature of human health protection against arthropod-borne diseases, including vector resistance. A further irony, some might note, is that North American media in concert with environmental and consumer movements would skewer certain insecticide use such as *organophosphates* in food production yet approve—or even champion—the direct exposure of large numbers of people during mosquito vector control operations. Apparently it is not appropriate to expose people to minuscule residues in the diet, but inhalation and contact exposure for human health protection are less newsworthy.

Regulations

When addressing the scope of North American resistance development, new regulations dealing with resistance are of critical interest. For example, with the promulgation of regulations governing the registration of genetically modified plants containing insecticidal proteins, resistance management plans were required as a prominent portion of the registration portfolio (USEPA 2002). With one exception, all of the current conditional registrations for genetically modified plants containing insecticidal proteins have a resistance management plan based on high dose and refugia strategies (the single exception is Mon 863 for corn rootworm control) (USEPA 2003).

The European Union (EU) also has recently taken some strides to require resistance management guidelines in its regulatory system. The EU-EPPO-PP1/213(1) guidelines require resistance risk assessment, development, and implementation of a resistance management plan and baseline monitoring of resistance for all new registrations within the EU (EPPO 2003). The 1996 FQPA also has a provision for resistance monitoring contained in its details. Essentially, this prescription for resistance monitoring is worded much like a series of recommendations by the U.S. Board on Agriculture of the National Research Council, one of which states that, "Federal agencies should support and participate in the establishment and maintenance of a permanent repository of clearly documented cases of resistance" (Dover and Croft 1986). To our knowledge, however, no divisional program within the U.S. Environmental Protection Agency (EPA) has ever followed up on this part of the FQPA law other than voluntary reporting of resistance development by registrants.

Presumably one measure of the impact of recent regulations on the availability of resistance management tools is the number of different formulations, pesticide and *biopesticide* modes of action, effective natural enemies, and other management strategies, tactics, and tools. Approximately 6,000 pesticides have been cancelled or their uses reduced significantly since passage of the FQPA (see Figure 1.2.2). On the other hand, the FQPA and related activities of the EPA have accelerated the registration of *reduced-risk pesticides* and organophosphate alternatives. Unfortunately, however, this legislation also has practically eliminated the experimental use permit process whereby land-grant universities, private technical service providers, and commodity researchers historically have adapted new pesticide tools to various production systems. In addition, the FQPA has provided an array of new risk-science developments estimating the aggregate exposure to pesticides that exhibit common modes of action, the cumulative human pesticide exposure over a lifetime, and the impact of endocrine disruption on nontarget organisms. Potentially all of these risk-science innovations could have unique or integrated impacts on resistance and resistance management in North America as the EPA evolves these policies.

As previously mentioned, resistance is a genetic-based decrease in the susceptibility of a population to a control measure. It has been observed across herbicides, fungicides, and bactericides, as well as insecticides and miticides. An array of evolving pest biotypes or races also has overcome conventionally selected crop varieties showing host-plant resistance. Perhaps even cultural control strategies such as crop rotation may be overcome by genetic adaptation in a pest (Levine and Oloumi-Sadeghi 1991; Levine, Oloumi-Sadeghi, and Ellis 1992). The economic, social, and environmental consequences for the various types of resistance include pest control failures, disrupted pest management systems (including limitations in the development of integrated pest management options), and increased pest control costs. Such costs have been classified variously as (1) pest managers forced to resort to newer, higher-priced pesticide alternatives and (2) additional applications.

Certainly there are arrays of environmental, social, and disrupted ecosystem consequences of the increased pesticide use induced by resistance. Functionally, disrupted ecosystems and environmental impacts could be measured in increased off-target effects on biodiversity and/or endangered species. Additional social impacts may include consequences on humans from increased pesticide residues, worker exposure, or increased disease spread where vector control is diminished as a result of resistance.

Summary

In summary, globalization and environmentalism likely will continue to impact the availability of pesticides as well as the social and economic determinants that will dictate overuse of pesticides leading to resistance. Heightened concerns over homeland security, particularly in the United States, may have collateral effects in terms of fighting bioterrorism with additional pesticide use. The emergence of biotechnology and genetically modified organisms with various pest selection processes could result in further expansion of resistance problems. On the other hand, monitoring and diagnostics in resistance management should improve dramatically with the application of new high-throughput technology developed initially for HIV/AIDS and cancer detection. In addition, the pesticide industry, through market and regulatory incentives, is beginning to deliver an expanding array of novel and ecologically softer pesticides. This fresh collection of new modes of pesticide action should allow pest managers a greater diversity of management tools to focus on target pests, thereby decreasing the rate of resistance selection. Obviously the dissemination of various regulations will continue to impact the availability of resistance management tools. Certainly society is witnessing the rapid and expansive response of the private sector to reduced-risk and organophosphate-alternative incentives through the EPA. One might only speculate on the development of new resistance management strategies, tactics, and tools if some of the focus and resources currently employed to regulate pesticides in North American societies were allocated to monitoring and measuring resistance, the loss of susceptibility in resistant-prone species, or the dysfunctional ecosystems resulting from resistance development. This resistance conference highlights several efforts to document resistance development in weeds, fungicides, and arthropods. These efforts are essential from our perspective, because “what gets measured gets managed.”

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1.2 Arthropods Reported to Be Resistant to Pesticides

Mark E. Whalon, Patrick S. Bills,
David Mota-Sanchez, Robert Hollingworth,
Gary D. Thompson, and David Ehnis

Since the first report of a “resistant” insect (Melander 1914) there have been 543 arthropod species reported to be resistant to one or more pesticides. Our work on a resistance database at Michigan State University (MSU) updates that of Georghiou and Lagunes-Tejeda (1991). The resistant arthropod count is based on an examination of over 3,863 peer-reviewed journal articles. This information currently resides in an electronic database at the MSU Department of Entomology and is available via the Internet at <http://www.cips.msu.edu/resistance/rmdb/index.html>

Resistance is the microevolutionary process of genetic adaptation through the selection by various agents including biocides (Whalon and McGaughey 1998). Resistance consequences include the failure of a plant protection tool, tactic, or strategy to control a pest where susceptibility is lost.

The global annual economic impact of pesticide resistance has been estimated to exceed $4 billion annually in 1991 and estimated again at $1.4 billion in 2002 (Hart and Pimentel 2002). Most resistance scientists and workers agree that resistance is a very important driver of change in modern agriculture, and that effective integrated pest management (IPM) may be severely disrupted by a resistance episode. In fact, the development and cascade-like effects of insecticide or miticide resistance often have perturbed pest management programs significantly.

In potato agroecosystems for example, the Colorado potato beetle, *Leptinotarsa decemlineata* (Say), has developed resistance to 40 insecticides (Figure 1.2.1). This insect is a strong candidate for the archetypal multiple-resistant species. Because of the evolution of resistance to nearly all chemical classes of insecticides in Maine, Pennsylvania, Michigan, Wisconsin, and New York (Long Island), farmers in these states historically have employed alternative tactics, including the use of propane flamers and plastic-lined ditches to stop the destruction of their crops by this pest. Apparently even one of the most recent broad-spectrum insecticides, the neonicotinoids, may not succeed against this pest for long due to resistance.

The Database of Arthropods Resistant to Pesticides

Resistant Arthropod Profile: *Leptinotarsa decemlineata*

coleoptera	CHRYSOMELIDAE	Colorado potato beetle	AG	eggplant, pepper, potato, tomato

There are 40 pesticides that this arthropod has documented resistance to:

Pesticide	Regions
aldicarb	USA(New Jersey), USA(Connecticut)
aldrin	Austria, Canada(Alberta), Canada(Ontario), Italy, Portugal, Switzerland, USA(New York), USA(Virginia)
azinphos-methyl	USA(Virginia), USA(Michigan), USA, Canada(Quebec), Poland, USA(Connecticut), USA(Massachusetts), USA(New Jersey), USA(New York)
Bacillus thuringiensis CRY3AA	USA
carbaryl	Canada(Quebec), Italy, Poland, USA(Connecticut), USA(New Jersey), USA(New York)
carbofuran	USA(Michigan), Canada(Quebec), USA(New York), USA(New Jersey), Canada(New Brunswick), USA(Connecticut)
cartap	Poland

Figure 1.2.1. Profile of resistance for *Leptinotarsa decemlineata*.

Economic impact, crop displacement, and rapid transition to alternative strategies, tactics, and tools are not the only effects of insecticide resistance. Efforts to control resistant pests often lead to the overuse of pesticides, which contributes to externalities such as environmental pollution, residues in food, and greater nontarget effects. When resistance disrupts a pesticide-intensive pest management system and it is replaced with a more strategically appropriate biologically intensive IPM system, however, the outcome of resistance may in fact result in a more sustainable pest management system.

In 1957, J. R. Busvine first published a list of resistant insects (Busvine 1956). Soon after, A. W. A Brown, the first director of the Pesticide Research Center at Michigan State University, also published resistance tables for the World Health Organization (WHO) and other agencies from the 1950s into the early 1970s (Brown 1958). In the 1980s, Brian Croft and Karen Theiling collected documentation of resistance of arthropod biocontrol agents, emphasizing the “*selectivity*” of some resistant biological control agents

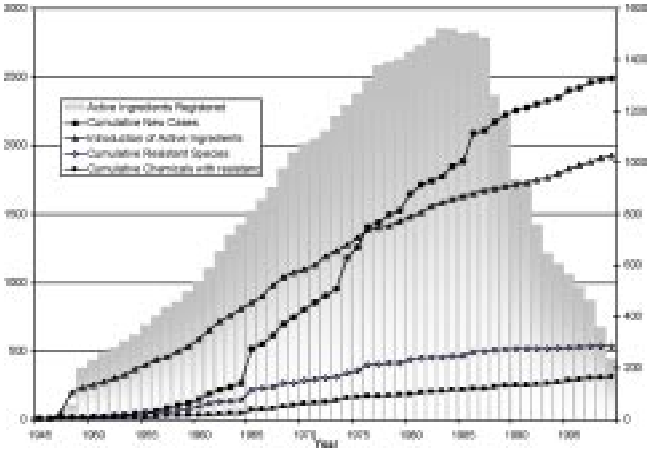

Figure 1.2.2 Timeline of arthropod resistance and pesticide registrations in the United States.

and their resultant *fitness* in biointensive IPM programs (Croft 1990; Theiling and Croft 1988). Georghiou and Legunes-Tejeda, supported by the United Nations Food and Agriculture Organization (UN FAO), published a compendium of resistance cases in 1991.

The U.S. Board on Agriculture of the National Research Council made a series of recommendations, one of which states that "Federal agencies should support and participate in the establishment and maintenance of a permanent repository of clearly documented cases of resistance" (Dover and Croft 1986). This recommendation was incorporated into the Food, Agriculture, and Trade Act in 1990, which again called for a U.S. "national pesticide resistance monitoring program." The U.S. Food Quality Protection Act of 1996 (FQPA) also provides for resistance monitoring in its language.

The MSU arthropod resistance database (<http://www.cips.msu.edu/resistance/rmdb/index.htm>) builds on all of these previous efforts. To date, the MSU database has utilized only science-based, peer-reviewed journals. Standardized methods for resistance detection and reporting do exist. For instance, the UN FAO has been publishing standardized tests for species affecting human health since 1969. The MSU database initially relied on a review of the values of the median lethal doses (LD_{50}), median lethal concentration (LC_{50}), median lethal time (LT_{50}), median knockdown (KD_{50}), and discriminating doses. The primary objective involved examining the statistical differences between resistant populations and a susceptible reference colony for previously unreported species, compounds, and/or regions. A *resistance ratio* (RR), the ratio of *dose-mortality* of the tested strain defined by the statistic used (e.g., LD_{50}, LC_{50}, KD_{50}, or TL_{50}) to a known susceptible strain, of 10 or more has been a general threshold for defining a resistance "case." Occasionally, reports with an RR less than tenfold are included when the authors clearly demonstrated that resistance was high enough to cause field failure.

Laboratory cases of resistance that clearly demonstrate the potential for resistance development to compounds that have not been observed to fail in the field also are reported in the MSU database as a harbinger. Therefore, the factors involved in deciding to accept a resistance report relied on the Whalon and McGaughey definition of resistance (1998): intrinsic and extrinsic factors of the test itself (Busvine 1968) and the statistical significance of the bioassay used to report the resistance level.

The MSU database makes every effort to include all scientifically validated reported cases of resistance, but we are hesitant to say that we have uncovered all cases in our review given the scope of this worldwide phenomenon. For instance, our review focused primarily on journals published in English. A number of Russian, Spanish, French, and Italian journals, however, also have been included. Still, there are undoubtedly other documented cases of resistance that should be included. To facilitate this process we have developed a web-based resistance survey tool: <http://cips.electric-software.com:8080/survey>. In addition, there are four distinct data tables updated regularly on the database. For instance, example database outputs summarize the documented cases of arthropods resistant to pesticides (Table 1.2.1 and Figure 1.2.2). Please see the website for further data (<http://www.cips.msu.edu/resistance/rmdb/index.htm>).

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Table 1.2.1. Summary of documented cases of arthropods resistant to pesticides

Compound mode of action/ Chemical class	# of compounds with resistance	Category of resistant arthropods					Total cases by chemical class	
		Agricultural, forest, and ornamental plant pests	Medical, veterinary, and urban pests	Predators / Parasites	Other / miscellaneous arthropods	Pollinators		
Organophosphates	112	715	358	52	10		1135	44.1%
Organochlorines	26	484	329	10	15	2	840	32.6%
Pyrethroids	33	133	74	11	1		219	8.5%
Carbamates	35	132	57	14	1		204	7.9%
Bacterials	38	42	4				46	1.8%
Miscellaneous	30	37	8	1			46	1.8%
Fumigants	6	21					21	0.8%
Insect Growth Regulators	10	16	2	3			2	0.8%
Organotins	3	8					8	0.3%
Formamidines	2	4	2				6	0.2%
Arsenicals	2	2	11				13	0.5%
Avermectins	2	2	3	1			6	0.2%
Chloronicotinoids	1	2	1				3	0.1%
Rotenone	1	2					2	0.1%
Dinitrofenols	1	1			1			0.0%
Sulfur compounds	2	1		1			2	0.1%
Phenylpyrazoles	1		1				1	0.04%
Total cases by arthropod category		**1602**	**850**	**90**	**30**	**2**	**2574**	
		62.2%	33.0%	3.5%	1.2%	0.1%		

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1.3 Scope and Magnitude of Herbicide-Resistant Weeds in North America

Ian M. Heap

Introduction

In the developed world, and increasingly worldwide, herbicides are the primary method of weed control, and their effectiveness is largely responsible for the current abundance of food globally (Avery 1995). Herbicides have become the primary method of weed control because of their efficacy and cost effectiveness; however, heavy reliance on herbicides has resulted in the widespread occurrence of herbicide-resistant weeds. Herbicide resistance continues to increase globally, causing significant yield losses and increasing the cost of food production. The first herbicide-resistant weeds occurred in the United States. This paper will outline some of the current and future problems of herbicide-resistant weeds in the United States.

Herbicide Resistance

In presenting the introductory herbicide resistance paper to this CAST symposium I will give a brief definition of resistance and its causes in weeds.

"Herbicide resistance" is the *evolved capacity* of a previously herbicide-susceptible weed population to withstand a herbicide and complete its life cycle when the herbicide is used at its normal rate in an agricultural situation (Heap and LeBaron 2001).

"Evolved capacity" in this definition implies that resistance is caused by a heritable change (mutation) in the genetic makeup of the weed that confers the ability to withstand a herbicide. Most herbicides act by inhibiting a specific enzyme (different for different herbicide modes of action) within the plant (Devine, Duke, and Fedtke 1993). The majority of herbicide resistance cases are due to the selection of rare individuals with genes that code for a modification of the target enzyme such that the herbicide no longer binds to or inhibits the enzyme. Classic examples of this are commonly found in acetyl-CoA carboxylase (ACCase) inhibitor, *acetolactate synthase (ALS) inhibitor*, dinitroaniline, 5-enolpyruvylshikimate-3-phosphate synthase (EPSPS), and triazine-resistant weeds. Overexpression of the target enzyme also can result in resistance.

In addition to altered *target sites* weeds may evolve resistance due to the exclusion of herbicides from the site of action (reduced absorption, reduced translocation, or sequestration) or by rapid detoxification of herbicides. It is this final mechanism, rapid detoxification conferred by elevated cytochrome P450 monooxygenase activity, that often results in resistance to a wide array of chemical modes of action and indeed is one of the mechanisms found in *Lolium rigidum* Gaudin. (Christopher et al. 1991; Cotterman and Sarri 1992).

To add to the complexity of resistance there are many instances where more than one resistance mechanism is found in a population (*multiple resistance*), and often within the same individual. The most complex examples are those of multiple-resistant *Lolium rigidum* (Hall, Tardif, and Powles 1994; Heap and Knight 1982, 1986; Holtum and Powles 1991) from Australia, and *Alopecurus myosuroides* Huds. (Hall, Tardif, and Powles, 1994; Moss and Cussans 1991; Sharples and Cobb 1996) from Europe, where rapid detoxification and a number of target site resistances often occur in the same population, making research into the mechanisms of resistance difficult and advice to the farmers about effective alternatives even more difficult (Willis et al. 1997).

Occurrence of Resistance

A few reports of weeds exhibiting reduced (less than fivefold) levels of control with 2,4-D in the 1950s did not receive much attention by farmers or scientists. The discovery of simazine-resistant *Senecio vulgaris* L. populations in a Washington state nursery in the late 1960s (Ryan 1970) is commonly cited as the first case of herbicide resistance. This case received a great deal of attention because it had major implications for triazine-dependent maize producers in the United States and Europe, and indeed more than 30 triazine-resistant weed species were identified in maize by the end of the 1970s. Triazine-resistant weeds were extensively researched but did not inflict as much economic damage to producers as first feared because alternative herbicide modes of action had arrived to market in time to avoid serious weed control problems.

The United States Versus the World

In April 2003 the International Survey of Herbicide-Resistant Weeds recorded 275 herbicide-resistant weed biotypes in 59 countries (Heap 2002). The United States has the highest number of herbicide-resistant weeds, having documented 100 resistant weed biotypes in 59 species (Tables 1.3.1 and 1.3.2).

A new resistant biotype refers to the first instance of a weed species evolving resistance to one or more herbicides in a herbicide group. *Amaranthus* spp. are particularly troublesome herbicide-resistant weeds in the United States and account for 7 of the 59 resistant species and a significant percentage of the area infested with resistant weeds. There also are numerous instances where *Amaranthus* spp. have evolved resistance to more than one herbicide *mode of action*, which complicates control strategies.

Table 1.3.1. Number of herbicide-resistant biotypes reported by country for the top ten countries

Country	Resistant biotypes
United States	100
Canada	39
Australia	38
France	30
Spain	26
United Kingdom	24
Israel	19
Belgium	18
Germany	18
Japan	16

The rate of identification of new herbicide resistance cases is surprisingly constant for both the global and the U.S. data. Worldwide there have been approximately nine new cases of resistance per year since 1980, and in the same time period the United States has added about four new cases each year (Figure 1.3.1).

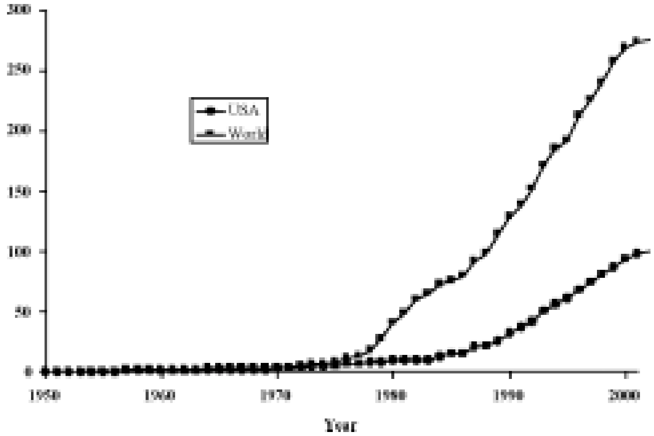

Figure 1.3.1. Chronological increase in the number of herbicide-resistant weeds in the United States and worldwide.

The ALS and ACCase inhibitors account for the largest increases in new resistance cases worldwide and in the United States (Figures 1.3.2 and 1.3.3).

Table 1.3.2. Herbicide resistance summary table for the United States[a]

Herbicide group	HRAC/WSSA classification	Example herbicide	Total
ALS inhibitors	B/2	Chlorsulfuron	35
Photosystem II inhibitors	C1/5	Atrazine	18
ACCase inhibitors	A/1	Diclofop-methyl	15
Synthetic auxins	O/4	2,4-D	7
Dinitroanilines and others	K1/3	Trifluralin	6
Thiocarbamates and others	N/8	Triallate	5
Ureas and amides	C2/7	Chlorotoluron	4
Bipyridiliums	D/22	Paraquat	3
Glycines	G/9	Glyphosate	2
Nitriles and others	C3/6	Bromoxynil	1
PPO inhibitors	E/14	Oxyfluorfen	1
Carotenoid biosynthesis inhibitors	F1/12	Flurtamone	1
Organoarsenicals	Z/17	MSMA	1
Pyrazoliums	Z/8	Difenzoquat	1
Total number of unique herbicide-resistant biotypes	100		

[a] HRAC = Herbicide Resistance Action Committee; WSSA = Weed Science Society of America; PPO = protoporphyrinogen oxidase; MSMA = monosodium salt of methanearsonic acid.

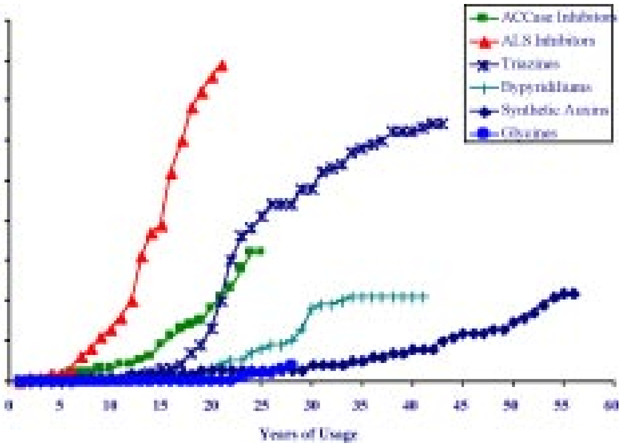

Figure 1.3.2. Chronological increase in the number of herbicide-resistant weeds worldwide to six herbicide classes.

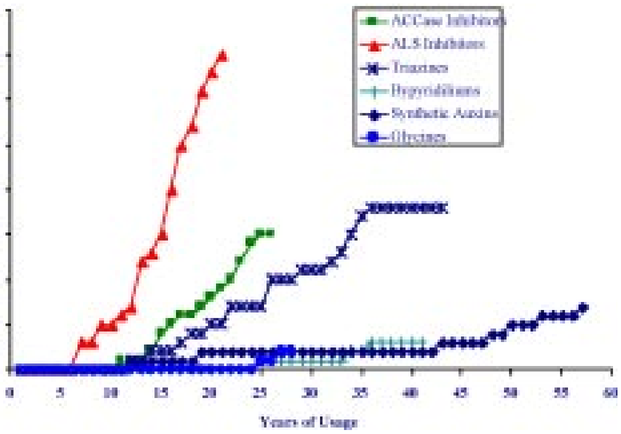

Figure 1.3.3. Chronological increase in the number of herbicide-resistant weeds in the United States to six herbicide classes.

There are 79 *ALS inhibitor*-resistant weed species worldwide, and 35 of these occur in the United States. The ALS-resistant weeds are found in all major crops and have become particularly troublesome in cereal production in the Pacific Northwest and in corn/soybean production in the Midwest. Of the 32 grass species resistant to ACCase inhibitors 15 can be found in the United States, primarily in cereal crops and the corn/soybean rotation (Heap 2002; Table 1.3.2). The graphs and data presented in this paper are summaries of the International Survey of Herbicide-Resistant Weeds (Heap 2002).

Glyphosate Resistance

Glyphosate was first commercially available in 1974 and is the most successful and most important herbicide in the world today. It has achieved this status in part because it is broad spectrum, translocated, is used postemergence, has low soil residual, has low nontarget toxicity, and has low environmental impact. It became available as a selective herbicide in Roundup Ready crops in 1996 and is widely used on a variety of those crops in the United States and many other countries.

While there were early reports of artificial selection of glyphosate-resistant plants, such as birdsfoot trefoil (*Lotus corniculatus*) (Boerboom et al. 1991) and perennial ryegrass (*Lolium perenne*), the first glyphosate-resistant weed (*L. rigidum*) was selected in the field in 1996, 22 years after the first commercial use of glyphosate. Thus it is clear that glyphosate is a "low risk for resistance" herbicide when used nonselectively. The introduction of Roundup Ready crops has led to the potential use of glyphosate two or more times a year, each year, however, dramatically increasing the selection pressure for glyphosate-resistant weeds. The cases of glyphosate-resistant *L. rigidum* and cases of glyphosate resistance in three other species (*L. multiflorum* L., *Eleusine indica* (L.) Gaertn., and *Conyza canadensis* (L.) Cronq.) have major implications for the management of glyphosate-resistant crops globally. Although it is clear that glyphosate is a low-risk herbicide for selection of resistant weeds, these cases have made it equally clear that glyphosate-resistant weeds will appear given sufficient selection pressure and time. *Conyza canadensis* is the first glyphosate-resistant weed to appear in Roundup Ready crops and has spread rapidly since its appearance in Delaware in 2000. It now infests over 200,000 acres in six states and likely will be found in much of the range of Roundup Ready soybean in the United States over the next few years, due to its rapid spread by airborne seed. Undoubtedly there will be several new cases of glyphosate-resistant weeds that appear in response to the increased use of glyphosate in Roundup Ready crops over the next 10 years. The real challenge will be to limit their impact on the utility of this valuable herbicide.

Resistance Management Strategies

In North America and Europe the primary *resistance management strategy* has been the use of *herbicide rotations*, mixtures, or sequences that involve different herbicide modes of action. Common resistance-management strategies currently used (to varying degrees) by farmers around the world include:

- **Herbicide rotation.** Rotating between herbicide modes of action from year to year is one of the most widespread and probably most cost-effective methods of resistance management.
- **Herbicide mixtures or sequences.** In this strategy different herbicide modes of action are used at full rates to control the same weed species, thus making the probability of target site resistance extremely low, as the same individual would require a mutation to both herbicide modes of action. Expense usually is the major deterrent to using mixtures or sequences, particularly with sequences, as they require additional applications. Care must be taken to choose herbicides that will not select for metabolism-based resistance to both modes of action.
- **Cultural/Nonchemical control.** Strategies that include nonchemical control often are suggested in resistance management but rarely adopted unless they provide immediate economic benefit to the farmer—usually this happens after the appearance of resistance. Most strategies are aimed at reducing seed production or the seed bank before cropping. They include crop rotation, stubble burning, cultivation to stimulate weed germination, delayed sowing to maximize pre-sowing weed kill, spray-topping, crop-topping, hay cutting, and capture of weed seed during harvest (Mathews and Powles 1996). Establishment of a highly competitive crop probably is the best example of a cultural control that provides immediate economic benefits.

Adoption of Resistance Management

Over the last 30 years scientists have studied the mechanisms of herbicide resistance, *cross-resistance* patterns, distribution of resistance, genetics, gene flow, biology, and ecology of resistance. All of these studies are necessary for an understanding of herbicide resistance and are useful in the development of resistance management strategies. Often the devised strategies are extended to farmers via fact sheets, workshops, and the popular press. Unfortunately, the weak link in the chain is the adoption of resistance management strategies by farmers. While the research and development arm of industry has been proactive in supporting herbicide resistance research, and the development of resistance management strategies, the sales and marketing arm of industry often ignores this advice and promotes repeated use of the same product year after year.

In addition, there is a common (and so far relatively accurate) perception by farmers that by the time they have a resistance problem, industry will provide a new herbicide to effectively solve the problem, thus making proactive and expensive resistance management strategies unnecessary. This is a dangerous assumption, as the economic consequences are severe if/when industry is unable to provide the next solution in time.

Glyphosate is the most important herbicide resource that farmers have left, and the introduction of Roundup Ready crops provides them with a useful tool for controlling existing resistant weeds. Unless carefully managed, however, Roundup Ready crops are not likely to be a long-term “silver bullet.” Widespread appearance of glyphosate-resistant weeds will take considerably longer than it took for widespread resistance to ALS- or ACCase-inhibitor herbicides, but complete reliance on glyphosate for weed control both preplant and postemergence probably will spell the beginning of its demise within a decade.

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1.4 Pathogens

Wolfram Koeller

Introduction

Most of our economically important plant diseases are caused by fungal pathogens. They are eucaryotic micoorganisms and reproduce exclusively or predominantly asexually. This clonal character of reproduction, which has impact on the monitoring and combat of fungicide resistance, differentiates fungal plant pests from insects and weeds. Most fungicides in the United States currently are used in the production of grapes, tree and berry fruits, vegetables and potatoes, and in the maintenance of turf with its high recreational value in an urban environment. This list of commodities does not include major field crops such as wheat, corn, or soybean. All seeds used in the United States, however, are coated with fungicides to protect seedlings from soil- and seedborne diseases. Fungicide resistance rarely has become a problem in such seed dressing applications, because most soil pathogens reproduce and disperse slowly and only infect plants during the relatively brief seedling stage.

Resistance has become a problem in foliar applications of fungicides indispensable in the production of numerous high-value crops. Here, losses caused by fungal diseases have become increasingly costly. For example, apples grown on 200,000 acres are affected by apple scab, a disease routinely managed with four to eight fungicide applications per season. The market potential of apples produced for the fresh market is $6,000–$8,000 per acre. A single blemish caused by the apple scab fungus will lead to the downgrading of apples to 10% of their fresh market value. Commercially acceptable apple cultivars and biological control agents are not available, leaving fungicides as the only option in the management of the disease. Numerous high-value crops cultivated in the United States mirror the apple scab example.

Fungicides and Fungicide Resistance

The first disease-control agents introduced over a century ago were sulfur and the copper fungicides. Although both are still in wide use and certified in organic food production, the level of disease control achieved with sulfur and the copper fungicides is low for many of the important diseases to be managed. More efficacious organic fungicides were introduced during the 1940s and 1960s, with the ethylenebisdithiocarbamates (EBDCs), captan, and chlorothalonil as important examples. Their commonality is a nonspecific mode of action through the indiscriminate chemical modification of numerous enzymes (Köller 1999). In order to avoid phytotoxicity, these fungicides must be confined to the surfaces of plants, where they inhibit the germination of attacking fungal spores. This inherently protective rather than curative mode of physical action is of limited value in integrated pest management (IPM) programs with their “only when needed” paradigm of pesticide use. An additional concern is the B2-carcinogen classification of several of these older fungicides, a characteristic remaining under the scrutiny of the Food Quality Protection Act (FQPA). The advantage of conventional protectants is that resistance never has become a limitation. This positive experience with resistance combined with low treatment costs is the major reason for the continued use of these conventional protectants.

Curative postinfection control of plant diseases requires systemic uptake of fungicides and, therefore, pathogen-specific modes of actions. Starting in the late 1960s with the introduction of the benzimidazoles, several classes of specific foliar fungicides have been introduced and widely used: the dicarboximides in the 1970s, the phenylamides and sterol demethylation inhibitors (DMIs) in the 1980s, and the new class of broad-spectrum strobilurins in the 1990s. The various classes of pathogen-specific fungicides allowed growers to manage diseases with postinfection applications and at prolonged spray intervals. The inherent disadvantage of these specific fungicides was that resistance has developed more or less rapidly to all classes (Brent 1995; Köller 2001).

The first case of practical fungicide resistance in the United States was reported in 1960 for the aromatic hydrocarbons used in the postharvest control of citrus rot caused by *Penicillium*. The first case of resistance to a foliar fungicide was reported in 1968 for dodine used in the postinfection control of apple scab (Brent 1995). Since then, all major fungal pathogens managed with pathogen-specific fungicides have developed resistance to at least one of the pathogen-specific fungicides. The current concern is that several pathogens have developed multiple resistance. For example, the apple scab fungus has responded consecutively with resistance to dodine, benzimidazoles, and the DMIs, and clear indications of resistance to the new class of strobilurin fungicides exist. Several powdery mildews have become resistant to the benzimidazoles, the DMIs, and more recently, the strobilurins. Indications are that repeated development of resistance might even accelerate the speed of future rounds of resistance (Köller and Wilcox 2001).

Antiresistance Strategies

The sharp rise of fungicide resistance in the 1980s required the development and implementation of antiresistance strategies. Goals of such strategies are to delay the speed of resistance development and to manage resistance once first cases of practical resistance have emerged. These two goals are not exclusive. Initial occurrences of resistance most often are restricted to particular regions, and management of resistance in these regions can and should be combined with delaying tactics in other regions. The first antiresistance strategy introduced in the late 1970s for the benzimidazoles was to mix a fungicide under risk with a conventional protectant. Initially this strategy was implemented through recommendations. Later, implementation was enforced by the marketing of prepacked mixtures in the control of high-risk diseases. The advantage of this mixture strategy was that resistant subpopulations of pathogens were managed by the protective partner. Respective mixtures, however, did not delay the selection of resistant subpopulations when they were used in postinfection applications typical for the systemic partner (Köller and Wilcox 1999). Consequently, contributions to the overall level of disease control achieved by the systemic mixture components declined over time. At a given threshold level of resistance frequencies, management of diseases entirely depended on the conventional protectant (Köller and Wilcox 1999). Although mixtures of two fungicides with postinfection activities might delay the development of resistance (Köller and Wilcox 2000), they have been studied or used rarely.

Strategies for the delay of resistance development have included rotation among different classes of fungicides. This rotation strategy was enforced for the new class of strobilurins by restricting the number of applications allowed per season. While the rotation among chemical classes will undoubtedly delay the speed of resistance development when measured in numbers of useful seasons, the inherent problems to such rotation programs are the restricted availability of rotation partners. In many cases, alternatives have been and will be the conventional protectants with their inherent limitations, because previous rounds of resistance already have affected the postinfection alternatives.

Another delaying tactic is the use of fungicides at high doses (Köller and Wilcox 1999). High doses will be effective only in cases of multiple-gene resistance, however, where resistant phenotypes continue to respond to the inhibitors. This type of resistance has been identified for the DMIs (Brent 1995; Köller 2001; Köller and Wilcox 2001). For many other fungicides, resistance is caused by target site mutations rendering mutants to respond immune to any feasible dose of the inhibitor (Brent 1995; Köller 2001). In these cases, high doses will not slow the selection of resistant phenotypes.

In summary, fungicide resistance has curtailed the sustained usefulness of most of our modern postinfection fungicides. Antiresistance strategies employed have been mixtures of these fungicides with a conventional protectant or the rotation among chemical classes of fungicides. Limitations imposed on these strategies are that conventional protectants in mixture do not delay resistance development when used in postinfection applications and the limited choices of postinfection fungicides not yet affected by previous rounds of resistance. A second matter of concern relates to the fact that growers cannot expect nor predict substantial crop losses caused by resistance. Such crop losses are experienced first during the initial emergence of practical resistance and by growers, who continue to rely on certain fungicides without the addition of other management practices. This status quo determines the future challenges.

Challenges

The delay of resistance development to a new fungicide is most effective, if strategies are implemented from the start of their commercial use. Appropriate antiresistance strategies will vary for different fungicides and different pathogens. For example, a high-dose strategy will be effective only in cases of multigenic resistance but ineffective in cases of target site mutations rendering immunity (Köller 2001; Köller and Wilcox 1999). The nature of expected resistance can be examined in proactive risk assessment studies. Such risk assessments have been implemented in a European Union Registration Directive, but reliable tools for risk assessments and their interpretation remain coarse and unreliable. For example, most risk assessments had predicted a moderate risk for the new class of strobilurin fungicides (Brent and Holloman 1998). Instead, resistance developed rapidly for many diseases in spite of limitation in the number of applications allowed per season (Bartlett et al. 2002). In view of current uncertainties, the implementation of antiresistance strategies derived from risk assessments must be accompanied by the continuous monitoring of pathogen responses to pathogen-specific fungicides. Only reliable monitoring procedures already in place will allow for adjustments of antiresistance strategies before threshold levels of practical resistance are reached. At present, monitoring programs are primarily aimed at the confirmation of resistance once it has reached a level of commercial ineffectiveness. At that stage, implementation of antiresistance strategies will be too late in many cases.

Both the improvement of methodologies employed in resistance risk assessments and the monitoring of pathogen responses to pathogen-specific fungicides require substantial commitment to the task. The financial resources presently committed by both the private and the public sectors are very small in comparison with the economical importance of plant diseases controlled with modern low-risk fungicides. But even if the level of financial resources were increased, it will hardly be possible to assess the relative risks and to monitor population responses for all diseases managed with modern postinfection fungicides. Results obtained for key pathogens with model character will have to be transferred to the majority of diseases affected by fungicide resistance.

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2.1 Resistance Issues in Fruit and Vegetable Production Systems

Charles Mellinger

Every season brings new adventures in managing resistance wherever fruits and vegetables are grown on large-scale, intensive farm operations. Resistance has triggered far more profound changes in our South Florida integrated pest management (IPM) systems and pesticide use patterns than regulation. Plus, resistance often beats the Environmental Protection Agency (EPA) to the punch. Resistance-triggered change in pesticide use is one reason our grower-clients have for the most part not been impacted adversely by implementation of the Food Quality Protection Act (FQPA), at least not yet.

Looking ahead though, we see tough new challenges. The phaseout of methyl bromide is bound to bring about big changes in pest management systems in tomatoes and peppers. Some growers are making the transition in an orderly, incremental manner, whereas other growers are betting that methyl bromide will get a reprieve and the day of reckoning will be delayed several years. If this latter group is wrong and the phaseout proceeds on the current schedule, some farmers will be scrambling and a few may find themselves excessively reliant on certain pesticides, making resistance management more difficult. Newly arrived invasive species also can trigger major changes in pesticide use patterns and dramatically change resistance management dynamics.

My task is to summarize pressing fruit and vegetable resistance management issues. There is fairly widespread agreement on the most pressing challenges in weed, insect, and plant disease control.

Insect Management

The first priority is preserving the efficacy of the nicotinoids including imidacloprid (Admire, Provado), thiamethoxam (Actara, Platinum), acetamiprid (Assail), and thiacloprid (Calypso). Key target pests likely to develop resistance, or already showing signs of slipping efficacy in some regions include Colorado potato beetles and whiteflies. Other pests belong on this list in certain regions.

The second priority is preserving the efficacy of spinosad (SpinTor, Conserve). Key pests vulnerable to resistance or already showing signs of slipping efficacy include diamondback moth in a number of geographical regions and certain thrips species in the Southeast.

Spinosad is a remarkably versatile product that meets a number of pressing needs for a softer midseason insecticide. Its range of uses, coupled with its specific mode of action, makes spinosad vulnerable to resistance. Farmers and IPM practitioners must resist the temptation to rely too heavily on this excellent new tool if they are to preserve its efficacy.

A significant level of adult pest movement from one crop to the next is being reported, where spinosad might be used several times in the same period for a range of pests. (Adult pest movement also is a big concern in managing whitefly and aphid resistance to nicotinoids.) Complicated patterns of spatial and temporal selection pressure pose equally complicated resistance management challenges.

The third priority is managing the development for resistance to avermectin (Agrimek) in dipterous leafminers and various mites. Mite control is a tough challenge, in large part because of the propensity of mites to develop resistance to new acaricides quickly. We continue to focus much effort on managing resistance to avermectin in citrus rust mites and two spotted spider mites on various crops. Other recently registered miticides pose important resistance management challenges, as well. The application rate of avermectin for leafminer control has increased twofold during the past decade, a clear sign we are losing ground.

The fourth priority is keeping old organophosphate (OP), carbamate, and synthetic *pyrethroid* chemistry effective. We will have a very difficult time managing resistance to reduced-risk chemistries, insect growth regulators (IGRs), and the nicotinoids without the ability to apply a relatively hot, broad-spectrum material from time to time. Not having methamidophos (Monitor) for control of western flower thrips as a rotation partner for spinosad (SpinTor) is an important example. But virtually all of these products already are compromised to some degree by resistance, and all are highly vulnerable if even a few farmers choose to build their control programs on them.

Managing resistance to OPs and carbamates is made more difficult—and important—by limits imposed on their use by the FQPA. As fewer of these materials are available, the remaining products likely are to be used more intensively, possibly leading to a proliferation of resistance insects and in some cases, control failures. For example, methomyl and oxamyl are excellent rescue pesticides for control of *Thrips palmi* in peppers. If either one should become unavailable, the use of the remaining active ingredient will certainly increase, even if only by a few applications per growing season.

On the soilborne insect and nematode front, we face some emerging resistance management challenges. If, and as, methyl bromide is phased out, many growers will increase their use of Telone and other fumigants and soil insecticides. We need to be vigilant in monitoring resistance in *pest complexes*, which could lead to dramatic shifts in species composition and root feeding damage. Glades Crop Care is working hard to develop new scouting and sampling techniques to understand better the scope and distribution of nematode problems across a field. How to deal with resistance management as control programs change will have to be figured out in real-time, which leaves little room for experimentation or error.

Disease Management

Managing Resistance to Strobilurin Fungicides

For years we have struggled in South Florida to keep up with blight diseases of tomato and potato and bacterial spot in tomatoes and peppers. Over the years the EPA has placed progressively strict limits on the total pounds of ethylenebisdithiocarbamates (EBDCs) that can be applied, forcing growers to introduce other fungicides into their programs. The strobilurins are very welcome new tools, yet are much more vulnerable to resistance than the EBDCs, coppers, and chlorothalonil. Indeed, already we are facing resistance to the strobilurins in the gummy stem blight pathogen in cucurbits. Fortunately, some other new fungicides that employ novel modes of action are well along the registration pipeline and will provide some additional options.

Avoiding Use of No-Longer Effective Products

Because of resistance, some fungicides just do not work anymore. For a variety of reasons, though, they are still used, costing farmers money and possibly making matters worse. Somehow the pest management community needs to find a more effective way to stop the use of legal products in places where resistant phenotypes have taken over target-pathogen populations. The steps necessary to monitor susceptibility are known, but the resources are not routinely accessible to get the job done. I hope this symposium will trigger some new thinking regarding how to overcome this practical reality.

In some parts of the country, processors and buyers also need to rethink the mandatory fungicide treatment requirements they impose on grower-contractors. These companies have an obligation to their growers, and the communities in which they work, to assure that any mandatory fungicide or fumigant applications are worth the expense and that risks are manageable.

Monitoring Chlorothalonil Susceptibility

Chlorothalonil (Bravo) remains a very valuable, affordable product. It is heavily used in many fruit and vegetable systems, and for the most part, resistance has not been a major concern. There is some evidence, I am told, (Holm et al. 2003) of modest levels of resistance in certain potato pathogens in a few states. It seems unlikely that chlorothalonil efficacy will collapse suddenly, but we should not take this product for granted. More systematic resistance-monitoring efforts should be put in place in a number of major growing regions until we are certain that resistance ratios are stable.

Weed Management

Managing Resistance to Sulfonylurea and Other Acetolactate Synthase (ALS) Inhibitor Herbicides

A half-dozen major crops drive herbicide discovery and registration priorities. The minor use crop problem is severe and persistent, although vegetable growers are pleased to have access to some new sulfonylurea herbicides. Sulfonylurea herbicides have a rich history in triggering resistance. A visit to <www.Weedscience.org>, the excellent global database of herbicide-resistant weeds, shows 79 species of weeds resistant to ALS inhibitors. Instances of resistant weeds have been documented in many countries. So as vegetable and fruit growers get a chance to rely on this chemistry family, we should be forewarned to manage resistance carefully.

Paraquat Resistance in Weedy Hosts for Crop Insects and Pathogens

Paraquat resistance in nightshade was documented in Florida in the late 1980s (Bewick et al. 1990; Stall, Kostewicz, and Brown 1987). Until recently, we did not understand some of the most serious implications of this fact. In our South Florida pepper-production regions, it turns out that nightshade is a preferred alternate host for pepper weevil, the insect that drives insecticide use in peppers. We have had some success in decreasing pepper weevil populations and insecticide treatments where we have spot-treated surrounding areas for control of nightshade using alternatives to paraquat. Unfortunately, nightshade is not the only weed infesting our production fields, and paraquat often has been the product of choice for controlling these other pests. This situation results in expensive tank mixes that often lead to crop injury because of environmental conditions or application issues. To keep damage and costs down, our growers will continue to need paraquat for control of weed hosts. Through the wise choice of tank mix or rotation partners we should be able to maintain the efficacy of paraquat against those weeds it still controls.

Current Resistance Management Efforts, or What Is Being Done?

Mode of Action Rotation

By far the most common resistance management tactic being used on fruit and vegetable farms is rotation of pesticides by mode of action. This strategy is important yet is not sufficient by itself to meet emerging resistance management challenges. This is because so many pests can and do move across the landscape, spending time in different crops and facing highly variable, and sometimes intense selection pressure.

Preventive Practices

We need to diversify resistance management tactics in intensive fruit and vegetable production systems. This effort will involve developing and implementing preventive practices to take pressure off the actual use of pesticides. For example, by rearranging the order in which pepper fields were planted on a client's farm, applications of methomyl were decreased by approximately 50% in the first season and an additional 50% the following year. The new planting order avoided movement of adult beet armyworms from fields being destroyed into younger fields.

By replacing some of the methomyl applications with *Bacillus thuringiensis (Bt)* applications, selection pressure was decreased, and in the second season after the planting change, the control afforded by each application of methomyl was much greater than in the high-pressure situation during the first season.

Exploit Susceptibility Windows

We need to identify windows in the life cycle of various pests when they are most vulnerable to a given family of chemistry, in the hope that short-term intensive use of a pesticide will drive populations down to low levels, giving plants a chance to get beyond vulnerable periods or setting the stage for economic biological control. Accomplishing this refined timing of applications, however, places greater pressure on scouts, who not only must accurately count insects in a field, but also accurately differentiate instars. In addition, applicators must respond quickly when a product only active on first and second instars is recommended in a field where insects are developing rapidly.

Information on susceptibility windows will help devise more effective rotational patterns that not only manage resistance but also have potential to minimize pesticide use and costs. The hurdle in turning potential cost savings into actual profits is to obtain and properly respond to accurate scouting data. Collecting such data, though, comes at a cost. In many cases, scouts and pest managers would rather "hedge bets" by recommending use of a product that controls all or most instars, rather than gamble on applying a product that works well only against young or mature insects. Insect development and timing issues obviously come into play prominently in use of IGRs such as tebufenozid.

Resistant Varieties

When resistant varieties become available for managing a particular pest it is important not to put all of the resistance management pressure on the resistance gene. It is critical to spread the pressure around by continuing to use all feasible preventive measures, including judicious use of pesticides. For example, we now have tomato varieties resistant to tomato spotted wilt virus. The best way to manage this gene is to not allow high populations of viruliferous thrips to continually spread pathogen inoculum that challenges the tomato plant's resistance. Rather, we need to use a combination of tactics, such as killing some vectors with pesticides and managing alternate hosts of the virus. Combinations of tactics are just as essential in maintaining the value of our resistant varieties as they are in managing pesticide resistance—and for exactly the same reasons.

A second essential ingredient for sustainable resistance management is taking some pressure off pesticides, especially where population levels are forcing farmers to apply multiple products one or more times each week. Heavy and routine reliance on pesticides is a sign that a farming system has become too accommodating for some pests and that changes are in order to either prevent the influx of pests or to deal with them in other ways when they approach damaging thresholds.

Barriers to Resistance Management

Unfortunately there are plenty of barriers to resistance management, including:

- Attitudes and expectations
- The comfort zone that comes with applications of "silver bullets"
- Information—both conflicting and lacking
- Aggressive marketing efforts, especially incentives and discounts linked to volume purchases
- Products only available in premixes
- Grower aversion to the risk of crop losses; and unrealistic, unsustainable control objectives
- Preference for simplicity in pest management systems
- The lack of infrastructure supporting the preventive practices essential to make *biointensive IPM* profitable

A full discussion of all of these constraints is not possible here. In closing, I will address briefly a few of these important barriers.

Grower attitudes are a big problem. Too many growers and pest managers expect the chemical industry to keep finding and commercializing new families of chemistry as they have done the past 30 years. Too many farmers think there is no significant difference—in terms of the prevention of resistance—between the OPs, carbamates, pyrethroids, *Bt*s, nicotinoids, and other reduced-risk chemistries. I think farmers should hedge their bets now by making a commitment to preserving the really good, affordable, reduced-risk products currently on the market, in case future products are simply not as good.

The goal for resistance management is another issue. Some people think that resistance can be managed, whereas others argue prevention must be the goal. We prefer to think that avoidance should be the goal. One needs to avoid resistance becoming obvious in a population by using correct management practices. From our experience, once resistance emerges to some active ingredients, there is no going back. In such phenotypes, resistance is relatively stable and quickly reaches critical levels in the face of continued selection pressure.

In other instances, though, resistant populations regain susceptibility relatively quickly. Avermectin resistance in citrus rust mites is an example. We think that avoidance should be the goal for resistance management, unless and until solid science and field experience documents that resistance is unstable in target populations.

Lack of information is another huge barrier. We need real-time, accurate data on resistance ratios in our field populations. We are working with academic partners to monitor resistance in a few very high-priority instances such as whiteflies and imidacloprid, but we see the need in future years for much more routine, localized monitoring of resistance for many more pest-pesticide combinations.

Perhaps in the future, pest managers will collect or somehow gain access to information on susceptible gene pools that is as accurate and timely as contemporary soil test data. The infrastructure to generate this information is not in place. What will this infrastructure and testing cost, and who will pay for it? Who will pay if we do not find ways to meet emerging resistance challenges, and what will that price tag look like? I sincerely hope we never have to find out.

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2.2 Resistance Issues in Cotton Pest Management

Patricia F. O'Leary and Robert L. Nichols

Introduction

Cotton (*Gossypium hirsutum*) is a major agronomic crop, grown on 5–6 million hectares (12–15 million acres) in the southern half of the United States from Virginia to California. The value of the crop averages approximately $6 billion per year. Pesticides are important tools used to protect the crop each year from a diverse complex of pests. It is not surprising that pest resistance has become a problem with some of the more frequently used products.

Current Status

Insects

Serious problems with insecticide resistance began to develop shortly after the chlorinated hydrocarbon insecticides were adopted for general use on cotton after World War II. At that time, resistant populations of two species were reported (King, Phillips, and Coleman 1996). Today, ten cotton insect pests have been identified by the Insecticide Resistance Action Committee (IRAC) as having populations resistant to one or more classes of insecticides (Table 2.2.1; IRAC Resistance Survey: Cotton Working Group 2003). Of these, the tobacco budworm (*Heliothis virescens*) and the cotton bollworm (*Helicoverpa zea*) are the most destructive, costing the cotton industry more than $250 million in 2002 (Williams 2003). Pyrethroid resistance in the tobacco budworm was first detected in the mid-1980s (Platt, McWhorter, and Vance 1987). Resistant populations now have become prevalent in the eastern portion of the Cotton Belt, and pyrethroids are no longer recommended for tobacco budworm management in several mid-Southern states.

Resistance in *Lygus* spp. and cotton aphids (*Aphis gossypii*) does not appear to be stable. In these species, variation in susceptibility occurs from year to year, among locations, and depending on the pesticide, within the season. As an example, *L. hesperus* populations monitored for susceptibility to various insecticides in California's San Joaquin Valley over several years were found to be resistant to organophosphates and carbamates, but the level and frequency of resistance fluctuated from year to year. In contrast, pyrethroid resistance was quite high and intensified over the study period (Grafton-Cardwell et al. 2000). Louisiana researchers have found that susceptibility of populations of *Lygus lineolaris* to cypermethrin, acephate, and oxamyl decreases

Table 2.2.1. Cotton insect pests with populations resistant to one or more classes of insecticides (IRAC Resistance Survey: Cotton Working Group 2003)

Pests	Pesticide class			
	Pyrethroid	Carbamate	Organophosphate	Organochlorine
Tobacco budworm	X	X	X	X
Cotton bollworm	X	X	X	
Beet armyworm	X			
Fall armyworm	X	X	X	X
Soybean looper	X	X	X	
Boll weevil				X
Cotton aphid	X	X	X	X
Silverleaf whitefly	X		X	
Lygus	X	X	X	
Western flower thrips	X	X	X	X

throughout the growing season (Halloway et al. 1998).

In the early 1990s resistance to pyrethroids and pyrethroid–organophosphate combinations led to devastating outbreaks of the silverleaf whitefly (*Bemisia argentifolii*) in cotton–vegetable systems in southern California and Arizona. Substantial economic losses were sustained by growers due to exorbitant costs of insect control. In addition, whitefly feeding deposits honeydew on exposed cotton lint, creating "sticky cotton." Not only was the cotton discounted over the entire region, but also, the reputation for stickiness has had a negative impact on domestic sales and export orders of cotton from the Southwest (Ellsworth et al. 1999).

Weeds

The Herbicide Resistance Action Committee (HRAC) and the Weed Science Society of America (WSSA) list five weed species that are common and troublesome in cotton and are resistant to one or more herbicide modes of action (Table 2.2.2; International Survey of Herbicide Resistant Weeds: USA 2003). As might be expected, most incidences of resistance have been reported in the mid- and southeastern states where herbicide use is heaviest. Johnsongrass (*Sorghum halepense*) is a major weed in agronomic crops throughout the southern half of the United States. Johnsongrass was heavily treated with postemergence graminicides following their introduction in the early 1980s, and as a result, resistance to herbicides with inhibition of acetyl CoA carboxylase (ACCase) as their mode of action occurred in the mid-South in the 1990s.

Inhibition of acetolactate synthase (ALS) is a common mode of action in herbicides. Registration of the ALS herbicide Staple® in 1994 was a major step forward, because Staple could be used as a true over-the-top herbicide in cotton. ALS resistance in populations of cocklebur (*Xanthium strumarium*) and more recently in Palmer amaranth (*Amaranthus palmeri*), however, has limited the utility of this otherwise very valuable compound. In addition, many of the locations affected by cocklebur resistant to ALS herbicides also have cocklebur resistant to the organoarsenical herbicides, MSMA and DSMA, the principal class of chemistries used for management of cocklebur escapes in cotton before the registration of Staple. In South Carolina, Palmer amaranth also is resistant to dinitroaniline herbicides.

With the advent of transgenic, herbicide-resistant technology, glyphosate (a glycine herbicide) has become the dominant herbicide in U.S. cotton and soybeans (Carpenter and Gianessi 2001). A recent and troubling development is the identification of resistance to glyphosate in the United States (van Gessel 2001). Although resistance to glycine herbicides has occurred previously in other weed species, positive identification of glycine resistance in horseweed (*Conyza canadensis*) is the first incidence that has affected row-crop agriculture directly (Feng, Pratley, and Bohn 1999; Lee and Ngim 2000). There is additional concern because of the extensive adoption of Roundup-resistant varieties in cotton, soybean, and other crops where glyphosate may be used two, three, or more times per season and is sometimes the only herbicide used. Such patterns of use represent strong challenges to the maintenance of glyphosate susceptibility.

Table 2.2.2. Weeds in cotton with populations resistant to one or more herbicide modes of action (International Survey of Herbicide Resistance Weeds: USA 2003)

Pests	Mode of action				
	Organoarsenicals	ALS[a]	Glycines	ACCase[b]	DNA
Cocklebur	X	X			
Horseweed			X		
Johnsongrass				X	
Goosegrass					X
Palmer amaranth		X			X

[a] Acetolactate synthase.

[b] Acetyl CoA carboxylase.

Pathogens

Fungicides are used chiefly in cotton as seed or hopper box treatments, or applied in furrow at planting for control of seedling diseases caused by *Pythium* spp. and *Rhizoctonia solani*. There are no known instances of pesticide resistance in the organisms that cause diseases in cotton.

Management Strategies

Strategies for managing pesticide resistance have been developed on a case-by-case basis. There are two components common to most situations, however: monitoring and the development of management plans and guidelines.

Monitoring

Monitoring programs for insect pests to certain insecticide families has been conducted at both local and regional levels. Entomologists in Louisiana have monitored cotton pest populations since 1986 for susceptibility to various insecticides. This program has tracked the evolution of pyrethroid resistance in tobacco budworm, providing information to tailor management recommendations to match the current level of resistance.

A recent example of a multistate resistance-monitoring effort is a program sponsored by IRAC and Cotton Incorporated. Following reports of field failures in several southern states, a program was initiated in 1998 to assess the extent of pyrethroid resistance in cotton bollworm populations. The monitoring effort involved 21 scientists in 12 states: Alabama, Arkansas, Florida, Georgia, Louisiana, Mississippi, Missouri, North Carolina, South Carolina, Tennessee, Texas, and Virginia.

Whereas insects generally produce multiple generations per year in temperate regions, weeds generally reproduce once annually, even when they germinate throughout the year. Thus, assaying resistance in weeds is a multiyear process. Through the present time, weed resistance has almost always been discovered after the fact. Weed scientists are currently exploring how best to assemble information for the purpose of recommending programs to decrease the potential for early development of resistance to herbicide modes of action.

Management Plans and Guidelines

Resistance management plans and guidelines have been developed for several cotton insect species. These guidelines have taken many different forms, depending on the pest, location, and pesticide class or mode of action involved. Basic guidelines for managing resistance, such as those found in Oklahoma State University's "Cotton Aphid Resistance Management Guidelines" (Karner 1997) and the University of California's "Herbicide Resistance—How to Delay or Prevent Problems" (Vargas and Wright 2001), are based on integrated pest management (IPM) practices to minimize the chance of a widespread infestation of the pest.

Other plans have been developed that are similar to those drafted for managing pyrethroid resistance in *Heliothis armigera* in Australia (Pyrethroid 1983). A "windows" approach is used to schedule insecticide applications to decrease selection pressure and to preserve a specific product for use against the most damaging pest population. The most widely adopted plans were developed to manage pyrethroid resistance in the tobacco budworm in the mid-South (Luttrell and Roush 1987) and to preserve susceptibility of two insect growth regulators and manage pyrethroid resistance in the silverleaf whitefly in Arizona and California (Ellsworth, Dennehy, and Nichols 1996; Goodell and Godfrey 2002). The whitefly plan is still an important component of pest management recommendations in the West, whereas the tobacco budworm plan is less used today due to the introduction and widespread adoption of *Bacillus thuringiensis* (*Bt*) transgenic cotton and the loss of pyrethroid insecticides as effective management tools for tobacco budworm in the mid-South. The plan has been modified, however, and is still in place in locations where potential pyrethroid resistance in cotton bollworm and tarnished plant bug exists.

Current Concerns

Sustainability of Transgenic Varieties

The cotton industry has a major investment in *transgenic technology*. In 2002, 71% of U.S. cotton acreage was planted in varieties that either express introduced genes for herbicide resistance or insecticidal proteins, or both (USDA 2003). A resistance management plan is a requirement for use of the *Bt* cottons, but is not required with the herbicide-resistant varieties.

Pyrethroid Resistance in Cotton Bollworm

The cotton bollworm is still relatively susceptible to the pyrethroid insecticides. In the last few years, however, there has been an increase in the number of reports of populations with increased *tolerance* to pyrethroids. In the multistate monitoring program described earlier, mean survival of cotton bollworm to a diagnostic dose of cypermethrin increased sixfold from 1998 to 2001 (Payne et al. 2002).

Susceptibility of Boll Weevil to Malathion

After 25 years and over $1 billion in program costs, the Boll Weevil Eradication Program is nearing completion. Entire states have been declared weevil-free, with total eradication nationwide expected by 2006. Malathion is essential to the success of the program. In 2002, approximately 4 million hectares (9 million acres) of cotton were in the active phase of the program, putting tremendous selection pressure on this insect from one insecticide.

Decreased Efficacy of Aldicarb

Aldicarb is the most widely used chemistry available for effective management of nematodes. Recently there have been reports of ineffective field applications of this nematicide against the reniform nematode (*Rotylenchulus reniformis*) in Mississippi and Alabama. Accelerated degradation of the product is suspected as the cause (McLean and Lawrence 2003).

Barriers to Resistance Management

Barriers to the implementation of effective resistance management programs are not unique to cotton. Two barriers reflect a lack of confidence in the availability of new products and concern about the economics of such programs.

Confidence in Availability of New Products

The crop protection industry has been prolific in providing tools for managing pests in cotton. Many growers, consultants, and agrochemical distributors still believe that there is an infinite stream of new pesticide products in development. Moreover, the concept of resistance still is met too often with one of two mutually exclusive forms of denial: either the pest will never be resistant to a specific chemical, or resistance is inevitable. In fact, development of resistance is a risk to the sustained use of any pesticide.

Economic Factors

The overriding influence on decisions made by many growers and apparently by certain pesticide manufacturers is the short-term bottom line. Unless there is a crisis, resistance management strategies have to show immediate economic benefits before they will be implemented. Short-term solutions are popular and easy to invest in because an immediate benefit can be realized. Resistance management is often unpopular because the benefit is delayed. Further hindering resistance management, consultants and growers are relatively adverse to risk. “Insurance spraying” of pesticides is not uncommon to protect investment in the crop.

Development of resistance is a risk to the sustained use of any pesticide. That risk depends on the pest, the pesticide, the pattern of use in the crop, and the pattern of use in the local cropping system. Our task is to develop means to manage such risks.

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2.3 Resistance Issues in Potatoes

John Keeling

Thank you for the opportunity to provide remarks to the Pest Resistance Management Symposium on behalf of the National Potato Council (NPC) and the potato growers we represent. There are 18 major potato-producing states in the United States that produced a number of potato varieties with a total farm gate value of more than $3 billion in 2001. In that same year U.S. potato producers planted 1.27 million acres of potatoes. Although both of these figures are significant, the size of the potato industry in the United States is small compared with major row crops. For that reason potatoes are considered a minor crop.

Potatoes are a capital-intensive crop with significant pest and disease pressures requiring a lengthy and complicated rotational regimen. The cost of planting an acre of potatoes is more than $2,500, and rotation with other vegetable and small grain crops results in potatoes being planted on a single piece of ground only every 3 to 5 years. Potatoes are vulnerable to yield or crop loss from fungi, insects, viruses, and weeds. Resistance management for these pests is critical to successful crop production and is a key component in the cropping plan of most potato growers. The unique characteristics of potato production offer both challenges and opportunities toward managing pest resistance.

The NPC believes that effective resistance management is broadly dependent on two key components: grower education and adequate availability of crop protection chemicals or biological agents capable of controlling pests of concern. The NPC is strongly committed to delivering the educational component to growers.

Although decreasing pesticide use is not 100% synonymous with managing resistance, the NPC believes that decreasing the overall amount of the active ingredient used while maintaining efficacy will result in significantly less resistance pressure from all pests. Good stewardship of pesticides almost always is going to lessen resistance pressure. The NPC emphasizes that the smart, reasoned use of pesticides makes good sense environmentally and economically.

Potatoes are subject to infestation from insects, fungi, viruses, and weeds. The most critical threat at any given time may vary, but aphids, Colorado potato beetles, and late blight often are the most challenging pests. Maintaining efficacy for these pests is critical.

The NPC has made the adoption of resistance management a key component of the Environmental Protection Agency's (EPA) Pesticide Environmental Stewardship Program (PESP). The PESP program is a partnership between the EPA and agriculture to increase grower adoption of pesticide strategies that decrease the overall risk from the use of pesticides. The NPC believes successful resistance management delivers the dual benefits of effective crop protection and overall decrease in pesticide application, which decreases environmental and worker risk.

The potato industry was an early adopter of integrated pest management (IPM) techniques and was among the first commodities to develop an industry-wide IPM protocol and to establish a baseline for evaluating farming IPM practices. The NPC regularly administers a grower survey that evaluates grower adoption of IPM techniques. Adoption of resistance management techniques is an integral part of that survey. For example, the following practices are specifically identified in the survey as key decisions impacting resistance management:

Preplanting decisions

- Rotate crops where the preceding crop is a non-pest host for potatoes
- Maintain spatial diversity from previous and present potato fields
- Use only minimum tillage in the spring to develop a reservoir of beneficial insects

Weed management decisions

- Maintain and review individual field weed histories
- Use mechanical tillage
- Base chemical applications on scouting and determination of efficacy
- Rotate herbicide mode of action
- Clean equipment when moving between fields
- Use chemicals on rotational crops not labeled for potatoes

Insect management decisions for Colorado potato beetles

- Use trap or barrier crops to house beneficial insects
- Leave a *refuge* or breeding ground for nonresistant pests
- Limit use of broad-spectrum pesticides
- Use chemicals on rotational crops not labeled for potatoes
- Restrict number of times and classes of pesticides applied to a single generation of insect
- Apply spot or border treatments where possible
- Base pesticide selection decisions on results of mortality test kits
- Use mechanical means when practical (vacuum or flamer)

Insect management decisions for aphids

- Use narrow-spectrum or reduced-risk biological compounds
- Only use reduced-rate application where recommended
- Use spot or field border spray
- Use chemicals on rotational crops not labeled for potatoes
- Restrict number of times and classes of pesticides applied to a single generation of insect
- Use beneficial insects timed to aphid arrivals
- Segregate seed production to isolated areas
- Scout

Insect management decisions for potato leafhoppers

- Scout using sweep nets and review migration progress reports
- Use narrow-spectrum or reduced-risk biological compounds
- Use same pesticide only once a year
- Use spot sprays

Insect management decisions for spider mites

- Scout fields using hand lens
- Treat only at economic thresholds
- Use narrow-spectrum or reduced-risk biological compounds

Insect management decisions for wireworms

- Bait and calculate economic thresholds for larvae
- Rotate with alfalfa and small grains for 3–4 years
- Sample soil
- Deep-plow alfalfa fields in August

Potato disease management decisions

- Use disease-forecasting models
- Remove volunteer potatoes
- Assess blight genotype prior to treatment
- Use biological control where possible
- Rogue virus-infected fields and eliminate all cull piles
- Vine-kill infected fields

Farm management decisions

- Maintain records of all applications and effectiveness
- Calibrate sprayers and use positive displacement application equipment
- Manage storage diseases

The process used by successful growers to make pesticide application decisions can decrease dramatically the development of resistance on individual farms and in limited geographic areas. But positive actions by any one commodity or geographic area will be ineffective without widespread adoption by all producers. There are limited chemistries and modes of action available to producers. Particular chemicals are labeled for a variety of crops, likely giving pests some exposure even before that product is considered for use on a potato farm. The educational effort must extend to all growers in all regions of the country.

The key barriers to addressing pest resistance effectively are limited grower educational efforts and difficulty in obtaining the registration or reregistration of the broadest toolbox of chemical and biological controls possible. The NPC believes that grower input and participation in EPA programs including the PESP helps ensure that strategies developed to address resistance management are practical and workable in the real world. The development of a clear industry definition of IPM and resistance management techniques in conjunction with the EPA has helped the NPC develop a consistent and effective educational message. Conducting grower surveys on a regular basis has helped evaluate grower understanding and adoption of key resistance management practices.

Continued availability of effective chemical and biological controls is largely a function of the regulatory process and economic decisions made by chemical manufacturers. Due to the fact that potatoes are a minor crop, the economic issues for pesticide registrations always will be a significant obstacle. Development of controls with unique modes of action that are less susceptible to resistance development clearly should be a priority. Continuing to evaluate the effectiveness of the Interregional Research Project Number 4 (IR–4) in assisting the registration of pest control products for minor crops or minor uses should be a priority. Expanded federal funding for the IR–4 program should be evaluated and supported by the industry if the program directly addresses actual grower needs.

The NPC appreciates the opportunity to provide comments to this symposium. Our growers take the issue of resistance management seriously and support the efforts of the Council for Agricultural Science and Technology and the EPA to create a forum for these discussions.

2.4 Resistance Issues in Corn/Soybean Cropping Systems

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Introduction

Corn and soybeans were grown on an estimated 61.3 million hectares (ha) (151.4 million acres [a.]) in the United States in 2002, representing approximately 47% of the field crop acres in the nation (NASS 2002). Corn was grown on an estimated 25.1 million ha (61.9 million a.) in ten midwestern states (Illinois, Indiana, Iowa, Kansas, Minnesota, Missouri, Nebraska, Ohio, South Dakota, and Wisconsin), 79% of the estimated corn acres in the United States. In these same ten states, soybeans were grown on an estimated 22.9 million ha (56.45 million a.), 77% of the estimated soybean acres in the United States. Throughout these ten midwestern states, corn and soybeans are rotated annually for improved production of both crops and management of pests, whose populations would increase if either crop were grown continuously. Consequently, the corn/soybean cropping system is the most prevalent type of cropping system used in field crops grown in the United States.

The corn/soybean cropping system presents unique opportunities and challenges for management of pests (insects, pathogens, and weeds) and the potential for pest resistance, especially in the twenty-first century. The amount of land devoted to production of transgenic corn and soybeans has increased significantly since the introduction of those crops (CBI 2003). The prospective plantings of transgenic soybeans and corn have been estimated at 80% and 38% of all U.S. soybean and corn acres, respectively, in 2003 (NASS 2003). The success of the current transgenic corn hybrids and soybean cultivars will encourage the development of new and different transgenic hybrids and cultivars that will be major factors in pest management well into the future. The advent of transgenic crop technology also has had an impact on development of new chemical pesticides, decreasing the number of active ingredients being developed by companies. As a consequence, the number of classes of chemical fungicides, herbicides, and insecticides has declined to just a few that are being used or could be used on most of the planted corn and soybean acres. Finally, the development of conventional corn hybrids and soybean cultivars (i.e., with traditional plant breeding methods) resistant to specific pests will continue, with the concomitant concern about the target pest's ability to overcome the crop's resistance.

The aforementioned issues will be discussed within the following sections: insect management, nematode management, plant disease management, and weed management. An overview of the pest resistance management issues will be presented, with references to specific current and potential challenges. Although interactions among all pests and pest resistance management programs in corn and soybeans are likely, such interactions will not be discussed in this paper.

Insect Management

Since the mid-1990s, the most widely discussed and hotly debated issue associated with insect resistance in the corn/soybean cropping system has been the potential for target insects to become resistant to *Bacillus thuringiensis (Bt)* in transgenic *Bt* corn. To address this concern, the U.S. Environmental Protection Agency (EPA) requires companies that submit *Bt* plant-incorporated protectants for registration also to submit insect resistance management plans (EPA 2002). Such plans for *Bt* corn are intended to prevent or to slow down the development of resistance to *Bt* within populations of target insects. Until 2003, all *Bt* corn products registered by the EPA were transgenic hybrids developed for control of Lepidoptera pests, primarily the European corn borer and southwestern corn borer. Other Lepidoptera pests controlled by some or all of these registered *Bt* corn products include armyworm, black cutworm, corn earworm, and fall armyworm. In February 2003, the EPA registered a *Bt* corn product for control of western, northern, Mexican, and southern corn rootworms. The insect resistance management plan for all *Bt* corn products to date includes a requirement for a 20% structured refuge of non-*Bt* corn. In the near future, corn hybrids with traits for resistance against both Lepidoptera pests and corn rootworms will be available.

Another recent development in management of corn insect pests has been the increase in use of insecticidal seed treatments for control of subterranean insects, including corn rootworms, white grubs, and wireworms. All of the most recently registered insecticidal seed treatments—Gaucho and Prescribe (active ingredient imidacloprid), and Cruiser (active ingredient thiamethoxam)—have been in the nicotinoid chemical class, and all of these insecticides are systemic. Another nicotinoid seed treatment—Poncho (active ingredient clothianidin)—is being developed, although it was not registered at the time this paper was written. The current *Bt* corn products for rootworm control do not control other subterranean insects such as white grubs and wireworms, pests for which rescue treatments are not effective. Consequently, all *Bt* corn for rootworm control will be treated with one of the nicotinoid seed treatments. In addition, the required non-*Bt* corn refuge can be treated for control of corn rootworms, so it is possible that a large percentage of refuges will be planted with corn seeds treated with a nicotinoid insecticide. Despite this possibility, the EPA has not required a resistance management plan for registration of these nicotinoid seed treatments or for other chemical insecticides. Furthermore, the companies that have manufactured the nicotinoid seed treatments are pursuing registration for their use on soybean seeds for control of bean leaf beetles and soybean aphids. It is possible that a significant percentage of the corn and soybean acres in the ten midwestern states indicated previously will be treated with nicotinoid insecticides in the relatively near future.

Although insects that feed above ground in corn or soybean fields are not controlled with insecticides on as many acres as insects that feed below ground in corn, it is important to note that most of the foliar-applied insecticides currently registered for use in corn and soybeans are pyrethroids. Due to their effectiveness and economics, pyrethroids are used preferentially when outbreaks of insect pests of corn and soybeans occur.

Two other issues regarding insect pest resistance in corn are associated with western corn rootworms. As a result of wide-scale spraying of insecticides for multiple years in succession to manage adult western corn rootworms in Nebraska, some populations have developed resistance to methyl-parathion and carbaryl (Meinke et al. 1998). In the eastern Corn Belt, a strain of western corn rootworm that lays eggs in crops other than soybeans has developed, probably as a consequence of intense selection pressure imposed by rigid annual rotation of corn and soybeans (Levine et al. 2002). The western corn rootworm has had a history of adapting to intense selection pressure (including development of resistance to chlorinated hydrocarbons throughout the Midwest, first reported in Nebraska [Ball and Weekman 1962]), so there is reason for concern regarding widespread exposure of this pest to a limited number of pest management tactics.

While we have fixated on the potential for development of insect resistance to *Bt* in transgenic *Bt* crops, we have ignored some basic principles of integrated pest management (IPM). Applying chemical insecticides only when an insect population density has reached an economic threshold is one of the tenets of IPM. This simple tenet is both economically and ecologically sound. One of the refuge requirements for event MON 863 (the event from which YieldGard Rootworm corn was derived), however, is contrary to this tenet. The EPA's Notice of Pesticide Registration, EPA Reg. Number 524-528, February 24, 2003 states: "Growers will not be permitted to apply CRW [corn rootworm] labeled insecticides to the refuge for control of insect pests while adult corn rootworm are present unless the Cry3Bb1 field is treated in a similar manner." If the pest density in the YieldGard Rootworm field has not exceeded an economic threshold, the requirement suggests that concerns about economics and the environment are subordinate to insect resistance management.

Finally, the crop protection industry is focused primarily on development of products that are prophylactic, rather than responsive to insect densities–*Bt* proteins for control of corn rootworms and European corn borers and insecticidal seed treatments for both corn and soybeans. Many acres of corn and soybeans will be "treated" unnecessarily, placing considerable selection pressure on many species of insects. Although insect resistance management is important for a viable future in crop protection, insect resistance management strategies should be developed within a framework of IPM, the very foundation of sustainable crop protection programs.

Nematode Management

Nematodes are responsible for significant yield losses in both corn and soybeans throughout the United States (Koenning et al. 1999). The species that causes the greatest concern throughout its range, and for which many specific resistance management strategies have been developed, is the soybean cyst nematode (SCN). The use of resistant soybean cultivars has become the standard for management of SCN, and resistant cultivars are available from both public breeders and private companies. Unfortunately, the lack of diversity among SCN-resistant cultivars poses a challenge. For example, 93% of the SCN-resistant cultivars in Illinois have the same source of resistance—PI88788. Because SCN populations adapt readily to sources of resistance, most soybean cultivars labeled as SCN-resistant can be damaged by approximately 50% of the SCN populations that occur in the state. Consequently, growers experience lower-than-anticipated yields and become dissatisfied with plant resistance for managing SCN.

Management recommendations for SCN in soybeans differ in different areas of the United States. The most common recommended cropping sequence in the South is (1) nonhost, (2) SCN-resistant cultivar, (3) nonhost, and (4) susceptible cultivar. The rationale for the susceptible cultivar is that nonvirulent SCN within the population will reproduce the most, stabilizing selection within the SCN population (Young 1998). The recommended cropping sequence in Iowa is (1) nonhost, (2) SCN-resistant cultivar type 1 (PI88788 resistance), (3) nonhost, (4) SCN-resistant cultivar type 2 (Peking resistance), (5) nonhost, and (6) susceptible cultivar. The susceptible cultivar can be grown safely after two cultivars with different sources of resistance have been grown during the two preceding years when soybeans were planted. The recommendation in Illinois is to rotate different SCN-resistant cultivars with nonhost crops and never grow a susceptible cultivar. The ultimate goal of all of these recommendations is to protect subsequent crops of soybeans by decreasing the population densities of SCN with resistant varieties without exerting excessive selection pressure on the SCN population.

New ways of labeling SCN-resistant cultivars and assessing the virulence of SCN populations may help growers match sources of SCN resistance with virulence of SCN (Niblack et al. 2002). Also, public breeders are emphasizing a search for new sources of resistance to improve diversity. Ultimately these efforts should result in better management of SCN and associated SCN resistance management strategies.

Although there are some sources of resistance to some nematodes that attack corn, host resistance is not a common practice for managing nematodes in corn. Unfortunately, corn nematode damage often goes unnoticed because it cannot be diagnosed easily from symptoms of injury. When some organophosphate and carbamate insecticides (e.g., Counter, Furadan, Mocap) were applied more widely to control corn rootworms and other insect pests, these products also offered some control of nematodes. No known cases of resistance of nematodes to these insecticides were reported. The insecticides used most frequently today have little to no activity against nematodes in corn. Current *Bt* corn products have no effect on nematodes in corn.

Plant Disease Management

Host plant resistance is the cornerstone for management of plant diseases in corn and soybeans. In corn, major problems with pathogens overcoming resistance in host plants have not occurred. Consequently, no formal resistance management programs have been implemented. In soybeans, however, races of the *Phytophthora sojae* fungus, which causes root rot, have adapted to the major genes for resistance in some locations (Kaitany, Hart, and Safir 2001; Schmitthenner, Hobe, and Bhat 1994). Although many different genes for resistance against *Phytophthora* are widely deployed, in some areas none of the major genes is effective for managing the fungus. Breeders are looking for new genes for resistance to *Phytophthora*, and some genes for partial resistance (i.e., tolerance) have been deployed. In the meantime, in places where *Phytophthora* seems to have overcome the genes for resistance, growers are encouraged to select soybean cultivars with the highest rated levels of partial resistance.

The use of seed treatments has been a standard practice for decades to protect corn and soybean seeds and seedlings from fungal infections. Although the use of foliar fungicides in corn and soybeans has not been as common as the use of fungicidal seed treatments, foliar fungicides can be applied to manage fungal leaf blights, gray leaf spot, and rust in corn and white mold, pod and stem blight, and anthracnose in soybeans. To date, no incidents of resistance of fungal pathogens to fungicides in corn or soybeans have been confirmed. Concern about the potential development of resistance in some populations of fungi may escalate, however, because many new foliar fungicides for corn and soybeans are in the same class—strobilurins. Azoxystrobrin, a strobilurin, is the active ingredient for the widely used product Quadris, and trifloxistrobin is one of the active ingredients in the recently registered fungicide Stratego. SoyGard is a recently registered fungicidal seed treatment for soybeans, and one of its active ingredients is azoxystrobin. New seed treatment products containing azoxystrobin are under development and may be labeled soon for control of seed and seedling diseases of both corn and soybeans. Strobilurins all have the same specific site of action in the target fungi, so the danger for development of strobilurin resistance is real. Widespread use of strobilurin-based fungicides potentially will place considerable selection pressure on populations of fungi in both corn and soybeans.

The most effective strategy for avoiding the development of resistance to widely used fungicides is to abide by simple IPM practices to minimize dependence on the use of fungicides, decrease the overall prevalence of disease organisms, and keep the population size of pathogens low. If application of a fungicide is justified, the number of applications per season should be limited, the number of consecutive applications should be limited, the fungicide should be applied during an early stage of disease development, and different types of fungicides should be used to minimize selection pressure by one class of fungicides. The IPM principles form the foundation, and resistance management strategies should be compatible with these principles.

Weed Management

The registration of Roundup Ready crops, especially Roundup Ready soybeans, has altered significantly the way in which growers manage weeds. As indicated in the "Introduction," the prospective plantings of transgenic soybeans, primarily Roundup Ready soybeans, have been estimated at 80% of all soybean acres in the United States (NASS 2003). The acres of Roundup Ready corn have been more limited because the European Union will not accept imports of the grain. If Roundup Ready corn becomes acceptable for export to Europe, it is possible that glyphosate (the active ingredient of the herbicide Roundup) will be used in both corn and soybeans every year, subjecting weed populations to significant selection pressure.

Concern about glyphosate resistance among different species of weeds is widespread in agriculture. Weed species that have become resistant to glyphosate have been confirmed throughout the world (Heap 2003): horseweed or marestail (*Conyza canadensis*) in Delaware, Indiana, Kentucky, Maryland, New Jersey, Ohio, and Tennessee; goosegrass (*Eleusine indica*) in Malaysia; Italian ryegrass (*Lolium multiflorum*) in Chile; rigid ryegrass (*L. rigidum*) in Australia, South Africa, and California; and wild radish in Canada. Although not all of these weed species have been found in corn/soybean cropping systems, the ability of weeds to become resistant to glyphosate has been documented.

Few new herbicides with different modes of action are being developed, contributing to the concern about development of glyphosate resistance in weed populations. Because the system of applying glyphosate in Roundup Ready soybeans is quick, easy, inexpensive, and effective for weed control, it has replaced the use of other herbicides and significantly slowed the development of new herbicides.

Resistance of weeds to herbicides other than glyphosate also has been verified. In Illinois alone, the list of weeds resistant to acetolactate synthase (ALS)-inhibiting herbicides, protoporphyrinogen oxidase (PPO) herbicides, and triazine herbicides is relatively lengthy. Waterhemp populations are resistant to ALS-inhibiting herbicides, PPO herbicides, and triazine herbicides. Smooth pigweed and kochia are resistant to ALS-inhibiting and triazine herbicides. Common cocklebur, giant foxtail, giant ragweed, and common ragweed are resistant to ALS-inhibiting herbicides, and common lambsquarters is resistant to triazine herbicides.

Weed scientists throughout the United States have prepared guidelines for minimizing the risk of development of herbicide-resistant weeds. As with so many other IPM strategies, minimizing the risk of herbicide-resistant weeds begins with scouting to determine the species of weeds present and whether weed densities justify a herbicide application. Nonherbicide alternatives—mechanical cultivation, delayed planting, weed-free crop seeds—should be considered. Regarding the application of herbicides to minimize the risk of herbicide-resistant weeds, the following resistance management strategies are recommended:

- Rotate crops with a concomitant rotation of herbicides to avoid using herbicides with the same site of action in the same fields.
- Limit the number of applications of a single herbicide or herbicides with the same site of action within a single growing season.
- Use mixtures or sequential treatments of herbicides that control the weeds in question, but use herbicides with different sites of action.
- Clean equipment before leaving fields that are infested with or suspected to have resistant weeds.

After herbicide application, fields should be scouted to detect weed escapes or shifts. If a potentially resistant weed population is detected, available control methods that prevent seed deposition in the field should be used.

Recommendations specifically for minimizing the risk of development of glyphosate-resistant weeds begin with all the aforementioned strategies. Other glyphosate resistance management strategies include using other herbicides with other sites of action in a corn/soybean cropping system; monitoring intensively for changes in weed populations; using sequential herbicide programs with a soil-applied herbicide with a different site of action, specifically for waterhemp and giant ragweed; spraying weeds at the proper time and with the proper rate; and avoiding continuous planting of glyphosate-resistant crops.

It is imperative that growers heed these recommendations to slow down or prevent the development of herbicide resistance in additional populations of weeds. Continued reliance on glyphosate applications in glyphosate-resistant soybeans and corn will be costly in the long run. If weeds develop widespread resistance to the few types of herbicides currently on the market, the lack of new herbicides with different modes of action limits the alternatives for weed management.

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2.5 Resistance Issues in Golf Course Turf

Wendy Gelernter and Larry Stowell

Introduction

The turfgrass industry, encompassing golf courses, parks, athletic fields, and home lawns, has grown in tandem with the urbanization of the U.S. population. Golf course turf, the most intensively managed segment of this industry and the focus of this paper, was responsible in 2000 for direct revenues of $20.5 billion (SRI International 2002). As a rough comparison, the 1994 retail value of cotton, corn, soybeans, and wheat were $120.6, $99.0, $72.0, and $24.0 billion, respectively (National Cotton Council 1994). There currently are approximately 16,000 golf courses in the United States serving 35 million golfers (SRI International 2002). With roughly 40.5 hectares (ha) (100 acres [a.]) of managed turf and landscape plantings per course, golf courses represent approximately 648,000 ha (1.6 million a.) of managed landscape.

Competition among courses for golfers, the popularity of televised tournaments, and demands by golfers for high-quality turf are continually rising, placing added pressures on turf managers to provide perfect, blemish-free turf. This backdrop underlies the discussion of issues and barriers in the implementation of resistance management programs for golf course turf.

Pesticide Resistance Issues

Pesticide resistance management for golf course turf is characterized by a complex interplay between factors that create high risk for development of resistance and those that act to decrease that risk significantly. High-risk factors include the following:

- **Perennial crop.** With crop rotation as one of the key tenets of resistance management, the perennial nature of turfgrass is a significant and inflexible barrier in avoiding the development of resistance. In the turfgrass system, there is no option to rotate to a nonsusceptible crop, no ability to lay fallow, and no opportunity for deep cultivation practices that may decrease inoculum or bury weed seeds.
- **Pest complexes.** Frequently, no one pest dominates control practices on golf course turf. Instead, pesticide applications usually are targeted at a complex of diseases, insects, or weeds, thus increasing the exposure of several pests simultaneously to a given product.
- **Role of stress in increased pest infestations.** Most golf course turf, particularly the 2–3 acres per golf course used for putting greens, is grown under severe stress conditions that increase the likelihood and the damage associated with pest infestations, as well as the frequency of pesticide treatments. Stress factors include heavily trafficked, highly compacted soils; decreased photosynthetic capacity due to low mowing heights; lack of appropriate cultivation; and suboptimal irrigation practices due to their interference with golf play.
- **Demand for blemish-free turf leads to preventive programs.** Unlike many crops in which successful management is judged primarily on yield, golf course turf is judged exclusively on appearance (color, uniformity, density) and playability. As a result, there is significant pressure on turf managers to prevent pest infestations before they develop. This reliance on preventive programs, although necessary for preservation of current expectations for turf quality as well as for the superintendent's job, results in more pesticide applications per year than for crops with higher damage thresholds.
- **Lack of independent information sources.** Because retail markups for turf products are high and competition among product sales forces is stiff, turf managers are one of the most heavily serviced end-user groups in agriculture. Because a turf manager typically is visited by several distributor or agrochemical company representatives each week, it is not surprising that sales people are the most popular source of agronomic information for turf managers. In contrast, the influence of university research and extension efforts has diminished over the past few decades, as funding for applied research has decreased. This

lack of funding has the additional (and perhaps unintentional) effect of strengthening the link between university research programs and the agrochemical industry, which funds an increasing proportion of the university's applied research programs. The result is a further decrease in the number of completely independent sources of agronomic and pest management information. The issue of influence and independence extends beyond university and extension programs to private consultants and contract researchers (including PACE Turfgrass Research Institute), whose research programs typically are funded, at least in part, by the agrochemical industry. While the credibility of university, extension, and independent private consultants still is quite high among end users (based on continued production of high-quality research and a determined, successful effort to remain independent of product sales), there are few, if any, research or educational organizations whose operations remain completely unassociated with the agrochemical industry.

- **Lack of proven benefits and guidelines for resistance management.** Turfgrass researchers who deal with the question of pest resistance are not unified in their approaches to resistance management. Recommendations range from a focus on rotations among pesticide classes to a "use it or lose it" strategy of sequential applications of the same or similar products; and from an emphasis on mixtures of low-labeled pesticide rates to a reliance on high-labeled rates of single products. These disagreements are highly publicized and well known to end users, who are exposed regularly to the arguments in continuing education courses and through a tight-knit, nationwide communication network of turf managers. The confusion that this lack of unity creates is buttressed by a lack of concrete data that demonstrate the benefits of one approach versus another—or even the benefits of any resistance management program at all—for avoidance of resistance. Without a clear set of guidelines available, and without evidence that investment in resistance management efforts will yield results, turf managers are likely to relegate resistance management to a low priority as they design their management programs.

Factors that decrease the risk of pest resistance in golf course turf systems include the following:

- **Emphasis on cultural management practices.** Turf managers are well educated on the relationship between pest infestations and plant stress. As a result, there is a strong emphasis on cultural practices including regular soil and water testing; optimized soil nutrition programs; irrigation management; aerification to promote gas exchange and improve soil properties; regular monitoring for soil salinity, weather patterns, and pest infestations; and selection of pest-resistant and climate-appropriate turf varieties during new construction or renovations. As a result, many potential pesticide applications are avoided.
- **Diverse spectrum of pesticide products.** A large number of products, representing different pesticide classes, typically are available in the turf market. This selection allows end users to rotate among pesticide classes if they choose to do so, and importantly, allows turf managers to find effective substitute products easily when other products are rendered ineffective by resistance.
- **Availability of broad spectrum products.** Fungicides such as chlorothalonil and mancozeb have been used with success for many years, with no reports of pest resistance. Although there are new regulatory restrictions on the use of these products, they continue to play an important role in disease control and in avoiding reliance on single-site products that are more likely to cause resistance.
- **Reservoirs of susceptibility.** For mobile pests such as insects, the existence of large reservoirs of untreated turfgrass (in the form of home lawns, parks, and less-maintained areas of the golf course such as roughs) can act as a tool for preserving pest populations that are unexposed and, therefore, susceptible to pesticides. The constant mixing of these susceptible populations with treated (and potentially resistant) pest populations may decrease the likelihood of resistance.

The result of the interaction between these high and low risk factors is that several documented cases of resistance have occurred on golf course turf (Tables 2.5.1–2.5.3), but usually in relatively localized populations. Product failures due to resistance typically have been limited in scope, due to the availability of substitute products with alternate modes of action. Because of a lack of clear guidelines for avoidance of resistance, turf managers generally place a low priority on incorporating resistance management practices into their programs. The relatively low frequency of resistance problems is therefore more a

Table 2.5.1. Turfgrass diseases that have been reported to have resistance to fungicides (FRAC 2003; Vargas 1994)

Disease	Fungicide
Dollar spot	Rubigan, Bayleton, Banner, Chipco 26019, Vorlan
Pythium	Subdue and related products
Pink snow mold	Dicarboximides (Chipco 26019, Vorlan)
Anthracnose	Heritage, Compass, thiophanate-methyl (Cleary's 3336, Fungo)
Gray leaf spot	Heritage, Compass

Table 2.5.2. Turfgrass insects that have been reported to have resistance to insecticides (Potter 1998; Vittum, Villani, and Tashiro 1999)

Insect	Insecticide
White grubs	Chlordane, dieldrin
Chinch bugs	Diazinon, chlorpyrifos
Black turfgrass ataenius	Aldrin, chlordane, dieldrin, heptachlor
Sod webworms	Aldrin, dieldrin

Table 2.5.3. Turfgrass weeds that have been reported to have resistance to herbicides (WeedScience.com 2003)

Weed	Herbicide
Goosegrass	Team and related DNA products (Balan, Surflan, Pendulum)
Annual bluegrass	Simazine (Princep) and related triazine products; Prograss
Smooth crabgrass	Acclaim and related aryloxyphenoxy products (Fusilade)

fortuitous outcome of good integrated pest management (IPM) practices and availability of a wide spectrum of products, rather than a result of a concerted effort to avoid resistance.

Barriers to Adoption of Resistance Management Programs

Obstacles in the path of more proactive resistance management programs exist as a result of information deficits, agrochemical company economic pressures, and lack of end-user incentives. Specific barriers include the following:

- **Lack of data on benefits of resistance management.** The lack of hard data demonstrating the operational, economic, or environmental benefits of implementation of turfgrass resistance management programs has resulted in a parallel lack of incentive among agrochemical companies and end users to invest in what is considered by some to be an unproven academic theory. The mixed messages delivered from the turfgrass research community on optimal resistance management strategies further exacerbate this situation.
- **Economic realities within the agrochemical industry.** Competition among companies that market products with the same mode of action is a strong disincentive to resistance management stewardship. For example, in the instance of a new class of site-specific pesticides with a high level of risk for causing resistance, companies have choices on how to market their products. A company that acts "responsibly" by voluntarily restricting product use based on resistance management principles will be willing to limit their sales (via restrictive label language, sales programs, etc.) because they believe that their actions will extend the life (and sales) of the product. But if there is a less scrupulous company that markets a product within the same pesticide resistance management group without regard to avoiding resistance, the benefits of resistance management are destroyed. When resistance and cross-resistance finally develop as the result of indiscriminate use of one or more of these products, the "responsible" company will be penalized by

failing to capture sales in the early, nonresistant window of time. The less responsible companies will be conversely (and contrarily) rewarded for implementing more aggressive marketing strategies that ignore resistance concerns.

In an age in which product development costs are increasing and the effective life of a patent is shortened by the length of time involved in getting a product to market, the emphasis is on achieving maximum profitability as soon as possible. The benefits of "saving" a product from resistance, thus ensuring its long-term use, is intellectually appealing but may not make practical sense to company planners and stockholders.

- **Fear of "global warning."** Researchers, in their attempts to transmit information responsibly, are sometimes excessively cautious in relaying their suspicions that resistance may be involved in product failures. Unfortunately, by waiting until resistance can be documented conclusively before warning end users of a problem, researchers sometimes inadvertently support additional applications of products to which resistance has developed, resulting in additional product failures and crop damage.
- **Unwarranted optimism.** Company claims that development of resistance to new pesticide chemistries is nearly impossible are sometimes accepted with a minimum of skepticism. Yet it seems prudent, especially in light of recent "surprise" cases of resistance (e.g., QoI fungicides and *Bacillus thuringiensis*) to assume that resistance development is likely to occur, at least until proven otherwise. Under this assumption, all products would be handled as if resistance were an imminent threat, rather than waiting for resistance to appear before management guidelines are put in place.

Solutions

The short-term solutions described here are those used by the PACE Turfgrass Research Institute and are based on the assumptions that the issues and barriers described in this paper remain unaddressed, but that knowledge of biology and resistance management experiences in other crops (along with a sprinkling of common sense), can form the basis for reasonable turfgrass guidelines.

- Based on current understanding of resistance, the products and pests most at risk for resistance should be identified, as shown in Tables 2.5.4 and 2.5.5, and should be the focus of research, education, and prevention efforts.

Table 2.5.4. Risk factors for pest resistance in turfgrass: High-risk pesticides. Pesticide classes and products characterized by frequent usage, single-site and/or specific modes of action, systemic activity/long residual activity, and/or with a history of causing resistance are considered high risk. For some of the products listed, resistance has not yet been detected among turfgrass pests, but we believe the likelihood of detection in the future is high if frequency of application is not limited in some fashion

Pesticide class	Examples
QoI fungicides	Azoxystrobin, pyraclostrobin, trifloxystrobin
Benzimidazole fungicides	Thiophanate-methyl
Dicarboximide fungicides	Iprodione, vinclozolin
Phenylamide fungicides	Mefonoxam, metalaxyl
Chlorinated hydrocarbon insecticides[a]	Aldrin, dieldrin, chlordane, DDT, heptachlor
Organophosphate insecticides (acetylcholinesterase inhibitors)	Chlorpyrifos, diazinon
Pyrethroid insecticides	Bifenthrin, cyfluthrin, deltamethrin, cyhalothrin
Acetyl chlorine receptor agonists/ antagonists insecticides	Imidacloprid
Ecdysone agonist/disruptor insecticides	Halofenozide
Triazine herbicides	Atrazine, simazine
DNA herbicides	Benefin, oryzalin, pendimethalin
Sulfonylurea herbicides	Chlorsulfuron, metsulfuron, foramsulfuron, trifloxysulfuron, rimsulfuron
Aryloxyphenoxy herbicides	Fenoxaprop, fluazifop

[a] No longer labeled for use in turf in the United States.

Table 2.5.5. Risk factors for pest resistance in turfgrass: High-risk pests. High-risk pests have one or more of the following characteristics: dominate control practices on a consistent basis, multiple generations per year, sexual reproduction, high reproductive rates, and/or a history of resistance to pesticides

Diseases	Insects	Weeds
Anthracnose Dollar spot Gray leaf spot Pink snow mold Pythium	White grubs (Japanese beetle, black turfgrass ataenius, chafers) Chinch bugs Sod webworms	Annual bluegrass Crabgrass Goosegrass

- In the absence of more specific information, products at risk of resistance should be used in block rotations, with no more than two sequential applications of each product.
- For products with longer residual activity that are applied only once or twice per year (imidacloprid and halofenozide), alternating annual single applications of one product per year should be considered.
- The use of pesticide rotations based on the resistance management groups proposed by the Fungicide Resistance Action Committee (FRAC 2003), the Herbicide Resistance Action Committee (HRAC 2002), and the Insecticide Resistance Action Committee (IRAC 2002) should be followed.
- When product failures do occur and resistance is suspected to have a role, the company involved should be notified, qualified university researchers should be involved to determine the existence and nature of resistance, and end users should be advised of the situation and informed that the existence of resistance is suspected, but not yet proven. They also should be provided with alternate pest management programs that have decreased reliance on the suspect pesticide class for control of the supposed resistant pest.

Longer-term solutions to address the deficits and barriers described in this paper include the following:

- Conduct field research programs to demonstrate the benefits achieved from specific resistance management programs.
- Accept that it is in neither the pesticide company's nor the end user's interest to promote resistance management programs, especially if the benefits of resistance prevention programs have not been demonstrated effectively.
- When a class of pesticide chemistry (or the susceptible genes to this class of chemistry) is deemed an important enough resource, consider more aggressive regulatory involvement in enforcement, more restrictive labeling, mandatory monitoring, and public reporting programs. This approach, however, is feasible only if there are data available to support the use recommendations that would receive regulatory oversight. Without strong science as its basis, additional regulation will do nothing to delay or to avoid resistance, and will squander time, money, and credibility.

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2.6 Resistance Issues in Organic Cropping Systems

Kevin Brussell

Organic farmers have encountered few problems with pest resistance. Organic farms do not base pest-control management on killing pests; it is used only as a last resort. The focus is on preventing pest development in the first place. Outbreaks of pests really are indications of problems that should be addressed culturally. We work on figuring out why the pest occurs in significant numbers, what happened to create a favorable condition/environment for the pest, and how to implement management measures that correct the underlying problem. The bottom line for organic farmers is soil health = plant health = animal health. A healthy plant in a healthy environment is seldom bothered by pests.

The foundation for preventing pest problems in organic farming is developing and maintaining the highest-quality ecosystem possible. A diversified 3- to 7-year crop rotation, alternating spring- and fall-planted crops, is key. This rotation creates a different environment in a given field each year. Row crops are alternated with solid-seeded crops and crops of different botanical families. Cover crops are planted between cash crops to improve soil structure, support a diversified soil microbe population, and provide beneficial insect habitat. A soil with a balance of species diversity works to keep pathogens in check. Only biocides that do not harm beneficial species are used, and then only as a last resort. Anything that disrupts the balance of microbes in the soil creates an environment favorable for pests.

A good example is Robert Boettcher's organic farm in the Big Sandy area of Montana. Wheat stem sawfly, a significant pest in conventional wheat, is almost nonexistent in his organic wheat, which is rotated with sunflowers and lentils instead of the conventional wheat-barley-summer fallow rotation.

Other beneficial management practices used to prevent pest problems include tillage, flaming, and vacuuming. Manipulation of the crop canopy for shading or sunlight inhibits weeds and diseases. Proper use of manures and compost greatly improves soil health; soil mineral balance of major and minor elements also is important in controlling weeds, insects, and diseases. For instance, corn borer seems to affect only corn significantly when there is a fertility imbalance. A connection between plant chemistry and the attractiveness of the plant to insects has been demonstrated by Dr. Larry Phelan at Ohio State. This study showed that European corn borer, given a choice between organic plants and conventional plants, would avoid laying eggs on the organic plants.

The biggest barrier to pest resistance management is industrial monocropping. We need to design the entire agricultural system around diversity, and to do this we need to think outside the box. University research and extension systems already have the infrastructure to accomplish this if they so choose.

3.1 Triazines, Acetolactate Synthase Inhibitors, and Protoporphyrinogen Oxidase Inhibitors

Les Glasgow

Introduction

In contrast to entomologists and plant pathologists who have been dealing with pesticide resistance for approximately 50 years, weed scientists have been relatively free from dealing with herbicide resistance up until the past 20 years. Scientists hypothesized as long ago as the 1950s, however, that resistance would develop in plants (Abel 1954; Harper 1956). This speculation occurred about the time of introduction of the first triazine—atrazine—that was registered for use in corn in 1958. Although weed resistance first was documented, in 1962 (*Daucus carota* to 2,4-D on a roadside in Canada), the resistant population did not spread, nor has resistance to auxin herbicides become a major problem. There are a number of probable reasons for the slow early development of herbicide resistance:

1. There was usually only one application of a product per year (low selection pressure).
2. Populations were diluted with sensitive individuals emerging from the seed bank.
3. Tillage normally was used before and after planting.
4. Herbicides with multiple modes of action were used.
5. Applications were made preemergence as well as postemergence.

Triazines

History and Evolution of Resistance

Herbicide resistance first was noted in 1968 with the identification of a biotype of common groundsel that was resistant to simazine (Princep). Resistance to atrazine was first documented in the 1970s in Pennsylvania, Virginia, Delaware, and Maryland. Since 1968, more than 60 triazine-resistant species (or biotypes) have been identified (40 dicots and 20 grasses in 35 genera) worldwide; they have been found in 31 U.S. states and in 18 countries (Heap 2003). The occurrence of new triazine-resistant populations has not been as rapid as with acetolactate synthase (ALS) inhibitors and some other herbicide modes of action during the last decade.

Despite the occurrence of atrazine-resistant populations, its use has been constant over the years. Atrazine is applied to approximately 70% of the U.S. field corn area, and to 65–70% of the sorghum area. In sugarcane, depending on the state, this can be as high as 90% of the crop area.

Factors Influencing Resistance Evolution and Management

- **Mechanism and fitness.** Although there are two examples of resistance due to increased herbicide metabolism in velvetleaf and rigid ryegrass, resistance in most cases is target site based, which is due to a change in the herbicide-binding domain on the D1 protein of PSII (Gronwald 1994). Because the D1 (QB) protein is a chloroplast gene product, triazine resistance is inherited maternally. This mutation not only decreases affinity of D1 for triazines, but also decreases the rate of electron transfer between PSII acceptors. Because this effect occurs in a process that is fundamentally important for plant survival and growth, it is not surprising that resistant biotypes have reduced photosynthetic rates, biomass production, fecundity, and competitiveness relative to susceptible biotypes.
- **Frequency.** Studies have shown the initial frequency of the triazine resistance trait in weed populations to be low, 1×10^{-10} to 1×10^{-20}, compared with that of other herbicide groups such as ALS inhibitors, 1×10^{-6} (Gressel 1991).
- **Multiple and cross-resistance.** Multiple and cross-resistance occur, but are limited in extent considering the 45 years of use and having been documented in only eight species, of which three (*Amaranthus rudis, Kochia scoparia, and Portulaca oleracea*) are found in the United States (Heap 2003). This relatively low occurrence of multiple or cross-resistance probably is a

reflection of the fitness penalty apparent in triazine-resistant biotypes that makes them more sensitive to other herbicides.

- **Herbicide mixture and rotation.** The use of herbicides with alternative modes of action, and hence a decrease in selection pressure, has been the primary reason for atrazine and other triazines remaining viable and valuable tools for farmers. There are several other herbicides used in corn with different modes of action and a broad range of activity, such as the chloracetanilides in tank mix and dicamba or 2,4-D postemergence, that provide good control of the species that have evolved triazine resistance and are used in combination with triazines.
- **Crop rotation.** In arable crops, triazine-resistant weeds first proliferated in those areas of the Northeast where continuous corn cultivation was practiced and growers relied predominantly on atrazine for broadleaf weed control. For economic reasons, growers rotate corn with other crops such as soybeans and alternative herbicides that have excellent activity on resistant biotypes and have been used for many years in those crops. It is unlikely with these rotations and availability of alternative herbicides that triazine resistance will escalate as a problem.
- **Tillage.** Until the advent of Roundup Ready most soybean crops in the rotation received tillage. Where tillage was not employed, crops received a sequence of applications, including burndown with mixtures such as paraquat and triazines and multiple herbicides applied preemergence.
- **Performance assessment.** It is important to note that for many years Syngenta and its legacy companies have provided, and still provide, a service for detection of resistance to its herbicides. Syngenta representatives can send samples of suspect plants or seeds to Vero Beach Research Center for bioassay. Susceptibility to other herbicide chemistries or modes of action also is determined and advice on control of the resistant biotypes is provided.
- **Education.** Partly because of the major dependence of farmers on triazine herbicides and the quick response of industry, researchers, extension personnel, and farmers, as soon as weeds evolved resistance to these herbicides the information was distributed and changes were made in the herbicide use in order to avoid more serious and widespread problems (LeBaron, H. M., personal communication 2003).
- **Label statements.** For more than 20 years the following statement has been included on all Syngenta triazine labels (Syngenta 2003):

> Following many years of continuous use of this product and chemically related products, biotypes of some of the weeds listed on this label have been reported which cannot be effectively controlled by this and related herbicides. Where this is known or suspected, and weeds controlled by this product are expected to be present along with resistant biotypes, we recommend the use of this product in combinations or in sequence with other registered herbicides which are not triazines. If only resistant biotypes are expected to be present, use a registered non-triazine herbicide. Consult with your state Agricultural Extension Service for specific recommendations.

Conclusion

The use and value of atrazine, and other triazines, will continue into the future because they are effective, economical, and the cornerstone of residual weed control in corn, sorghum, sugarcane, and other crops. They remain important tools for weed control in many crops as a component of a program, and despite the presence of resistant biotypes, they provide excellent control of a wide range of other species and susceptible biotypes.

ALS Inhibitors

History and Evolution of Resistance

The first ALS-inhibiting herbicide, chlorsulfuron, was introduced for weed control in cereals in 1982. Chlorsulfuron and other sulfonylurea (SU) herbicides are active at very low rates; gram (g)/hectare (ha) rather than the kilogram (kg)/ha for those previously developed. Since their introduction, there are now four additional chemical classes that inhibit ALS: imidazolinones (IMI), triazolopyrimidines (TP), sulfonylamino-carbonyl-triazolinones (SCT), and pyrimidinyl-thio-benzoates (PTB).

Significant changes in herbicide potency, selectivity, and weed control are achieved by relatively small structural alterations within a herbicide class. Consequently, many chemical manufacturers, including Syngenta, continue to develop ALS-inhibiting herbicides with better properties and/or new uses. All inhibit the ALS or acetohydroxyacid synthase (AHAS) enzyme, which is the first enzyme common to the biosynthesis of the branched chain amino acids isoleucine, valine, and leucine.

Selection of resistant weed populations with ALS-inhibiting herbicides became apparent in 1987, with the discovery of chlorsulfuron-resistant biotypes of prickly lettuce *(Lactuca serriola)* and kochia (*Kochia scoparia)* in wheat in United States. Since then, ALS-inhibitor resistance has been documented for at least 23 monocot and 50 dicot weed species in a total of 25 countries (Heap 2003).

In contrast to the triazines, ALS-inhibitor resistance has become so common and so widespread that it poses a real threat to the continued use of these herbicides in certain cropping systems. For example, so much of the waterhemp (*Amaranthus rudis*) in Illinois is resistant to ALS inhibitors that these herbicides are no longer recommended for its control (Hager et al. 1997). A similar situation exists for control of kochia in wheat where resistant biotypes now are widespread in intensive cereal crops in the United States and Canada (Guttieri, Eberlein, and Thill 1995).

Factors Influencing Resistance Evolution and Management

- **Mechanism and fitness.** The ALS inhibitors are at high risk for the evolution of resistance in weeds because they have a single target site, are effective against a broad spectrum of weeds, are used extensively on many crops, and are relatively persistent, often providing season-long control of germinating seeds. All data on the ALS-resistant biotypes show they are equally as fit and vigorous as the susceptible native populations, or differences are very subtle (Saari, Cotterman, and Thill 1994).

- **Selection pressure.** A major factor in the appearance of resistance is the high selection pressure imposed by ALS-inhibitor herbicides on very sensitive weed species. Predominantly, resistance occurs as a result of decreased sensitivity of the target ALS enzyme to inhibition by the herbicide, although there are biotypes that have evolved a lower level of resistance through increased herbicide metabolism and rapid detoxification thereof.

- **Inheritance.** During selection pressure from the herbicide, resistant *ALS* alleles are dominant over susceptible alleles. Although *ALS* functions in plastids, *ALS* is a nuclear gene and follows normal Mendelian inheritance. Hence, in contrast to the situation with target-site, triazine resistance, resistant *ALS* alleles are disseminated by both pollen and seed.

- **Target-site plasticity.** Several single amino acid substitutions that convert ALS from a herbicide-sensitive to a herbicide-resistant enzyme have been identified. Target-site resistance to ALS inhibitors in all weed biotypes, investigated thus far in natural populations, has been caused by substitutions at one of five conserved regions of the gene with multiple substitutions having been identified for two of these amino acid domains (Tranel and Wright 2002). Thus there is a relatively large amount of flexibility in the herbicide-binding site of the ALS enzyme (i.e., this site can tolerate substitutions with minimal consequences to normal catalytic function of the enzyme). A likely explanation is that the ALS-binding site is different from its active site, although probably in close proximity.

- **Cross-resistance.** Data for all ALS-inhibiting herbicides and ALS substitution combinations are far from complete; nevertheless, several trends have become apparent in recent years (Tranel and Wright 2002). It is common to find that once a weed has evolved resistance to one ALS inhibitor, the resistant biotype is cross-resistant or less sensitive to many of the other herbicides in this class. Although exceptions exist, resistance caused by ALS inhibitors generally can be classified into three types on the basis of cross-resistance:

  1. SU and TP
  2. IMI and PTB
  3. SU, IMI, TP, and PTB (broad cross-resistance)

There is limited information about the newer chemistries, and thus earlier descriptions of cross-resistance were made as follows:

1. SU-specific
2. IMI-specific
3. Broad

Target-site insensitivity has been used to develop a number of sulfonyl-urea-resistant crops, including varieties of wheat, oilseed rape, tomato, soybean, and others. In addition, IMI-resistant crops such as rice and corn are available.

- **Multiple resistance.** Crucial to resistance management and using other herbicides is the degree of multiple resistance present in an ALS-resistant population. Although not as prevalent as cross-resistance, there is substantial evidence for multiple resistance involving ALS inhibitors in a number of species (17 species worldwide, Heap 2003). Syngenta has provided a performance assessment service for ALS-inhibitor resistance for Company representatives and advice on use of alternatives. With an understanding of the patterns of multiple or cross-resistance and careful consideration of alternative or complementary herbicides, which could include the older, established herbicides such as 2,4-D, dicamba, atrazine, chloracetanilides, and glyphosate, ALS resistance is managed. Recent observations of decreased sensitivity of waterhemp populations to glyphosate, however, along with resistance to other herbicides, make it essential that growers plan their weed-control programs with resistance management in mind.

- **Label statements.** In common with their statements for the triazine herbicides, Syngenta has included resistant-management statements on their ALS-inhibitor product labels for many years (Syngenta 2003):

> This herbicide controls weeds by inhibiting a biochemical process which produces certain essential amino acids necessary for plant growth. The inhibited enzyme system is acetolactate synthase (ALS). Occurrence of ALS-resistant weeds can be prevented or delayed by using this product in sequence or tank mixtures having a different mode of action, and by using some form of mechanical control or a herbicide with a different mode of action to control weed escapes before they set seed. Both modes of action should provide acceptable control of the specific weed if applied alone at the rates used in tank mixture.

Conclusion

Resistance by a single weed species does not necessarily prevent the use of that herbicide for the many other target species in a cropping system. There must be careful consideration of the tactics used, however, to avoid proliferation of this resistance into an intractable, economically significant, long-term problem. Despite the decline in their use in certain crops, such as soybeans and rice, ALS inhibitors remain important tools as part of a more complex, long-term, and perhaps more sustainable, integrated approach to weed control using crop rotations, *herbicide mixtures*, or rotations and tillage.

Protoporphyrinogen Inhibitors

History and Evolution of Resistance

The first inhibitors of the enzyme protoporphyrinogen oxidase (Protox) were launched during the 1970s and soon were established as excellent postemergence-applied herbicides for control of broadleaf weeds. Although there has been decline in their use with the advent of genetically modified crops, over 5 million ha of crops were treated with these herbicides in 2001.

There are now eight different Protox-inhibiting chemistries, including diphenyl ethers (DPEs), *N*-phenylphthalimides, oxadiazoles, oxazolidinediones, phenylpyrazoles, pyrimidinediones, thiadiazoles, and triazolinones, plus three additional herbicides that are as yet unclassified. Of these, the DPEs, *N*-phenylphthalimides and triazolinones are the most commonly used in the United States.

Despite the extensive use of Protox inhibitors over the past 30 years, the first-ever case of evolved resistance was documented in waterhemp in 2001 in Kansas (Heap 2003). The grower had used acifluorfen (and ALS inhibitors) for many years prior to 2000. Researchers at Kansas State University demonstrated that this biotype was resistant to all the Protox inhibitors tested and also to ALS inhibitors (Shoup, Al-Khatib, and Peterson 2003). Although the mechanism of resistance is not yet known, no differences in absorption or translocation of foliar-applied herbicide between the sensitive and resistant biotypes have been observed.

At a recent North Central Weed Science Society meeting, researchers from Kansas State University, University of Illinois, Southern Illinois University, and University of Missouri gave papers on the occurrence and management of waterhemp biotypes resistant to Protox inhibitors. Resistant biotypes were 10–40 times more tolerant than susceptible biotypes to foliar applications of DPEs (acifluorfen, fomesafen, and lactofen).

Factors Influencing Resistance Evolution and Management

- **Mechanism and fitness.** Protox-inhibiting herbicides have a complex mechanism of action (Duke et al. 1997). Protoporphyrinogen is a key enzyme catalyzing the last common step in heme and chlorophyll biosynthesis (i.e., conversion of protoporphyrinogen IX to protoporphyrin IX). Protox inhibition results in accumulation and leakage of protoporphyrinogen into the stroma and or cytoplasm where it is converted into protoporphyrin IX causing light-dependent membrane damage and cell death. This complicated mechanism of action provides several sites at which resistance could evolve.

Weed resistance to Protox inhibitors may not have evolved previously because of the usually short-lived selection pressure of most of the herbicides that have been used, as well as their use as part of a program, in mixture or in rotation (alternate years) with herbicides with different modes of action. There currently is no evidence for decreased fitness in resistant biotypes, although this may be a factor considering the site of action of the Protox inhibitors. In addition, there has been considerable work on adjuvants to optimize and strengthen the activity of postemergence-applied Protox inhibitors.

The absence of evolved resistance for many years is surprising—Protox inhibitors appear to have a single site of action at which they are highly potent as inhibitors at the molecular level. Many structurally diverse effective Protox inhibitors have been discovered, implying that the protogen-binding site is plastic, like the binding sites for other herbicides that have large numbers of effective herbicides (e.g., ALS inhibitors).

- **Cross-resistance.** It has become apparent in a number of field and greenhouse studies that the biotypes tested are resistant to a range of foliar-applied Protox inhibitors. Soil-applied Protox inhibitors still were effective against these resistant biotypes, however.

- **Multiple resistance.** University of Illinois researchers also reported a waterhemp biotype that exhibited resistance to triazines, ALS inhibitors, and Protox inhibitors (Patzolt, Hager, and Tranel 2002). This resistance pattern leaves glyphosate as the only postemergence herbicide available to control this particular biotype in soybeans, and there are concerns from university researchers that waterhemp biotypes also are showing decreased sensitivity to glyphosate.

- **Performance assessment.** In common with their service for the other herbicide groups mentioned earlier, Syngenta provides a monitoring service to Company representatives for resistance to Protox inhibitors, determines susceptibility to herbicides with alternative modes of action, and provides advice on controlling the resistant biotypes.

- **Education.** Although resistance to Protox inhibitors is not widespread, Syngenta sponsors a field program with universities to test resistance management strategies. Pending test results, Syngenta as well as state extension scientists are recommending a two-pass program, with preemergence and postemergence applications such as:

> Boundary or Dual II Magnum at the highest rate for your soil type followed by either Flexstar or Touchdown (only in Roundup Ready™ soybeans), applied at the appropriate use rate for the size of waterhemp present.
>
> In those situations where Protox-resistant waterhemp is present or suspected, use Boundary or Dual II Magnum at the highest rate for your soil type, followed by Touchdown, applied at the appropriate use rate for the size of waterhemp present.
>
> The use of a Protox-inhibiting herbicide such as Canopy XL, Authority, or Valor preemergence followed by a Protox-inhibiting herbicide such as Flexstar, Ultra Blazer, Phoenix, or Cobra postemergence for waterhemp control should be discouraged because use of the same mode of action will apply additional selection pressure.
>
> When used properly, herbicide mode of action rotation can reduce the likelihood of weed resistance development, whereas repeated use of the same mode of action can lead to the selection of resistant weeds (Syngenta unpublished).

Conclusion

Although resistance to Protox-inhibitor herbicides has not, as yet, become as widespread as that to other herbicide groups, it is important to implement resistance management strategies in these early days of its discovery. The Protox inhibitors have an important place in weed management, and for them to remain effective it is essential that their performance be carefully monitored and best management practices put in place that avoid intensive selection pressure, which leads to the evolution of resistant populations.

Barriers to Resistance Management

The barriers to resistance management are common to all herbicide groups and are probably similar for all agrochemicals, although their significance may vary:

- Suitable, cost-effective alternatives are unavailable—fewer alternative chemistries or modes of action will be available.
- Efficacy on many weeds is still excellent—the product still is used at the same intensity and without mixture or alternation of mode of action.
- Potential for resistance development is not recognized—selection pressure is too high with too many applications of a single mode of action and decrease of application rates, leading to selection of tolerant individuals.
- Resistance is not recognized—other explanations, such as wrong growth stage at application, poor conditions for activation of the herbicide, misapplication, and late weed emergence are given for failure to control individuals in a population.
- Growers may be reluctant to use alternative methods or products—the cost of the solution can be higher or there is a cost increase with small or no short-term benefit. Alternative programs also may have a cost in complexity and a need for more knowledge of new or different techniques.
- Industry may be reluctant to recommend tactics that decrease sales—there is a concern that establishment of resistance management tactics can decrease individual company competitiveness.

Overall Conclusion

Growers with the problem of controlling herbicide-resistant weeds are advised to use good management practices. These include cultivation, use of full labeled rates, rotation of herbicide mode of action as crops are rotated or in a continuous crop rotation, use of tank mixtures or sequential applications to control specific weeds, and prevention of seed production and spread. Well-designed, integrated management systems exist that will delay the onset of, or control existing, resistant weeds. Industry long has supported and will continue to support efforts to ensure responsible use of herbicides in resistant weed management.

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3.2 Glyphosate: A New Model for Resistance Management

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Introduction

For Monsanto, product stewardship is a fundamental component of customer service and business practices. The issue of glyphosate resistance is important to Monsanto because it can adversely impact the utility, sales, and life cycle of its products if it is managed improperly. The risk of developing resistance and the potential impact of resistance on the usefulness of a herbicide vary significantly across modes of action, however, and are dependent on a combination of different factors. As a leader in the development and stewardship of glyphosate products for almost 30 years, Monsanto invests considerably in research to understand the proper uses and stewardship of the glyphosate molecule, including some of the factors that can contribute to the development of weed resistance.

Today, some 275 herbicide-resistant weed biotypes have been identified in various cropping systems in the United States, many of which are resistant to the triazine, imidazolinone, and sulfonylurea herbicide families (Heap 2003; Holt and Le Baron 1990; Shaner 1995). The development of resistance depends on a number of factors including chemical properties of the herbicide and its *target-site specificity*, characteristics of the plant, and agronomic practices. The onset of resistance to glyphosate has taken 23 years and affected far fewer weeds with a lower level of resistance than with other herbicides. Based on current use data and the criteria listed here, glyphosate is considered to be a herbicide with a low risk for weed resistance (Benbrook 1991; Heap 2003). After almost three decades of worldwide use, confirmed resistance to glyphosate exists in biotypes of *Lolium rigidum* (annual ryegrass) in Australia, South Africa, and California; *Lolium multiflorum* (Italian ryegrass) in Chile; *Eleusine indica* (goosegrass) in Malaysia; and *Conyza canadensis* (marestail) in certain states of the eastern United States.

The development of weed resistance to glyphosate is considered rare due to the following characteristics:

1. Most weeds and crops are inherently susceptible to glyphosate, and the long history of extensive use of glyphosate over the past 28 years has resulted in few instances of resistant weeds (Bradshaw et al. 1997);
2. Selection for glyphosate resistance using whole plant and cell/tissue culture techniques was unsuccessful, and therefore is expected to occur rarely in nature under normal field conditions.
3. Glyphosate has many unique chemical properties, such as its mode of action, small biomimetric chemical structure, limited metabolism in plants, and lack of residual activity in soil, which make the development of resistance less likely.

Chemical Properties of Glyphosate

Target-Site Specificity

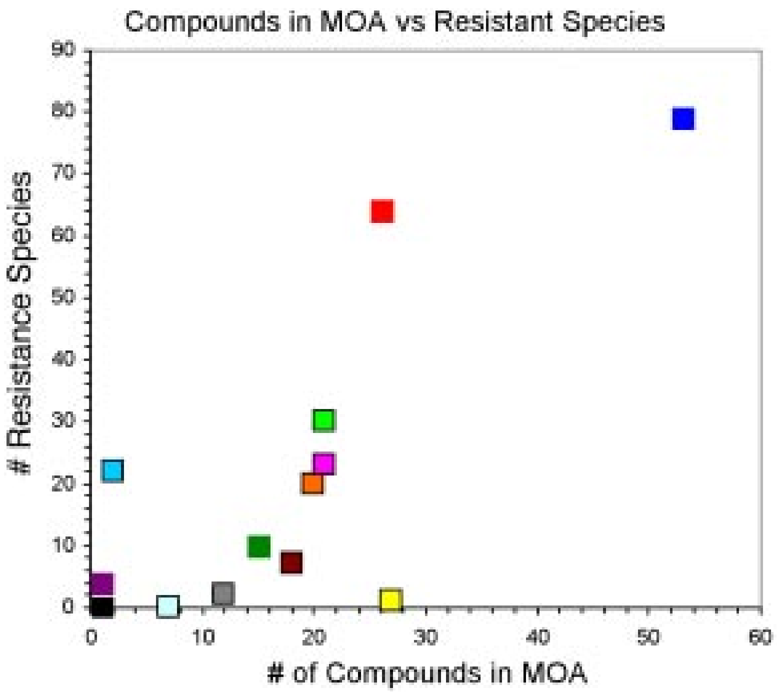
Target-site alteration is a common resistance mechanism among many herbicide classes (e.g., acetolactate synthase [ALS]-inhibitors and triazines). Glyphosate competes for the binding site of the second substrate, phosphoenolpyruvate (PEP) in the active site of 5-enolpyruvylshikamate-3-phosphate synthase (EPSPS) and is a transition state inhibitor of the reaction (Steinrucken and Amrhein 1984). This was recently verified by X-ray crystal structure (Schonbrunn et al. 2001). As a transition state inhibitor, glyphosate binds only to the key catalytic residues in the active site. Catalytic residues are critical for function and cannot be changed without a lethal or serious fitness penalty. Furthermore, very few selective changes can occur near the active site of the enzyme to alter glyphosate's competitiveness without interfering with normal catalytic function. Therefore, target-site resistance is highly unlikely for glyphosate. This was further illustrated in that laboratory selection for glyphosate resistance using whole plant or cell/tissue culture techniques was unsuccessful (Jander et al. 2003; OECD 1999; Widholm et al. 2001).

A herbicide's mode of action is classified by the interference of a critical metabolic process in the plant by binding to a target protein and disrupting the required function. The "specificity" of this interaction is critical for the opportunity to develop target-site-mediated resistance. Because the herbicide contacts discreet amino acids during protein binding, changing one of these contact point amino acids can interrupt this binding. The question of how important these particular amino acids are to the protein's structure and function versus their importance in herbicide binding warrants further discussion.

There are three classes of amino acids in a protein's primary sequence: (1) those critical for the function that describes the "active site"; (2) those important for structure (i.e., configuring the exact geometry of the active site); and (3) those not important for structure or function. In terms of those critical for function, changing one of these few amino acids almost always incapacitates or creates a very "unfit" protein. In comparison, changing one of the many amino acids responsible for structure, the second class, sometimes can be accomplished while maintaining functionality if the substitution is homologous. Finally, in most proteins many amino acids are not critical for structure or function and changing them is easily accomplished while maintaining functionality (Fersht 1977). These changes represent the majority of genetic diversity in a particular gene.

Specificity of inhibitor binding is dependent on the number and type of the amino acids serving as contact points and can be measured indirectly by counting the number of unique compounds that can bind in the same site (Figure 3.2.1). On one extreme, glyphosate is the only herbicide compound that can bind to EPSPS. Single amino acid substitutions near the active site have been observed for EPSPS, and while glyphosate binding is slightly weaker, these enzymes also are less fit. Similarly, high specificity also is observed for glutamine synthetase, binding three compounds including phosphinothricin in the active site (Crespo, Guereo, and Florencio 1999). Paraquat and diquat are the only two herbicides inhibiting photosystem I. No target-site mutations have been reported to be responsible for resistance in these systems (Powles and Holtum 1994).

On the other extreme are target enzymes that are efficiently inhibited by a wide array of compounds



(Legend for Figure 3.2.1.)

Modes of Action^{a}		Compounds	Species
ALS	🟦	53	79
PPO	🟨	27	1
Triazines, C1	🟥	26	64
ACCase	🟩	21	30
Auxins	🟪	21	23
Ureas, C2	🟧	20	20
Thiocarbamates	🟫	18	7
Dinitroanilines, K1	🟩	15	10
Chloroacetamides	◼	12	2
HPPD	🟦	7	0
Quats	🟦	2	22
Glyphosate	🟪	1	4
Phosphinothrecin	⬛	1	0

Figure 3.2.1. Compounds in modes of action versus resistant species.

[a] Mode of Action (MOA), Compounds, Acetolactate synthase (ALS), Protoporphyrinogen Oxidase (PPO), Acetyl Co-A carboxylase (ACCase), Chloroacetamides were limited to just chloro derivatives, 4-Hydroxyphenyl-Pyruvate-Dioxygenase (HPPD). Number of compounds taken from Herbicide Resistance Action Committee (2002). Classification of Herbicides According to Mode of Action, <http://www.plantprotection.org/HRAC/> The number of resistant species was taken from the species count at <weedscience.com>, April 2003, (Heap 2003).

(e.g., ALS) is inhibited by 53 and acetyl CoA carboxylase [ACCase] is inhibited by 21 separate herbicide compounds that bind both within and outside the active site; (HRAC 2003; Tranel and Wright 2002). These cases demonstrate that numerous noncritical amino acids are involved (outside the active site) offering a relatively large range of permissible mutations. In these two cases, a single amino acid change can result in virtual immunity to the class of herbicides and has led directly to the preponderance of resistant weed species for these mode-of-actions (MOAs), 79 and 30, respectively.

Limited Metabolism in Plants

Metabolism of the herbicide active moiety often is a principal mechanism for the development of herbicide resistance. The lack of glyphosate metabolism or significantly slow glyphosate metabolism has been reported in several species and reviewed in various publications (Coupland 1985; Duke 1988), and therefore, it is unlikely that this specific mechanism would come into play with glyphosate.

Lack of Soil Residual Activity

Herbicides with soil residual activity dissipate over time in the soil resulting in a sublethal exposure and in effect low-dose selection pressure. Glyphosate adsorption to soils occurs rapidly, usually within 1 hour (Franz, Mao, and Sikorski 1997). This binding makes glyphosate unavailable to plant roots, and hence no impact to plants is observed from soil-bound glyphosate. Glyphosate's postemergent-only activity allows the use of a high-dose weed management strategy.

Weed Management Strategies for Glyphosate

A key element of good weed management is using the correct rate of glyphosate at the appropriate window of application for the weed species and size present. Higher herbicide doses result in higher weed mortality and less diversity of resistance genes in the surviving population (Matthews 1994). Low herbicide rates also may allow both heterozygous- and homozygous-resistant individuals to survive (Maxwell and Mortimer 1994), further contributing to the buildup of resistant alleles in a population. As resistance is dependent on the accumulation of relatively weak genes, which may be the case for one or more of the four weed species that have evolved resistance to glyphosate, using a lethal dose of herbicide is critical.

Results that support these strategies are beginning to emerge from recent field research studies at several universities where it is documented that studies must be done in the field in the crop (Roush, Radosevich, and Maxwell 1990). Various weed management programs have been evaluated since 1998 to determine how they impact weed population dynamics. Studies were initiated in Colorado, Kansas, Nebraska, Wyoming (Wilson, R. G., et al. 2002, unpublished data), and Wisconsin (Stoltenberg 2002) to evaluate continuous use of Roundup Ready technology with exclusive use of glyphosate or inclusion of herbicides with other MOAs, and rotation away from Roundup Ready technology. These treatment regimes were compared with a conventional herbicide program for each crop evaluated. General observations after 5 years are the following:

1. Use of a continuous Roundup Ready cropping system with either glyphosate alone at labeled rates or incorporation of herbicides with other MOAs resulted in excellent weed control with no weed shifts or resistance reported.
2. Use of glyphosate at below-labeled rates resulted in a weed shift to common lambsquarters at two locations (Nebraska and Wyoming).
3. In Wisconsin, ALS-resistant giant ragweed was selected for in the broad-spectrum residual herbicide regime implemented in the conventional corn cropping system. The continuous glyphosate system (using labeled rates) resulted in no significant weed shifts.

The use of glyphosate at the recommended lethal dose has prevented the buildup of weeds with greater inherent tolerance, and any potential resistance alleles have been avoided over the duration of these studies. Rotating herbicide MOAs every other year has been postulated as a way to prevent or significantly delay resistance to glyphosate. It is not well understood, however, whether occasional abstinence from using a weed control tool will have any substantial impact on delaying resistance development. It may depend on the characteristics of the specific herbicide or method of control. Gressel (2002) states that abstinence that allows weed seed buildup can have very negative effects. Preliminary results from the university studies mentioned previously indicate that continuous Roundup Ready systems used over several years did not create weed shifts or resistant weeds when the correct rate of glyphosate was applied and good weed management was practiced.

Much of the industry's experience with weed resistance is based on triazine and ALS resistance. With over 130 weeds resistant to these chemistries globally (Heap 2003), most weed management recommendations are based on traditional weed management recommendations that include rotation of herbicide MOA and tank mixing. Because this has driven current industry recommendations, Monsanto believes it is critical to study the epidemiology of specific cases.

ALS Herbicide Case Study in Iowa

This information outlines general herbicide use in a typical corn/soybean rotation.

Corn from 1990 through 1997:

- 84% of the corn acres were cultivated.
- 58 to 72% of the corn acres were treated with atrazine.
- 35 to 60% of the corn acres were treated with metolachlor, alachlor, or acetochlor.
- 24 to 50% of the corn acres were treated with dicamba or 2,4-D.
- From 1991 to 1997, 5 to 17% of the acres were treated with nicosulfuron, which has no activity on waterhemp.

Soybeans from 1990 through 1997:

- 22 to 74% of the soybean acres were treated with imazethapyr.
- 54 to 73% of the soybean acres were treated with pendimethalin or trifluralin (National Agricultural Statistics Service 2002).

Based on the above information, growers in Iowa utilized crop rotations that resulted in a herbicide use pattern with multiple MOAs that were effective on waterhemp. Even with this commonly promoted and accepted practice for preventing weed resistance, waterhemp resistant to ALS herbicides was selected rapidly.

Summary

Glyphosate has unique characteristics that have made it difficult for plants to avoid its lethal effects, so we should not assume that employing weed resistance management tactics developed for other herbicides is appropriate for glyphosate as well. Development of weed resistance is a complex process that is very difficult to predict accurately, and no single agronomic practice will mitigate resistance for all herbicides or all weeds. As a result, weed resistance needs to be managed on a case-by-case basis and tailored for the particular herbicide and grower needs. Using good weed management principles built on achieving high levels of control through proper application rate, choice of cultural practices, and appropriate companion weed control tools will allow continued, effective use of glyphosate.

The key principles for effective stewardship of glyphosate use, including Roundup Ready crops, include (1) basing recommendations on local needs and using the tools necessary to optimize weed control; (2) establishing proper rate and timing of application; and (3) responding rapidly to instances of unsatisfactory weed control.

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3.3 Demethylation Inhibitor Fungicide Resistance in Fruit Crops

Wayne F. Wilcox

Introduction

Scab (*Venturia inaequalis*) and powdery mildew (*Uncinula necator*) are the two most common targets of fungicides applied to apples and grapes, respectively, both in the United States and internationally. In the United States, sterol demethylation inhibitor (DMI) fungicides have been registered for the control of both diseases since the 1980s and have been used heavily for these purposes since then. Practical resistance to the DMI fungicides (unacceptable disease control attendant with a selection of resistant pathogen phenotypes) first was suspected for *V. inaequalis* within 5 to 6 years after commercial introduction of the fungicides, and documentation finally was published in 1997 (Köller et al. 1997). Now, DMI resistance is considered common in regions with intensive apple scab pressure such as Michigan and New York, where the utility of these materials in disease control programs has been limited seriously as a result. Resistance also is widespread in the apple-growing regions of Europe and is suspected (but not documented) in parts of South America. Similarly, compromised control of grapevine powdery mildew was noted a comparable time after the DMIs first were registered on this crop (e.g., Travis and Muza 1991). Practical resistance was documented in both California (Gubler et al. 1996) and New York (Erickson and Wilcox 1997) a few years later, and now is considered to be widespread in the United States and Europe; it also has been documented in South Africa and is suspected (but not documented) in parts of Australia and South America. Although the DMIs still are used to control this disease, their importance is now diminished seriously from what it was previously.

Practical resistance to some types of fungicides (e.g., the benzimidazoles) develops as a result of disruptive selection. Although the vast majority of the *baseline population* of the target fungus is highly sensitive to the toxicant, a distinct subgroup is virtually immune and undergoes rapid selection as the material is used in disease management programs, resulting in the potential for a sudden loss of control (Köller and Scheinpflug 1987). Such selection is not affected by the fungicide dose. In contrast, practical resistance to the DMI fungicides results typically from directional selection, whereby fungicide sensitivities within the original baseline population are distributed normally and unimodally, with no immune subgroup. When fungicide exposure rates are decreased, through such factors as dilution within the growing plant, inadequate spray coverage, or an intentional decrease of use rates, the least-sensitive members of the population are selected and gradually come to predominate. Losses in disease control often are gradual and incremental over time (Köller and Scheinpflug 1987).

Management of the Problem

A three-pronged approach was taken in the northeastern United States to managing DMI resistance in apple and grape production systems: (1) Defining the problem within a commercial context; (2) Determining the utility of theoretical resistance management (RM) strategies under field conditions; and (3) Using this information as the basis for educating growers and their advisors about the issue.

Defining the Problem

Prior to the introduction of DMI fungicides into the apple market, a resistance-monitoring technique was developed for *Venturia inaequalis*, and baseline sensitivity distributions were determined (Köller, Parker, and Reynolds 1991; Smith, Parker, and Köller 1991). When commercial control problems subsequently arose, these techniques and data were used to compare the fungicide sensitivities of pathogen populations within affected orchards with those in baseline settings. Such comparisons showed that the least-sensitive members of the pathogen population, which were present at a frequency of <2% under baseline conditions, had been selected to a frequency of ≥40% in orchards where scab control with DMI fungicides had been compromised. Such phenotypes therefore were defined as resistant, and it was shown that commercial rates of the labeled DMI products provided approximately 50–75% control of them versus 100% control of sensitive phenotypes in greenhouse evaluations (Köller et al. 1997).

Similarly for *Uncinula necator*, the least-sensitive phenotypes that originally constituted a mere fraction of the baseline population were found to constitute >90% of the population in vineyards where practical resistance to triadimefon had developed, and the median ED(50) (the effective dose for 50% inhibition of mycelial growth) was 30-fold higher than in baseline populations. In contrast, median ED(50) values for two other DMIs, fenarimol and myclobutanil, had increased by only two- to eightfold in the same vineyards, and these materials still were providing acceptable powdery mildew control, although prospects for their continuing efficacy was considered tenuous (Erickson and Wilcox 1997).

Field Tests of Resistance Management Strategies

For *Venturia inaequalis*, a 3-year trial was conducted in an orchard where the frequencies of phenotypes deemed resistant to fenarimol and the unrelated fungicide, dodine, were representative of commercial settings in which sensitivity shifts had begun but were still well short of conferring practical resistance. The RM strategies investigated were (1) use of a high DMI rate (30 versus 15 micrograms (μg)/milliliter (ml) fenarimol); (2) application of the DMI fungicide in mixture with a surface protectant (mancozeb); and (3) application of the DMI in mixture with another, unrelated, systemic compound (dodine). Each year, disease incidence and severity data were gathered and fungicide sensitivity distributions were determined for a collection of single-spore isolates from each treatment population. From these data, the control of both the sensitive and resistant subpopulations was calculated for each treatment.

Whereas both fenarimol rates provided statistically equivalent control of the DMI-sensitive and DMI-resistant subpopulations, the lower rate provided intense selection pressure for the resistant phenotypes (i.e., it provided only 25% as much control of the resistant subpopulation as of the susceptible population). Tank mixing with mancozeb improved control of both subpopulations equally. Therefore, although mixing mancozeb with a low rate of fenarimol decreased the overall level of disease relative to the fenarimol-only treatments, it did not decrease the frequency (selection) of DMI-resistant phenotypes within the pathogen population that survived treatment with this mixture. Thus, inclusion of a protectant fungicide in mixture does not allow a decrease of the DMI rate from an RM viewpoint, and use of both strategies (high DMI rate plus inclusion of a protectant) is the preferred tactic (Köller and Wilcox 1999a). In contrast, mixing a second systemic compound (dodine) with a low rate of fenarimol distinctly decreased selection of the DMI-resistant isolates. It was concluded that mixing DMI fungicides with protective compounds such as mancozeb does not decrease the selection of DMI-resistant phenotypes because the two fungicides inhibit the fungus in spatial and temporal isolation. In contrast, dodine and fenarimol inhibit the fungus in concert both temporally and spatially; hence selection will occur only for fungal isolates that are resistant to both (Köller and Wilcox 1999a, 2000).

Resistance management strategies for *Uncinula necator* were tested over 4 years in a commercial vineyard where practical resistance to triadimefon had been documented, but where sensitivity shifts with respect to myclobutanil, another DMI with greater intrinsic activity, was less pronounced and this material was still effective. The specific strategies tested were (1) using a high DMI rate (112 versus 56 grams (g)/hectare (ha) of myclobutanil); (2) limiting DMI use (three applications of myclobutanil rotated with three of sulfur versus six of myclobutanil only); and (3) limiting the size of the pathogen population against which DMIs are applied (three sprays of myclobutanil early in the season followed by sulfur versus the converse; i.e., applying at the start of the epidemic rather than once it is in progress). Disease control and myclobutanil sensitivities within treatment populations were determined as stated previously.

The full 112 g/ha rate of myclobutanil provided equivalent disease control when used in all six applications or only three times at the start of the season; however, improved control of the resistant subpopulation (less selection) was provided by the lower spray frequency. Furthermore, this rate also was significantly less effective, both with respect to disease control and the selection of resistant phenotypes, when applied in the last three sprays rather than the first three. Halving the myclobutanil rate to 56 g/ha decreased disease control by approximately 50%, and control of the resistant subpopulation by 50–75%, relative to the full rate (Wilcox 2003).

Educational Efforts

The theory of resistance development, basic RM strategies, and the results of supporting research projects were presented to growers and advisors through a repeated series of oral presentations, statewide newsletter articles, and regional and national trade publications (e.g., Köller and Wilcox 1999b; Wilcox 1999, 2003; Wilcox and Köller 1996). In 1999, a survey was commissioned among the majority of wine grape growers in New York, to determine the relative importance that they attached to RM with respect to other factors that might influence their choice of a fungicide. These factors, in decreasing order of importance to the respondents (% respondents rating the factor as "highly important") were: (1) efficacy (100); (2) resistance management (86); (3) handler and worker safety (50); (4) cost (43); and (5) environmental toxicity (36) (G. B. White and W. F. Wilcox unpublished). Such data demonstrate that the importance of RM is recognized by growers, although it does not indicate to what extent growers employ the recommended practices. Anecdotal observations suggest that compliance is high, however, provided that the recommended practices are practical and overtly connected with efficacy in growers' perception.

Barriers to Resistance Management

Various economic, technical, and social barriers exist with the potential to limit RM, most of which apply to other at-risk fungicides in addition to the DMIs. They include cost, technical limitations of alternative fungicides used in rotation or tank mixes, regulatory issues, conflicts with marketing strategies, and lack of research support.

Cost

The use of high rates and the inclusion of a tank mix partner involve an additional cash outlay relative to avoiding these practices. Experience suggests that cost is a more important factor in the choice of fungicide options than indicated in the grower survey referenced in the preceding section. For instance, there may be a tendency to decrease the rates of both components of a tank mix to more closely approximate the cost of using either one alone. This is not a good RM practice.

Technical Limitations of Alternative Fungicides Used in Rotation or Tank Mixes

Paramount, perhaps, among several limitations is the actual or potential occurrence of resistance to many of the fungicidal alternatives to the DMI materials; for example, *Venturia inaequalis* versus dodine (Köller, Wilcox, and Jones 1999), *Uncinula necator* versus boscalid, and both pathogens versus the QoI fungicides. In fact, it seems that pathogen populations that already have been selected for resistance to one group of fungicides may be predisposed to developing resistance to additional unrelated groups (Köller and Wilcox 2001). Another limitation is the temporal and spatial separation of protectant compounds from the DMIs when the two are applied in mixture. For example, DMI fungicides function against *V. inaequalis* from within the plant after infection has occurred, whereas traditional protectant compounds (e.g., mancozeb, captan) prevent infection by inhibiting spore germination on the outer tissue surfaces. Thus, if a DMI is applied within a few days after an infection has occurred (the only time that it is effective), the protectant fungicide mixed with it will provide no additional control of that infection event (i.e., it will do nothing to decrease the selection of DMI-resistant isolates that might result from that particular spray).

Regulatory Issues

Broad-spectrum protectant fungicides (captan, chlorothalonil, mancozeb, ferbam, etc.) have been used for over a half century with no development of resistance and are common components in RM programs in fruit and other crops. Many of these compounds will be reviewed under the Food Quality Protection Act as potential carcinogens, however, and their regulatory future is uncertain. Furthermore, regulatory issues have precluded the use of DMIs with higher intrinsic activities than those that are now allowed. For example, the ED(50) for baseline populations of *Venturia inaequalis* with respect to flusilazole, a DMI that is registered for use on apples in both Europe and Canada, is 0.008 μg/ml. In contrast, those with respect to fenarimol and myclobutanil, the two standard DMIs registered for apple scab control in the United States, are approximately five- and ninefold as great, respectively (Köller, Parker, and Reynolds 1991). Substituting one DMI of greater activity than another is tantamount to increasing the rate of the original; and in fact, flusilazole and a similarly active compound (difenconazole) are the only two DMIs that still provide some control of scab in European orchards where practical resistance is rampant. Neither is registered in the United States.

Conflicts with Marketing Strategies

Although high use rates are an important component of RM strategies for DMI fungicides, these products often are priced so that only marginal rates are economically competitive. Recently the conflict between marketing and RM strategies has become apparent with respect to the new QoI fungicides, which have supplanted the DMIs to some extent for use against both *Venturia inaequalis* and *Uncinula necator*. Although it is known that use of the QoI materials in a curative (rather than preventive) mode provides significant selection pressure favoring the least-sensitive segment of a fungal population (Wong and Wilcox 2002), such a use pattern is being promoted for these products by some advertising and sales personnel in order to improve the products' commercial appeal.

Lack of Research Support

Effective RM recommendations should be based on proven principles rather than dogma or guesses. Furthermore, experience shows that growers are far more likely to implement recommended strategies when their utility has been demonstrated rather than merely pontificated. Thus, it is both perplexing and disquieting that public support for the science of RM has all but vanished. Resistance management is too "applied" for the National Research Initiative and other programs pertaining to agricultural research that focus on fundamental sciences. The preservation, rather than replacement, of registered pesticide tools—even those considered "reduced risk" by the Environmental Protection Agency—does not appear to fit the priorities of national integrated pest management research programs. Those concerned and impacted by RM have not marshaled the political wherewithal to get this topic recognized as a legitimate objective within new, narrowly targeted programs. As old pesticides are replaced by newer and often safer materials, these will face increasing risk of loss to resistance if it is not possible to discover how best to maintain their longevity.

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3.4 Diamondback Moth Resistance in Crucifers

Anthony M. Shelton and J. Z. Zhao

Background

Crucifers are a diverse plant family containing many species of weeds, vegetables such as cabbages and broccoli, and the field crop rapeseed/canola. In North America and Central America in 2002, 119,431 hectares (ha) of vegetable crucifers and 3,720,990 ha of rapeseed/canola were harvested (FAOSTAT 2003). The climatic conditions for growing crucifer crops in North America vary dramatically, but the diamondback moth (DBM), *Plutella xylostella*, can be a problem in all areas where crucifers are grown. It is especially problematic in warmer areas where crucifers are present year-round. In the temperate parts of North America, DBMs may not be able to overwinter and must be reintroduced into these areas by aerial movement of adults (Hopkins 1999) or on plant material grown in other areas (Shelton et al. 1996). Because of their high cosmetic standards, vegetable crucifers generally sustain higher losses by DBMs than do field crucifers. The area grown to the field crucifer rapeseed is more extensive, however, and in some years DBM can cause considerable damage.

Diamondback moths have become a problem in several parts of the world, primarily for two reasons: it has been able to develop resistance to a number of different insecticide classes, and the use of broad-spectrum insecticides has decreased its natural enemy complex. Diamondback moths appear able to develop resistance to some insecticides faster than one of their principal natural enemies, *Diadegma insulare*, and this can exacerbate the problem (Xu, Shelton, and Cheng 2001). Diamondback moths were the first agricultural pests to develop resistance to DDT (Ankersmit 1953), and since that time some populations of DBMs have been able to develop resistance to every major class of insecticide (Talekar and Shelton 1993). There are biological characteristics of the insect and agricultural characteristics of crucifer production that seem to enhance the development of resistance. For example, DBMs have rapid life cycles in which a generation may be produced in less than 2 weeks. An individual adult also may produce nearly 200 eggs, and adults may travel hundreds, or even thousands, of miles so resistant genes may be spread rapidly over a large geographic area (Talekar and Shelton 1993). There also is evidence of considerable variation in esterase activity between DBM populations, leading to differences in susceptibility to specific insecticides (Maa 2001). From an agronomic standpoint, in areas in which crucifers are grown continuously DBMs can move from one crop to the next and be selected for resistance while they reside in each crop.

Early Surveys for Resistance

For decades DBMs have been reported as pests throughout the United States, but generally they were able to be controlled with the available insecticides. In the late 1980s at a national entomology conference, there was considerable discussion about how insecticidal control of DBMs seemed to be failing in many parts of the United States. In 1988, a cooperative program was developed to examine the susceptibility of DBM populations throughout much of North America (Shelton et al. 1993a). Forty-four populations of DBMs were collected from 19 states within the United States, Mexico, Canada, and Belize during the peak activity of DBMs in each area. Using a leaf dip assay, the populations were examined for susceptibility to three commonly used classes of insecticides: pyrethroid (permethrin-Ambush 2E), carbamate (methomyl-Lannate 1.8L), and organophosphate (methamidophos- Monitor 4E). Resistance ratios (RR) varied the most for methomyl (up to 780-fold); 15% of the populations had RR values ≥50, and 46% had values <10. The highest RR value for permethrin was 81; 17% of the populations had RR values >50 and 56% had values <10. The highest RR value for methamidophos was 42; none had values >50 and 83% had values <10. No geographic patterns for resistance were evident, because different populations within the same state or region may have varied considerably in their susceptibility. From this survey and an assessment of field performance where the samples were taken, provisional concentrations were developed to categorize susceptibility to each insecticide.

Another survey was conducted in 1990 with 11 populations of DBMs collected from six U.S. states to assess susceptibility to methomyl and permethrin and two different products containing *Bacillus thuringiensis* subsp. *kurstaki*. In this survey (Shelton et al. 1993b) the highest RR value for methomyl was 875, and for permethrin 237. The highest RR value was 178 for Dipel 2X and 211 for Javelin WG and this occurred in a population from New York, an area in which DBMs do not overwinter. Two populations from Florida had RR values to Dipel 2X > 50. In a subsequent survey that just focused on populations from Florida, one population had an RR of 1,641 to Javelin (Shelton et al. 1993b). A follow-up spray trial conducted in Florida in 1992 (Shelton et al. 1993b) indicated that both formulations provided <30% control in the field. Another product, XenTari, containing *Bacillus thuringiensis* subsp. *aizawai* with its additional Cry1C protein, provided 60% control. Since that time, however, populations resistant to Cry1C also have been noted (Cao et al. 1999).

Results from these early surveys indicated high levels of resistance to some of the major insecticide classes used at that time. The differences within states and regions were assumed to be caused by practices of individual growers. To examine this hypothesis more carefully, it is worthwhile to discuss the development of resistance in individual states.

Examples of Resistance Development in Individual States

New York

The 1988 and 1990 surveys indicated that some of the highest levels of resistance to commonly used insecticides occurred in New York. This was surprising for several reasons. First, there may be only five to seven generations of DBMs in New York, far fewer than the approximately 20 generations that can be produced in warmer areas of the county. Hence, selection pressure for the development of resistance should be far less in New York. Second, it is commonly considered that DBM populations cannot survive the cold winters of upstate and western New York, where the majority of cabbage is grown. Thus, even if a DBM population developed resistance within a single growing season, it would be eliminated during the winter and not be present for the next year. Therefore, we hypothesized that resistant DBM populations may be moving into New York either through aerial movement of adults or through contaminated transplants. Although long-range movement of adult DBMs has been documented to occur (e.g., Hopkins 1999), contaminated transplants may be a more direct source because the majority of cabbage grown in New York originates from transplants grown in southern regions. Transplants, grown in the field or in greenhouses, enable earlier production of cabbage in the northern regions of the United States.

Samples collected from 1989 to 1992 documented that DBMs were introduced into New York in the early spring on cabbage (Shelton et al. 1996). During 1989, transplant shipments from five transplant companies in Florida, Georgia and Maryland were sampled for DBMs, and the seasonal average infestation per company ranged from 1.3 to 3.5 DBMs per 100 transplants. One shipment in June, however, when the majority of transplants arrive, had 8.2 DBMs per 100 transplants. In 1990, the seasonal average infestation per company ranged from 1.8 to 12.0 DBMs per 100 plants, but one shipment had 17.4 DBMs per 100 plants. It was discovered that some DBM populations on these transplants had RR values >200 to methomyl and up to 20 to permethrin. Thus it was concluded that the high levels of resistance observed in New York in the 1988 national survey likely were the result of bringing transplants into New York that were contaminated with resistant populations of DBMs. Because of this, most New York growers have become far more cautious and demanding about the quality of transplants they use. Likewise, there has been an effort in the transplant production areas to use a more integrated approach to decrease DBM populations. Some practices that transplant growers can do include not locating transplant beds near production beds (a source of DBM infestations), raising transplants in screened-in areas, and rotating insecticides to decrease resistance to any single insecticide. Another technique that seems to work quite effectively is the use of better application techniques. A Maryland grower who had a seasonal infestation of 3.5 DBMs in 1989 was able to lower it to 0.3 in 1990 and keep it < 0.5 per 100 transplants in 1991 and 1992 through improved scouting practices and switching from aerial to ground applications of an insecticide.

Florida

Unlike in New York, populations of DBMs can occur throughout the year in Florida, and this ability increases the opportunity for resistance. The principal insecticides used in Florida in the 1980s were pyrethroids, but beginning in the mid-1980s growers started to notice control failures (Leibee and Savage 1992). By the winter of 1986–1987, pyrethroids in general provided no control of DBMs. A population of DBMs collected from central Florida that was resistant to fenvalerate also was resistant to methomyl (a carbamate) but susceptible to several organophosphates, thiodicarb (a carbamate), and a *Bacillus thuringiensis (Bt)* product. Once growers switched from pyrethroids, intense use of the alternative insecticides produced populations resistant to a number of different products, including *Bt*. Beginning in the last 5 years, growers have been able to use new insecticides with novel modes of action, including spinosad (SpinTor), emamectin benzoate (Proclaim), and indoxacarb (Avaunt). These products seem to be the choice of growers at present, but there is a high likelihood of developing resistance to these materials if they are not used properly.

California

During an outbreak of DBMs in California in 1997, nine populations of DBMs were collected from the major broccoli areas throughout the state and assayed for their susceptibility to currently used materials (*Bacillus thuringiensis* subsp. *kurstaki*, permethrin, and methomyl). Elevated levels of resistance were seen only with permethrin, and seven of the nine populations had RR values >100 (Shelton et al. 2000).

These data indicate that resistance to at least one of the commonly used insecticides (permethrin) may have played a role in the outbreak during 1997. Other factors may have been at least equally important, however. The winter of 1996–1997 was warmer than normal, and during the period from February through August of 1997, the amount of rainfall was <50% of normal. Hot and dry conditions are known to be conducive to outbreaks of DBMs.

Hawaii

In the mid-1990s in Hawaii, resistance in DBMs to all available insecticides was so severe that marketable yields of crucifers were decreased, and crucifers were imported to supplement local production (Mau and Gusukuma-Minuto 2001). Spinosad was commercialized for pest control in crucifers in Hawaii in April 1998 and provided excellent initial control of DBMs (Mau and Gusukuma-Minuto 1999). In some areas in Hawaii, however, control failures became evident in 2000. To examine whether these failures were due to resistance, 12 populations of DBMs in total were established from three islands (Oahu, Maui, and Hawaii) between September 2000 and April 2001 and examined in the laboratory using leaf-dip assays (Zhao et al. 2002). Results from this study indicated that 6 of the 12 populations were highly tolerant to spinosad (TR >100-fold). Two populations resistant to spinosad also were examined for potential cross resistance to emamectin benzoate (Proclaim) and indoxacarb (Avaunt), two new insecticides from novel classes. Fortunately, no cross-resistance was observed. A "postmortem" examination of the development of resistance to spinosad was done to determine what had caused resistance, and the following conclusions were drawn. Insecticide resistance management (IRM) strategies had been incorporated into the label for spinosad prior to its introduction. The manufacturer recommended an IRM strategy that limited use to ≤3 applications in a 30-day period, followed by at least 30 days of nonuse, and a maximum of 6 applications per crop. Such IRM restrictions probably were helpful in maintaining spinosad susceptibility in populations of DBM in most areas. In some areas of Hawaii, however, resistance developed despite labeled restrictions designed to prevent overuse. Although the guidelines may have been followed, they did not take into account a more "regional" approach for resistance management where as many as 50 applications per year might have been made to a common DBM population due to continuous sequential plantings on adjacent farms. Crucifers were planted and harvested to meet fresh-market needs every week of the year.

Spinosad was voluntarily removed from some areas in Hawaii when control failures occurred. Fortunately, as resistance to spinosad was developing, Proclaim and Avaunt became available. Since spinosad's removal from the market, continued monitoring has indicated a decline in resistance in many populations in Hawaii, so it is gradually being reintroduced, and this will take some of the pressure off Proclaim and Avaunt (Mau, R. 2003. Personal communication). Time will tell whether growers in Hawaii will be able to develop a more durable IRM for DBMs.

Transgenic Plants

Because DBMs are the only insects to have developed resistance to *Bt* toxins in the field, it also has served an important role in helping to evaluate resistance management strategies for transgenic plants that produce *Bt* toxins. In greenhouse (Tang et al. 2001) and field trials (Shelton et al. 1999) the value of a refuge for conserving susceptible alleles and the importance of refuge placement within the system have been shown empirically. Likewise, field tests also examined the strategy of spraying the refuge to prevent economic loss to the crop while maintaining susceptible alleles in the population. Results indicate that great care must be taken to ensure that refuges, particularly those sprayed with efficacious insecticides, produce adequate numbers of susceptible alleles.

In addition to the currently available resistance management strategies for plants that express a single *Bt* toxin at a high dose, plants also have been developed plants that will only express *Bt* toxins when induced to do so, thereby creating a "within-plant" refuge until the plants need to be protected (Cao, Shelton, and Earle 2001). This strategy may be useful for crops in which the marketable portion is produced during the latter half of the plant's growth (e.g., many vegetables such as sweet corn, tomatoes, broccoli, etc.), and for which the plant can withstand some level of early infestation. Likewise, the DBM/*Bt* crucifer system is being used to confirm the value of pyramiding *Bt* genes into plants to delay the onset of resistance to each gene if it were introduced either sequentially or simultaneously in separate plants (Zhao et al. 2003).

Lessons Learned and Recommendations

The DBM has shown a tremendous ability to develop resistance to nearly every insecticide used intensively against it. If there is a lesson to be learned from the development of resistance in DBMs, it is that sole reliance on a single class of an insecticide will fail. To avoid the development of resistance, growers should take the following actions:

1. Make sure they are not bringing DBM-contaminated plants into an area.
2. Rotate classes of insecticides to lessen the pressure for resistance to develop to any single class.
3. Use insecticides that are softer on natural enemies.
4. Destroy DBM-infested crop debris to decrease movement of DBMs between plantings.
5. Use alternative strategies besides the sole use of sprays of insecticides.
6. Develop area-wide resistance management programs, not just management on individual farms.

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3.5 Insect Resistance Management for Transgenic *Bt* Crops

Graham P. Head

Introduction

Insect resistance management (IRM) plans have been proactively implemented for all transgenic *Bacillus thuringiensis (Bt)* crops that have been commercialized. Central to these IRM plans has been the two-pronged strategy of expressing a highly effective dose of the insecticidal protein in all relevant plant tissues together with the provision of refuge areas for susceptible insects. These approaches have been combined with measurements of baseline susceptibility for the target pest species, routine and reactive monitoring for resistance in the target species, integration of IRM into existing pest management systems, intensive educational programs for farmers, and development of subsequent generations of products with multiple insecticidal proteins. For any particular *Bt* crop and country, the specific implemented IRM practices have been carefully adapted to local needs, reflecting local and regional differences in pest biology and agronomic practices. Differences in the size of structured refuge required among crops and countries illustrate this process of local adaptation. The most important lesson for the design of IRM plans has been the need to balance technical considerations with the practical and economic needs of farmers. Because implementation of IRM practices by farmers is critical to the success of IRM for *Bt* crops, farmers must be aware of their responsibilities, understand the need for IRM, and regard the required IRM practices as logistically and economically feasible. This underscores the need for inclusion of such considerations in the design phase of IRM plans and highlights the critical nature of farmer education programs.

IRM Approaches

Insect resistance management aims to delay or prevent resistance development through appropriate product design and deployment. Three general IRM approaches have been proposed and pursued over the past three decades:

1. Minimize the selection pressure for resistance. This can be achieved by ensuring that a product contains only a relatively low dose of the active ingredient or by limiting the use of the product in the field. The latter approach can occur uniformly by requiring a low-labeled use rate or heterogeneously by setting aside locations where the product will not be used at all (i.e., “refuges” for susceptible individuals).
2. Remove resistant alleles from the target pest population. In contrast to the first strategy, this approach typically involves using high enough doses of an insecticide to control heterozygous resistant insects, thereby making resistance functionally recessive.
3. Use multiple selection mechanisms in combination. This approach can work through mixing insecticides with different modes of action (or pyramiding insecticidal genes in transgenic plants) or rotating insecticides over time.

Because of a desire to ensure their durability, all three approaches have been proactively applied in the case of transgenic crops engineered with genes conferring protection against certain pest insect species (so-called *Bt* crops). Subsequent sections discuss how and why this has been done, and what lessons have been learned in doing so.

Relevant Characteristics of *Bt* Crops

With the development of genetic engineering techniques, it has become possible to achieve high, constitutive, season-long expression of insecticidal proteins in certain crops. These techniques have been used in field corn and cotton (and, on a smaller scale, in a number of other crops such as potatoes) to produce plants that are protected from a set of important lepidopteran pests. The proteins expressed are derived from the common soil bacterium, *Bacillus thuringiensis*, and are crystalline endotoxins (hence known as Cry *Bt* proteins). Because of the high, season-long levels of expression of the insecticidal protein in each instance, it is recognized that high adoption of these products without careful management could strongly select for resistance. This is one of the reasons that IRM plans have been proactively implemented for all of these products. At the same time, the nature of *Bt* crops provides an opportunity to employ IRM strategies that were not feasible for most conventional insecticides. First, the high expression levels of *Bt* protein (much higher than can be achieved using *Bt* proteins in foliar sprays) mean that these products deliver a high dose of insecticide throughout the life of most of the target pest species. As noted previously, this helps to ensure that resistance will be functionally recessive. For example, the expression of Cry1Ab protein achieved in all important tissues of a transgenic YieldGard corn plant exceeds the LC99 of the primary target pest, the European corn borer (*Ostrinia nubilalis*), by several orders of magnitude. Second, the defined in-plant distribution of insecticidal protein makes it possible to manipulate how much of the pest population is exposed through the creation of refuges. It also makes it possible to combine multiple insecticidal genes and thus to express multiple insecticidal proteins within a single plant. The first such product has just been commercialized in the United States in the form of Bollgard II cotton, which expresses the Cry1Ac and Cry2Ab proteins for control of lepidopteran pests.

IRM for *Bt* Crops

The basic IRM strategy employed for all *Bt* crops thus far commercialized builds upon the opportunities provided by the nature of *Bt* crops themselves. The two-pronged strategy involves expressing a highly effective dose of insecticidal protein throughout the transgenic plant to make resistance functionally recessive where possible, together with ensuring that refuge areas are provided for susceptible pest insects. The many susceptible insects coming from the refuge areas can mate with the few resistant insects surviving on the *Bt* crop, thus diluting out the resistant alleles in the pest population. Note that the refuge need not be something specifically planted by a farmer for that purpose (a structured refuge); the refuge can consist of nontransgenic plants of any species that can be used as a host by the target insects.

This is not the full extent of IRM for *Bt* crops, however; other complementary practices also are employed. These practices include the following:

1. Establishing baseline measurements of *Bt* protein susceptibility for each target pest species prior to widespread commercialization of the *Bt* crop. This practice is the basis for future assessments of resistance.
2. Monitoring for resistant insects in populations of the target pest species. This practice is based on routine monitoring of pest populations in potentially high-risk areas, reactive monitoring for suspect populations, and broad monitoring of product performance. In all instances, the baseline measurements are used for comparison purposes.
3. Using alternative insect control methods where appropriate (including cultural, biological, and chemical tools), as a part of fitting IRM practices into existing integrated pest management systems.
4. Targeting comprehensive educational programs at farmers and other relevant stakeholders.
5. Developing subsequent products that express multiple *Bt* proteins with different insecticidal properties. As described previously, the first such product already has been commercialized.

Adapting IRM for *Bt* Crops to Local Conditions

Bt crops have been commercialized at a global level, with the use of both *Bt* corn and *Bt* cotton in North and South America, Asia, and Africa; and *Bt* corn in Europe. A critical piece of this effort has been to develop locally appropriate IRM plans for each product in each country involved. In doing so, local, crop-specific aspects of target pest biology, agronomic practices, and grower behavior have been taken into account. Where resistance risks are higher because of aspects of pest biology and the nature of agronomic practices, more conservative IRM practices may be needed. Conversely, where resistance risks are inherently low because of these same factors, IRM practices can be adapted accordingly. Similarly, IRM practices must fit with local grower needs and agricultural practices.

An illustration of this local adaptation can be seen in the specific details of the refuge strategy used with different crops in different countries, and even for a given crop in different regions of the same country. For example, in the United States, *Bt* corn has a required refuge size of 20% in the main Corn Belt, but a 50% refuge is required in southern cotton-growing areas. In both instances, these refuges can be treated as needed for lepidopteran pest species. The larger refuge size for *Bt* corn in cotton-growing areas reflects the additional selection pressure for *Bt* resistance exerted by the use of *Bt* cotton in these areas. In contrast to the requirements for *Bt* corn, *Bt* cotton in the United States requires either a 20% refuge that may be treated with insecticides (comparable to the *Bt* corn option in the main Corn Belt) or a 5% refuge that cannot be treated for the target lepidopteran pests of *Bt* cotton. The unsprayed refuge option is included because cotton farmers in some regions of the United States need a high adoption option for economic reasons, and because few alternative control methods are available for the target pests. In Argentina, *Bt* corn requires a 10% refuge that may be treated with insecticides. The smaller refuge size in Argentina relative to the United States is based on apparently lower resistance risks for the target pests, primarily because of their broad host range. This situation is seen in a more extreme form in countries such as China with many small-holder farmers. In China, farmers are not required to plant any structured refuge in association with their *Bt* cotton because alternative host crops of the key target pest, the Old World bollworm (*Helicoverpa armigera*), provide a substantial source of refuge for *Bt* cotton.

Lessons Learned about How to Make IRM Successful

Seven years of experience with corn and cotton farmers in the United States, and comparable amounts of experience in countries as diverse as Argentina, Australia, and China, have provided valuable lessons on what sorts of IRM strategies can be effective technically and implemented successfully.

First and foremost has been the recognition of the importance of farmers in making IRM successful. Because the IRM plans associated with *Bt* crops require a variety of actions on the part of farmers, such as planting refuges, farmers must be aware of their responsibilities, they must understand the need for IRM, and they must regard the IRM practices that are required of them as logistically and economically feasible. This highlights the need for consistent and effective educational programs and illustrates why the needs of farmers must be considered in the design of IRM plans.

Second, but related to the first point, IRM plans must take into account the local and regional variation present in farming practices. Farming practices vary because of differences in agricultural systems, as well as because of chance environmental factors that constrain farmers' options at any given time. Consequently IRM practices must be flexible, and IRM plans should include multiple options that are adapted to different systems. This local adaptation of IRM practices for practical reasons complements the local adaptation that occurs for technical reasons (see the earlier discussion of differences in refuge size in different countries).

Third and equally important, it must be recognized that the IRM practices required for *Bt* crops are costly for farmers, in terms of both money and time (the opportunity cost of the practices). This issue can be addressed partially by ensuring that IRM practices are sufficiently adapted to existing agricultural systems to be simple and inexpensive for farmers to implement. Educational programs also are critical in this respect.

More generally, the design of IRM plans must balance the technical need to mitigate the risk of resistance development with the practical and economic needs of growers. The former dictates that IRM plans must have a strong scientific base to be effective. They also must be flexible over time because scientific knowledge is continually increasing. These technical considerations, however, cannot be so rigidly applied that they limit the availability of the product to farmers. If farmers regard IRM practices as impractical or unaffordable, they may choose not to use the product, and both they and society lose the benefits that product adoption could have brought. Alternatively, farmers simply may not implement the IRM practices and the durability of the product will suffer. Thus carefully balancing the various factors involved in IRM is the key to developing effective and implementable IRM plans.

4.1 What Have Insect Resistance Management Models Taught Us?

Nicholas P. Storer

Introduction

As with all models, insect resistance management (IRM) models can be constructed with varying degrees of complexity. At one extreme, grossly simplified models can provide overly simplistic answers that may not provide useful insight into the processes affecting resistance evolution in the field. At the opposite extreme, overly complex models that aim to simulate the real world are very costly and require significant knowledge of the system being modeled. Interpretation of such models in order to draw useful conclusions can be very difficult. The literature provides a wide range of examples between these two extremes. Simple models tend to be descriptive and deterministic, exclude population dynamics, handle spatial processes only in abstract ways, and simulate a fixed environment (e.g., Roush 1989). More complex models account for population dynamics and migration between patches (e.g., Caprio 2001; Comins 1977; Georghiou and Taylor 1977a,b). The most complex models are more mechanistic, integrate system-specific processes, and can incorporate stochasticity, model spatial relationships more explicitly, and even account for variable environments (e.g., Onstad and Gould 1998; Onstad et al. 2001; Peck, Gould, and Ellner 1999; Storer et al. 2003). Proponents of the simple approach cite the broad applicability and generality of the results and the ability to produce analytical solutions to specific questions. Proponents of the complex models cite their utility in understanding more fully the unique aspects of any insect resistance evolutionary system. The easy access to powerful computers enables mechanistic simulation models to be more common.

Some Learning from Simple Models

Simple models, beginning with Comins (1977), have taught some very important principles of resistance management. Such lessons have led to the development and widespread deployment of IRM strategies for transgenic insecticidal crops (*Bacillus thuringiensis [Bt]* corn and *Bt* cotton) in the United States and Australia. The models have helped to provide an understanding, for example, of the "high-dose + refuge" strategy, and the conditions upon which the effectiveness depends (Gould 1998). It has been learned that larger refugia and higher doses give longer durability (Roush 1997), and that deployment of two insecticidal traits in a stack can extend significantly the durability of each (Gould 1986; Roush 1997).

Adding Complexity—Spatial and Stochastic Processes

The simpler models mentioned previously are very generalized and have lent themselves to additional development to better understand the underlying processes. For example, one of the conditions that favors the effectiveness of the high-dose + refuge approach is that there is random mating among insects produced from the refuge and from the transgenic crop. In order to understand how the real world impacts this condition, it is necessary to examine the effect of the spatial distribution of refugia and transgenic fields, and how the insects move among the different patches.

Several models have suggested that high levels of dispersal between patches can accelerate the spread of resistance, whereas very low levels of dispersal can allow localized foci of resistance to develop (Caprio and Tabashnik 1992; Mallet and Porter 1992; Peck, Gould, and Ellner 1999). By further accounting for stochasticity in models, Peck, Gould, and Ellner (1999) showed that the balance between dispersal preventing the buildup of foci of resistance and the dispersal allowing resistant populations to spread can depend critically on random factors, such as patch distribution and local population size. Indeed, Peck, Gould, and Ellner (1999) showed that there are several scenarios in which extinction of a resistance allele in the tobacco budworm, *Heliothis virescens*, is more likely than its spread in the face of intense selection pressure from *Bt* cotton.

Handling Uncertainty

One criticism often leveled at IRM models, especially as they become more complex and system-specific, is that there is uncertainty around the processes and parameters included in the model. Many of these are naturally highly variable (such as nonspecific mortality, weather, dispersal patterns) or not predictable with accuracy (such as grower adoption). It is therefore very important to interpret the output of IRM models with this uncertainty in mind. Insect resistance management models generally provide a prediction of the change in frequency of resistance alleles over time, and the results often are expressed as the number of years until some frequency of the alleles is reached. As the actual rate is unpredictable due to the process and parameter uncertainties, such output should be considered in relative terms. Storer (2003) expresses model output as rate of adaptation relative to a standard benchmark. For example, a relative adaptation rate of 2 means that adaptation is expected to occur at twice the rate of, or in half the time of, the benchmark. This output variable therefore allows direct comparison of the effect of different IRM practices or different circumstances on the durability of an insect-control tool.

Applications of Spatial Models

Storer (2003) provides an example using a model simulating adaptation to rootworm-protected maize. This model predicts that if the refuge is held in the same location each year then the durability of the rootworm-protected maize is many-fold longer than if the refuge locations are random each year (thus usually on land that was planted to the rootworm-protected crop the year before). This results from the fixed refuge supporting large populations of susceptible rootworms over many years, increasing the effectiveness of the refuge. Such a finding can be used to improve the design of refuge-based IRM programs for rootworm transgenics, and would not be evident from a simple, nonspatial model.

These more complex spatially explicit models enable additional questions to be addressed. They can be used to investigate the effect of different farmers employing different pest-control tactics on the rate of adaptation to any one tactic. For example, they can be used to examine the effect of a patchy distribution of *Bt* crops and non-*Bt* crops on the spatial distribution of resistance alleles through time and help to understand the effect of a structured refuge at different levels of technology adoption (e.g., Storer et al. 2003). Such models provide insight into pest adaptation to competing technologies, such as different rootworm-resistance traits in maize (N. Storer, unpublished data). This analysis leads to an improved understanding of the way pest adaptation occurs in complex environments, improved understanding of the need to manage resistance, and improved understanding of the effectiveness of different IRM strategies.

Although models generally have been used to examine proactive resistance management strategies, they also have been used to design effective reactive strategies once resistance has appeared (Sisterson, M. 2001. Personal communication). Much of the uncertainty in assumptions and parameter values can be resolved once resistance occurs, such as the fitness of heterozygous- and homozygous-resistant insects on different crops, cross-resistance (or negative cross-resistance) to other control technologies, and the number of genes involved. The models, therefore, can be regarded as being more predictive in absolute terms (although considerable uncertainty will remain). Options for reactive plans generally consist of easing the selection pressure across the affected area and may include additional measures designed to impact resistant genotypes differentially over susceptible genotypes. Spatially explicit models can provide useful indications of the area over which such actions should be taken, and provide predictions of the time until reversion to susceptibility under different remedial action plans.

Conclusions

`Insect resistance management models by definition represent a simplified reality and often fail to account for all the uncertainties inherent in evolutionary genetics. Therefore, care must be taken in interpreting them for real-world applications. There is uncertainty in the future agricultural environment, uncertainty in the value of input parameters, and uncertainty that all relevant processes have been accounted for. Furthermore, IRM models are difficult to validate. The models make predictions over many years, even decades. If a model's predictions were to coincide with actuality, there would be little certainty that the actual events resulted from the processes exactly as modeled. Alternatively, if actuality fails to follow predictions, there would be uncertainty as to whether the model processes, assumptions, or parameter values caused the discrepancy. Partial validation can be possible, for example, by comparing predictions of pest population dynamics in the absence of or the presence of the insecticidal technology. For several important pests there are additionally documented historical instances of resistance that can be compared with model predictions.

The cautious approach to the application of results of computer models to the real world is similar to that for the laboratory (e.g., with *Plodia interpunctella* described in Roush 1994), greenhouse (e.g., with *Plutella xylostella* by Tang et al. 2001), or small-scale field experiments (e.g., with *P. xylostella* by Shelton et al. 2000). Each of these environments provides insight into natural processes, under controlled conditions, and therefore provides a valid forum for investigating IRM strategies. Physical experiments, however, are necessarily limited by the size of the test arena, by the number of different selection regimes that can be tested, and usually by the duration of the grant/publication cycle. Full field experiments on IRM are impractical, as the necessary control treatments will be designed to create the very problem that IRM is designed to avoid. Cyberspace provides the only suitable environment to perform long-term, large-scale IRM experiments testing multiple IRM strategies under multiple sets of assumptions.

Interpreting model output as relative predictions helps to account for much of the uncertainty and allows the true value of the models to be revealed. The models enable IRM practitioners to improve their understanding of a pest/crop/geography system. Through sensitivity analysis, models enable IRM researchers to focus their resources on understanding those processes that have the largest effects on resistance evolution. Insect resistance management models enable objective evaluation of IRM strategies that minimize the risk of pest adaptation while maximizing the benefits of the pest control technology.

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4.2 Resistance Management Strategies: Have Models Helped?

Richard Roush

Introduction

"*Ignorance ain't what you don't know, it's what you do know that ain't correct.*"
—*Will Rogers, American humorist*

Resistance management is a scientifically and practically vexing problem in pest management. As scientists, we prefer to test ideas with experiments before making recommendations on management, but long-range movement of pests and diseases, and the time frames required for any meaningful results, makes it very difficult and costly to conduct convincing experiments on resistance management. Due to pest and disease dispersal, however, realistic field experiments for some of the most vexing pests for resistance management would require tens of square kilometers. Couple this with the need to maintain the experiments for at least 4 to 7 years (about the minimum time for resistance in many key pests and weeds), not to mention the ethical issues of including treatments expected to generate resistance faster than the alternatives being tried (Tabashnik 1986), and the prospects of proving through experiments about how to manage resistance are dim.

Still, even in the absence of experiments that generally can be accepted as informative, decisions about the deployment of pesticides and transgenic crops must be made, especially by regulators. On the basis of history, it can be asserted that resistance will evolve, generally far too rapidly, if proactive steps are not taken to slow it down. As a consequence of this reality, and not with any joy, scientists have let mathematical models assume a critical role. At the very least, by forcing a precise statement of assumptions and the mathematical implications thereof, models have played an essential role in building a conceptual framework for resistance.

Especially during the last 15 years, this framework has revealed clearly the condition described by Will Rogers. Much of what is commonly believed about resistance management simply is not supported by the logical analysis forced by the models. This includes "urban myths" such as that high doses (or application rates) are more effective than low doses, and that pesticide mixtures are more effective than rotations. Although mixtures and high doses can be the more effective strategies in certain special cases, they generally are not so. Indeed, experiments on these ideas have given results that are inconclusive with respect to general rules in managing resistance, and the models have explained why (e.g., Roush 1994, 1997a,b, 1998).

Space limitations prohibit a detailed explanation of these conclusions. Instead, the aim here is to provide a summary and to point readers to other papers that provide more detail and lead to the primary literature.

High Doses Versus Low Doses: The Importance of Heterozygotes

It was once a popular idea that low application rates could be good for managing resistance because they would allow some susceptible individuals to survive. Simple arithmetic and simulation models, however, show that one must allow a large proportion (10–20%) of the treated individuals to survive if resistance is to be delayed significantly. In general, this would be impractical because it can allow too much damage to occur (Curtis 1985). One can illustrate this by using the dose response data for *Bacillus thuringiensis (Bt)* resistance in the diamondback moth to set the fitness at each dose to be considered (Roush 1994). For example, a dose of 1 part per million (ppm) kills 95% of susceptible individuals and approximately 70% of heterozygotes (Roush 2003; Tang et al. 1997).

On the other hand, another popular idea is that use of high doses generally will delay resistance. With the high-dose approach, resistance could be delayed in theory because the great majority of resistant heterozygotes (carrying one R and one S allele), the most common carriers of resistance, and perhaps even many resistant homozygotes are killed by the dose of toxin used. The survivors are so rare that the overwhelming majority will mate with susceptible homozygotes that escaped treatment and thereby produce heterozygous (effectively susceptible) offspring. As clearly demonstrated in modeling by Tabashnik and Croft (1982), however, the doses needed often must be very high and yet cannot interfere with the successful mating of resistant survivors of the treatment with susceptible immigrants. Further, the resistance frequencies must be low, so the strategy cannot be very effective if not adopted before resistance is first observed. In fact, the doses needed must kill approximately 95% of the heterozygotes to delay resistance significantly (Roush 1989, 1994, 1997a,b, 2003). These conditions rarely are met for insecticides. Worse, high doses generally destroy biological control agents needed in integrated management programs for insects and mites (Roush 1989; Tabashnik and Croft 1982).

Given the high resistance levels found in heterozygous herbicide-resistant weeds, it also seems unlikely that high doses will help for herbicides, nor have experiments shown a consistent advantage for fungicides (Brent 1995). It is conceivable that higher doses may help somewhat for cases of polygenic resistance, as may be true for fungicides.

High expression of toxins looks promising for *Bt* transgenic crops (Roush 1994, 1997a,b), however, illustrating how models identify the key assumptions that drive the success of one strategy or another. The models also show the importance of effective refuges to provide susceptible insects to mate with any survivors of the transgenic plants. This is consistent with the longer history of resistance management (e.g., Roush and Croft 1986; Tabashnik and Croft 1985). Recent experiments also have supported the use of refuges specifically for *Bt* crops (Liu and Tabashnik 1997; Shelton et al. 2000; Tang et al. 2001).

Models developed for addressing this debate also illustrate the factors that are critical to the evolution of resistance. The reason the high-dose strategy attracted such attention even in the late 1970s (see Tabashnik and Croft 1982) reflects the fact that simulation models clearly demonstrated the critical importance of the survival of heterozygotes to the rate of selection. A twofold increase in mortality of heterozygotes from 50% to 100% can mean more than a fivefold increase in the number of generations to resistance. By contrast, even a 100-fold difference in the initial frequency of the resistance allele generally makes less than a fivefold difference in the time to resistance (Roush 1997a,b). Given that the survival of heterozygotes cannot be measured until resistance in the pest has evolved somewhere, this is a key factor that limits the ability of the models to make some predictions.

Two Toxins: Mosaics, Rotations, and Mixtures

Another choice often faced in resistance management arises when there is more than one pesticide or toxin that can be used. Historically, the introduction of new pesticides has been uncoordinated and generally is driven by market considerations. This means that insecticides have been used in haphazard mosaics in which neighboring crops carrying interbreeding populations of pests are treated with a few different pesticides. Models (Roush 1989) and experiments (Roush 1993, 2003), however, show that mosaics never are better and often are worse than rotations.

It seems widely believed that mixtures of pesticides or toxins generally will or nearly always will delay resistance better than using them individually in sequences or rotations. This is not supported by experiments (Tabashnik 1989) or by models (Comins 1986; Gould 1986b). In contrast to the high-dose strategy, in which heterozygotes are controlled by applying enough of a single pesticide, the mixture strategy relies on a second pesticide to control the individuals heterozygous for resistance. This means that each of the toxicants must be used at doses that effectively kill completely susceptible individuals twice, which has been called "*redundant killing*" (Comins 1986; Gould 1986a). As with the high-dose strategy, however, mixtures are effective only if the mortalities of susceptible insects are very high (>95%) when exposed to each individual toxicant. Even then, resistance to at least one of the pesticides must be somewhat recessive for resistance to be significantly delayed (Gould 1986b; Mani 1985; Roush 1989, 1997a,b, 1998, 2003). Mixtures of insecticides are not promising due to incomplete coverage of the treated habitat (i.e., very few pesticides provide even 95% control) and residue decay (as pesticides break down, susceptible pests that have dispersed into the habitat or emerged from protected sites will not always be killed).

Again, running a few numbers in models shows that what seems a good idea does not stand up; it is the rigor of the model that exposes the weaknesses of the mixture strategy, which otherwise seems intuitively appealing. As with *Bt* crops and the high-dose strategy, however, the same kinds of models suggest that pyramiding two *Bt* toxins in the same plants can be effective in managing resistance, because the key assumptions are more likely to be met (Roush 1998). Similarly, although pyramiding classical host plant resistance factors generally may not provide much advantage (Gould 1986a), in the specific case of the Hessian fly, the available data suggest that pyramiding would be very effective (Gould 1986b).

Validation

Although it is very difficult to test these models explicitly, many of the models' predictions, such as the importance of refuges and problems with mosaics, have been tested, as discussed in this paper. Other predictions also have been met, at least in terms of population dynamics. For example, predictions of a "halo" of low pest density in nontransgenic crops near *Bt* crops have been met in the field (Andow and Hutchison 1998). Roush (1997b, Fig. 9) predicted that resistance in the pink bollworm to *Bt* cotton in Arizona would take at least 20 generations to evolve, even if the proportion of nontransgenic cotton was only 20%, but that the population of pink bollworm would begin to decline because it would be unable to replace itself. In fact, pink bollworm populations have begun to decline after adoption of approximately 65% *Bt* cotton, and still there are no resistance problems after approximately 24 generations (6 years) of use (Carriere et al. 2003).

Have models helped in managing resistance? They certainly have, by informing the decision-making process when no other means were available. Models clearly help to compare different strategies under the same range of conditions and thereby to identify which strategies are likely to be most effective across any set of assumptions. Models also can identify which features about the genetics, ecology, and management of resistance are most likely to be most important, and have played a key role in regulatory decisions. Scientists need to continue testing their intuition with the models and the models with experiments. Otherwise they run the risk of repeatedly acting out the mistake articulated by Will Rogers. What is today's ignorance? What do we actually "know"? These are the continuing challenges for resistance modeling.

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4.3 Herbicide Resistance Models: Have They Helped?

Carol Mallory-Smith

The first model to predict the occurrence of herbicide resistance was published by Gressel and Segel in 1978. This model, which was fairly simplistic, included the parameters of mutation rate, selection pressure, fitness, and seedbank. The authors drew from the information available about resistance to other pesticides and heavy metals. The model was developed nearly 10 years after the first report of a herbicide-resistant weed (Ryan 1970). The authors contended that resistance would be an infrequent event in part because there were few herbicides with high enough selection pressure or persistence. They also suggested that the resistant weed biotype would be less fit than the susceptible biotype and so would be less competitive when the herbicide was not used and the buffering capacity of the soil seedbank would maintain susceptibility in the population. In 1978, data about herbicide resistant weeds were limited, and the only major resistance reported was resistance to the triazine herbicides.

It should be noted that although there are analogous features among insects, diseases, and plants, the differences are so great that one should be cautious in transferring predictions or recommendations from one system to another. If some of the differences are evaluated, it is apparent why caution is needed. Plants are stationary, although pollen and seed do move. A refuge would not have the same impact for weeds as it does for insects. The highest degree of cross-pollination occurs between adjacent plants, so there would not be enough movement of susceptible genes into the population to maintain susceptibility. In most cases, the generation time for weeds is much longer than for insects or microbes. The most significant difference is that there is not the dissimilarity between the host and the pest that exists with insects and microbes. When herbicides are applied, the goal is to kill one plant, the weed, and not injure the other plant, the crop.

In the ensuing 25 years since the Gressel and Segel model (1978) was published, several other theoretical models have been created. These models included more parameters or were more specific. The model constructed by Maxwell, Roush, and Radosevich (1990) included gene flow and population dynamic aspects. Other models have addressed specific weed species, herbicide classes, or the impact of herbicide-resistant crops on the system (Cavan, Cussans, and Moss 2001; Diggle and Neve 2001; Hanson, Ball, and Mallory-Smith 2002; Shaner, Feist, and Retzinger 1997).

Predictive Role of Models

With or without models, it still would be predicted that the herbicide that exerted the highest selection pressure would be at risk to select a herbicide-resistant biotype. Selection pressure includes the efficacy of the herbicide combined with the number of applications. It would be predicted that the most sensitive weed species would be the most likely to evolve resistance.

The models are descriptive of what had happened but have not been particularly effective in resistance prevention or management. It still is not possible to predict when or where resistance will occur or why one species and not another will develop resistance. High- and low-risk herbicides have been identified, after the fact.

How Models Were Used to Identify Data Gaps

All of the models contain common parameters. The models made it very apparent that there were data gaps related to predicting the occurrence of herbicide resistance in a weed species or to a specific herbicide. In order for the models to be accurate, better data were needed. The models also raised questions about the assumptions included in the models. Researchers have addressed components of the models, but still there are major data gaps 25 years later. In part this is due to the long-term nature of the studies that would be needed and the cost of conducting the studies. It also is because there are no experimental methods to determine some of the parameters such as mutation rate.

- **Mutation rate.** Mutation rates for resistance are unknown and are theoretical, so any number included in a model is highly suspect. The fact that resistance appears in some populations of a species but not in other populations of the same species at other sites raises the question of how mutations for resistance arise.
- **Mode of inheritance.** The models assumed that the trait would be a single gene and nuclear-encoded trait. Polyploidy was not considered in the models. A limited number of studies have been conducted to determine the mode of inheritance of herbicide resistance.
- **Fitness.** It was assumed that there would have to be a cost associated with resistance, and that the resistant biotypes would be less fit. There has been, and still is, a great deal of debate over how fitness should be evaluated and which parameters should be measured. Some researchers have argued that in order to get an accurate measurement isogenic lines must be used, and that the studies must be conducted under typical field conditions (Jasieniuk, Brule-Babel, and Morrison 1996). By the time a resistant population is identified, it often is difficult to find a susceptible plant in the same population. It could be argued just as logically that weed populations are diverse so multiple biotypes of both resistant and susceptible plants should be used. In addition, “typical field conditions” do not exist; environmental conditions differ every year.
- **Gene migration.** Gene migration through seed or pollen movement was included in the Maxwell, Roush, and Radosevich (1990) model. The authors contended that a susceptible gene migration from a susceptible population would slow resistance. Jasieniuk, Brule-Babel, and Morrison (1996) concluded that gene migration from a susceptible population to a resistant population would not slow the occurrence of resistance.

Uncertainty Associated with Various Parameters

Even though there has been considerable research on herbicide-resistant weeds, there is still a great deal of uncertainty associated with various parameters. Data gaps still exist, and weed scientists continue to debate the parameters and their importance.

- **Mutation rate.** Mutation rates are unknown, and mutations are random events. It is obvious that mutations for certain resistance alleles are more common than others, but the actual rate still is unknown. Mutations for resistance to the acetolactate synthase (ALS) inhibitors are frequent, and multiple mutations occur that provide resistance to these herbicides. Mutation rates for other herbicides such as glyphosate and 2,4-D are lower.
- **Mode of inheritance.** Caution should be taken with interpretation of inheritance data because the number of studies on inheritance is limited. Polygenic resistance has not been documented but is expected to be responsible for multiple resistance that is metabolism based. Most often resistance has been due to mutations in a single nuclear-encoded gene (Jasieniuk, Brule-Babel, and Morrison 1996). Resistance to the sulfonylurea and imidazolinone herbicides has been reported to be a single, nuclear-encoded dominant or semidominant trait. There is only one report of resistance as a recessive trait. Resistance to the triazines is maternally inherited, so the trait does not move in with pollen.
- **Fitness.** In the absence of the herbicide, fitness and competitive differences between resistant and susceptible biotypes have been compared. The only consistent differences have been measured between triazine-susceptible and triazine-resistant biotypes. In most studies for the parameters measured, the triazine-susceptible biotype was more fit than the triazine-resistant biotype. Negative consequences for resistance to other herbicides have not been shown.
- **Gene migration.** Field data still are not available for gene migration. None of the models included prediction of movement of resistance from one site to another. Research in gene migration has increased not to determine the influence that susceptible plants could have on the decrease of resistance in weeds but because of the question of gene flow from herbicide-resistant crops into weedy and native species. Pollen movement will be responsible for short-distance movement of a trait, and seed movement has the potential for short- or long-distance movement, depending on the dispersal mechanism.
- **Selection pressure.** Selection pressure for most herbicides can be estimated. Efficacy data are collected over a wide range of environments and for many weed species. A national data base containing this information would be useful for predicting which species might be most likely to evolve resistance to a particular herbicide. Soil

persistence is determined as part of the herbicide-development process, and half-lives under different environments are known. The impact of herbicide rotation versus herbicide mixtures on selection pressure is not known, however. Decreased herbicide rates have been suggested as a way of decreasing selection pressure. Theoretically, this practice might be a viable means to decrease selection pressure; however, the idea of maintaining a weed population, susceptible or not, is unacceptable to most growers. Prediction of cross-resistance has proved difficult. The supposition was that if a weed was resistant to one herbicide in a group then it would be resistant to other herbicides within that same group. This is not always the case.

- **Seedbank longevity.** The longer seed lasts in the soil, the longer susceptibility could be maintained in a population. Many weeds have a soil seed life from 2 to 5 years. Unfortunately, by the time that resistance is recognized in a field, much of the susceptible seedbank would be depleted. The seedbank is analogous to the refuge for insects but is not as renewable.

Validation of Models

The models for the most part have not been validated. In order to truly validate them, the components should be tested, which requires the production of a resistant biotype based on the parameters of the model. The resistance gene must occur in the population, and this is a random event. Resistance in a weed species may or may not occur under similar conditions.

Resistance is an economic and social issue for growers. Many growers do not see the value in prevention of herbicide resistance, and instead of using a proactive approach, will react if and when the problem occurs on their farm. Resistance management requires long-term planning and commitment. In many regions of the United States, the agricultural economy does not allow farmers to choose a production practice that might be more costly in the short term, even if it would be a good resistance management strategy. This may seem shortsighted but it is the reality of production agriculture today.

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4.4 Lessons Learned in Predicting and Assessing the Risk of Fungicide Resistance: Have Models Helped?

Hendrik L. Ypema

Introduction

The main purpose of this presentation is to assess whether models addressing development of fungicide resistance have been helpful in the effort to improve resistance management (RM) strategies for fungicides. It provides a brief overview of the role of models in predicting or assessing development of fungicide resistance, and in identifying factors that influence the time period in which resistance develops to the point of compromising fungicide efficacy. A general description of a model found in several dictionaries is the following: A preliminary pattern representing an item not yet constructed, and serving as the plan from which the finished work, usually larger, will be constructed. Specifically in fungicide resistance research and management, a model is a tool to aid in predicting how fungicide resistance will develop in nature and to identify factors important for resistance development. The design of models is based on three concepts, which all can be found in the general description of a model just cited. First, a model is a "preliminary pattern," therefore it is based on assumptions about reality. Second, it is "representing," therefore the goal is to approach reality with the model. Third, the real-life project, in this case occurrence of resistance, is "not yet constructed," in other words has not been detected yet.

Models Addressing Fungicide Resistance Development

There are a large number of publications available on modeling for fungicide resistance development (Josepovits and Dobrovolszky 1985; Kable and Jeffery 1979; Levy and Levy 1986; Levy, Levi, and Cohen 1983; Milgroom and Fry 1988; Shaw 1989a,b, 1993, 2000; Skylakakis 1981, 1982). For the design of a model, several factors need to be quantified as accurately as possible to approximate the real-life situation. Some of these factors are the following:

1. Nature of the mode of action of the fungicides in question;
2. Estimated frequency of individuals in the population that is completely controlled, partially controlled, or not controlled;
3. Rate of pathogen reproduction;
4. Numbers of genes involved in resistance development;
5. Use of the product (number of applications: in a sequence and throughout the season, use in mixes, or as a solo product, rates);
6. "Fitness" of resistant isolates; and
7. Levels of exposure of the pathogen to a fungicide: rates, coverage, degradation, unexposed sub-populations, and fungicide distribution properties.

Unfortunately, for a newly introduced fungicide many of these factors cannot be estimated accurately, because the data on which the estimates are based are difficult or impossible to quantify (Brent 1995; Brent and Hollomon 1998).

Model Assumptions

Models predicting or describing scenarios of resistance development are likely to be most precise when the assumptions underlying their operation are closest to the situation in nature. In many cases, factors important for resistance development are estimated from past experiences with other fungicide-pathogen combinations or from laboratory experiments. For instance, fungicide-target fungi such as *Botrytis* spp. and powdery and downy mildew fungi have shown in the past to be prone to resistance development; therefore they are assumed to be the first to develop resistance to newly introduced fungicides (Brent 1995). Multisite inhibitors were shown to be at a lower risk of encountering resistant strains of target fungi compared with single-site inhibitors. Introduction of a new *single-site inhibitor*, therefore, may raise more immediate concern about resistance development (Brent 1995). Past resistance risk assessments of single-site inhibitors do not always represent resistance risk of future single-site inhibitors, however. For instance, resistance to benzimidazoles and phenylamides compromised use of these products against some pathogens after one or two seasons of use, whereas it took approximately 7 years of use of sterol-inhibitor fungicides before resistance became a concern (Brent 1995; Brent and Hollomon 1998). Would it have been possible to predict the resistance risk of *Quinone outside Inhibitor* (QoI)-fungicides when they were introduced commercially in Europe in 1996 based on past experiences with other fungicides? Probably not; the last major group of fungicides encountering resistant strains of target pathogens in the field were the demethylation-inhibitor (DMI) fungicides, where resistance levels increased in a gradual pattern, whereas with QoI fungicides resistance development has been more disruptive (Brent 1995; Brent and Hollomon 1998).

An Example: Resistance Development to QoI Fungicides

Most QoI fungicides currently marketed were developed from strobilurin A, a fungal metabolite of *Strobilurus tenacellus*, and all share the same mode of action. The antifungal activity of strobilurin A helped the fungus compete with other fungi in establishing itself on its food source of decaying pine cones on the forest floor. The metabolite was chemically modified for better utility as a fungicide and has stood at the base of several QoI fungicides currently marketed (Ypema and Gold 1999).

Looking at the factors that needed to be quantified to predict and manage the development of resistance at the moment when QoI fungicides were launched commercially, it becomes clear that many could not be quantified adequately. Because a model system—a fungus producing the lead fungicidal molecule—was available, the mode of action of strobilurin A could be elucidated fairly quickly, and for the majority of fungicides currently commercialized the mode of action is known. Several QoIs exhibited excellent activity against a number of pathogens with many short vegetative generation cycles and high reproduction rates that were shown to be prone to resistance development, such as the powdery mildew fungi. At the moment of introduction, however, it was not known whether resistance would affect QoI fungicides similarly compared with, for instance, benzimidazoles. Although the QoI lead molecule, strobilurin A, was extremely active against several target fungi at extremely low rates in in vitro assays (Ypema and Gold 1999), there was no information as to which proportion of the population was actually controlled by field application. The same was true for most other fungicides at the time of their introduction.

Recently, a few publications have addressed survival of individuals of the apple scab fungus, *Venturia inaequalis*, in an orchard population following applications of half and full rate of DMI fungicides alone or in combination with protectants (Köller 1995; Köller and Wilcox 1999). At the moment of introduction, there was no clear information about the numbers of genes involved in resistance development to QoIs. Several target site mutations were identified in yeasts, hinting at a resistance scenario that would be multigenic in character, and hopefully leading to a gradual development of resistance in the field (Jordan et al. 1999). Upon introduction, it was not known how use of QoIs with regard to rates, number of applications, and intervals would impact the development of resistance. At the moment of introduction, true resistant strains of target pathogens had not been encountered; therefore, indications of all characteristics that make up "fitness," the ability to compete (sporulation, growth, lifecycle, survival), certainly were not known. Also unknown was how patterns of exposure of the pathogen to a fungicide based on distribution properties of the fungicide, applied rate, coverage achieved, and the presence of unexposed subpopulations in, for instance, untreated areas or on alternate hosts, affected development of resistance. These factors all have been estimated and used in models to assess development of resistance (Josepovits and Dobrovolszky 1985; Kable and Jeffery 1979; Levy and Levy 1986; Levy, Levi, and Cohen 1983; Milgroom and Fry 1988; Shaw 1989a,b, 1993, 2000; Skylakakis 1981, 1982). But it was impossible to quantify these factors for most fungicides accurately at the moment of introduction.

A few years after introduction of QoI fungicides, more information was gathered about certain factors influencing resistance development (Heaney, Hall, and Olaya 2000). Compared with the moment of introduction, the mechanisms of resistance and underlying mutations that were found in target pathogens in treated areas were much better known, and some mutations were found to be quite different from the original target-site mutations identified in yeasts. Limited information also was known about the fitness of resistant isolates collected from treated areas and mutants generated in the laboratory (Heaney, Hall, and Olaya 2000). Any study conducted with these strains, however, was limited to only a small sample of one to a very few individuals. Conclusions based on the study of these individuals were difficult to extrapolate to the large pool of genetic variation and potential resistant phenotypes in a fungal population in nature, making it impossible to provide a general prediction for the development of resistance to QoI fungicides. Information about how rate of pathogen reproduction, use of the product, and level of exposure affect development of fungicide resistance in detail is still elusive, several years after QoI fungicides were launched. It can be concluded that many factors underlying the development of resistance still could not be quantified accurately several years after introduction of QoI fungicides at a time when the first cases of resistance were encountered in the field, limiting the utility of models to predict development of resistance in practical situations. The situation has been similar for most other fungicides several years after their launch.

Have Models Helped?

Did models help in predicting development of resistance or in identifying factors that influence fungicide resistance development? To date, knowledge of resistance and RM is based mainly on past experiences with fungicides to which resistance has developed. It continues to be difficult—if not impossible—to assess accurately the resistance risk to a newly introduced fungicide compound until resistance develops. Verification of the actual success and validity of a model in predicting risk of resistance development and identifying factors important for resistance development for a given fungicide-pathogen combination has been difficult, because many factors identified by models as being important in influencing resistance development cannot be quantified accurately in nature. Those factors include fitness of resistant strains in a fungal population, level of exposure to a fungicide, and the presence of untreated target pathogen subpopulations. Although the predictive power of models to assess the risk of resistance development of a given fungicide-pathogen combination is limited, models have been and will be very useful in identifying factors that may influence the development of resistance in general.

Conclusions

As for today's formulation of fungicide RM strategies before detection of resistance, such recommendations are based primarily on factors that the end user can manipulate with ease, such as the number of applications of a particular fungicide, the concentration at which a fungicide is applied, and whether it is applied alone or in a tank mix with other fungicides. Such recommendations focus primarily on reduction of selection pressure and satisfactory, economically feasible control of most individuals in a pathogen population with multiple types of chemistry. Other factors identified by models as being important are not at all or only superficially included in the formulation of RM guidelines, because they cannot be measured accurately or because they cannot be controlled by the end user. For the foreseeable future, due to the difficulty in accurately quantifying these other factors, the role of models to predict "real-life" resistance risk scenarios likely will remain limited. This may change only when future research is directed more toward fields and orchards where fungicides are used. The role of models as a tool in understanding resistance development and factors important to resistance development will continue to be important.

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5.1 Pesticide Resistance Management: Is There a Role for Consumers?

Doug Gurian-Sherman

Introduction

Consumers are an untapped resource, and a potentially powerful force, for promoting pesticide resistance management (PRM). They are largely unaware of the importance of PRM, but they are concerned about the effects of pesticides on health and the environment. Those concerns about pesticides could provide an avenue for consumer support of PRM if a concerted effort were made to promote such support. Consumer support for PRM could be mobilized by incorporating PRM into integrated pest management (IPM), which in turn may be supported through the marketplace or by consumer groups.

Pesticide resistance management needs IPM as a vehicle for consumer support because otherwise PRM is too specialized and complex to attract consumer attention. Both PRM and IPM may promote decreased pesticide use, which is an important consumer goal that arises from concern about the safety of pesticides. Consumer groups may additionally recognize the value of "safer," or reduced-risk, pesticides and may support PRM for those pesticides. Resistance management of safer pesticides can, like pesticide use reduction, be accomplished through IPM.

Pesticide resistance management is a resource conservation issue, and consumers support conservation. Like many natural resources, pesticides can be "used up" if not conserved. And as natural resources can be conserved by judicious use, pesticides can be conserved by PRM. Loss of pesticides as a resource through pest resistance can have negative impacts on the environment. For example, estimates of crop yield losses in the absence of pest control typically range from approximately 20% to 80% depending on the crop and where and how it is grown. In the absence of adequate pest control, the acreage needed for farming could increase to offset yield losses. The additional acreage devoted to agriculture would decrease land available for other uses and increase the environmental impacts associated with agriculture. And loss of reduced-risk pesticides may result in replacement by more dangerous pesticides.

Although resource conservation has broad public support, pesticides typically are not viewed as a resource by the general public. Instead, pesticides often are equated with environmental and human harm. At best, the public considers pesticides to be a "necessary evil," the use of which should be minimized. As already noted, however, a decrease of pesticide use is compatible with both PRM and IPM.

Despite the importance of PRM/IPM, there are barriers that prevent consumers from supporting it. Those barriers are the lack of understanding that pesticide use can be decreased under IPM, the lack of standardized IPM goals that are consistent with consumer interests, and the sometimes-divergent needs of farmers and consumers concerning pesticide use. Those barriers are not insurmountable, and suggestions for overcoming them are provided.

Consumer goals of decreasing pesticide use and adopting the use of safer pesticides can coincide with the goals of PRM and the needs of farmers. That intersection of interests can be incorporated into IPM, if IPM is defined and standardized properly, thereby providing a vehicle for consumer support and benefits to society.

Consumers, Pesticides, and PRM

Although there is no evidence that consumers are concerned about pest resistance, their aversion to pesticides can be used to support PRM. Consumer concern about pesticides leads to a desire for decreased pesticide use, which could contribute to PRM. Decrease of pesticide use facilitates PRM generally by decreasing selection pressure on pesticides, thereby decreasing the likelihood of resistance. The goal of decreased pesticide use also is a goal of organic farming. The exclusion of many pesticides under organic farming standards, however, limits the value of organic farming for PRM. In contrast, IPM is less restrictive about the kinds of pesticides used, can decrease the use of pesticides, and is supported by consumers.

Consumers want decreased pesticide use because they generally equate pesticides with environmental and human harm. The long shadow of *Silent Spring*

(Carson 1962) remains, occasionally reinforced by stories about the recovery of ospreys and eagles after the banning of DDT, atrazine-deformed frogs, and hermaphroditic alligators found in lakes on flooded farmland.

Concern about pesticides also can be seen for the new technology of *genetically engineered* (GE) pesticidal plants. For example, a laboratory study suggested that GE corn pollen containing an insecticidal protein from *Bacillus thuringiensis* (*Bt*) bacteria may have harmed Monarch butterflies (Losey, Rayor, and Carter 1999). Although later field experiments concluded that it was very unlikely that *Bt* corn pollen harmed Monarchs (Sears et al. 2001), the damage to public perception already had occurred.

An indication that consumers are concerned about pesticides can be found in consumer surveys. A recent survey conducted by the Center for Science in the Public Interest showed that 76% of consumers desired labeling of food from crops treated with pesticides, more than the percentage that desired labeling for GE crops (Center for Science 2001). In fact, despite concern about GE foods, approximately 21% of consumers said that GE foods that decrease pesticide use are safer than conventional foods, whereas only 7% felt GE foods without pesticide reduction were safer. A recent survey by Rutgers University found that pesticide residue on food was an important food safety concern (Govidasamy et al. 1998).

Organically grown food often is purchased because it is produced without using synthetic pesticides. Sales of organically grown food can therefore act as an indicator of consumer interest in decreasing or eliminating pesticides. In recent years, consumption of organically grown food has increased at over 20% per year according to U.S. Department of Agriculture data (Dimitri and Greene 2002). These dramatic increases have occurred despite substantial premiums, often over 50%, charged for organically grown food. Although organically grown food makes up only a very small percentage of U.S. agricultural production, the Rutgers survey indicated that over two-thirds of consumers would buy organic food if it were not so expensive. That potential market for organically grown food suggests a parallel interest among consumers for decreased pesticide use.

It does not necessarily follow, however, that consumers who favor organically grown food also would favor crops grown using IPM. Although both organically grown and IPM-grown food may decrease pesticide use, they are distinguished by several other practices, as well as by a general philosophy of natural farming that only organic farming embodies. For example, organically grown food allows the use of different pesticides than IPM-grown crops allow. In particular, pesticides approved for organic farming are derived from natural substances rather than synthetic ones. That gives organic pesticides an aura of safety. On the other hand, consumers may be interested in purchasing IPM-grown food that uses less pesticide even if certain other goals of organic production are not accomplished.

A survey conducted by Rutgers University about consumer attitudes toward IPM revealed that consumers would respond positively to the decreased use of conventional pesticides. Seventy-one percent of consumers surveyed were willing to purchase IPM-labeled food, and 88% of those consumers were willing to pay a premium for food grown using IPM methods (premiums ranged up to 20%) (Govindasamy et al. 1998). Respondents, however, typically did not understand IPM prior to reading definitions supplied with the survey. This indicates that consumers must be educated about how IPM addresses their concerns about pesticides to market IPM-grown food effectively.

An indication of the market potential for IPM-grown food is demonstrated by IPM-labeled food sold by the Wegman's grocery chain of the northeast United States. With the help of Cornell University, Wegman's began labeling food grown using IPM in 1995. The crops grown for the Wegman's IPM label expanded from 1,413 hectares (ha) in 1996 to an estimated 3,654 ha in 1998 (Cornell University 1999). The Wegman IPM program includes pesticide reduction, with adoption of 80% of the recommended IPM methods giving a predicted 30%–50% decrease in pesticide use (Cornell University 1999).

Integrated pest management also may have an economic advantage over organic farming, even in the absence of the high premiums paid for organically grown food. That is because organic production, with its philosophical as well as biological justification, may sacrifice yield and increase labor compared with conventional farming. By comparison, IPM is based on maintenance of high yields, thereby allowing higher profit at lower prices than for organically grown food.

A second means for consumers to support PRM is through environmental and consumer advocacy organizations that recognize the importance of PRM. This does not require most consumer-members of those groups to understand the details of PRM, but only to trust the consumer organization to represent their interests concerning the broader goals of human health and environmental protection. By this means the problem of technical complexity being a barrier to consumer understanding and support of PRM may be avoided.

Consumer organizations are unlikely to support IPM if they believe that all uses of chemical pesticides are harmful and unnecessary. Certain environmental groups may support organic farming, for example, as an alternative to conventional farming in part because synthetic pesticides are not used.

But certain consumer activists and consumer groups have shown support for IPM, including the use of certain nonorganic pesticides. For example, Charles Benbrook, a prominent agricultural environmentalist and critic of agricultural biotechnology, has supported the use of synthetic pyrethroid insecticides in arguments against the use of *Bt* crops (Union 2001). In a publication for the Consumers Union, Benbrook defines "Biointensive IPM" as a "range of preventative tactics and biological controls to keep pest population within acceptable limits. Reduced-risk pesticides are used if other tactics have not been adequately effective, as a last resort and with care to minimalize [sic] risks" (Gold 1999, p. 18). At least one other prominent environmental organization that endorses biointensive IPM, the World Wildlife Fund, considers PRM to be critically important (World Wildlife Fund 2003).

The specific acceptance by certain consumer groups of reduced-risk pesticides, as opposed to synthetic pesticides generally, should not be overlooked. Understanding the acceptance by consumer groups of certain synthetic pesticides, such as synthetic pyrethroids as opposed to organophosphates, is critical to gaining the support of those groups for IPM/PRM.

Support of biointensive IPM by consumer groups indicates a willingness to accept, if somewhat grudgingly, a legitimate role for certain synthetic pesticides. By implication, if pesticides are accepted as having a legitimate role in biointensive IPM, then it follows that their effectiveness should be conserved. Therefore the recognition of pesticides as a resource by environmental organizations represents an opportunity for them to endorse PRM practices to conserve those resources.

Several types of reduced-risk pesticides are registered by the Environmental Protection Agency (EPA). Unlike the narrower spectrum of pesticides approved for organic farming, synthetic pesticides are included among the reduced-risk pesticides registered by the EPA. According to a recent EPA list, 32 pesticides are registered under the reduced-risk program (plus several previously registered pesticides have been reclassified as reduced-risk) (EPA 2003). Those reduced-risk pesticides include 10 fungicides, 11 herbicides, and 12 insecticides (one of which functions as both insecticide and herbicide). In addition, biopesticides, such as biological control agents like microbial *Bt* and other microbes, often are considered reduced-risk pesticides. A recent EPA list includes 195 biopesticides (not including transgenic crops or beneficial pest-eating insects such as ladybugs—the latter are not included because they require no EPA registration) (EPA 2002).

One measure of pesticide safety or perceived safety may be based on the origin of the pesticide, in particular whether it is derived from a naturally occurring substance. For example, synthetic pyrethroid insecticides derived from the botanical insecticide pyrethrum often are considered to be acceptable and relatively safe. Other new and effective pesticides are synthetic versions of compounds found in nature. For example, the strobiluran fungicides are synthetic versions of antifungal compounds found in fungi of the genus *Strobilus*.

A specific example of the support of PRM by consumer organizations as well as their impact on PRM policy is found in insect resistance management (IRM) for genetically engineered *Bt* crops. Environmental organizations, along with agricultural scientists and regulators, promoted the development of mandatory resistance management plans for *Bt* crops. The high-dose refuge strategy that emerged from the debates concerning *Bt* crops is unique, inasmuch as no regulations mandate PRM for other pesticides.[1] In addition, *Bt* crops have led to a decrease in chemical insecticide use in *Bt* cotton in several parts of the United States. Due to the controversy surrounding GE crops, however, acceptance by many consumer groups of *Bt* crops as an alternative for chemical pesticide use currently is not an option.

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[1] Support for *Bt* IRM by consumer organizations initially was motivated by the desire to prevent cross-resistance to microbial *Bt*s used by organic growers. Advocacy for *Bt* IRM has continued for new *Bt* products, however, such as MON 863 for corn rootworm, for which there is no important microbial counterpart used by organic growers.

Barriers to Consumer Support for PRM

There are several barriers to consumer support for IPM/PRM resulting from problems in marketing IPM/PRM or from IPM standards (or lack of standards) that do not meet consumer goals of decreasing pesticide use or using safer pesticides. Marketing barriers include lack of consumer understanding of IPM and inconsistent market supply (Pool, W. 2003. Personal communication).

Another potential barrier could develop concerning standards for reduced-risk pesticides that may differ between consumer groups and others interested in IPM. For example, GE pesticidal crops are registered along with other biopesticides as de facto reduced-risk pesticides, but often are considered to be unacceptable by environmental groups. The definition of other reduced-risk pesticides by the EPA also may not be stringent enough to suit certain environmental groups.[2] Similarly, definitions of acceptable pesticides under biointensive IPM/PRM by consumer organizations may not always be acceptable to farmers. That divergence between how farmers apply IPM/PRM and how consumers define IPM may act as a barrier to consumer support for PRM.

Farmers may not want to be restricted to the use of reduced-risk pesticides, or even to the preferential use of such pesticides. Many reduced-risk pesticides are relatively new and still under patent protection, and therefore often are more expensive than old nonreduced-risk pesticides. Furthermore, reduced-risk pesticides may not be available to control all pests on all crops for which nonreduced-risk pesticides are available. Even when available, some reduced-risk pesticides may be less effective than available nonreduced-risk pesticides. This often may be the case for the reduced-risk biopesticides. Additionally, many pesticides are safer because they have a narrower spectrum of activity and therefore are less likely to harm nontarget organisms. But a narrow spectrum of activity also may mean that fewer types of pests are controlled than by nonreduced-risk, broad-spectrum pesticides. Farmers may not want to be restricted to nonreduced-risk pesticides if a decrease in yields is a consequence.

In practice, decreased pesticide use depends on adequate pest control at lower levels that is sometimes difficult to achieve. Decreased pesticide use in certain instances actually could accelerate resistance if not done in a biologically sound manner. For example, resistance management plans for *Bt* crops have depended on the use of a high effective dose of the insecticidal *Bt* Cry protein. That is because resistance alleles that can overcome high pesticide doses typically are present at much lower frequencies than alleles effective at lower doses. Often such high-dose alleles also are recessive. The recessive nature of the resistance genes facilitates PRM by necessitating the mating of two heterozygous parents that each carry a resistance allele, the chances of which are decreased by planting non-*Bt* "refuges" (Shelton, Zhao, and Roush 2002). For *Bt* crops, a high level, or dose, of the pesticidal protein is therefore considered to be desirable for resistance management. Similar principles also may apply to certain other pesticide uses.

Integrated pest management standards acceptable to farmers do not always require a decrease in pesticide use or PRM compared with conventional farming, although often they include pesticide reduction as a laudable goal. For example, applying insecticide based on a measure of insects reaching an economic threshold, a common IPM practice, may result in higher pesticide application than scheduled spraying under conventional farming in certain circumstances.

Perhaps due to disagreements concerning acceptable definitions of IPM, and unlike the situation for organic farming, there is no standardization of IPM that allows broad certification of IPM/PRM-grown food. That lack of standards also limits both the kind of commercial marketing that might otherwise be done to promote IPM/IRM and the broad promotion of IPM/PRM by consumer groups. It also limits the availability of food grown under IPM protocols acceptable to consumers.

Solutions and Conclusions

The IPM/PRM standards that provide for substantial decreases in pesticide use and the use of reduced-risk pesticides will encourage consumer acceptance of IPM-labeled foods. The IPM standards also allow product discrimination that facilitates marketing and willingness of consumers to pay a premium for foods labeled as IPM. Consistency between those standards regionally or nationally will facilitate an adequate

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[2] The requirements for reduced-risk status are essentially a demonstration of less risk in any of several categories compared with currently used pesticides. The amount of risk reduction is not specified clearly.

supply of IPM/PRM-grown food. Such standards also allow a consistent message to be conveyed to consumers that such foods are grown with less pesticide and safer chemicals. Because of regional variation in growing conditions, such as climate and pest pressure, however, such standards will require flexibility regarding implementation details.

Consumer representatives, grower organizations, and IPM/PRM scientists need to come together to agree on standards for IPM/PRM that best accomplish the requirements of all those concerned. Although standards for IPM that completely satisfy all stakeholders are unlikely, an adequate compromise may be possible.

Farmers may be willing to accept occasional small losses of yield due to limitations of options under certified IPM/PRM if they can rely on guaranteed markets or premiums that compensate for those losses. On the other hand, the willingness of consumers and consumer groups to support premiums for IPM/PRM food will depend on a willingness of farmers to fulfill consumer goals. Consumers might compromise on the use of certain nonreduced-risk pesticides if they are used only as a last resort, in order to achieve the broader goal of substantial decreases in pesticide use.

Pesticide resistance management can be an issue that consumers, scientists, and farmers agree on if their mutual interests are recognized and all are willing to compromise to promote the broader goals that all parties desire.

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5.2 Role of Stakeholders in Resistance Management: Crop Consultants

Roger Carter

Introduction

Resistance management (RM) is considered the mainstay of many agricultural consultants' repertoire of strategies. Although RM is considered to be "something new" or a "key word," independent agricultural consultants have been recommending practices supporting RM for more than 40 years.

Without RM, agricultural producers would find it difficult to remain in business. Yet there is the misconception that RM is not as widely adopted as necessary to facilitate environmental enhancement. Because of this misconception, there must be dialog to discuss the role of all players in the RM scheme.

Barriers to RM and How to Eliminate Them

A few consultants and producers lack appreciation for RM science. Many of these are of the "old school" and have not realized yet that the key to profitability is the adaptation to "new thinking," including the "updated version of RM." They have developed apathy not just to RM, but also to other scientifically proven programs to enhance profitability. Training those from the old school and putting more independent unbiased consultants in the field will increase the chances that apathy will not be an issue in the future.

There also seems to be a lack of ethics necessary for self-imposed compliance. The repeated use of the same chemistry on the same insect spectrum and transgenic refugia abuse are two examples. Both practices can be "controlled" by industry's imposing stricter punishments for abusers. Abusers can be found through more stringent monitoring programs conducted by industry. As a last resort, government regulation may be necessary to dictate punishment.

Producers and consultants currently are relying on the most efficacious and profitable treatments and practices due to poor farm economics. Increasing government payments for increased use of "healthy" RM programs will increase participation in RM programs. An improved cost-of-production crop insurance program will ensure a firmer economic base for farmers and thereby improve participation. Guaranteeing profitability through either government payments or insurance programs if growers adapt updated versions of RM will enhance participation.

There is currently a severe lack of different tools to control many pests. A prime example is the control of the brown stinkbug in soybeans. Methyl parathion is the only efficacious and practical treatment to control this insect. Both the government (i.e., the U.S. Environmental Protection Agency [EPA]) and industry must give RM practitioners more tools. The more tools consultants have in their bags, the more likely we are to have a good RM program. A bag will never get too full of tools. Certainly, the more tools consultants have, the harder the decision-making becomes, but at least there will be multiple choices in order to practice RM.

Economic restraints caused by yield or quality reduction from certain practices, programs, or treatments designed to embellish RM put hardship on producers. The cost of alternative control practices often can be very great. These constraints must be paid for by the public (the government) through payments or insurance designed to offset losses. Or, the public (the government) can help to pay for the development, through industry, of new practices, programs, or products that work in RM programs without desecrating profit.

Many producers are in a short-term survival mode due to the poor farm economy. Improving the farm program with payments on what is produced (not on base acres), crop insurance reform (adopting the cost of production insurance), and a change in foreign trade policy will be necessary to improve short-term cash crunches and to help the producers and consultants adopt long-term goals. And integrated pest management (IPM) programs must be created with long-term vision in order to facilitate those goals.

Management skills of a few producers may impede RM adoption by agriculture as a whole. The RM programs often can be complicated, yet workable. Education of the next generation of producers will enhance the adoption of the most efficacious RM programs.

Goals of Independent Agricultural Consultants

Although consultants work with a diversity of crops, pests, and conditions, our goals are similar.

1. We must maintain long-term vision and not look only at short-term relief. The key to most RM programs is longevity.
2. We also must maintain RM as a facet of IPM and integrated crop management (ICM). One of the results of good IPM and ICM programs is a good RM program. The sciences of all embellish each other.
3. While monitoring crops, consultants must be looking vigilantly for the early warning signs of resistance and communicating their findings as quickly as possible to the scientific community.
4. Consultants must educate their clientele constantly regarding RM. And they themselves must remain updated constantly on all facets of science that affect RM.
5. Consultants also must help industry and public research develop updated RM programs and evaluate those programs before they are fully implemented in the fields.
6. Consultants must maintain contact with all other stakeholders. All stakeholders in RM should “work and play well with others.” A consistent interaction must be maintained among all stakeholders.

Perception of Other Stakeholders’ Goals

Consultants perceive that the goals of all other stakeholders should be the following:

1. to work and play well with other stakeholders,
2. to consider economics at all times,
3. to see everything from the farmers’ perspectives,
4. to keep goals do-able,
5. to look “outside the box,”
6. to protect American technology, and
7. to evaluate new RM strategies before implementing them.

The producers’ number one goal should be economic survival. They also should have long-term vision and a goal of working with nonbiased consultants to implement RM programs.

Researchers (industry and public) should search for new chemistry and strategies. They should develop RM programs for ever-changing pest complexes, cropping systems, and management tools, and they should pursue new thresholds and scouting techniques to be used with new technologies. Finally, researchers should develop novel transgenic or conventional pest control or pest resistance traits.

Industry should develop new chemistry and technology (new and more tools). Companies should monitor and help to develop RM programs—rotating programs, modes of action, etc.—especially in weed management. Mandating compliance through closer inspections and stiffer penalties should be a priority. Activation of terminator genes is a must for biotechnology. Another key concern should be protecting U.S.-developed technology so that U.S. producers do not subsidize foreign competitors, as is occurring now. And, finally, industry must keep marketing and sales balanced with RM programs.

Government’s goals should include establishing federal guidelines or restrictions developed with consultants, industry, and grower groups. It should monitor the effects of RM programs on farm economics and on the environment. It should also protect U.S.-generated technology from foreign competitors. Establishing “fast-track” clearance on novel products to increase RM tools is necessary. The U.S. government should finance university and private research brainstorming activities that seek novel approaches. And government should promote independent, unbiased agricultural consultants as the medium best suited to deliver the most-efficacious RM systems to the end users—the producers.

Economics Should Always Be First

Grower groups, independent consultants, the EPA, the U.S. Department of Agriculture, university research and extension, and industry (basic to dealer) each have a role to play if efficacious, profitable, and long-term RM programs are to be embellished. Although certain goals are somewhat unique, each stakeholder should list economics first and foremost as a backbone to any viable program. If it doesn’t show a profit on the farm, then don’t waste the time, manpower, and money to try to make it fit. The producer must have a profit from every investment. Otherwise, the practice will be dropped.

Summary

There are certain barriers to achieving complete adoption of all RM techniques. These barriers can be decreased primarily by making it economically feasible for producers to adapt RM programs through government support or through improved yields and quality at a lower cost per unit. Secondly, the continued development of more efficacious, more easily managed RM tools and programs will decrease barriers. And third, communication among all stakeholders is imperative. Having an unbiased opinion as a delivery mechanism for RM systems and techniques is one key to the success of RM.

5.3 Role of Producers in Management of Resistance

Frank L. Carter

Introduction

This session is on the role of stakeholders in resistance management. My topic is to discuss the role(s) of producer stakeholders. I will give an overview of the current pest situation in cotton and specifically address each of the three questions posed to this panel.

Background

I am an entomologist with the National Cotton Council. I am not a cotton producer. My remarks are based on a long-standing professional interest in resistance and 22 years of experience working with national cotton producer groups. I also have worked closely with the Insecticide Resistance Action Committee (IRAC) for the more than 15 years. For this discussion, I will confine my remarks to cotton producers only.

The history of resistance in the cotton system has been well documented. At this workshop alone, cotton has been the "poster child" in several sessions. Dr. O'Leary outlined cotton resistance issues, and cotton was the topic in four of the seven presentations in the "Lessons Learned" session. Glyphosate resistance in weeds in cotton was discussed by Dr. Heering, and Dr. Bagwell gave an overview of insect resistance in mid-Southern cotton. Dr. Dennehy talked of resistance issues in Western cotton, and Dr. Head discussed resistance management (RM) in *Bacillus thuringiensis (Bt)* crops, including cotton.

Current Cotton Pest Situation

We now are in a new era in cotton. I think that this will set the stage for future RM strategies in cotton because the insecticide use in cotton has been decreased significantly. There are two reasons for this. First, boll weevil eradication expanded in the mid-1990s and effectively has removed the boll weevil along with the associated insecticide use. About the same time, in 1996, *Bt* cotton was introduced and rapidly adopted. *Bt* cotton further decreased insecticides applied for control of lepidopterous pests. As a result, pesticide use per season declined from an average of 6.7 applications per season in 1995 to 3.2 in 2003.

In addition, several new products have been developed recently for cotton, giving cotton a selection of modes of action (MOAs) with both transgenes and conventional chemistry now available for insect pests. Weed control under the current trend of minimum tillage is in need of new MOAs. Resistance management planning should focus on this environment rather than the 30-year history of dealing with resistance in cotton.

Question #1: What Are the Barriers to RM?

The following is a list of some of the barriers to resistance management from the viewpoint of producers. These are listed in no particular order of importance.

- **Must be alternatives available.** Effective RM capabilities improve when two or more MOAs are available to be used in some combination, either in mixtures or in alternating applications.
- **Pick your RM target.** Cotton, like most other crops, has a long list of pests. Cotton has 12 insect pests; 25 or more weed pests; a list of diseases including seedling diseases, root rots, vascular wilts, and boll rots; and 3 major nematode pest species. Obviously, we cannot conduct an RM plan for each pest-by-product combination. This very likely is unnecessary anyway.
- **RM plan.** Producers look to others to identify priority needs for RM.
- **Lack of ownership or leadership.** In some cases, resistance management leaders are bound by state lines or other geographic boundaries. Possibly more important, especially in today's "lean and mean" environment, most of those leaders are spread too thin in their responsibilities to

look beyond simply meeting the next deadline. Planning and executing an RM plan requires a time commitment that may be a luxury in today's work environment.

- **Survival mode.** Producers often are in a survival mode. Their philosophy is "Let's take care of this season first!"
- **Lack of incentive.** Incentive may not be the correct word here, but I think that producers need a good reason to support RM plans aggressively. Recent examples are the *Bt* cotton refuge RM plan to protect that valued technology and the whitefly RM plan in Arizona to avoid return to the crisis mode with whitefly. In this vein, I think that producers are more willing to support RM after emerging from a crisis situation.
- **Must be cost neutral.** Producers generally desire that RM strategies are cost neutral. Again, the exception is after recovering from a crisis, as Arizona did with whitefly.
- **Impediment to new replacement or competing technology.** It may sound strange at this meeting where RM is considered a method to preserve existing technology, but there is some truth to the idea that preserving one technology actually may serve as an impediment to a new replacement or competing technology. Other speakers have referred to this already in this workshop.

Question #2: What Are the Goals of RM Implementation for Producers?

The goals of RM are more straightforward. These are listed here, and there may be more goals that could be included.

- Clearly identified objective
- Effective plan and strategies
- Practical strategies that are producer friendly
- Strategies that are cost neutral to producers
- RM plan that covers host range of the target pest

Question #3: What Are the Goals of Others in Pest RM?

Effective RM requires the participation and involvement of stakeholders involved in production of a commodity. The following is a list of some of the specific roles of others that I think are most important.

- **Scientific community.** Producers must rely on the scientific community for science-based proposed RM plans, and the research community must be responsible for monitoring the effectiveness and progress of the plans.
- **Private industry.** Private industry has a huge role in resistance management. Protecting existing products against resistance development and developing alternative products are obvious responsibilities. Private industry plays an important role in the IRAC, the Fungicide Resistance Action Committee, and the Herbicide Resistance Action Committee programs. Interactions with producer groups, consultants, and the scientific community are key roles.
- **Extension and consultants.** Extension and consultants must work with scientists and growers to evaluate proposed plans.
- **Extension, consultants, and producer organizations.** Extension, consultants, and producer organizations are needed for communication to those ultimately responsible for carrying out RM strategies.
- **Economists.** Economists must provide input on the economic impact of protecting the technology and the cost of implementing such measures.
- **Producers.** Producers are needed to provide grower input on modifications or new plan strategies, to serve as a reality check on proposed strategies, and to help evaluate science-based strategies.

Summary of Questions

The important barriers in the view of producers include alternative tools, a clear target or objective, leadership, and identified incentive. Key goals considered by producers are clear need, effective plan, practical strategies, minimal economic economical impact on producers, and a good monitoring plan. The roles of others include key roles for the scientific community, private industry stewardship, extension and consultants for education, and research for monitoring and modifications to the plan as needed. Producers have important roles in carrying out successful RM plan strategies.

Producer Perspective Summary

In summary, the cotton industry is entering a new era, one in which insecticide input is decreased significantly. Producers now expect that consideration of RM plans should be conducted in light of these new developments and not on the 30-year-old history of resistance and insecticide use in cotton. Producers expect that target-specific RM plans will be identified on those pest–by-product(s) combinations that are thought to be high resistance risk. Producers want RM strategies to be of minimal economic impact to them and suggested practices to be practical in nature. Producers ultimately will make or break any RM plan, so it makes sense to strive for practicality when choosing RM strategies. Last but not least, producers will not be in favor of increasing regulation of RM. Producers encounter an increasing regulatory environment in all farm practices, so they do not want to see RM regulated.

5.4 Industry's Perspective on Insect Resistance Management and Its Implementation

Caydee Savinelli, Graham P. Head, and Gary D. Thompson

Introduction

Pest management resistance is a serious issue for the agricultural chemical industry. The development of pest resistance to a company's product poses significant problems, in terms of poor product perception in the eyes of the customers, loss of tools for the growers, and revenue loss for the company. The decrease in product use is a significant motivation for the industry to engage in the issue of pest management. Companies are aware of the consequences of resistance development, and it is imperative that they take the lead in developing strategies that will manage resistance both for new product development and current product maintenance, with the goal of sustaining product use in a resistance management framework. The essence of the resistance management programs needs to be flexible in nature to fit the local conditions.

Industry Goals

The agricultural chemical industry has several goals in the development and implementation of resistance management programs. One goal for resistance management implementation is to have insect resistance management be a key component of the company's product stewardship departments. Management plans that delay or minimize resistance are an integral part of new product development and current product maintenance. As part of new product development, sensitivity baselines are established and monitored after the product is registered. Another example of company product stewardship efforts in resistance management is the annual review of products and resistance management plans. Other efforts in product stewardship include the development of resistance management plans for transgenic plants; such plans include technical teams who oversee the deployment of insect resistance management plans in the field. Certain companies also have resistance management pages on their websites.

Key Tactics

Once the industry goals are established for resistance management, there are a number of key tactics employed by companies in their resistance management programs. It is important to define the mode of action of a product. Because not all products have the same mode of action, this is an important step in identifying which products may be used or should be avoided in a resistance management program. It also is essential that the effective rates are labeled because this minimizes selection pressure. Labeled use patterns, both in terms of application timing and numbers of applications, should be consistent with good resistance management principles. If it has been determined that continual use of one product has the potential to cause resistance, then it is important that the manufacturer has labeling that addresses this issue. This labeling decision needs to be made by the manufacturer and not as a regulatory requirement.

Another key tactic in a resistance management program is to monitor key pest populations for changes in sensitivities to specific technologies or products. For example, when pyrethroid resistance was first observed in cotton, the manufacturers formed a task force that monitored the insect resistance levels and coordinated resistance management strategies.

Other key tactics for resistance management programs include product labels and educational literature. Resistance management statements on product labels can limit the applications to be made in a season as well as indicate the types of chemistries that should be avoided or alternated. Educational literature that increases awareness to resistance management issues should be developed and used in training programs. Industry should involve the research community in the development of resistance management strategies. It also is important that industry communicates with regulatory authorities about the status of resistance management efforts.

Barriers

In spite of the efforts of industry to develop resistance management programs that are flexible and adapted to local conditions, barriers to resistance management implementation still exist. Knowledge about resistance management is increasing, and resistance management plans need to be reviewed regularly and to reflect the state of the current science. The complexity of insect biology, cropping practices, and the size of the systems makes it difficult to have one plan that fits every situation. With this complexity, it is a challenge to implement resistant management plans efficiently and to make programs as practical and flexible as possible. Another barrier in the implementation of resistance management plans is relying on a single tactic in order to save costs.

Some barriers to resistance management implementation are strict regulations that may conflict with local resistance management programs. If the label has mandated recommendations for resistance management that conflict with local resistance management programs, there will be confusion as to which is the correct program to use.

Industry views restrictive regulations as decreased incentives for development of new insect management options. Resistance management regulations have the potential to increase the amount of time and resources required for the development and maintenance of new crop protection technologies that would be important tools in insect management. Potentially, restrictive regulations may add little or no benefit to managing insect resistance and may decrease or delay the number of new options for resistance management.

Resistance management regulations also can add a significant burden to the registration process and be a deterrent for minor use registrations. Additionally, with strict regulations, there will be a shift of resources to the implementation of resistance management programs that would focus on a less-effective tactic, that of label enforcement rather than education.

Another consequence of complex insect resistance management programs is that growers will not use these programs. The net result is that the growers will not avoid using the product but will avoid using the insect resistance management plans. Growers are aware of the costs of IRM practices and will implement those practices that are affordable, simple, and flexible.

Industry holds the view that there needs to be participation from all stakeholders in the development and implementation of insect resistance management programs. The involvement of the U.S. Environmental Protection Agency (EPA) and other regulators in insect resistance management discussions has elevated the importance of this subject. The EPA also has realized the complexities of insect resistance management and has kept most insect resistance management proposals on a voluntary or trial basis. Growers provide valuable practical input and need to be more active in insect resistance management plans. The technical community should help in the development of flexible programs based on sound science.

Conclusions

Delaying the development of pest resistance or maintaining susceptibility is the desired goal of all stakeholders in this debate. But good intentions turned into permanent regulations or requirements in this situation create as many, or more, problems as they solve. History has demonstrated clearly that resistance situations can change rapidly and that at least annual reviews and revisions to programs are needed. The rapidly escalating costs of implementing insect resistance management, borne as they are today by the manufacturers, growers, universities, and extension services, can decrease the incentive for developing and adopting new insect management options and distract from more effective educational efforts.

Resistance management is a dynamic, evolving science that should be widely debated at all levels within academia and by industry and growers. Industry has the most to gain or lose from actions or inactions. Industry can manage and react to resistance issues more effectively without specific regulatory requirements. For resistance management to work effectively, there needs to be active participation and buy-in from the entire crop protection community, including growers, crop consultants, commodity groups, university and extension personnel, and industry.

5.5 Role of Stakeholders in Resistance Management: Pesticide Manufacturers

Gilberto Olaya

Introduction

Fungicide resistance risk studies, the establishment of baseline sensitivity distributions, and the implementation of resistance management strategies are key components of the research, development, and commercialization of a new fungicide in the agrochemical industry today.

Several factors associated with either the fungicide, the plant pathogen, the epidemiology of the disease, or the programs implemented for disease control could contribute to the development of resistance to a fungicide. In many cases, fungicide resistance is caused by misuse of the product. In the past, growers decreased the impact of fungicide resistance by switching to new, very efficacious products. But few new fungicides are reaching the market today because higher quality standards are required for the registration of new fungicides, including increased safety for users and the environment.

The implementation of fungicide resistance management programs requires that several different fungicides with different modes of action be available to the user to avoid or delay resistance development. Resistance management is essential for stewardship and preservation of the fungicide products. General resistance management guidelines can be drawn from estimated resistance risk studies, which consider all the chemical and physical characteristics of the fungicide and all factors related to the biology of the fungus and the epidemiology of the disease. Fungicide resistance should be managed at the local level, however, according to the epidemiology of the disease in the area, the use pattern of the fungicide, and the overall fungicide spray programs used by growers.

Barriers to Resistance Management Implementation

The positioning of a new fungicide in the market usually generates much debate between scientists and marketing managers in the industry. The potential number of sprays, number of sequential applications, and possible resistance management guidelines are discussed. A new fungicide is ready to be introduced into the marketplace when an agreement between technical managers and sales managers is reached based on studies completed on the efficacy of the fungicide, the resistance risk, and marketing plans.

One of biggest limitations for implementation of resistance management programs is the lack of registered alternative chemistries to rotate or to tank mix with the fungicide at risk. For example, there were no suitable alternatives to azoxystrobin for control of foliar diseases on pistachios in California. Due to this limitation, the resistance risk was high for strobilurins on this crop. Another barrier to resistance management implementation could be the sales price of alternative chemistries. The potential fungicide partner for rotation or tank mixing with the fungicide at risk may be very expensive, thereby limiting the acceptance of the resistance management program. This circumstance often leads growers to cut use rates or to stretch spray intervals.

To identify the potential for resistance development as new fungicides move closer to market introduction, resistance risk studies are implemented. These studies focus on historic information on fungicides in similar classes of chemistry as well as on studies on the mode of action. If this information raises any level of concern, isolates of candidate fungi are collected for use in baseline sensitivity studies and evaluation of potential cross-resistance. The specific company or the industry (if fungicides with a similar mode of action are already in the market or are to be introduced shortly) can then design and implement a strategy to minimize the risk of resistance. After the commercial launch of the product, the resistance management program that was implemented could change depending on the evolution of resistance. Lack of fungicide resistance risk studies and/or characterization of the mode of action could affect the prediction regarding the stability and inheritance of the resistance and whether resistance is triggered by changes at the target site.

Education of the user, disease control professionals, consultants, regulators, extension plant pathologist, distributors, and technical and sales personnel is very important for the success of resistance management implementation. Some users believe that resistance is not their problem and that new and better products are coming from industry. The users' focus is on the control of the diseases in their crop in this season and in their profitability. This short-sighted view can lead to development of resistance, which impacts other growers and the entire agrochemical industry.

Goals of Resistance Management Implementation

Resistance develops in plant pathogens after a high selection pressure is exerted by the use of a fungicide. The goal of any resistance management program in industry or any other institution is to manage the potential for resistance by decreasing the selection pressure, which is usually done by decreasing the number of applications.

There are critical studies that help in the implementation of resistance management. These studies focus on the mode of action, resistance risk assessments, baseline sensitivity distributions, and the identification of the mechanism of resistance. Studies of this nature are conducted by industry and in many cases, in collaboration with universities. The research programs can focus only on key representative plant pathogenic fungi. Another component required to implement resistance management properly is the identification of the level and extent of cross-resistance among related members of a fungicide chemistry. This information guides the use of fungicides and decreases potential selection pressure through restricting the use of fungicides in the same cross-resistance group. For example, most of the studies described here have been conducted on the newly developed QoI fungicides. Predictions about resistance development based on those studies have been relatively accurate whereas with other fungicides, the information has been limited and has failed to lead to the appropriate prediction.

After fungicide resistance management programs are developed for the targeted crop diseases, resistance monitoring usually is initiated to monitor the performance of the product and to detect early development of resistance. Industry has been proactive in the implementation of resistance monitoring with studies done in-house or in collaboration with universities. Resistance monitoring has helped to improve or optimize resistance management guidelines. The North America QoI subgroup of the Fungicide Resistance Action Committee (FRAC) also has been very active in the implementation and modification of resistance management programs and has been working toward the industry goal of product stewardship and prolonging the market life of QoI fungicides.

Fungicide producers also need to develop resistance management programs to fit the programs currently in place. For example, there are new fungicide products that are in the same cross-resistance group as the current fungicides on the same crop but that target different diseases. For example, there are QoI inhibitors with strength on the Oomycetes versus the QoI inhibitors that are more efficacious on Ascomycetes and Basidiomycetes.

Fungicide resistance management programs implemented by industry also need the support of universities and extension plant pathologists. Our experience with universities and the QoI-based fungicides has been very positive and has helped us ensure the proper use patterns of the fungicide by growers. Industry also brings the message about the appropriate use of the fungicides to sales and technical service personnel inside the company. This program of resistance management is key for the success of the fungicide strategy and needs to be improved further in the future.

After all studies on efficacy and resistance are completed, the recommendations for use and resistance management are in place, and collaboration and guidelines are in agreement with university and regulatory agencies, we wait for resistance developments hoping that they do not show up.

Goal of Others in Fungicide Resistance Management

A major objective of agrochemical producers is to match a resistance management strategy with state recommendations and IPM programs. The growers would better handle single and local resistance recommendations. Users, disease control professionals, consultants, regulators, extension plant pathologists, distributors, and technical and sales personnel all need to get all involved and contribute to resistance management.

University research could include studies on mechanisms of resistance and influence on epidemics as well as studies on baseline sensitivity distributions. Proper education and training of fungicide users as well as personnel from the different sectors involved in agriculture is required. Extension bulletins always have been an excellent part of grower education.

Fungicide resistance management by industry and working groups also should be supported by FRAC International. The EPA needs to evaluate label language on the resistance management recommendations. Industry and users could be benefit if the review of the resistance recommendations could be expedited.

5.6 Barriers to Implementation

Marvin Schultz

Introduction

Weed resistance to herbicides concerns many sectors of the agricultural community: growers, advisors, researchers, registration authorities, and the agrochemical industry. Weed resistance is of concern to herbicide manufacturers as it may adversely impact the sales and longevity of a product if not managed properly, decreasing the number of tools available for growers to ensure an abundant food supply and profitable production. Resistance management strategies must be effective, reliable, practical, and economical. These strategies, along with the necessity of proper stewardship, must then be communicated effectively to the grower.

To help achieve these goals, the Herbicide Resistance Action Committee (HRAC) fosters cooperation between industry, government researchers, advisors, registration authorities, and growers. The HRAC is an industry-based group chartered by CropLife International to foster stewardship and to communicate the basic principles of herbicide resistance including

- Promotion of a responsible approach and proper use of herbicides;
- Support and participation in research, conferences, and seminars, which increase understanding and scientific knowledge of the causes and mitigation of herbicide resistance;
- Communication of the causes and consequences of herbicide resistance;
- Communication of herbicide resistance management strategies and support for their implementation through practical guidelines;
- Promotion of active collaboration between public and private researchers, especially in the areas of potential problem identification, management strategy development, and implementation; and
- Facilitation of discussion of proper product stewardship among industry representatives.

Barriers to Implementation

The HRAC believes there are a number of barriers that prevent the implementation of effective weed resistance strategies, and it looks for ways to alleviate these barriers as part of its goals and objectives.

One major barrier is the lack of sufficient information available to understand the resistance complex and mitigation practices. A number of factors impact the development of weed resistance to various herbicides. It is important to understand how these factors contribute to the development of the management strategy appropriate for a specific situation. For instance, how do characteristics of the herbicide (molecular, physical, and environmental) impact resistance development? How does the way we use herbicides impact resistance development? Can we identify which weeds, modes of action, and cropping systems are most prone toward selection for resistance? Why does resistance occur in certain field situations but not in other fields with similar use patterns? Can we predict where or when herbicide resistance will occur? One of the goals of the HRAC is to work with academic researchers to identify these information gaps and to promote incentives, including funding, to improve our pool of knowledge about what these factors are and how they impact each other.

Another barrier, related to the lack of technical information already mentioned, is that herbicide resistance management strategies need to be tailored, targeted, and practical in each particular situation to be effective—a “one-size-fits-all” approach is not appropriate. From a global viewpoint, herbicide-resistant weeds are a minor issue, because only a few weeds have developed resistance in a few areas, fields, or patches. At a local level, however, it can be a significant issue. Therefore, resistance management strategies must be tailored to a specific situation and location.

The risk of resistance varies among products, weeds, cropping systems, and cultural practices. Blanket prescriptive approaches cost growers money and may not be appropriate for all products. Instead, strategies must be clear, flexible, and practical for the grower to use. As a result, the HRAC believes that rigid mandatory federal regulations are not the appropriate method to improve implementation of resistance management strategies. Instead, tailored strategies based on product characteristics and grower practices should be developed and promoted through cooperative industry efforts where appropriate.

Still another barrier is that growers generally care about resistance only when it happens on their farm, and also they believe that when it does occur it usually can be managed fairly easily. This perception is based on their history and experience with weed resistance problems. In most cases, alternative products or practices have been and still are available to manage weeds that become resistant to a particular herbicide. And growers generally believe that herbicides with new modes of action will continue to become available to control the resistant weed. It also is important to note that most herbicides control many target weed species and maintain most of their value to the grower despite cases of resistance to a particular weed species. In this way herbicides may differ from other pesticides such as insecticides and fungicides that have fewer target species, and growers may perceive the impact of weed resistance to be less serious than pesticides with a smaller number of selective target pests. Perhaps most importantly, growers will focus on short-term economics and most often will optimize weed control for a current season. Preventative resistance management strategies may require additional input costs without any obvious benefit to the grower’s bottom line.

One of the goals of the HRAC is to improve grower understanding of potential product-specific resistance risks through educational efforts. Another goal is for industry to continue its investment in research and development to identify and fill market needs. To that end, it is important to consider that mandatory regulatory requirements are likely to burden and delay the registration process, thus negatively impacting effective herbicide resistance management by discouraging research investment and registration of new weed control tools.

Finally, one of the greatest challenges to implementation is simply education. Management strategies, once developed, need to reach multiple levels of the distribution chain including manufacturers, retailers, extension personnel, consultants, farm managers, landlords, and growers. Furthermore, educational efforts need to be tailored to reach each of those target audiences. Enhancing education efforts to raise awareness of herbicide resistance and product stewardship is a primary goal of the HRAC.

Stakeholders’ Interests

The HRAC views the goals of other stakeholders to be similar in many cases to its own. For instance, there is general consensus that all sectors of the agricultural community have a role to play in weed resistance management. The ultimate audience is the grower who needs to hear consistent resistance management messages from all stakeholders. The HRAC believes that other stakeholders also would like to see industry expand its educational efforts to raise grower awareness of weed resistance and encourage proper product use, and we share this goal. The HRAC believes that other stakeholders share its view that increased research is needed to improve our understanding of the mitigation and economics of weed resistance management. At this time, there is a lack of consensus regarding the role of federal regulations in herbicide resistance management. Some stakeholders believe that resistance management can be mandated through regulations, whereas others believe, as does the HRAC, that a more flexible and tailored approach fostered through industry is appropriate.

5.7 The Environmental Protection Agency and the Pest Management Regulatory Agency: Pest Resistance Management Goals and Challenges

Sharlene R. Matten and Pierre Beauchamp

Introduction

The U.S. Environmental Protection Agency (EPA) and the Pest Management Regulatory Agency (PMRA) of Canada are committed to promoting and endorsing proactive pesticide resistance management. Under the auspices of the North American Free Trade Agreement (NAFTA), the United States and Canada have joined together to develop and publish guidelines for voluntary pesticide resistance management labeling for implementation in North America: PR Notice 2001-5 and DIR 99-06, respectively. The development of these guidelines was part of the activities of the Risk Reduction Subcommittee of the NAFTA Technical Working Group on Pesticides. Both countries believe that a harmonized approach based on rotation of target site/mode of action for pesticide resistance management would help reduce the development of pest resistance. A uniform approach to resistance management labeling will help support a harmonized approach to joint registration decisions in any or all NAFTA countries and worldwide.

Overall Pesticide Resistance Management Goals

The Environmental Protection Agency

The EPA endorses and promotes the use of effective, proactive resistance management for pesticides to delay pest resistance. For resistance management, the EPA may examine under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) whether pest resistance will pose an increased environmental or human health risk or if resistance would lead to an increase in pesticides that not only would increase pollution but also might pose higher human health and environmental risk. Two of the EPA's strategic goals are (1) to ensure the protection of food safety from the use of pesticides including adoption of reduced-risk pesticides and biopesticides and (2) pollution prevention. Resistance management helps preserve these goals.

Under FIFRA, the EPA has considered the development of pesticide resistance in its regulatory decisions, but it does not have an official overall policy or standard data requirements in place yet. Although lacking an overall policy, the EPA has endorsed and promoted the use of proactive resistance management to decrease the likelihood of resistance and potentially the use of pesticides that pose higher risks to humans and the environment. It is in both the user's and the public's interest to prevent or to manage pesticide resistance. The EPA has developed voluntary resistance management labeling guidelines based on the rotation of mode of action as part of a joint activity under NAFTA. These guidelines are published as EPA Pesticide Registration Notice 2001-5 (USEPA 2001). The EPA believes that this approach to resistance management is sound and would be highly beneficial to pesticide manufacturers and pesticide users.

Because of the adoption of the Food Quality Protection Act (FQPA), pesticide resistance management has become more critical to achieving the EPA's performance goals. This is because FQPA has led to the elimination of many uses of two broad-spectrum pesticides classes, organophosphate and carbamate, that were key components of resistance management programs. Pesticides within these two classes have been noted to pose risks to human health and to the environment. Loss of these broad-spectrum pesticides will put more selection pressure on pests to develop resistance to the remaining pesticide product classes, especially the narrower spectrum, reduced-risk classes, and transgenic crops. Without broad-spectrum pesticides, such as the organophosphate insecticides, minor pests are becoming more major problems and resistance is expected to increase. Pesticide resistance is, thereby, expected to increase in importance as the diversity of broad-spectrum active ingredients decreases and the target spectrum is narrowed.

The Pest Management Regulatory Agency

A key goal of the Canadian PMRA is to prevent or at least delay the development of pest resistance. It is an important part of sustainable pest management and, in conjunction with alternative pest management strategies and integrated pest management programs, can make significant contributions to decreasing risks to humans and the environment. The PMRA believes that all pesticides registered for commercial/agricultural use should incorporate resistance management statements and the Mode of Action (MOA) classification system on the label as specified in DIR 99-06 (Health Canada 1999) by January 1, 2004. The primary focus of this goal—implementation of DIR 99-06, the voluntary pesticide resistance management guidelines based on mode/site of action rotation—is considered to be the linchpin of any program to delay or to prevent development of pest resistance. In addition, the PMRA believes that resistance management should be part of the core pesticide use training at all levels: users, industry, academia, provincial, and federal. Finally, the PMRA feels that it is important to harmonize resistance management efforts under NAFTA, as well as globally.

Status of Mode of Action Labeling under NAFTA

The EPA and the PMRA endorse and promote the use of voluntary pesticide resistance management strategies for all pesticides to mitigate the development of pest resistance. One such pesticide resistance management strategy is the rotation of mode of action of pesticide classes to decrease the selection pressure posed by reliance on only one class of chemistry, thus increasing the likelihood of resistance. As previously noted, the EPA and the PMRA developed voluntary resistance management labeling guidelines based on the rotation of mode of action as part of a joint activity under NAFTA. These guidelines are published as EPA Pesticide Registration Notice 2001-5 (USEPA 2001) and Canada Regulatory Directive DIR 99-06 (Health Canada 1999). These voluntary guidelines provide a numerical system of classification to identify the mode of action of the pesticide on the front panel of the label and to provide resistance management labeling statements in the “Use Directions.” The labeling statements encourage users to (1) rotate between pesticides with different modes of action; (2) monitor for loss of field performance; (3) use integrated pest management (IPM) programs that include resistance management; (4) use up-to-date technical information regarding resistance management, provided by technical representatives from industry, academia, extension, and consultants; and (5) report any suspected instances of resistance.

The EPA and the PMRA believe that this approach to resistance management is sound and would be highly beneficial to pesticide manufacturers, pesticides users, and the public. It is hopeful that registrants will embrace this approach and work with the EPA and the PMRA to implement the PR Notice 2001-5 and Regulatory Directive 99-06 for all relevant products. Both the United States and Canada believe that this approach is an important element of international harmonization. A uniform approach to resistance management labeling will help decrease the development of pest resistance and support a harmonized approach to joint registration decisions in any or all NAFTA countries and worldwide.

To date, the PMRA has approved nearly 300 pesticide labels having either the classification and/or the resistance management labeling statements. This represents approximately 18% of the 1,600 eligible pesticide products registered as approved for agricultural uses in Canada. In contrast, the EPA has approved only 6 pesticides labels with both the classification and resistance management labeling statements. The PMRA has set a target date of January 1, 2004 for full implementation of these guidelines. The EPA has not set a target date, but feels that harmonization with the PMRA is important.

Other EPA Resistance Management Regulatory Activities

Section 18 Policy Revisions

The EPA also believes that effective resistance management should be considered in its issuance of emergency exemptions under Section 18 of FIFRA. This is not currently allowed under existing Section 18 regulations, however. Approximately 30–50% of the 600 Section 18 requests per year cite resistance problems with existing registered alternatives as part of the basis of their request. The EPA is in the process of developing criteria for public comment as to when an unregistered pesticide could be used for the purposes of resistance management.

Mandatory Insect Resistance Management for *Bt* Crops

In contrast to the program for synthetic pesticides, the EPA has mandated an unprecedented insect resistance management (IRM) program for *Bacillus thuringiensis (Bt)* plant-incorporated protectants (PIPs), or *Bt* crops. The EPA believes that *Bt* IRM is important because of the threat insect resistance poses to the high benefits and low risk of using *Bt* proteins in transgenic crops (*Bt* PIPs) and in *Bt* microbial sprays. Both IRM for *Bt* crops and pesticide resistance management for pesticides, in general, were discussed at the Office of Pesticide Program Dialogue Committee (PPDC) in July 1996. At this meeting, the PPDC indicated that the EPA should play a role in pest resistance management, but that it should not make resistance management mandatory for all instances for all pesticides. The PPDC agreed, however, that genes from *Bt* were in a special category and that protection of their susceptibility was in the “public good.” The EPA has mandated seven basic IRM elements for *Bt* PIPs: (1) structured refuges, (2) grower agreements that impose binding contractual obligation on the grower to comply with the IRM requirements and annual affirmation of these obligations, (3) grower education programs, (4) grower compliance assurance programs, (5) annual resistance monitoring programs, (6) remedial action plans should resistance be suspected or confirmed, and (7) annual reports (sales, research, compliance, monitoring).

Special Review

The EPA also has considered pesticide resistance when determining whether an unreasonable adverse effect could occur if registered uses of a pesticide are suspended or cancelled as part of a Special Review process under FIFRA Section 6 (Matten et al. 1996). To date, pesticide resistance was a primary consideration in assessing the benefits of the continued use of the ethylene bisthiocarbamate fungicides (e.g., mancozeb, maneb, metriam, and nabam). There were no reports of fungicide resistance to this class, which is widely used in fruit and vegetable crops.

Adverse Effects Reporting

In 1998, the EPA revised its adverse effects reporting rule (FIFRA Section 6[a]2) to require that substantiated incidents of resistance be reported to the Agency. The Agency’s goal was to use the substantiated incidents of resistance as a way to gauge the extent of resistance in the United States to a particular pesticide. Since this change went into effect, the EPA has received approximately 50 substantiated reports of resistance.

Barriers to Proactive Resistance Management Implementation

The EPA and the PMRA have identified several important barriers to implementation of proactive resistance management strategies. These barriers are the following:

1. A lack of endorsement and implementation of proactive resistance management strategies because of different stakeholder values, beliefs, interpretation of available data, and cost.
2. A lack of research funding and focus for development and implementation of proactive resistance management strategies.
3. Industry reluctance to develop and promote the adoption of voluntary resistance management guidelines, PR Notice 2001-5 and DIR 99-06.
4. A general lack of information on the effectiveness of resistance management strategies. This means that proactive resistance management strategies are adopted before they can be validated in the field.
5. In the United States, a lack of stakeholder consensus on the need for EPA involvement in resistance management. This is especially true for mandatory resistance management requirements.
6. In the United States, a lack of a clear resistance management policy. Under FIFRA, the EPA has the authority to examine the likelihood of resistance (resistance risk) and the consequences of resistance to human health and the environment as well as the benefits of resistance management.

Challenges to Proactive Resistance Management Implementation

The EPA and the PMRA have identified several important challenges that must be tackled before there can be effective implementation of resistance management. These challenges are the following:

1. The need for appropriate incentives to implement proactive resistance management strategies. For example, one possible incentive mechanism would be to use promotional programs for adoption of resistance management that would reward users and the pesticide industry. This may be achieved through regulatory and nonregulatory mechanisms.
2. The need for a more consistent dissemination, diffusion, and adoption of resistance management strategies. That is, pesticide education programs should have a strong focus on proactive versus reactive pesticide resistance management and its long-term (vs. short-term) economic and environmental benefits.
3. The need for clearly identified ways to minimize the use of negative marketing and sales campaigns that impact the adoption of proactive resistance management strategies. That is, there is a concern that if one registrant adopts resistance management strategies for products within a particular mode of action class, they will be at a competitive disadvantage if another registrant with products in the same class does not. There should be a "level playing field."
4. The need for further discussion of resistance management strategies, policies, and mode of classification systems on a global scale.
5. The need for a greater focus on proactive resistance management for reduced-risk pesticides including both chemical and biopesticides. In the United States, implementation of the FQPA has led to a decrease in the number of broad-spectrum active ingredients used for pest control. This has led to a greater focus on resistance management for the remaining active ingredients, including reduced-risk pesticides and biopesticides including plant-incorporated protectants (e.g., *Bt* crops) that are more targeted, focus on a single target site of action, and are believed to be more prone to resistance development. The same changes also are occurring in Canada through the reevaluation of already registered products.

Roles of Other Stakeholders in Resistance Management

The EPA and the PMRA have indicated that all stakeholders have important roles to play in developing and implementing proactive (or reactive) resistance management strategies. These roles, which are roughly the same in the United States and in Canada, are described briefly here.

1. Industry: The primary role of industry is to provide leadership, education, and financial support for the development and implementation of proactive resistance management strategies. This should include development of new reduced-risk active ingredients that can be used in existing integrated pest management programs, as well as innovative ways to use nonchemical alternatives to minimize resistance development or its spread.
2. States/Provinces: The primary role of states/provinces is to provide regulatory oversight, leadership, education, and financial support for the development and implementation of proactive resistance management strategies.
3. The U. S. Department of Agriculture (USDA)/Agriculture and Agri Food Canada (AAFC): The primary role of the USDA/AAFC Canada is to provide leadership in active research, education, extension, funding, and promotion of proactive resistance management and its integration into pest management programs. These federal institutions should be especially important in developing innovative pest management technologies for minor uses that are financially less attractive to industry.
4. Academia and Extension: The primary role of academia and extension is to perform research on proactive resistance management strategies (i.e., testing and evaluation). In addition, both academia and extension are critical to pesticide education and implementation of resistance management strategies. This includes evaluation of the cost effectiveness of different pest control technologies as well as dissemination and distillation of resistance management information into simple, effective messages.
5. Consultants: The key role of consultants is to provide advice to growers on appropriate resistance management practices and strategies for a particular farming operation. They are critical to the successful implementation of proactive (or reactive) resistance management strategies.
6. Users: The primary role of users is to adopt resistance management strategies. They are the key to the success of any resistance management program whether it is proactive or reactive in nature.
7. Public Interest Groups: The primary role of public interest groups is to foster debate and demand

accountability by all stakeholders to use resistance management to provide for continued and improved food safety and environmental health.

Summary

The EPA and the PMRA believe that proactive pesticide resistance management is important to decrease the likelihood of resistance. Both countries have adopted similar voluntary resistance management guidelines based on rotation of mode of action, PR Notice 2001-5 and DIR 99-06. To date, these guidelines have not been adopted fully; approximately 300 labels in Canada and only 6 labels in the United States have used these voluntary labeling guidelines. There are many barriers and challenges to the successful adoption of resistance management strategies, and all stakeholders play a vital role in the development and implementation of proactive strategies.

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5.8 Issues in Pest Resistance Management

Eldon E. Ortman

Introduction

Resistance management has taken a more prominent role in integrated pest management (IPM) programs with an apparent ever-increasing number of occurrences of pest resistance or adaptation to control tactics. The development of pest resistance is a constant reminder of the plasticity of biological systems. Pest resistance, or adaptation to control tactics, is not confined to resistance to synthetic pesticides, although that arena provides the most obvious examples of this phenomenon. Adaptation has occurred with resistant cultivars created by traditional plant breeding mechanisms and to cultural pest control practices. The most notable recent example of the latter is Western corn rootworm (WCRW) laying eggs in soybean fields, which can have a significant impact on the subsequent year's corn crop. In a significant area of the Corn Belt, the use of (an annual) soybean/corn rotation as a primary option for managing the WCRW is no longer efficacious.

Recommended Resistance Management Strategy

What should be our resistance management strategy(s)? I propose drawing on and paraphrasing the PAMS approach used to describe IPM: prevention, avoidance, monitoring, and suppression. Taking those actions that will prevent or avoid the development of pest resistance should be the first and primary approach. Monitoring is an important step; however, resources likely will be a limiting factor in the development and deployment of sampling and monitoring technology. Therefore, it will be critical to prioritize the pest/tactic combinations that are the highest priority for a monitoring activity. Finally, suppression/remediation must be done when a tactic fails. The basic causes for failures should be identified and the more sustainable approaches to mitigating pest problems should be sought.

Questions about Pest Resistance

When pest resistance occurs, one question should be, "Why did this happen?" Generally, the primary situation that leads to pest resistance is the unilateral or overuse of a single pest control tactic. Why is there "overuse"? The tactic's "silver bullet" properties in terms of cost, ease of use, and efficacy are a common cause. Overuse may have resulted from a lack of viable alternatives, inadequate education, regulatory constraints, or a profit-maximizing position. In many parts of the world the overriding consideration for using a control tactic is cost. New chemistries are expensive to develop, market, and deploy. The target specificity of some newer products is problematic for growers/users in areas where economics is limiting. An inexpensive, broad-spectrum product may be affordable and provide control, whereas a more targeted material frequently is more costly and may require use of additional tactics.

Another question might be, "Has IPM failed when pest resistance occurs?" It seems that some of the basic elements, including the use of multiple management tactics and a pragmatic education on the biology and ecology of the target pest as components in an IPM program, may not have been in a highly operative or productive mode.

A third question might be, "Is the best approach to pest resistance management voluntary or regulatory?" The voluntary approach is the most desirable when all involved parties in the public and private sector can reach consensus on the right approach. A basic belief is that people will do the "right thing" if there are good options and these options are clearly articulated (i.e., a good educational program). There have been problems in gaining broad-scale commitment in a voluntary program, however. Further, some options may be costly or problematic to implement, and thus there may be a need to consider incentives. For example, when an alternative presents an increased cost to the user, is it appropriate for a producer to bear the entire burden for a higher-cost alternative when the basis is a general benefit to the environment or to the general public? If it is "a public good alternative," would it be appropriate for the public to share some of the costs? In addition, some alternative tactics or materials may present a greater risk to production. Is some form of insurance a viable option? The regulatory approach is fraught with complications: who regulates, and on what basis; who pays; how is enforcement implemented; what is the cost, etc? The cost for a potentially broad regulatory approach likely will be prohibitive.

Questions about Regulation

Currently there is a limited number of resistance management plans logged in an enforcement or regulatory mode. *Bacillus thuringiensis (Bt)* is a prime example for which there are significant questions about regulation. Some questions have included

- Why is *Bt* regulated in a genetically modified organism (GMO) but not as a spray or dust?
- Why are other pesticides that are created, for example, by the culturing of a natural organism not required to have a regulatory protocol for resistance management?
- Why are other GMO crops not required to have a resistance management plan in force?
- Why are resistance management plans not in place for regulation of synthetic chemicals when already there are hundreds of examples of pest resistance?

There are numerous significant issues that would need to be addressed in developing the basis for a regulatory approach.

A Final Example

A voluntary, research-based, genetic deployment of insect-resistant wheat has been employed in a limited east/central wheat area. Host plant resistance to Hessian fly developed via conventional breeding has been the primary control tactic for decades. An annual survey was conducted to monitor the Hessian fly field population for virulent strain development. Alternative, resistant, host genes were deployed in subsequent years when virulent strains were detected. This approach made it possible to stay ahead of pest evolution and maintain a traditional host plant resistance breeding program as a viable control for Hessian fly.

In addressing the matter of pest resistance management it would seem most advantageous and sustainable to place the primary emphasis on research and education through public and private sector collaboration rather than regulation. Furthermore, prevention should be of higher priority than remediation.

5.9 Interregional Research Project No. 4 Program and Minor Crops: Developing Choices for Pest Resistance Management

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Introduction

The Interregional Research Project No. 4 (IR–4) was organized in 1963 to obtain regulatory clearances for crop protection chemicals on specialty or minor food crops. Most of the minor crops are fruits and vegetables. This paper focuses on how the IR–4 enables growers to make choices in pest control products. More specifically, it describes how biopesticides can be used in pest resistance management. The objective of this paper is to describe some aspects of the IR–4 activities on the registration of conventional crop protection chemicals and biopesticides and how they pertain to pest resistance management. The issues addressed include biopesticides, reduced-risk products, crop grouping, and biotechnology.

Choices in Pest Management

As part of growing crops, producers make choices about varieties and cultural practices that can influence crop yield. Pest management is based on making choices among available pest management tools including chemical and biological methods. The development of resistance to pesticides can be influenced by those choices. Subsequently, the management of pest resistance also is based on making choices in control techniques management. If cultural methods are not adequate and pesticides are deemed necessary for control, the proper tools must be available so that choices can be made. Whereas poor choices may increase the risk or perpetuate resistance problems, lack of available options can leave producers without the ability to choose. Because choice is the key component of pest resistance management, the availability of conventional crop protection chemicals and biopesticides is critical for pest resistance management. Registration costs, low acreage, limited potential for return on investment, and greater liability of minor crops have limited pesticide development in minor crops. Resistance problems are more likely to occur in minor crops because multiple pesticide applications often are needed to protect minor crops at a level necessary to maintain their marketability. In many minor crops there may be no registered product or only one for a given pest, thereby limiting the choices available for resistance management.

Although *varietal selection*, cultural practices, and all forms of pest management are important, IR–4 focuses on registration of crop protection chemicals. The IR–4 is the only program dedicated to assisting the registration of crop protection tools for minor crops. By increasing grower options, there is at least the opportunity to develop a pest resistance management program. The IR–4 program is involved with both conventional pest management products and biopesticides. Considering the resistance management problems and limited choices, both conventional chemicals and biopesticides are needed to develop a meaningful resistance strategy. In the early 1990s the IR–4 program focused on defending older products going through reregistration and had approximately 100 new conventional pesticide uses per year. As a consequence of the Food Quality Protection Act, a strategic partnership was developed between the IR–4 program and the Environmental Protection Agency (EPA). The cornerstone of the partnership was the decision to focus on reduced-risk pesticides for the magnitude of residue projects that facilitated the registration process. As a consequence of the reduced-risk strategy and other efficiencies since the year 2000, the IR–4 program has had approximately 500 new uses per year (Figure 5.9.1) (IR–4 2003). The development of "Super Crop Groups" that involve the development of residue data on reduced data sets has successfully hastened registrations for spinosad and azoxystrobin, and expanded uses of glyphosate into crops that have no preexisting registered products.

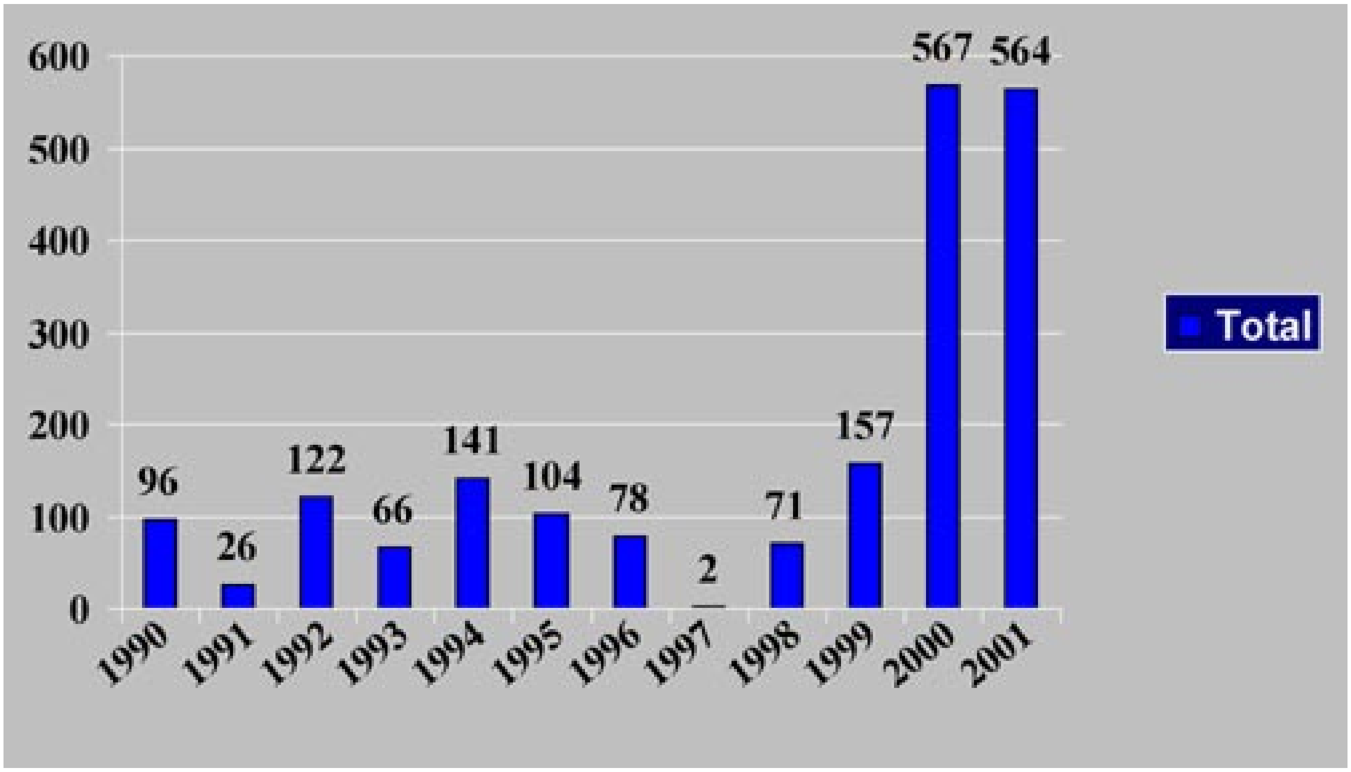

Figure 5.9.1. The number of new uses for conventional pesticides obtained through IR-4 petitions to the EPA, 1990 to 2001.

Biopesticides

Biopesticides are a key component in pest resistance management. In the 1970s IR–4 helped obtain tolerance exemptions for *Bacillus thuringiensis (Bt)* in minor crops. In 1982, the IR–4 formally started a biopesticide program. In 1995 the biopesticide program was expanded to include a grant program. The biopesticide program focuses on assisting registrants through the EPA regulatory process and has a grants program to promote the development of new biopesticides and expanded product uses. In 2002 the IR–4 was instrumental in obtaining 91 new biopesticide uses. Registrants need to develop efficacy data on their products to feel confident about placing additional pests on their label. Many biopesticide registrants are small venture capital companies and may consist of a single individual. There have been over $2 million in grant funds distributed to university and U.S. Department of Agriculture (USDA) researchers, with over $400,000 in 2003 alone. The grant program emphasizes efficacy studies. Projects are classified as early or advanced stage. Early-stage proposals are for products that have an incomplete toxicology package and are not registered yet. Advanced-stage projects are with products that are registered, and often involve label expansion, such as adding a new pest or new crop to the label. Through the grant program, IR–4 project members have been involved indirectly in the development of the most widely used biopesticides in production agriculture.

Reduced-Risk Products

Many of the newer, reduced-risk pesticides have narrow modes of action. Many registrants of strobilurin fungicides have constructed their labels with resistance management in mind. In order to maintain the use of their products they have limited the number of applications per crop. One criterion of being classified as a biochemical biopesticide by the EPA is that the product has a nontoxic mode of action (Jones 2001). Biopesticides tend to have broader modes of action, are generally safer on beneficial organisms, and offer less selection pressure for resistant individuals within the pest population compared with conventional products, making them useful in resistance management programs. Implementing biopesticides into a pest resistance program requires adoption by growers. As they are with conventional products, growers are keenly interested in the efficacy of the products they use. Part of the problem in adoption of biopesticides is that in the attempt to use them, there is a corresponding drop in replacements for conventional products. Conditions such as the age, size, and concentration of a pest influence the ability of a biopesticide to obtain adequate control. The potential range and consistency of efficacy should be considered in the selection of a biopesticide. Some biopesticides are suited better for use under early season, low-level pest pressure, or in rotation with conventional products. The early season use may extend the time that a pest is kept below economic thresholds through the combination of its own activity and the maintenance of beneficial insects or organisms. Use as a rotational product helps decrease the selection pressure toward resistance through repeated use of conventional products. A more proactive approach to the use of biopesticides would be helpful in avoiding pest resistance problems. There are other incentives that growers need to consider with biopesticides. Biopesticides also can be used in situations when a short reentry interval is needed to allow cultural practices to be conducted. In addition, using biopesticides close to harvest can help avoid possible residue problems from a conventional product. As part of the IR–4 Biopesticide Grant Program, it is requested that proposals be designed in an integrated pest management (IPM) program with biopesticides and conventional products to facilitate use in resistance management. Greater emphasis on IPM approaches to project design will be emphasized in the future.

Crop Grouping

The risk for pest resistance in ultra-minor crops is even greater because they are more likely to have very few pest control options. The IR–4 program has been addressing this issue through the use of crop groups. Crop groups are a system of crops with similar botanical and cultural potentials for pesticide exposure and dissipation modes, such that they can be grouped for purposes of setting residue tolerances. Within each crop group there are representative crops that are used for magnitude of residue studies, and the residue levels on the representative crops are used to set tolerances for all members of the crop group. Without crop grouping there would have to be individual tests on each crop. There are currently 19 crop groups in the United States and 20 in Canada. There still are many crops such as tropical fruit that are not currently in an official crop group, making it difficult to obtain registrations. The IR–4 recently held a Crop Grouping Symposium to develop new crop groups and expand current ones (Markle et al. 2002).

Risk avoidance is a key part of pest management decisions, and there are multiple barriers to biopesticide adoption that are beyond the scope of this paper. Incentives for adoption such as eco-labeling and improved market value would lead growers toward incorporating biopesticides into their pest management program and thus indirectly influence pest resistance management.

Several biopesticide products for which the IR–4 has assisted in the registration process (Benmhend, 1999) have been adopted or show great potential for adoption. They also offer pest management solutions under conditions prone toward resistance. Kaolin (trade name Surround) currently holds an approximately 70% market share for the control of pear psylla in pears of the Pacific Northwest (Sekutowski, D. 2003. Personal communication). Kaolin also has been found effective in decreasing glassy winged sharpshooter adults and oviposition (Puterka et al. 2003). Part of the IR–4 process involves obtaining project request forms from public sector scientists, commodity groups, and growers. Mites are a common pest in many minor crops. Mites are very prone to having resistance problems due to multiple generations being produced through a cropping season and great fecundity. Sucrose octanoate and sorbitol octanoate are two sugar esters that have shown good activity on mites and soft-bodied insects. Thymol (Api Life VAR) is a natural product found in thyme and is effective in control of Varroa mite in honeybees. Thymol for honeybees has generated more grower project requests than any biopesticide or conventional product in the 40-year history of the IR–4 program. It has been approved by the EPA for a Section 18 (an emergency use) in several states. Varroa mites already have been found to be resistant to fluvalinate (a pyrethroid) and coumaphos (an organophosphate), which currently are under a Section 18. This highlights the need for the EPA to take a more proactive stance in allowing for multiple Section 18 registrations whereby a conventional pesticide and a biopesticide could both obtain Section 18s as pest resistance management tools. This is especially important because Section 18s are commonly issued to products that have new chemistries and modes of action. The limitation to this one new mode of action accelerates the selection pressure that can lead to pest resistance problems. In addition, pests that need Section 18 approvals often are hard to control and are in outbreaks due to the pests' preponderance to develop multiple resistance to preexisting pesticide chemistries. When successful, new chemistries are developed, other analogs are rapidly produced; therefore, the selection pressure during Section 18 use can impact an entire new line of products.

Impacts of Biotechnology

Biotechnology has had positive and negative impacts on pest control for minor crops. Several pest control systems have been developed and some have been adopted for minor crops (Table 5.9.1) (Gianessi et al. 2001). Several of the developed technologies have not moved forward due to grower concerns about potential consumer reaction. Unlike major crops such as corn or soybeans, which can be stored for long periods, most fruits and vegetables are perishable. Any negative public perceptions of most minor crops would be disastrous. Plant incorporated protectants are evaluated in the Biopesticides and Pollution Prevention Division of the EPA, the same division that evaluates microbial and biochemical biopesticides. Plant-incorporated protectant data packages tend to have specialized studies resulting in greater resources being needed for their review. This also has delayed the time required to have a new product complete the review and registration process for non-transgenic microbial and biochemical biopesticide products.

One of the more prominent biotechnology advancements has been the development of crops resistant to glyphosate, which has provided an effective and less-expensive weed control program for corn, soybean, and cotton. Its success also has decreased the development of new herbicides for major crops. Development of new herbicides for minor crops is dependent on having new products developed for major crops first, because major crops dictate the decision of companies to move forward with the registration process. Therefore, the sharp decrease in herbicide development has greatly lessened the chance of finding new herbicides for minor crops. Most of the herbicides currently used in minor crops were developed over 25 years ago.

Some of the newer products that have adequate selectivity in vegetables are sulfonylurea herbicides. These herbicides are inhibitors of branched chain amino acid synthesis by inhibiting a single enzyme acetolactate synthase. The dependence on a single enzyme system has made sulfonylurea herbicides prone to develop resistance in weeds. Although the timeline for development of pest resistance generally has been shorter for insecticides and fungicides, the lack of new herbicide products makes the long-term prospects for herbicide resistance increase. Overall, the percentage of acres that have benefited from biotechnological approaches has been vastly greater for major than for minor crops.

In summary, the key to avoiding pest resistance problems is to have choices for pest management. The IR–4 program helps to register products for pest control in minor crops so that a greater number of choices are available. These choices are essential for the development of a pest resistance management program.

Table 5.9.1. Potential and adopted biotechnology-derived pest management in minor crops (Adapted from Gianessi et al. 2002)

Pest category	Approved and adopted uses	Potential uses
Diseases	Papaya, Squash	Citrus, Raspberry, Stone fruit
Insects	Sweet corn	Broccoli, Eggplant
Weeds	Canola	Sweet corn, Lettuce, Strawberry
Nematode	———	Pineapple

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5.10 Pesticide Education and Training Programs

Monte P. Johnson

Pesticide Safety Education Program Information

Each state/territory has a Pesticide Safety Education Program (PSEP) Coordinator who directs the training activities and typically conducts training sessions for commercial pesticide applicators. Training for private pesticide applicators—typically growers applying to their own land—mostly is done through county extension offices by county agriculture agents. Commercial applicators apply pesticides as a business and are grouped into specialized categories such as ornamental and turf, agricultural plant, aerial, or right-of-way. After successfully completing training and/or an examination, both private and commercial applicators will be certified to purchase, use, and supervise the use of restricted-use pesticides. The PSEP Coordinators also conduct recertification sessions, which allow applicators to retain their certification by accumulating a certain number of credits during the certification period.

Annual PSEP funding sources include Environmental Protection Agency (EPA) pass-through funds at $1.88 million, other federal funds (such as competitive grants) at $1 million, state funds at $3.93 million, and other funds (such as fees, etc.) at $2.34 million. The PSEP staff supported by these funds includes 55 full time equivalents (FTEs) by the EPA funds and 356 FTEs by other funds. The program also is supported by 1,956 volunteers.

The PSEP Coordinators submit work plans and annual reports through the Performance Planning and Reporting System. From these reports for fiscal year (FY) 2002, we learned that the number of people receiving initial certification training was 114,859, the number receiving recertification training was 311,634, and the number receiving noncertification training was 285,394, resulting in a total of 711,887 people.

Pest Resistance Survey

Thirty PSEP Coordinators responded to a recent survey on pest resistance training activities that asked the following questions:

- In your pesticide safety education sessions, do you address pest resistance? Yes—30; Comments: resistance management is covered extensively; particularly with vegetable and fruit growers; primarily private recertification.
- If you cover pest resistance, is it in initial training, recertification training, or both? Both—20; Initial—2; Recertification—8; Comments: covered in initial training materials; covered in IPM; category specific for commercial applicators.
- Is pest resistance covered in private or commercial training or both? Both—25; Private—1; Commercial—2; No Response—2. Comments: commercial only now, but plans for private; emphasized more for private applicators; emphasized more for commercial applicators.
- How do you cover pest resistance? Inclusion with organic agriculture so conventional growers understand impact; discussed with label comprehension, pesticide mode of action (MOA), IPM; discussions on alternative pest management practices; give examples, usually diseases and MOAs; discuss how resistance happens, cover species of resistant pests; resistance management statements on labels, complying with resistance management for transgenic crops; discuss how to assess MOA, cross-resistance, multiple resistance; discuss herbicide resistance in weeds; resistance management presented as a cost-savings tool; discussed as part of pest control failures; have weed specialists or entomologists cover it; covered in study guides.

5.11 Role of Stakeholders: State Pesticide Regulation

David Scott

Role of the Pesticide State Lead Agency

The current role of pesticide state lead agencies (SLAs) in the issue of resistance management (RM) seems to be somewhat limited. The SLAs are responsible primarily for pesticide product registration and pesticide use regulation in their respective states. For the most part, state product registration efforts are the result of state laws that originally were intended to provide truth-in-labeling for the consumer. States sample pesticide products for purity, focusing primarily on verifying the correct amount of active ingredients and screening for contaminants. Most SLAs rely on the U.S. Environmental Protection Agency for human and environmental screening and assurances. States also rely on the marketplace, researchers, and user and producer industries for efficacy issues, including pest resistance issues. In certain instances, however, states require the submission of efficacy data for registration when exaggerated or doubtful claims appear on product labels. Indiana is one of those states.

The SLAs also are active in product registration related to the federal processes involved in the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) Section 18 (emergency exemption) registrations and FIFRA Section 24c (special local needs) registrations. Although it has not been an issue in many registration decisions to date, a question for future consideration by states will be whether RM can be an acceptable emergency exemption for a product.

The other area for SLA involvement in RM is pesticide use regulation. Currently the use of RM language on product labels is voluntary, and where the label language does exist, it is advisory rather than mandatory. Therefore, there is no role for state enforcement.

Barriers to Resistance Management Implementation

The experience of the SLAs suggests that regulating effective use is a difficult task. In addition, regulating prudent use also is difficult. A good example of this is a review of states that have tried to mandate or regulate integrated pest management (IPM). Although IPM is a concept that most states embrace, developing rules and regulations to make it happen has not been successful consistently. As a further complication, pest resistance may be regional in nature, thereby requiring regional management plans. This does not bode well for national product labels.

From a regulator's perspective, motivating pesticide users to read and follow all parts of a label has been a life's work. Labels in general, however, already are too long and contain far too much advisory information. The longer the label, the less likely the user is to read it. In addition, most regulators have limited interest in lots of advisory language.

Goals of Resistance Management Implementation

Simply stated, the goals of RM implementation should be to keep safe products effective and available for as long as they are needed. With a record of limited success in dealing with pesticide efficacy issues, most SLAs would prefer to limit regulatory involvement. A more reasonable goal would be to educate and motivate pesticide users to implement RM for their own benefit.

5.12 Role of Extension in Management of Pest Resistance

Walter R. Stevenson

Introduction

The economical production of healthy, pest-free plants depends on the careful integration of multilayered components into effective pest management programs. During the past 50 years, however, some in agriculture often have viewed pest control as a "silver bullet" exercise in which a single tactic, typically dependent on a new pesticide or a new family of chemistry, solves a long-standing problem. If a particular material fails in a few years because of pest resistance issues, which is often the case, the sense is that there will soon be another pesticide with equal or even greater efficacy. And so goes the treadmill of optimism, pesticide evolution, and always-changing pesticide use patterns. Resistance management has long been a concern in the world of entomology. In recent years, however, as new herbicide and fungicide chemistries have evolved from multisite to single-site toxicants, weed scientists and plant pathologists have begun to pay much closer attention to managing pest resistance.

Agriculture has a dismal record in managing resistance of pests to pesticides. In short, the insects, weeds, and plant pathogens we are attempting to control are winning the battle. Pest resistance is turning out to be much more complicated than envisioned and the tools we are currently employing to manage resistance are simply not meeting the challenge. As the flow of new pesticide chemistries slows and older chemistries are no longer available for use because of toxicological and environmental concerns and regulatory restrictions, a crisis is unfolding that needs immediate focused attention. The question of the hour focuses on how we retain the efficacy of those pesticides currently in use and what will be our plan for use of new chemistries currently in the developmental pipeline so that we can continue to achieve an acceptable level of pest control.

Resistance Management Plans

Resistance management must be a team effort. Success over time will require a careful integration of thinking and actions of stakeholders including growers and their representative organizations, pest management consultants, pesticide manufacturers and suppliers, the U.S. Environmental Protection Agency (EPA) and government regulators, consumers, and those involved in university research and extension, all playing essential roles. It is in the best interest of all parties, present and future, that pest management systems remain as effective, safe, and as economical as possible.

In the past few years, there have been important breakthroughs in the development of "next generation" pesticides that are safer to the applicator, the environment, and consumers, and that often replace more risky pesticides targeted by the Food Quality Protection Act. Often these "reduced-risk" pesticides are characterized by a highly specific mode of action that can be overcome quickly by a single mutation in contrast to older, broader-based chemistries that have been used for years without the appearance of resistance in the target pest populations. The challenge before us is how to move the newer, safer chemistries into well-integrated pest management programs in which we can avoid selecting for pest resistance and ultimately losing these new materials. Because all stakeholders lose when pest resistance becomes widespread in a pest population, proactive approaches must be developed for stability in pest management programs.

Role of Extension

The traditional role of extension in pest management programs involves working with producers in understanding the pest problems they face, the control measures that are the most economical, effective, and safe to use, and the integration of multiple control tactics with crop production practices. Extension personnel regularly evaluate new and currently available chemistries for efficacy, effect on yield, and crop quality and then formulate state- or region-wide pest management recommendations based on extensive field trials and evaluation. Results of their observations and experience are shared with producers at educational meetings and field days, and in a variety of publications. Because of the complexity of pest resistance concerns and the need to pay much closer attention to the structure and effectiveness of resistance management plans, however, the role of extension in this arena needs to evolve at a rapid pace.

There is a critical need for extension to build upon its historical role and to serve as a leader, drawing together all stakeholders so that proactive, collective thinking can develop to assure routine, widespread compliance with effective resistance management strategies. Some of the areas where extension can play a critical role include the following:

- Establish the baseline of pest sensitivity to new pesticides prior to their introduction on the commercial market and continuously monitor changes in discriminating dosages.
- Provide critical evaluation of new pesticide chemistries in field trials with rate studies to determine the dosage needed for effective pest control.
- Cooperate with the EPA and pesticide manufacturers on focused Experimental Use Permit (EUP) programs before broadscale marketing of new products to better judge how new materials will fit into local and areawide crop pest management programs.
- Evaluate the likelihood of emerging resistance for each new chemistry (*Resistance Risk Profile*) based on projected use patterns, mode of action, and known genetics of target pests.
- Formulate Resistance Management Plans before commercial sales of each new chemistry, with special focus on plan efficacy in the first few years of widespread use.
- Work with pesticide manufacturers in the design of labels to include information on use patterns and resistance management information.
- Work closely with growers so that they are fully aware of the importance of resistance management and what they can do to decrease the risk of pest resistance.

The proactive management of pest resistance is not a goal that is easily achieved given how pesticides are marketed and used by most pest managers. At a time when extension resources are dwindling and there is less, rather than more, interaction between university research and extension faculty and growers, it is ironic and worrisome that the chemical industry also is going through aggressive consolidation leading to loss of field research programs and expertise and vast reductions in technical service to growers. There are intense marketing efforts directed at larger-scale corporate farms at a time when there is less direct contact with smaller-scale family farms that often need hands-on assistance in planning their pest management options. It is absolutely critical that collaborative relationships evolve between stakeholders with common goals and interests for the effective management of pest resistance to become a reality. I see extension acting as a catalyst in developing these relationships and playing the lead role in ensuring the development and implementation of effective resistance management tools.

5.13 Regulation, Research, and Funding

Thomas O. Holtzer

Introduction

Rather than simply providing my own opinions, I made a few phone calls to people who have been involved heavily in academic research on resistance management for some time. From these people I gleaned some good ideas and insights, and I appreciate their willingness to share their thoughts with me. What I will provide here is a distillation of some of those conversations.

Researchers' Interests

So what did I find out? Not surprisingly, it is safe to say that academic researchers are most interested in finding out how things work—that's why they do science. And many also are excited about focusing on how particular systems work so that the information they generate can help solve some very practical problems. Just as clearly, academic researchers do not want to be policymakers and regulators. On the contrary, most are very happy to have someone else doing that job.

Researchers are fully aware that policymakers and regulators have to weigh information and make judgments using factors and perspectives in addition to the sciences of ecology, evolutions, genetics, genomics, and the like. That is as it should be. Often, however, I heard the somewhat frustrated plea from academic researchers that they certainly want decision makers to understand the data and the interpretation of that data from a scientific perspective, and they want that research-based information to be given full and fair consideration in the decision process. In other words, they want decision makers to use the contributions of science to the fullest extent possible. The researchers also felt that they have much to offer decision makers in an advisory role, and that sometimes decision makers do not make extensive enough use of this expertise.

Along these lines, perhaps the most frustrated researchers were those who felt they had been excluded from being part of the advisory process because they had done research specifically related to a particular issue and that particular work had been supported financially by an involved corporation. Although there was some appreciation for the fact that there could be a perception of conflict of interest, there remained the frustration that those who actually know the most about the system under consideration often are excluded from the advisory process.

A much bigger issue for the research community relates to support for research. There is a strong sense that the need for sound research far exceeds the available funding—particularly regarding research that is longer term in scope and focused on the intermediate area between narrow product-oriented efforts and very basic investigations.

Funding

The obvious next question is: "Where should additional funding come from?" There were only two sources that surfaced as potential possibilities: the federal government and industry. Programs within the U.S. Department of Agriculture (USDA)/Cooperative State Research, Education, and Extension Service (CSREES) that could expand funding for resistance management research are the National Research Initiative, regional IPM grants, and the Biotechnology Risk Assessment program. The U.S. Environmental Protection Agency (EPA) also could become more involved in funding. Industry sources were seen as including pesticide manufacturers, corporations that provide seed for genetically modified (GM) crops, and pesticide users such as farmers and pest control operators.

Among the researchers I interviewed I found a variety of ways to look at the funding picture, depending on whether the researcher saw the benefits of research on resistance management as flowing primarily to the public or to private individuals or corporations. Benefits to the public are those that occur when, for example, the federal government builds a road that benefits everyone. With respect to resistance management, public benefits may be such things as longer useful lives of cheaper pesticides or GM crops that we already know a lot about (and therefore understand the risks associated with their use). Prolonged useful lives of some products (e.g., products known to pose low risks) would keep food costs lower and keep environmental and human health concerns in check. Another public benefit of longer useful lives of pesticides would be that public funds have been spent to register pesticides through the EPA and to expand the registration of pesticides through the USDA's Interregional Research Project 4 (IR–4) program. So by investing in resistance management research, the public would be protecting its previous, considerable investment in these pesticides.

Research that decreases pesticide resistance problems may benefit private individuals and corporations by increasing profit potential, by prolonging the profitability of the manufacture and sale of a particular pesticide, or by prolonging the profitability of the production and sale of a particular GM crop. Farmers might benefit from the prolonged effectiveness of a pesticide or GM crop that is cost effective from their perspective.

Regarding benefits to industry, in my discussions with researchers I heard the idea that research that improves our understanding of resistance management primarily benefits the manufacturers because their products remain profitable longer; but also I heard a contrasting perception that pesticide manufacturers actually benefit from the development of resistance. This is because the development of resistance gets rid of cheaper products that have been in the marketplace for a while and that may be off patent. Resistance facilitates replacement of these products by new ones that provide a higher profit potential to manufacturers.

In the course of my conversations, an old idea resurfaced. It goes something like this: a healthy research program could be established from a modest check off or tax on pesticide sales receipts. There also was a variation of this idea: the EPA could increase the fee on new registrations and reregistrations and use this source of funding to support a research program. In some of my conversations, however, the other side of the coin came up—that the beneficiary of resistance research was primarily the public and that the public should therefore fund the research out of general funds (not out of a tax on pesticide sales or a fee on registrations).

Partnership Opportunities

In the spirit of one of the main themes of the Fourth National IPM Symposium held just before this meeting, I would raise the obvious idea that there is a wonderful opportunity for a public-private partnership. My suggestion would be that the pesticide and GM crop producers join with the CSREES and the EPA to establish and fund a Resistance Management Research Program. The program would invest in research in the intermediate range of basic to applied—focusing on understanding the principles of resistance and addressing the most pressing applied research needs. It would not target narrow, specific product-oriented research, however. Detailed research priorities for the program would be developed by representatives of industry, the CSREES, the EPA, and other stakeholders.

Manufacturers would establish a funding mechanism (or request Congress to do so on their behalf) that would provide half the total dollars through a mechanism functioning essentially like a sales tax on pesticides. The CSREES and the EPA would join with industry (including farmers and other users) to request that Congress fund the other half of the program through a new investment of federal general dollars.

If the messages we received at the Fourth National IPM Symposium are valid, Congress would look quite favorably on a plan that brought together the pesticide and GM crop industries with the CSREES and the EPA.

6.1 Industry's Suggestions for Solutions and Working Together

Gary D. Thompson, Graham P. Head, and Caydee Savinelli

Introduction

The creation of this CAST conference and the large volume of work on resistance issues in recent years clearly illustrates that many of us believe that insecticide resistance can have serious consequences for a crop production segment and for the company that developed the product. You will, however, hear widely diverse opinions on how best to address resistance threats. The logic behind certain opinions comes from the fact that no compound has been totally lost because of the local and transient nature of resistance. It also is notable that susceptibility often can be managed after it develops. A good example is mite resistance to dicofol, or Kelthane, that developed over thirty years ago. Today, Kelthane still can be used a limited number of times in most locations and remains a valuable effective tool if growers follow the crop- and pest-specific recommendations. Regardless, there is widespread consensus in industry that resistance management is good for business and that it is most effective when practiced on a proactive basis with the first introduction of a product or trait.

Current Barriers

Before addressing solutions to barriers and improved ways of working together it is helpful to readdress briefly some of the current barriers seen by industry. Often cited are that the crop systems are too large, complex, and dynamic and that it is impossible to get consensus across all parties involved. Our knowledge is continually increasing, options are changing, and it ranges from difficult to impossible to validate resistance management theories due to the long evolutionary processes involved. With this backdrop, it is very difficult to get companies to work together—much less all stakeholders including growers, consultants, distribution, extension personnel, the U.S. Department of Agriculture–Agricultural Research Service (USDA–ARS), university research, and regulators—and to focus our limited resources on the task. The other root cause is that there are too few tactics or there is one tactic that is more cost effective, providing an incentive for growers to overrely on it.

Solutions

There is no easy solution to working together and coordinating efforts; it requires a lot of hard work. Controversy is common and consensus is rare when it comes to resistance issues. Industry has found, however, that for working on broad issues such as resistance management, participating in CropLife task forces such as the Resistance Action Committees (RACs) is much more effective than working alone as individual companies. An individual company does not have the resources or the need to focus continually on resistance management, and a single voice often has much less impact than a united one.

The Insecticide Resistance Action Committee (IRAC) also has facilitated workshops on resistance management for various audiences. We have found that large audiences and broad general debates can raise awareness, but they typically result in little progress towards tangible solutions. Likewise, attempts to provide general strategies on solutions through national regulations are very limited in their effectiveness due to the exceptions required for diverse crop production systems. What has worked well are workshops for growers and continued support of focused local or regional programs that involve growers. It is the growers' understanding of the value to sustainable profitability for their farms and their neighbors' farms that changes behavior from only using the least expensive or most effective tactic all of the time to something more sustainable and appropriate for insect resistance management . These local or regional programs must be practical, simple to implement, and flexible, with regular reviews that adapt to changing situations.

The IRAC also has found value in coordinating efforts on bioassay methodologies, conducting surveys, and providing a coordinated response when resistance first emerges. The IRAC has provided seed money to start research programs but feels that this effort should continue to be dominated by land-grant universities and the USDA–ARS. The IRAC also has played a role in education by developing literature and videos, and by placing ads in the popular press. Education is the activity that can have the greatest impact. Historically, extension services have had the lead role, but they have struggled to take on new projects during a prolonged budget cutting era. The needs here should be assessed and perhaps approached with more funding and partnerships on certain aspects. It is generally known what we should do and not do to manage resistance, but the information is not well distributed and constant reinforcement is needed to change behavior from a short-term focus to a longer-term sustainable one.

There are a few pest/crop situations for which there are too few tactics to keep pests off balance. Industry generally views these as economic opportunities and devotes resources to finding new tools, whereas the U.S. Environmental Protection Agency and the IR–4 have tried to decrease barriers to entry through preferred treatment for minor crops and vulnerable crops and through Section 18 justifications. All of these efforts should be reviewed with a longer-term approach rather than a crisis management approach—the latter being all too common.

Additional resources could be put to good use in many endeavors, but we believe that both current and additional resources should be focused on increased education and support of proactive local/regional programs. Many educational efforts could be general in nature and combine efforts from insecticides, herbicides, fungicides, and general integrated pest management messages. The local/regional programs must be driven by the commodity groups and state extension services with support from industry, academia, and other stakeholders as needed.

6.2 How Can We Alleviate Barriers?

Roger P. Kaiser

Introduction

The first ideas that come to mind when asked about "alleviating barriers" to implementing resistance management are not solutions, but problems. Our current economic system erects significant barriers to cooperation between individuals and companies as we compete in the marketplace. In the short term, one man's gain is another man's loss. When it comes to resistance management, however, the long-term loss of any one class of chemistry or tool for controlling pest populations is a loss for everyone.

Any discussions of resistance management must be held against the background of our economic system. We operate within a system that values individual freedom, personal property, and patent rights. This system is successful, and many alternatives are available to our growers because of competition between companies.

Current Efforts

Although there is some benefit from identifying the problems and defining exactly what is wrong with our current resistant management strategy, I will begin instead with a brief review of our current efforts and successes. We must recognize that there are already severe constraints on the selection and development of new pest control products. Besides the basic hurdles of efficacy, environmental impact, and toxicology, most companies monitor early-stage materials for loss of activity due to resistance. They may conduct "high pressure" trials in which materials are subjected to intense selection and pests are monitored for resistance development. They may run models or laboratory trials that predict resistance. In all instances, resistance management is included when developing the business plan and estimating the market size for a new product.

The Quinone outside Inhibitor (QoI) fungicide chemistry is a good example. Tens of thousands of analogues were synthesized in this area; many could have a unique fit into the marketplace. These differ in their volatility, longevity, intrinsic activity, systemicity, and curative ability, but they all share the same mode of action. The limits of market size, the development of resistance, and the high cost of completing the hundreds of tests necessary for registration have cut the number of new product candidates to a handful. Resistance always is considered when evaluating new compounds for development. The net result with the QoIs is that more resources are going into the development of chemistries with different modes of action and only a few QoIs will reach the marketplace.

With regard to fungicides, most new products have resistance management on the label. There is a recognized procedure for establishing new "Working Groups" within the North American Fungicide Resistance Action Committee (NA-FRAC) and the International FRAC organizations. Label changes are slow, and sometimes the process is painful, but significant progress has been made in reaching agreement on label language and guidelines. Resistance management is just one aspect, just one small extension of integrated pest management. Good product stewardship rewards both the customer and the companies selling the products.

People implement resistance management, not labels, laws, or educational programs. And people are strongly influenced by the culture that surrounds them. Much like the movement against smoking, which has changed the culture from smoking as an accepted practice to one of social disfavor, and like the "recycling" movement (though not as successful), which has made people aware of the limitations in resources and the need to reuse and conserve, resistance management responds to our culture.

The best example of a cultural shift in the pathology area of the agricultural industry has been the fight against late blight of potatoes. Through educational programs, grower meetings, and discussions over coffee at the local diner, late blight has become known as a "community disease." Growers who do not eliminate cull piles, plow down severely infected potatoes, or use clean seed and thereby introduce the pathogen into the township face irate neighbors and public condemnation. We can do the same for resistance management; it can become a community issue with good stewardship as the goal.

Eliminating Barriers

How do we create this same feeling of community in the resistance management arena? What can we do to eliminate barriers to the adoption of resistance management? Education is key. We must change the culture so that good stewardship is a civic responsibility. We must establish resistance management as a community problem with a community solution. Within the pest control service sector this means a strict adherence to the resistance management guidelines at all levels: the basic manufacturers, the dealers, the crop consultants, and the salespersons in the field. We must do what we can, working with the growers to eliminate off-label and nonrecommended uses. When we move the thought process from short-term solution and short-term goals to long-term thinking, then we will have widespread resistance management in the field.

What should be the role of government in this process? There is no question that the force of law and the threat of inspections can have a major impact on the adoption of specific behaviors. With resistance management, however, the issue is very complicated. Resistance management guidelines must be tailored to the local situation and the specifics of the pest and crop interaction. This is not an ideal environment for law and inflexible rules.

There are certain actions that can help, however. First, the regulatory authorities could streamline the process for label changes. The PR Notice on resistance management gives guidelines for making label changes by “notification,” but the language is unacceptable for most pesticide labels. Next, because getting a new product onto the U.S. Environmental Protection Agency work plan has become a major issue, we should discuss adding resistance management as a critical factor for determining “Expedited Review” status. Finally, and this is already underway, we should establish uniform group names and codes for each specific mode of action or cross-resistance group.

These actions, along with many of the other fine suggestions offered during this symposium, combined with an educational program and the efforts of our partners in extension and research, will shift the culture of resistance management. Good resistance management will be the norm within the agricultural community.

6.3 Ways to Work Together

Natalie DiNicola

Introduction

When seeking ways to work together to improve implementation of weed resistance management strategies, there are some general principles that the Herbicide Resistance Action Committee (HRAC) believes need to be considered. First, it is critical to note that herbicide resistance is an issue that affects all stakeholders. Research- and development-based registrants, generic suppliers, retailers, growers, extension agents, and other members of the agriculture community all have a stake in managing weed resistance. To that end, the HRAC believes that there is a benefit to all stakeholders to promote product stewardship, including the use of integrated weed management practices. Weed resistance is of concern to herbicide manufacturers because it can impact the sales and longevity of a product adversely if not managed properly, and members of the HRAC take product stewardship seriously. The HRAC believes that a balance of sound science, agronomic experience, and common sense should be used to manage herbicide resistance. An effective resistance management strategy is one a grower will implement. The HRAC provides a forum for consideration of these principles and development of consistent stewardship goals and best practice recommendations concerning herbicide-resistant weeds.

Goals

The HRAC is committed to a number of goals to promote product stewardship. A primary goal is the development of educational materials to be used by all stakeholders. The HRAC has developed a number of educational materials already, including a mode of action poster, a series of white papers on identifying, confirming, and managing weed resistance, and an HRAC website where interested parties can learn more about herbicide resistance. The HRAC intends to expand its educational efforts with additional materials targeted more directly to the grower, such as educational brochures, presentations, and other materials that can be communicated by members of HRAC and by other interested stakeholders.

A second stewardship goal is to continue to uphold the transparency of scientific findings. In many cases, the HRAC members conduct research, either internally or in collaboration with universities, to investigate the biochemical mechanism of resistance and to identify alternative control programs for resistant weeds. This research is made available to the scientific community and to other interested stakeholders through scientific meetings or publications. The HRAC will continue this practice to further increase our knowledge pool concerning the factors impacting weed resistance.

Perhaps one of the greatest contributions the HRAC has made has been consistent funding of the International Survey of Herbicide-Resistant Weeds website (www.WeedScience.com) managed by Dr. Ian Heap. That website catalogues instances of weed resistance globally and tracks their trends according to mode of action class and weed species. The HRAC will continue funding this website to serve as a resource for numerous stakeholders worldwide.

The HRAC will continue to encourage funding of basic research on herbicide resistance, both internally and externally, to improve our understanding of the resistance complex and to develop appropriate resistance management strategies and their proper implementation.

The HRAC will continue to encourage the development of mode of action-specific resistance management plans that provide a balance of sound science, agronomic experience, and common sense to manage herbicide resistance.

The HRAC has established regional working groups to focus needs at the local level. These regional groups, in turn, often interact with an informal network of national organizations. The HRAC will work to ensure consistency of positions and communications across these regional groups.

The HRAC also has identified certain key stewardship messages to communicate to growers as part of its resistance management campaign:

- Base weed control recommendations on local needs and use the tools necessary to obtain desired weed control.
    - Use the RIGHT PRODUCT, at the RIGHT RATE at the RIGHT TIME!
    - Use good agronomic principles such as cleaning equipment between fields, using certified seed, scouting, and monitoring.
    - Adopt sound agronomic practices such as strategic cultivation, narrow row spacings, multiple herbicides, and crop rotations, as appropriate.
    - Do not allow weeds to reproduce by seed or to proliferate vegetatively. Mow or spray noncrop vegetation to prevent seed production.

- Report instances of unsatisfactory control to your company representative for investigation.

The HRAC will continue to implement these goals to foster cooperation among all stakeholders and to improve resistance management implementation in the field.

6.4 Eliminating Barriers

Roger Carter

This paper represents the views of the membership of the National Alliance of Independent Crop Consultants. Eliminating the barriers to adopting, developing, and maintaining resistance management (RM) practices is paramount for the success of agriculture. All stakeholders should increase industry and governmental support in all three phases: development, adoption, and maintenance. Financial and technical support is needed. Development of more easily manageable and profitable tools or alternative treatments is of primary importance.

Accepting the role of professional, scientifically qualified, unbiased consultants as a medium to transport the technology to the end users (growers) will improve both the flow and the credibility of the information. Continuous training and education of consultants and growers is necessary; having economic incentives for both is a must. The bottom line is that if it isn't profitable for the grower, it won't get done.

All stakeholders must work in unison. Including growers, independent consultants, industry (majors, distributors, and dealers), the U.S. Environmental Protection Agency, the U.S. Department of Agriculture, and university research and extension personnel in each facet of RM is critical to the success of RM programs. Increased communication among all stakeholders is necessary. We should work first in smaller units and then in larger ones to facilitate communication. All information should be transferred in a timely manner.

Although it takes time and money, RM programs should be developed as products are developed. Having RM programs in place before a product (including transgenics) is marketed and selling that concept as a "package deal" with that product will enhance acceptance.

Continuous communication among all stakeholders is a must in development, adoption, and maintenance. Currently there is little dialog among all stakeholders in the development stage; most dialog is between research and industry, with little input from others.

6.5 Lessons Learned: Growers' Perspective

John Keeling

As the Executive Vice President and Chief Executive Officer of the National Potato Council (NPC), I thank you for the opportunity to provide remarks to the Pest Resistance Management Symposium on behalf of the National Potato Council and the potato growers we represent. I have been asked to address briefly the significant barriers to the adoption of resistance management protocols by the potato industry.

The NPC believes that effective resistance management is broadly dependent on two key components: grower education and the adequate availability of crop protection chemicals or biologic agents capable of controlling pests of concern. The NPC is strongly committed to delivering the education component to growers. The obstacles to advancing grower education and product availability are as follows:

- As a minor crop planted on slightly more than 405,000 hectares, potatoes offer relatively low returns to registrants and provide little incentive to new product development.
- The advent of herbicide-resistant, genetically modified organism grains has resulted in an exodus from herbicide development for major crops. Because most minor crop chemicals are developed based on research for major crops, this change will provide additional disincentive for minor product development.
- There are limited chemistries and modes of action available to producers. Particular chemicals are labeled for a variety of crops, likely giving pests some exposure before that product may even be considered for use on a potato farm. The availability of fewer labeled products encourages resistance development.
- Producer groups lack the financial resources to develop and implement grower education programs.
- Resistance management requires global planning and thinking. The efforts by an individual grower will be insufficient if the grower's neighbor is not involved. Organizing more-widespread resistance management efforts is difficult, and such efforts typically do not have the overall incentives necessary for widespread adoption.

6.6 Stakeholder Roles in Resistance Management: Time to Get with the Program

Charles Benbrook

Introduction

Resistance management is like virtue—everyone recognizes its importance yet it is largely dependent on the actions of others. Susceptible gene pools must be looked at, and managed, as public goods that belong to and can benefit everyone.

When resistance moves through a population and an active ingredient or family of chemistry fails, it is important to ask why. Typically, all major players can argue with conviction that fault lies largely somewhere else:

- The U.S. Environmental Protection Agency (EPA) was too slow in registering alternatives (especially if a minor use crop);
- The IR–4 program did not have the resources needed to get needed alternatives through the system, or pursued inappropriate priorities;
- A company pushed its product too hard, or a particularly talented and motivated regional salesman was too successful;
- Rotational product prices were set too high;
- Growers were too eager for a simple solution;
- Prevention-based integrated pest management (IPM) takes too much time and effort because the information needed to make it happen is hard to compile and to interpret properly;
- Resistance pests moved into the area from elsewhere, or are the fault of neighbors who overused the product; or, my personal favorite...
- "I thought the company/extension/my applicator/ a local IPM scout was watching out for resistance."

So the first barrier to resistance management is pretty obvious—we have to get it straight whose job it is. We have to make sure that the people and players in the pest management community responsible for resistance management (RM), or playing a supportive role in RM, have the tools needed to tackle this vital challenge realistically.

Whose Job is Resistance Management?

Is it industry's job? No—industry's job is to discover and bring to market products that will earn a good return on their shareholders' investments. Marketing goals almost always will trump the discipline needed for resistance management. Incentives in the pesticide industry are all volume and sales driven. Plus, resistance can actually be good for business in that it often renders older off-patent chemistry obsolete and opens the market to newer, usually higher-priced, proprietary chemistry and/or transgenic solutions.

Does industry have a major role to play in managing resistance? Absolutely. Their role, indeed their responsibility, is to develop and share the knowledge, science, and information databases from which sound resistance management plans can be crafted, evaluated, and as needed, upgraded.

Companies also must bring into the public arena the results of their annual monitoring of resistance levels in key pest populations around the world. Some king-size institutional innovation is going to be needed to accomplish this goal, because some companies will resist sharing this data for liability and competitive reasons. But somehow, a safe and acceptable mechanism must be discovered to make this critical information accessible to those working at the frontlines of resistance management.

Company technical experts need to work more openly with university specialists and IPM practitioners who are monitoring levels of resistance in local areas. The goal is simple and vitally important: creation of accurate, up-to-date databases on resistance levels in key target pests in all major production regions. Such databases are an essential input in testing and refining resistance management plans (RMPs)—what works, what doesn't, why, and what more is needed?

The huge monitoring task looming before us can be accomplished only through teamwork within an area and through networks linking local and regional teams so that "lessons learned" travel fast and new insights are shared quickly. Our Wisconsin-Florida biointensive IPM Risk Avoidance and Mitigation Program (RAMP) project is working now to create such a network focusing on the half-dozen reduce-risk chemistries that have made such a big difference in vegetable pest management in the Central Sands region of Wisconsin and in South Florida.

Is resistance management the EPA's job? No—the agency's job is to assess the safety of pesticides as proposed for use, and when needed, impose and assure compliance with risk mitigation measures.

By virtue of controlling the science that must support registrations and what goes on pesticide labels, however, the EPA has important roles to play in making sure that sound resistance management practices are identified and adhered to. The deep-set concern over *Bacillus thuringiensis (Bt)* transgenics triggering resistance forced the agency to develop technical expertise on resistance and IRM strategies. It has also established a key precedence: When circumstances warrant, the EPA can and should request data on resistance, including genetic and biochemical mechanisms, models, bioassays, discriminating dose baselines, and RMP strategies. Such data can and should be assessed prior to approving registrations; plus, the data can then be shared with the IPM community in support of initial RM planning.

The EPA also plays a key role as pesticide label gatekeeper. The agency deserves praise for recognizing the need to support resistance management through product labels; the joint EPA–Canada effort leading to today's voluntary labeling initiative started more than 4 years ago.

On the topic of the EPA's voluntary resistance management–mode of action labeling initiative, it is worth noting that nearly two years after the policy was finalized, only a few pesticide companies actually have stepped up to the plate and placed revised labels on products. BASF has the coding scheme on two pyraclostrobin (Cabrio, Headline) labels, Dow AgroSciences has placed it on one spinosad label, and that's it—out of more than 10,000 registered products. Three down; 9,997 to go. On the plus side, Syngenta has voiced support for the initiative and expects to have several products newly labeled this year.

Hopefully one tangible outcome of this meeting will be a pledge from each of the major companies to add the coding scheme to all product labels by the end of 2004. If adoption of the scheme remains spotty, the EPA should impose on the laggards a requirement to submit to the agency all data on discriminating doses and resistance ratios in the company's possession, as well as definitive science showing that resistance management is not necessary.

Are extension specialists and universities responsible for resistance management? No—their role is to enable and support grower activity, not motivate or compel compliance with needed RMPs. Their job is to generate, access, and integrate information needed to support sound resistance management. Our RAMP project team senses that universities and extension specialists need to be playing a more central role in two ways: (1) making sure that resistance management plans are working, and (2) driving the process of upgrading plans where resistance ratios are creeping upward.

Universities and extension are the only players in the system that can work on behalf of the whole system in defining how the efficacy of resistance management plans will be monitored and sustained. They should be given the responsibility of designing and overseeing the implementation of mechanisms to detect and deal with resistance quickly and decisively, such that the integrity of the susceptible gene pool is protected. They must be the ones charged with blowing the whistle when a train wreck appears imminent and should play a major, formal role in determining the scope of necessary additional resistance management practices. Others must shoulder the task of making sure their recommendations are followed.

Are farmers and field IPM practitioners responsible for resistance management? At the end of the day, yes, they are.

Only the people making day-to-day pest management decisions can make resistance management a reality. Resistance management is going to take systematic effort, focus, and resources. We cannot legislate it, mandate it, teach it, or pay for it. The steps needed to manage resistance successfully are too complicated, variable across time and space, and dynamic to capture in laws, regulations, program rules, or incentives. This nut must be cracked in unconventional ways.

Cracking the Resistance Management Nut

Teamwork in support of farm-level efforts and much more fluid generation of, and access to, information are two essential ingredients in cracking this nut. Grower associations and other formal and informal alliances across growers and their pest managers are vitally needed to deal with an inescapable reality—human nature. Resistance management requires collective action across landscapes. The resistance management effort is like a chain, no stronger than its weakest link. There must be a way for growers to work together to shore up weak links, and sometimes those links will be growers with a nonchalant attitude about resistance.

Whether and how growers and the IPM community will deal with cowboys who choose to ignore RMP essentials is a major, unresolved issue. As long as it remains unresolved, the inability to address weak links in the RM chain will loom as a major barrier to successful, sustained resistance management. There are actually some useful ideas and mechanisms in the *Bt* corn Insect Resistance Management (IRM) compliance and remedial action plans, including a process to prohibit further sales to growers not following IRM requirements, intensification of monitoring when a first case of resistance is found, and county- or region-wide suspension of sales and plantings (National Corn Growers 2002).

Do consumers and environmentalists have a role? Not directly, but they do have important supportive roles. They need to help convince legislators to invest in biointensive IPM, which is, after all, the only sustainable way to decrease reliance on high-risk pesticides. They need to keep the pressure on regulators to identify and deal with high-risk pesticide uses, while also working to streamline the registration of reduced-risk and biopesticide products. They also need to recognize that when and how a pesticide is used determines risk outcomes and that resistance management requires diversity in control measures, tactics, and products applied.

Although it is simpler to run a campaign just to ban all uses of a given pesticide, sometimes it is prudent to leave a few moderate-risk uses on the market, with labels limiting use to specific and narrow circumstances consistent with recommended resistance management plans. Pre-bloom stone and pome fruit uses of moderately toxic organophosphates are examples, to the extent that worker exposure and nontarget risks can be managed.

The public interest community has another key resistance management responsibility that is barely on their radar screen. As often-vocal advocates for organic farming, these groups are promoting policy and marketplace changes that will expand the acreage devoted to organic cropping systems. Pest managers on organic farms have a far more narrow pesticide tool kit to work with. As some of today's most promising reduced-risk chemistries gain approval for use by certified organic farmers, resistance management risks will be enormous and the challenge immediate.

Many experienced organic farmers have developed sophisticated, well-balanced cropping systems in which pests simply are not as serious a problem as on other farms. For them, minimizing selection pressure to manage resistance is rarely an issue. But there are many farmers transitioning conventional acreage to organic systems, and most of these growers start the process with the substitution of organically acceptable pesticides for synthetic pesticide products that are not allowed in organic farming. On such farms, the temptation will be great to rely excessively on cost-effective products such as spinosad (SpinTor) or *Bacillus subtilis* (Seranade). In addition, these farmers will have far fewer chemical rotation options, so their resistance management options will be curtailed.

Consumers and environmental advocates who want to see organic farming expand and thrive need to focus attention on the need for targeted research and education on resistance management practices and strategies compatible with organic farming rules. The organic farming community needs to quickly advise growers and certifiers of the risk of resistance and steps that are essential to avoid it. Without such an initiative, resistance to some important new reduced-risk chemistry likely will emerge from excessive use on a few organic farms, perhaps undercutting future sales on both organic and conventional crops. If this happens, few companies will bother again to go through the added effort and expense required to formulate a special product line for use on organic farms.

The Goal of Resistance Management

Our panel has been asked to address the goal of resistance management. This is a no-brainer—the goal of RM must be to preserve the susceptible gene pool in target pest populations such that there is no meaningful erosion in pesticide efficacy. When lifeguards are recruited and trained, their mission is not defined as managing the drowning process, their goal is pure prevention. The same core goal should apply in managing resistance.

What does "no meaningful erosion in pesticide efficacy" mean in the field? Are we flirting with another Delaney Clause? Pest managers can and should rely as heavily as possible on safe, effective products. The only way a pest manager can tell where the line between sustainable use and resistance lies is to push limits, a process that will eventually lead to a measurable loss of efficacy. A "not meaningful," and hence acceptable "erosion of efficacy" is defined as an increase in resistance ratios that is contained and reversible through proven and practical resistance management plans.

In terms of monitoring resistance in the field, a "meaningful loss of efficacy" occurs when a pesticide must be applied at a higher rate of application to achieve a given level of control, and/or delivers acceptable control over a shorter period of time. In the future, crop consultants, experiment stations, and companies will need to carry out well-designed trials to determine use patterns that impose "over the line" levels of selection pressure. Establishing such resistance-inducing use patterns in controlled, contained experiments is a logical way to alert field practitioners when it is time to diversify control tactics, as opposed to just ratcheting upward the intensity of pesticide use and waiting for growers to get hammered by a newly resistant population.

Wisconsin-Florida RAMP Project RM Goals

I am part of a biointensive IPM project focused on intensive vegetable production systems in Florida and Wisconsin. Our team includes Charlie Mellinger, Jerry Brust, Galen Frantz, and twenty-odd scouts working for Glades Crop Care in South Florida, along with several of their grower-clients, and the Wisconsin potato IPM team and its grower-cooperators who have worked together so well as part of the World Wildlife Fund, Wisconsin Potato and Vegetable Growers Association, and the University of Wisconsin collaboration.

In both Florida and Wisconsin, the registration of a number of low-impact, reduced-risk pesticides has set the stage for progress in decreasing reliance on high-risk pesticides targeted by the Food Quality Protection Act (FQPA). In particular, rapid adoption of the nicotinoid insecticide imidacloprid (Admire, Provado) in the mid-1990s and the strobilurin fungicide azoxystrobin (Quadris) in the late 1990s has greatly and positively expanded biointensive IPM options.

Because these products have proved so effective, they are now bearing a major share of the control burden for some major pests in both states. Indeed, selection pressure already is close to or exceeding the limits of sustainable use. Plus, additional active ingredients in the nicotinoid and strobilurin families of chemistry now have been registered, with several more coming. We expect even more intense marketing efforts in the years ahead and downward pressure on prices.

Over time, use of these materials surely will rise, as will the importance and difficulty of managing resistance. Charlie Mellinger, in his presentation, summarized our project's most immediate concerns. Walt Stevenson outlined some of the steps extension needs to take, and is taking in Wisconsin, to "ramp up" resistance management. Here I describe a new tool we are developing to support resistance management planning and practice.

Next Generation RMPs

We are convinced that RMPs in intensive fruit and vegetable production regions must quickly evolve beyond alternating pesticide modes of action in a given field. Mode of action rotation will remain an essential ingredient of resistance management, but will not be enough to sustain efficacy. This is because the movement of pests across landscapes can lead to multiple exposures to critical chemistries within a matter of weeks, highlighting the need for areawide approaches and adherence to recommended RMPs.

Our RAMP project team is developing "Resistance Risk Profiles" that are region-crop-pesticide-pest specific. Resistance Risk Profiles will be used in two ways: (1) to help determine the scope of the specific practices and tactics that should be initially incorporated in Resistance Management Plans, and (2) to monitor the efficacy of RMPs over time and help guide the process of annually upgrading RMPs, when and as needed.

A Resistance Risk Profile will project the likelihood of resistance emerging based on a pesticide's use pattern, mode of action, the genetics of resistance (to the extent known), and field studies where resistance has previously been monitored. Annual profile updates will track changes in discriminating doses and resistance ratios. An upwardly trending resistance ratio, or evidence of resistance in some other production region around the world, will highlight the need for more sophisticated measures to further decrease selection pressure. In this way, Resistance Risk Profiles and RMPs will evolve in tandem. Field experience will sharpen both.

Some of the information needed to complete a Resistance Risk Profile is readily available, but other information inputs will have to be generated through laboratory research and/or field experience. Annual discriminating dose levels are clearly key data inputs, and obtaining these data is a major technical and institutional challenge. It will require new investment, infrastructure, and cooperation to monitor annual changes in discriminating doses on the scale needed.

Our concept of resistance “risk” encompasses both the prospect of a resistant phenotype emerging, as well as the additional pest management and pesticide-related costs and risks that can emerge in the wake of resistance. Accordingly, our Resistance Risk Profiles also will include assessments of the consequences of resistance. In instances where there are many alternative pesticides that work about as well, cost about the same, and pose comparable risks, the consequences of resistance management, or lack thereof, will be much less severe than in instances such as imidacloprid for whitefly control in Florida or azoxystrobin for early blight management in potatoes.

Concluding Thoughts

The director of the IR–4 minor crop tolerance program in the United States, Dr. Bob Holm, has called this the “golden era of pest management” because of the proliferation of highly effective, lower-risk pesticides. Reduced-risk chemistries have indeed made enormous contributions in Florida and Wisconsin in lessening the adverse impacts of pesticide use. We are convinced that new resistance management tools and strategies are needed to sustain this golden era of pest management—and sooner rather than later. The tools must be locally adaptable, readily modified, widely used, and annually reviewed and updated. The scope of change must be driven by the rate of loss in the susceptible gene pool and projections of the consequences of resistance.

New ways must be found to think through resistance management challenges on an areawide basis and to implement management interventions strategically across time and space, notwithstanding field borders and each grower’s unique perspective on what is really driving resistance, who is responsible for it, or changes needed to prevent it.

Major changes in pesticide use patterns driven by exogenous factors such as FQPA implementation and phaseout of methyl bromide have the potential to trigger resistance management meltdowns. As a community, we have to pool resources, knowledge, and experiences to place resistance management innovation on the same timescale as that governing change within susceptible gene pools. I hope this symposium crystallizes our thinking on necessary first steps and reinforces the need to get moving in building resistance management infrastructure with more than a hope and a prayer of meeting contemporary needs.

Literature Cited

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6.7 Lessons Learned: Academic Research Perspective

Thomas O. Holtzer

In the session on the role of stakeholders, I discussed barriers from the perspective of academic research, and my primary focus was on improving the level of funding in support of research in the intermediate area between narrow, product-oriented efforts and very basic investigations. I suggested that much could be accomplished by a partnership bringing together the pesticide and genetically modified crop industries as well as the U.S. Department of Agriculture's Cooperative State Research, Education, and Extension Service and the U.S. Environmental Protection Agency.

Clearly, forging such a partnership would benefit from many people and entities joining together in the effort. But working together is much easier to talk about than it is to do. The folktale featuring the Little Red Hen offers some insights.

> One summer day the Little Red Hen found a grain of wheat. "A grain of wheat!" said the Little Red Hen to herself. "I will plant it." She asked the duck, "Will you help me plant this grain of wheat?" "Not I," said the duck. She asked the goose, "Will you help me plant this grain of wheat?" "Not I," said the goose. She asked the cat, "Will you help me plant this grain of wheat?" "Not I," said the cat. She asked the pig, "Will you help me plant this grain of wheat?" "Not I," said the pig. "Then I will plant it myself," said the Little Red Hen. And she did. Soon the wheat grew tall, and the Little Red Hen knew it was time to reap it. "Who will help me reap the wheat?" she asked. "Not I," said the duck. "Not I," said the goose. "Not I," said the cat. "Not I," said the pig. "Then I will reap it myself," said the Little Red Hen. And she did. So she reaped the wheat, and it was ready to take to the mill to be made into flour. "Who will help me carry the wheat to the mill?" she asked. "Not I," said the duck. "Not I," said the goose. "Not I," said the cat. "Not I," said the pig. "Then I will carry it myself," said the Little Red Hen. And she did. So she carried the wheat to the mill and the miller made it into flour, and she carried the flour home. When she got there, she asked, "Who will help me make the flour into dough?" "Not I," said the duck. "Not I," said the goose. "Not I," said the cat. "Not I," said the pig. "Then I will make the dough myself," said the Little Red Hen. And she did. So she put on a white apron and mixed the dough. Soon the bread was ready to go into the oven. "Who will help me bake the bread?" said the Little Red Hen. "Not I," said the duck. "Not I," said the goose. "Not I," said the cat. "Not I," said the pig. "Then I will bake it myself," said the Little Red Hen. And she did. After the loaf had been taken from the oven it was set on the table to cool. "And now," said the Little Red Hen, "who will help me to eat the bread?" "I will!" said the duck. "I will!" said the goose. "I will!" said the cat. "I will!" said the pig. "No, I will eat it myself!" said the Little Red Hen. And she did.

It is tempting when reading this tale to identify with the title role. Surely we all want to see ourselves as the one who takes charge and persistently does what needs to be done to reach the goal, even when we get no help. But implicit in the folktale is not just the question of whether we fit the title role, but also the question of how we will answer the call to become involved when we are needed most.

6.8 Potential Resources to Address Resistance Management

Eldon E. Ortman

Introduction

The U.S. Department of Agriculture's Cooperative State Research, Education, and Extension Service (CSREES) supports a broad portfolio of research, education, and extension programs in integrated pest management (IPM). Resources are made available in two different modes. The CSREES and the Land-Grant Universities (LGU) are partners in program development. To support that partnership, certain CSREES funds are made available to the LGUs on a formula basis. Those funds are matched by the LGU. The CSREES manages several competitive IPM grant programs that have different goals and objectives. The Request for Applications (RFAs) for each program are different and change over time. The RFAs for those competitive programs have not had a specific line or created a unique identity for resistance management. Within the context of several of the RFAs, however, there would be an opportunity to propose a project that is relevant to resistance management. Those persons interested in resistance management should review the grant program opportunities on the CSREES website for specific RFA information. Following is a brief description of the IPM programs in which CSREES invests resources.

Regionally Focused Programs

Regional IPM Centers (Centers)

Centers, through partnering with institutions and stakeholders, will facilitate the identification and prioritization of regional and multistate IPM research, extension, and education program needs. In fiscal year (FY) 2000, geographically based centers were formed in the north central, northeastern, southern, and western regions of the United States primarily to establish a national pest management information network. Centers of the future will be the focal point for team building efforts, communication networks, and stakeholder participation. Centers will bring together those with expertise, identify needs and priorities, and address a broad range of IPM research, education, and outreach issues. This is a Section 406 national competitive grant program.

Regional Integrated Pest Management Program (RIPM)

The RIPM Program is a regionally based program that supports development and implementation of new and modified IPM tactics and systems, the validation in production systems, and the delivery of educational programs to pest managers, advisors, and producers. The program builds stakeholder partnerships to address critical pest management needs in the region. This is a special research grant program that is regionally competitive and will be managed by the Centers.

Pest Management Alternatives Program (PMAP)

The program goal is to develop replacement tactics and technologies for pesticides undergoing regulatory action for which there are no effective registered alternatives. This program funds short-term development and outreach projects aimed at adaptive research and implementation of tactics that have shown promise in previous studies. The focus of the program is on developing replacements for specific tactics. The intent is to continue current program goals and convert this program to a component managed by IPM Centers. This is a special research competitive grant program.

Nationally Focused Programs (Discovery to Implementation)

Base Support to Land-Grant Universities

The underpinning of the national extramural agricultural research, education, and outreach capability is accomplished through a federal/state partnership with the LGU System. The CSREES provides oversight for the federal annual base support that is provided through the Hatch, Smith-Lever, McIntyre-Stennis, and Evans-Allen Acts. The federal funds are matched and multiplied by state and local resources in support of the national agricultural research, education, and extension infra-structure. This is a formula-based program.

National Research Initiative (NRI)

The NRI pest management research program supports fundamental and mission-linked research on the biology of insects, microbes, nematodes, and invasive plants. It also supports research on the interactions among pest organisms, species of agricultural importance, and their interaction with the environment. This research program is a foundation for the development of the next generation of IPM tools, strategies, and systems. This is a national competitive grant program.

Risk Avoidance and Mitigation Program (RAMP)

The RAMP supports the development and implementation of innovative IPM systems on an area or landscape basis. It is designed to maintain crop productivity and profitability and, at the same time, to address environmental quality and human health issues. The program will involve major acreage crops as well as key fruit and vegetable production systems. Projects funded by this program are long-term, involving systems approaches targeted at eliminating or minimizing pesticide residues in key foods, soil, and surface water. Funded projects tend to be multistate or regional in scale and typically involve multiple cropping systems with emphasis on enhanced stability and sustainability of IPM systems. This is a Section 406 national competitive grant program.

Crops at Risk (CAR)

The CAR program addresses intermediate-term, applied research, education, and extension in IPM for crop and cropping systems. The goal of this program is to develop or modify multiple-tactic IPM systems and strategies focused on specific crop production systems. This is a Section 406 national competitive grant program.

Minor Crop Pest Management (IR–4)

The IR–4 is the principal public program supporting the registration of pesticides and biological control agents for use on minor crops. This program provides coordination, funding, and scientific guidance for both field and laboratory research to develop data in support of registration packages to be submitted to the U.S. Environmental Protection Agency (EPA). IR–4 coordinates the cooperation of commodity producers, state and federal research scientists, and extension specialists in identifying and prioritizing pest control needs. This is a special research competitive grant program, with additional support from CSREES and the Agricultural Research Service base funds.

Methyl Bromide Transitions Program (MBT)

This program addresses the need to develop management technologies, systems approaches, and extension delivery programs for methyl bromide uses that may be cancelled. This is a Section 406 national competitive grant program.

Organic Transitions Program (OTP)

The goal of this program is the development and implementation of biologically based pest management practices that mitigate the ecological, agronomic, and economic risks associated with a transition from conventional to organic agricultural production systems based on national standards. This is a Section 406 national competitive grant program.

Extension IPM Implementation

This is a base program in each state and territory that facilitates the development and transfer of IPM from researchers to implementation by farmers, crop consultants, and other end users. Information outreach occurs through consultations, clinics, workshops, conferences, demonstrations, field days, and a wide variety of publications. This program provides the scientific foundation for IPM. This is a Smith-Lever 3(d) program with funds distributed according to a formula.

Pesticide Safety Education Program (PESP)

The primary focus of this joint EPA/USDA program is to provide educational programs that support the proper use of pest management technologies. A central focus is to provide pesticide applicators with the knowledge and training needed to safely and effectively use pesticides. Education is provided by LGU extension programs in conjunction with state regulatory agencies that certify and license applicators. The EPA provides funds (allocated on a formula basis) and the CSREES manages a national program connecting to the science education base in each state, the District of Columbia, and territories.

Biotechnology Risk Assessment Research Grant Program (BRARGP)

In addition to the IPM portfolio listed here, another potential source of competitive funds is the USDA Biotechnology Risk Assessment Research Grant Program (BRARGP), the purpose of which is to assist Federal regulatory agencies in making science-based decisions about the effects of introducing into the environment genetically modified animals, plants, and microorganisms. In FY 2003, applications must address one of the following program areas or seek partial funding for a conference that addresses science-based risk assessment or risk management of genetically modified organisms released into the environment:

- Research designed to identify and develop appropriate management practices to minimize physical and biological risks associated with genetically engineered animals, plants, and microorganisms.
- Research designed to develop methods to monitor the dispersal of genetically engineered animals, plants, and microorganisms.
- Research designed to further existing knowledge with respect to the characteristics, rates, and methods of gene transfer that may occur between genetically engineered animals, plants, and microorganisms, and related wild and agricultural organisms.
- Environmental assessment research designed to provide analysis that compares the relative impacts of animals, plants, and microorganisms modified through genetic engineering to other types of production systems.
- Other areas of research designed to further the purposes of the BRARGP.

6.9 Lessons Learned: State Regulatory Perspective

David Scott

In general, I believe we have learned that resistance management is not a simple, one-size-fits-all, issue. While that idea is tempting to some people, I do not believe that it is an issue for which there is a simple regulatory fix. Even if regulation were the answer or part of the answer, most states would be required to work it into existing priorities. It would not be a very high compliance priority for most states.

I also believe that if the U.S. Environmental Protection Agency and others feel that states do have a significant role to play in the issue of resistance management, the states must be more actively engaged by those stakeholders relative to the issue. Waiting to involve states, if truly needed, until the end of the process will limit the support from state lead agencies.

6.10 Public Sector Plant Breeding and Pest Resistance Management

Margaret E. Smith

Introduction

A primary objective for many plant breeding programs is improvement of pest resistance to produce varieties that suffer less loss of yield and quality due to pest damage. Not infrequently, such varieties have provided the selection pressure that has led to evolution of resistance in pest populations (e.g., stem rust in small grains [Dyck and Kerber 1985], Hessian fly in wheat [Gallun and Khush 1980]). Judicious application of plant breeding, however, also can contribute positively to pest resistance management, as described in the present paper.

Designing for Sustainability

A plant breeding approach that is designed for sustainability of the agricultural system into which product varieties will fit is most likely to be an approach that will contribute positively to pest resistance management. "Designing" implies an intentional approach, in which the goals and possible outcomes have been carefully considered in advance. "Sustainability" has been defined in many ways, but most definitions incorporate certain common elements. Among these are the ideas that sustainability is the capacity over the long term to satisfy human food and fiber needs, enhance environmental quality and the natural resource base upon which the agricultural economy depends, integrate (where appropriate) natural biological cycles and controls, and sustain the economic viability of farm operations (U.S. Congress 1990). Designing for sustainability, then, involves a thoughtful, intentional approach to developing long-term agricultural productivity in a way that takes advantage of biological cycles, enhances environmental and natural resource quality, and is economically viable.

As they relate to plant breeding, these principles suggest that resistant varieties are a desirable option for pest management (because they take advantage of natural biological controls and have few, if any, negative effects on the environment), that such resistance must be long-standing or durable, and that it must offer an economically viable level of pest control. Designing for sustainability means that plant breeders must seek ways to ensure long-term effectiveness of pest control measures—in other words, ways to manage pest resistance effectively. Several possible approaches to this challenge are discussed in the following sections.

Durable Resistance

Much has been written about horizontal, broad spectrum, or durable resistance (e.g., Gallun and Khush 1980, Simmonds 1999). Often it is equated with polygenic resistance, although this relationship does not always hold true. There are some classic examples of single gene resistances that have proved durable over long time periods (e.g., Simmonds 1999). Knowledge of pest biology often will suggest whether single gene resistance might or might not hold up over time. Highly mobile pests (e.g., airborne fungi) have much greater potential to evolve to overcome a single gene resistance than less mobile pests (e.g., soil-living pathogens).

In most instances, resistance that is durable will be partial resistance rather than complete immunity. Something short of immunity generally is sufficient to avoid economic losses to pests, and certainly decreases the selection pressure experienced by the pest population. The plant breeding challenge inherent in this is that immunity is easiest to spot in large breeding populations and simplest to select for. Selection for partial resistance requires quantification of relative levels of pest damage rather than simply looking for the "clean" plants, and thus is more time consuming and complex. It also is impossible to do in the presence of genes conferring immunity or near-immunity, because these genes mask any underlying variation in partial resistance. Nonetheless, programs that have explicitly targeted partial resistance generally have been quite successful.

Pyramiding multiple resistance genes was difficult or impossible to do based solely on phenotypic selection approaches, but now may be achievable using molecular genetic tools. Pyramiding can combine several different genes for resistance to provide polygenic resistance based on multiple mechanisms of resistance—a combination much more likely to be durable than single gene resistances. Molecular genetic markers also may allow combination of polygenic partial resistance with single genes conferring immunity, provided the markers can capture the majority of the variation for the partial resistance trait. The ability to detect quantitative trait loci that explain most trait variation still is limited, particularly for traits influenced by many loci each of which has a small effect, which is the nature of most partial resistance. With improved molecular genetic marker technology, this limitation should be overcome, and combining single gene immunities with a background of partial resistance should become possible.

Background Resistance Underlying Transgenes

Some of the first transgenic crop varieties that have been successfully marketed carry transgenes that confer near immunity to pests. These include the *Bacillus thuringiensis (Bt)* crops for insect resistance and several disease-resistant horticultural crops. In terms of selection pressure on the pest population, transgenes are no different from genes native to a crop species—immunity still exercises strong selection pressure on pest populations. As discussed in the previous paragraph, the probability of pests evolving resistance to these transgenes would be decreased by incorporating them into varieties that carry partial resistance. This would enhance the lifetime of the resistant transgene by ensuring that the varieties released with it had multiple mechanisms and multiple genes for resistance, thus decreasing the likelihood that a pest could evolve to overcome all of them simultaneously. To my knowledge, this has not been standard practice, but designing for sustainability suggests that it should be.

Identifying Optimal Refuge Varieties

A tactic central to pest resistance management for transgenic insect resistant varieties is the use of susceptible refuge plantings. Little plant breeding effort has been devoted to identifying and/or developing optimal refuge varieties, but this could be done. In a refuge, adult insects that can mate are actually beneficial, but yield or quality loss due to insect damage is undesirable (Losey, J. 2001. Personal communication). Tolerant varieties—those that support a relatively large insect population but suffer little/no yield or quality loss despite that—provide exactly what is needed in a refuge. Tolerance often has been dismissed in developing resistant varieties, because tolerant varieties can allow insect population buildup over time to the point where the variety no longer can withstand the insect pressure and yield or quality losses do occur. Tolerant varieties, however, should be optimal for use in refuge plantings. Plant breeders could certainly devote more attention to screening for and/or breeding such varieties.

Heterogeneous Varieties

Host plant resistance is no different from other pest control tactics in that varying pest control measures over space or time constitutes best integrated pest management practice. This is most apparent for those transgenic pest-resistant plants in which the resistant variety is simply a form of chemical control deployed through the genetic machinery of the plant. We would not advocate pest control through repeated application of exactly the same chemical pesticide over large areas and multiple years. We should not fall into the same trap with simple host plant resistance mechanisms, whether transgenic or not. Heterogeneous varieties can provide diversity in pest resistance mechanisms in the spatial dimension. This is not a new concept; the multiline approach was first suggested fifty years ago by Jensen (1952), but it is still relevant and useful. Varietal mixtures including both resistant and tolerant components would have a similar effect and have been considered for providing the required refuges for transgenic varieties in instances in which individual plants (as opposed to whole fields) can constitute effective refuges. Such mixtures have the advantage that by planting the seed, the farmer will automatically create a refuge. Knowledge about refuges and their management, agreement that refuges are important as a public good, and compliance all are taken care of as soon as the seed is purchased for planting. Heterogeneous varieties are probably an underutilized component for designing sustainable pest resistance management systems.

Novel Sources of Resistance

Fundamentally, plant breeding contributions to pest resistance management rely on the availability of multiple, diverse sources of resistance that differ in terms of their modes of action. Identifying such sources has long been a goal of most breeding programs, and this need will continue. Land races, old varieties, local farmer varieties, and wild and weedy crop relatives all may harbor useful resistance genes. Although such varieties have been good sources of single, simply-inherited pest resistance genes in plant breeding programs, they generally have not been used for extraction of the more complex, polygenic resistances that are undoubtedly also present. Such use has proved difficult due to the unimproved and often unadapted nature of the parent germplasm and hence the difficulty of phenotypically identifying desirable individuals and maintaining multiple resistance genes through a breeding process. Tanksley and McCouch (1997) describe new molecular genetic approaches for more efficiently mining the genetic potential of such varieties. Using these approaches, our gene banks could serve as a rich resource for designing more-sustainable pest-resistant varieties.

The Need for Public Sector Plant Breeding

Breeding and selection of polygenic or durable host plant resistance usually is a lengthy, gradual process. As described in this paper, it provides products that are clearly in the public interest to have available. But the paybacks to such research (e.g., profits) are not immediate. This is the classic description of the type of plant breeding that will most likely be done in the public sector—longer-term projects with unclear short-term profit potential, but that serve the public's interests. Unfortunately, as noted recently by Knight (2003, p. 568), "All over the world, conventional plant breeding has fallen on hard times, and is seen as the unfashionable older cousin of genetic engineering...Government funding of plant-breeding research has all but dried up...." If plant breeding is to continue to make significant contributions toward sustainable design for pest resistance management, this is a trend that clearly must be reversed—soon, and strongly so.

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6.11 Working Together to Remove Resistance Management Barriers and to Adopt Proactive Resistance Management Strategies: A U.S. Perspective

Sharlene R. Matten

Introduction

The mission of the U.S. Environmental Protection Agency (EPA) is to protect human health and the environment. Part of this mission can be accomplished through the adoption of proactive resistance management strategies. The EPA has worked with all stakeholders to achieve proactive resistance management. This has primarily been done on a voluntary basis, except for the case of specific resistance management requirements for *Bacillus thuringiensis* (*Bt*) plant-incorporated protectants (*Bt* crops). To promote greater success in implementation of long-term, proactive resistance management strategies, however, there should be more emphasis on determining common resistance management objectives and goals. This requires more intensive and iterative communication among stakeholders.

Removing Barriers and Working Together to Achieve Proactive Resistance Management

The following goals, objectives, and activities can remove barriers to developing and adopting proactive resistance management strategies. All of these activities involve extensive and intensive stakeholder participation and commitment to achieve success.

First, there must be a determination of common resistance management objectives and goals among stakeholders through both iterative and interactive processes. This common set of objectives will allow every stakeholder to participate in a "win-win" situation to achieve proactive resistance management. To create a common set of objectives and goals, all stakeholders must work toward consensus and motivate cultural changes that will allow full participation in the development and implementation of proactive resistance management. This interaction will allow more fully the development of positive relationships among stakeholders based on mutual respect and trust. Examples of processes and frameworks that are likely to facilitate development of consensus are public workshops, grower meetings, and scientific meetings.

It also is important to have transparent and consistent regulatory processes, policies, regulations, and requirements that are cost-effective and based on sound science. There should be clear economic advantages and incentives for the adoption of resistance management strategies. There also should be voluntary programs that promote the use of pesticide resistance management strategies.

Whenever possible, all stakeholders should work toward obtaining the necessary research funding to support the development, implementation, and adoption of proactive resistance management strategies. There should be a strong financial incentive to maintaining long-term resistance management programs as part of an overall integrated pest management program. All stakeholders must share in the common goal of proactive resistance management.

Summary

The EPA believes that proactive resistance management is important to its overall mission of protecting human health and the environment. There are many steps available to achieve successful proactive resistance management provided there are agreed-upon common goals and objectives. Whenever possible, all stakeholders must reach a consensus as to these common goals and objectives to remove resistance management implementation barriers and to work together more productively.

6.12 Working Together to Remove Resistance Management Barriers and to Adopt Proactive Resistance Management Strategies: A Canadian Perspective

Pierre Beauchamp

Introduction

The Canadian Pest Management Regulatory Agency's (PMRA) primary goal is to protect human health and safety and the environment while enabling access to effective pest management tools. Part of this goal can be accomplished through delaying the loss of pesticide effectiveness due to the development of resistance by pests. The PMRA, in concert with the U.S. Environmental Protection Agency (EPA) has developed specific resistance management labeling as a tool for growers in their day-to-day resistance management activities.

Removing Barriers and Working Together to Achieve Proactive Resistance Management

The Regulatory Directive 99-06 "Voluntary Pesticide Resistance Management Labeling Based on Target Site/Mode of Action" was published in October 1999. The Directive was made available to the industry through mailings, the Internet, presentations at scientific and regulatory meetings, and personal contacts. Unlike the EPA PR Notice 2001-05, DIR99-06 specifically mentions a target date of January 1, 2004 for full implementation of the label changes.

The new label statements proposed in the DIR99-06 can be separated into two parts: (1) assignment of each product to a standard group based on the target site/mode of action of the active ingredient; (2) specific recommendations on how to prevent the development of resistance. These label statements are considered to be the basic information needed by the growers to make the link between resistance management education/recommendation and how to choose and use products to delay resistance development in the field. This is why the addition of the resistance management statements on all Agricultural/Commercial products has been the main goal of PMRA since publication of DIR99-06.

In October 2001, 2 years after publication of the DIR99-06, only 30 labels contained the new resistance management statements. Following that finding, a decision was taken to incorporate in each letter of registration a paragraph asking the company to amend the label at next printing. For new active ingredients, the labeling changes were requested at first label printing.

As of January 2003, 288 products, or approximately 18% of eligible products, incorporate resistance management statements in their labels. It is expected that less than 40% of eligible products will have resistance management statements by the target date of January 1, 2004. At that time, an assessment of the progress will be made and a new approach to resistance management labeling may be considered.

Summary

The PMRA believes that resistance management labeling is essential to delay resistance development. The PMRA, in conjunction with the EPA and in discussion with industry, is hopeful that greater participation by registrants will be forthcoming. Voluntary resistance management labeling has been less successful than hoped and new approaches (e.g., mandatory statements) may be necessary after January 1, 2004.

7.1 Herbicide Resistance Management Strategies for Weeds

Dale L. Shaner

Introduction

Herbicide-resistant weed populations have been selected at a relatively steady rate of nine new biotypes per year for the last 30 years with no indication that this rate is decreasing (Heap 2003). This increase has occurred in spite of the fact that resistance management guidelines have been available and have been taught to growers beginning in the 1970s. The continued rise in herbicide-resistant weed populations indicates that there is some problem either with the resistance management guidelines or in our efforts to educate the farmer in how to use them or the ability of farmers to implement resistance management.

Proactive Versus Reactive Herbicide Resistance Management

Although it seems that it is better to manage resistance proactively rather than reactively, most farmers do not change their weed management practices until after a resistance problem has developed on their farm. One difference between herbicide use and either insecticide or fungicide use is the frequency of applications during a growing season. Insecticides and fungicides often are applied 4 to 10 times per season, whereas herbicides are applied only once or twice. Thus it may be easier to practice proactive resistance management for insects and diseases because there are more opportunities to use multiple mechanisms of action of insecticides or fungicides per season on the pest population.

Another reason for the lack of proactive herbicide resistance management is that the resistance management program will be more complicated and expensive than a program that depends on one highly effective herbicide or herbicide class (Peterson 1999). Furthermore, the cost of the cure for herbicide resistance is the same as the cost of prevention. An economic analysis by Pannel and Zilberman (2001) showed that there was no economic advantage for farmers who were early adapters of resistance management versus late adapters. Hence there is little economic incentive for farmers to practice proactive resistance management.

American Cyanamid introduced a program that attempted to manage proactively the selection of resistance to the imidazolinones (Shaner, Feist, and Retzinger 1997). The program contained multiple elements including education of sales staff, distributors, and users on herbicide resistance; recommendations for effective herbicide mixtures or sequential programs for resistance management; and incentives for farmers to implement these programs. The program was not very successful for various reasons. A survey of farmers indicated that they did not have a clear understanding of how resistance develops or on herbicide mechanisms of action. Their major concern, however, was the cost of implementation of resistance management.

What are consequences of this lack of proactive resistance management? One is that educational efforts to change farmer practices proactively are probably going to be unsuccessful. That does not mean that the farmers do not need to be informed on effective resistance management practices because they will need to know what to do when the problems occur. A survey conducted in Western Australia found that growers were more likely to implement a herbicide resistance management system if they had resistance on their farms and if they had easy access to information on resistance management (Llewellyn et al. 2002). Thus, the aim of educational programs may have to change from proactive management techniques to helping farmers recognize when resistance has been selected on their farms and giving them guidelines on what to do once it has occurred to prevent the problem from spreading.

Role of Resistance Monitoring

There are key technical and managerial elements involved in all antiresistance strategies (Schwinn and Morton 1990). The key technical elements include the following:

- Early evaluation of the inherent risks of selecting for resistance
- Establishment of baselines of resistance in weed populations and development of methods to detect resistance
- Determination of specific use parameters of the herbicide based on cropping patterns, product performance, and weed spectrum
- Development of programs for detecting and monitoring resistance under practical conditions

The managerial elements include the following:

- Determination of use recommendations for the herbicide (i.e., dosage, proportion of area treated, persistence, etc.)
- Integration with other weed control methods
- The ability to enforce recommendations
- Acceptance of recommendations by other companies, academia, and users
- Coordination of recommendations with manufacturers of herbicides with the same mode of action or herbicides used on the same crop
- Implementation of recommendations before resistant weeds develop

Based on these key elements for resistance management, companies need to have a resistance management program in place so they can give farmers the answers they need when resistance occurs. This program should be established during the development phase of a new compound and should include diagnostic tests as well as resistance management practices. Resistance monitoring plays a vital role in determining when and where resistance is occurring and should be part of a herbicide marketing program so that the problem can be detected early before it has spread too far. In Europe, one requirement of registration for a new pesticide consists of an estimate of the risk for selecting resistance, and the establishment of a monitoring system for resistance as well as a mitigation program for managing resistance (Shaner and Leonard 2001).

But it is difficult to conduct a monitoring program, particularly for a herbicide with a new mechanism of action and for which resistance has not yet occurred. Modeling, although imperfect, can be a means to rank weed species according to their probability of becoming resistant. Those species that appear to be the most vulnerable can act as the "canary test" for the selection of resistance and could possibly allow time for a change in herbicide usage that would slow the spread of resistance.

An example is the introduction of glyphosate-resistant crops. Shaner (2000) proposed that there would be an increase in certain weed species once glyphosate became the primary herbicide used. *Conyza canadensis* (horseweed) was identified as one of the species that could act as an early indicator of shifts in weed populations once glyphosate became the primary herbicide used for weed management in glyphosate-resistant crops. It has now been documented that this shift is occurring (Van Gessel 2001), and glyphosate-resistant *C. canadensis* has spread to large regions of the Southeast and East Coast in no-till glyphosate-resistant cotton and soybeans (Mueller et al. 2003). Although this weed is not a particularly hard problem to control with alternative herbicides, it should act as an early indicator of potential problems we may face in the future and a reminder that now is the time to change farming practices to decrease reliance on glyphosate for weed management.

Strategies for Herbicide Resistance Management

What practices have been shown to be the most effective in herbicide resistance management? Certain procedures that are effective in insect resistance management, such as providing refugia for susceptible weed biotypes, have not been shown to be an effective strategy. Unlike insects, weeds are not mobile and pollen flow may not occur at high enough rates to keep susceptibility in the populations. In addition, in many instances, the resistant trait is dominant or semidominant and heterozygous resistant plants will survive and set seed after treatment with a full-use rate of the herbicide. Therefore it is difficult to keep the resistant trait as a recessive trait within a population. Farmers also are reluctant to allow unfettered weed growth in even part of the field, because this location will act as a seed source for the rest of the field and the weed population can spread rapidly.

The generally accepted guidelines for herbicide resistance management are the following:

- Avoid continuous use of same herbicide or mechanism of action (MOA)
- Use other methods of weed control (e.g., physical) in addition to herbicides
- Rotate herbicide MOAs
- Use mixtures of herbicides with different MOAs

- If possible, rotate herbicide mixtures

Two of the most widely used methods for herbicide resistance management are rotating herbicides and using tank mixtures of herbicides with different mechanisms of action. The reason for this is that there is a very low probability of resistance being selected to two different mechanisms of action. But there are problems with this approach because both herbicide classes must be active on the same weed species in order for this to be an effective management strategy. In addition, the use of mixtures often increases the cost to farmers and they are reluctant to add the additional cost until after resistance has occurred, at which time the mixture is no longer effective as a preventive strategy.

One criticism of the use of tank mixtures is that there is an increased potential that resistance will be selected to both herbicides. Although this has not yet occurred, it is a possibility. A way to avoid selecting for resistance to two mechanisms of action simultaneously is to rotate tank mixtures rather than just rotating single mechanisms of action herbicides. These mixtures may not be available, however, and the cost will increase. In addition, it is unlikely farmers will adopt this practice until after resistance has occurred on their farm.

It is important to note that herbicide resistance management is a multiyear process. It has to be part of an integrated system and cannot be done on a year-to-year basis. Weed scientists have been seeking acceptance of integrated weed management (IWM) by farmers for many years (Buhler 2002). In Australia, herbicide resistance has been one of the key reasons for the adoption of IWM by the farmers (Llewelyn et al. 2002). The same could be true in North America.

In order for a resistance management program to be adopted it must to meet several criteria: it has to control the resistant weed(s) effectively, be simple and relatively easy to implement, and be economical. Using herbicide rotation and herbicide mixtures meets most of these requirements and helps explain why they are the most widely used methods for resistance management. With a decreasing number of companies searching for new herbicides and the loss of existing herbicides through reregistration, however, the choices available to farmers may become limiting. This means that we need to preserve the tools that are currently available. Limiting the number of times a particular herbicide mechanism of action is used over multiple years may help delay the selection of resistance (Beckie and Kirkland 2003), although it probably will not stop resistance. Farmers also need to be well educated on resistance management and on the mechanism of action of the herbicides they are currently using. Placing the mechanism of action on the label, which is currently done on a voluntary basis, should act as a good educational tool and help farmers make more informed choices (Beckie, Chang, and Stevenson 1999; Mallory-Smith 1999).

Ultimately, resistance management comes down to implementation at the farm level. The methods for management are straightforward and, in most cases, relatively easily done. Farmers, however, will change their practices when they see value in the changes or they are forced to make changes due to a resistance problem. Strategies need to be in place to provide answers to these problems as they arise and methods need to be developed to allow detection of the problem as early as possible, so that resistance does not spread.

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7.2 Pest Resistance Management Goals: Monitoring Insects

D. D. Hardee

Introduction

From 1996 to the present, the U.S. Department of Agriculture–Agricultural Research Service (USDA–ARS) at Stoneville, Mississippi has provided the only program for the U.S. cotton industry designed to monitor bollworm (*Helicoverpa zea* [Boddie]) and tobacco budworm (*Heliothis virescens* [F.]) for possible development of resistance to the Cry1Ac δ-endotoxin (*Bacillus thuringiensis* [*Bt*]) in transgenic cotton. To date, no significant and recurring changes in tolerance have been detected, nor have any field control failures due to such tolerance been reported. As novel proteins are introduced into *Bt* cotton for commercial use in the future, monitoring will of necessity be more complex, detailed, and expensive. The ARS, consultants, cotton producers, and state experiment stations are initiating proactive programs to improve the reliability of the monitoring program to ensure long-term effectiveness of this valuable technology.

Pests in Cotton

Worldwide, cotton (*Gossypium hirsutum* L.) is a pleasing target for insects of all types. United States cotton is no exception—at least 15 insect species in some years and in some parts of the U.S. Cotton Belt can cause moderate to extensive damage (Williams 2002). Insecticides remain the solution of choice for most of these pest problems in cotton fields. One of these pests, the boll weevil, *Anthonomus grandis grandis* Boheman (Coleoptera: Curculionidae), is on the verge of total elimination from the United States with the aid of a combination of insecticides, cultural control, and traps and lures (Hardee and Harris 2003). Need for insecticides to manage three other major pests, pink bollworm, *Pectinophora gossypiella* (Saunders) (Lepidoptera: Gelechiidae), tobacco budworm, *Heliothis virescens* (F.) (Lepidoptera: Noctuidae), and bollworm *Helicoverpa zea* (Boddie) (Lepidoptera: Noctuidae), has declined in some production regions since 1996 because of the commercial introduction and use of transgenic cotton (Hardee et al. 2001).

Genes from the bacterium, *Bacillus thuringiensis* Berliner, for the production of the insecticidal protoxin (Cry1Ac δ-endotoxin, or *Bt*) have been inserted into the genome of several crops, including cotton and corn, to control certain pests. The development of resistance to Cry1Ac in *Bt* cotton has been a major concern, because all parts of the cotton plant contain the toxin all season, and thus potentially resistant pests are afforded a greater opportunity to survive and to produce resistant populations (Gould 1998). Current resistance management plans for *Bt* cotton have the signal feature of relying on the "refuge/high dose" strategy that combines transgenic plants delivering very high doses of toxin, supported by the nearby presence of non-*Bt* plants, or refuges. A high-dose strategy based on simple models that used mostly results from laboratory studies (Gould 1986) and the requirement of plantings of non-*Bt* cotton as refuges to produce susceptible insects for mating with surviving resistant individuals have been mandated by the U.S. Environmental Protection Agency to retard total population resistance. Growers may choose one of the following refuge types for 2003:

1. Plant an external refuge of at least 20 acres (a.) of non-*Bt* cotton for every 80 a. of *Bt* cotton within 1.0 mile of the farthest *Bt* cotton to provide *Bt*-susceptible moths; refuges can be treated with any non-*Bt* insecticide for any insect
2. Plant at least 5 a. of non-*Bt* embedded refuge at least 150 feet (ft) wide for every 95 a. of *Bt* cotton as a contiguous block within the *Bt* field; the refuge may be treated with any insecticide applied to the *Bt* cotton
3. Plant at least 5 a. of non-*Bt* cotton for every 95 a. of *Bt* cotton; this acreage may not be treated with any insecticide labeled for bollworm (BW) and tobacco budworm (TBW) and must be at least 150 ft wide and within 0.5 mile of *Bt* cotton.

Depending on results from 2002–2003 alternate host studies, some of these options may be subject to change for the 2004 crop year.

Monitoring Program

In addition, the USDA–ARS at Stoneville, Mississippi was selected in 1995 to initiate and continue a U.S. Cotton Beltwide monitoring program to detect any changes in resistance or tolerance levels from year to year. Such changes in tolerance would then be used to recommend resistance management procedures and remedial action plans if levels of tolerance and/or resistance were detected. Since the 1996 crop year, the ARS's Southern Insect Management Research Unit (SIMRU), in cooperation with farmers, consultants, and state experiment stations and extension services across the southern United States, has conducted a monitoring program to compare colonies of TBW and BW collected in various states to highly susceptible, laboratory-reared colonies of both species (Hardee et al. 2002). These procedures have changed over the years but essentially consist of a larval bioassay in which insects are fed on an artificial diet containing a small dose of Cry1Ac found in a foliar *Bt* product, MPVII. This dose is similar to the concentration found in *Bt* cotton.

Fortunately for the entire cotton industry, with the exception of a slight but as yet unexplained increase in tolerance of BW in 1998 (Hardee et al. 2002), no changes in overall susceptibility in both species had been detected through 2002. Multiple reasons for the continuing effectiveness of *Bt* cotton with no sign of change in susceptibility have been suggested. Some of these include effectiveness of the refuge concept, higher than expected contribution of susceptible insects from alternate crops and weed hosts, small percentages of *Bt* cotton planted in many locations, and greater susceptibility of resistant BW and TBW to other factors such as winter kill, application of insecticides for other pests, and biological control agents. A combination of these reasons, and perhaps other unknowns, may be contributing factors. Regardless of the reason(s), we can state with confidence that through the 2002 growing season, no tolerance had been noted at a high enough level to cause control failures in the field.

It is not surprising that the refuge concept and monitoring program have both had their share of challenges and critics. The requirement of non-*Bt* refuges, regardless of the option chosen, has been met with considerable skepticism by growers, consultants, and certain cotton entomologists and geneticists, especially because certain assumptions of the models used to predict refuge needs are not met (Peck, Gould, and Ellner 1999), and no data exist supporting the efficacy of the refuges. Thus, the assumption that refuges are effective is based mostly on theory, not fact. Another criticism of the refuge concept currently in place is that all sections of the Cotton Belt, regardless of agricultural practices and pest complex, have the same refuge requirements. To obtain more defensible information on the production of susceptible populations of pest insects by other host crops, the ARS in Mississippi, Monsanto Ag, and cotton entomologists from Arkansas, Georgia, Louisiana, and North Carolina have just completed the first year of a 2-year study to determine the number of BW produced by corn, grain sorghum, peanuts, and soybeans in an agricultural environment. Preliminary results indicate that higher numbers of BW than expected were produced in most of these crops (refuges). This is an important finding because BW is less susceptible to Cry1Ac than TBW, Cry1Ac in *Bt* cotton is not considered high dose for BW, and this insect is predicted to be the most likely to develop resistance to Cry1Ac. Pyramiding genes for a two-toxin system to be introduced to the grower in 2003 in transgenic cotton (Adamczyk, Adams, and Hardee 2001; Sachs et al. 1996; Tabashnik 1994) may overcome the challenge to decreased susceptibility in BW, but the effect of dual-toxin *Bt* cotton on increased potential for cross-resistance is yet to be determined.

Skeptics of the monitoring program through 2002 have stated that we are not sampling a large enough field population to detect low levels of tolerance, and our use of moths from pheromone traps fails to test the possible presence of recessive resistant genes in the native population. Both of these concerns have merit. In order to test the numbers of insects suggested as being needed would require considerably more collective manpower and funds than currently are available for this program, even though we have consistently increased and improved our effort since 1996. While with the ARS at Stoneville, D. V. Sumerford (unpublished) attempted to detect recessive resistance through an F_2 screen (Andow and Alstad 1998; Andow et al. 1998; Venette, Hutchison, and Andow 2000) but was unable to show conclusively that any existed. In 2003, the ARS is taking proactive steps to study the possibility of recessive resistance genes by cooperating with entomologists in states and locations growing a high percentage of *Bt* cotton annually since 1996. These studies will include season-long collection of eggs from moths captured in light traps, followed by extensive bioassays and cross mating. In addition, we will increase our general monitoring program by at least 50% in 2003 to include more states and cotton-producing regions.

Bt resistance monitoring in the future undoubtedly will increase in importance and complexity.

For example, in 2003 alone there will be two dual-toxin systems introduced. These will involve the need to bioassay populations for susceptibility to not only Cry1Ac, but also Cry2Ab, Cry1F, and possibly their combinations. These make up the transgenic cottons known as "Bollgard II" (Monsanto Ag) and "Wide Strike" (Dow Agrosciences). In addition, on the horizon are other products such as "Vip" (Syngenta's Vegetative Insecticidal Protein). All of these new products offer a wide range of effectiveness against many other lepidopteran pests of cotton that may lead to the need for monitoring programs for other insects.

At the moment, Mid-South and Southeastern cotton entomologists are drafting a resistance mitigation plan for BW and TBW in *Bt* cotton. Because of the dual insect and multiple host situations in the Mid South and Southeast as opposed to the single host pink bollworm in the arid Southwest, an acceptable plan of mitigation will require the collective thinking of the entire cotton and chemical industries.

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7.3 Resistance Management Strategies for Plant Pathogens

Barry J. Jacobsen

Introduction

Plant protection pesticides have played and will continue to play a critical role in integrated disease management strategies for the foreseeable future. Until the 1970s, plant pathologists did not have to consider pathogen resistance to fungicides (Brent 1995), bactericides (McManus and Stockwell 2001) or nematicides. Today this is a major consideration when developing integrated disease management strategies that incorporate modern fungicides and bactericides. Resistance of nematodes to nematicides has not yet become more than a conceptual problem (Moens and Hendrickx 1998), whereas bacterial resistance to streptomycin and fungal resistance to benzimidazole, phenylamide, sterol demethylation inhibitors, and quinine outside inhibitors (strobilurin) fungicides have caused significant losses to farmers. Prevention of further losses and maintenance of the use of these valuable crop protection tools will require understanding of the scientific basis for development of resistance in plant pathogen populations, strategies for prevention, and a commitment to stewardship by manufacturers, dealers, extension educators, consultants, farmers, and federal and state regulatory agencies. Support for basic scientific research by both the public and private sectors dealing with development and persistence of resistance in plant pathogen populations is critical to developing appropriate strategies and regulation.

Plant pathogen resistance to transgenic events that provide host plant resistance have not yet been identified, but there is reason to expect that pathogens will express genes that allow them to attack these transgenic plants. It is critical that the risk of pathogen resistance to both transgenic plant protection events and to plant protection pesticides be assessed and strategies be developed to retain these valuable disease management tools.

Risk Assessment

The assessment of risk of pathogen resistance must serve as the basis for development of management strategies. Assessment of risk relative to fungicide resistance has been reviewed by Brent and Holloman (1998). Critical factors identified by these authors include mode of action(s) of fungicides, site specificity in the pathogen, genetic variability in pathogen populations, factors involved in cross-resistance, and factors involved in the selection and survival of resistant individuals in pathogens. These authors developed estimates of inherent risk of failure or diminution of control based on structural classes of fungicides and mode of action of fungicides. Based on field experience to date, the authors have estimated failure relatively accurately. Factors included primary and secondary mode(s) of action; site specificity and intensity of use of the fungicide; and characteristics of the causal agents of disease such as whether the pathogen is mono or polycyclic, capacity of the pathogen to produce and retain resistant individuals in the population, the isolation of the pathogen population, and implementation of other control strategies.

The Fungicide Resistance Action Committee (FRAC) has classified fungicide classes as having high, moderate, or low risk potential for performance failure (FRAC 2003 a,b). Those with high risk are characterized by having highly specific sites of action, use as eradicants, persistence, high dose strategies and intensive use without other effective tools being used for disease control. Those with low risk potential are characterized by having multiple modes of action, important secondary modes of action, lack of eradicant activity, and lack of observed cross resistance. Pathogen characteristics that create high risk are multiple cycles of infection on a crop, fast generation time, high level of reproduction, high potential for genetic variation due to sexual recombination, the parasexual cycle, or high mutation rate, high fitness of resistant individuals, isolated nonmigratory populations, and an obligate nature of parasitism. Another significant factor is the use or nonuse of integrated disease management strategies wherein the more diverse the management tools used, the lower the risk of development of resistance. The lack of basic information on pathogen genetic variability, inheritance, and fitness as well as on secondary modes of action of fungicides are significant obstacles to predicting risk with greater reliability. The considerations previously described for fungicides also are important for risk assessment for bactericides, nematicides, and transgenic pathogen control events.

Management of Plant Pathogen Resistance

Fungicide resistance management has been reviewed by Brent (1995) and Brent and Holloman (1998). The following key points are made by these authors, proved with field experience, and appropriate to all plant pathogen management tools:

1. Do not use products with high or moderate risk in isolation. Use two or more modes of action in combination or alternation in control programs. Specifically, integration of products with low risk potential with those of higher risk is desirable. Generally this has meant using high risk products with low risk ones either in combination or in alternation. In practice this has been relatively effective; however, the use of a protective contact material in combination with a systemic material does not prevent selection of resistant individuals by systemic materials inside the plant. The concept of combinations of protective contact materials and systemics for resistance management is weakened when the protective contact material has markedly shorter effective residue periods. Only the use of two systemic materials with different modes of action will decrease the probability of selection of resistant individuals within plant tissues.
2. Restrict the number of treatments of high risk products per season and avoid eradicant use. Intensity of selection pressure is clearly a factor in development of significant populations with resistance. Disease prediction and action thresholds clearly must take this into consideration.
3. Use full manufacturers' recommended dose. Clearly, that is the preferred strategy where major gene resistance is anticipated; however, where multistep resistance is anticipated, lower-than-recommended dose strategies may not lead to buildup of highly resistant populations. This latter point is not completely clear and more basic scientific information is needed.
4. Use disease control products integrated with other pathogen control strategies. Integrated or diverse strategy disease management programs are more stable than those dependent on a single factor. Disease control products should be used with other tactics such as traditional host plant resistance, crop rotation, biological control, cultural and regulatory controls, and with other strategies such as induced host resistance. Any factor that decreases pathogen populations and their survival will decrease the risk of pathogen resistance development.

Creating the Environment for Management of Plant Pathogen Resistance

Critical to the implementation of these management concepts is the availability of diverse types of pathogen management tools. This means continued registration of existing products with low risk for resistance development and registration of new products with different modes of action. New registrations must address the full range of disease control products including biological controls, pesticides, transgenic crops, and products that induce systemic resistance in plants. Equally important is development of a stewardship ethic by all stakeholders. Manufacturers and their marketing groups must take a long-term view of sales of moderate or high risk products. Consultants, food company pest control managers, extension educators, and farmers should emphasize integrated strategies based on sound science. Finally, private and public support for pathogen population resistance monitoring programs, basic science, regulatory programs, and educational programs that support pathogen resistance management must be in place.

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7.4 The Use of Information Technology in Resistance Management and Refuge Compliance

Dennis D. Calvin and Joseph M. Russo

Introduction

Information technology provides a framework to analyze complex problems and provide crop and pest management guidance. Managing resistance within pest populations against control technologies is a topic of increasing importance and one for which information technology can provide help (Ffrench-Constant and Roush 1990; Marcon et al. 2000). This paper is designed to show how information technology can (1) provide a valuable framework to analyze the need for using a pest management technology and (2) provide refuge compliance guidance. Before discussing the use of information technology in resistance management and refuge compliance, it may be instructive to discuss the value of *Bacillus thuringiensis (Bt)* corn hybrids today.

Value of *Bacillus thuringiensis* Corn Hybrids

In 1996, the first transgenic corn hybrids that produced the insecticidal protein Cry I A(b) were released commercially to protect against European corn borer (ECB) and several other Lepidopteran pests. These hybrids were the result of biotechnology methods used to transfer the gene that codes for Cry A(b) from *Bt* ssp. *kurstaki* into the corn plant genome. Since their initial introduction, *Bt* corn hybrids have captured approximately 22% of the corn market (National Corn Growers Association, 2003). The U.S. Department of Agriculture (USDA)–Economic Research Service (ERS) estimated that about 19% of the corn acreage in 2001 was planted to *Bt* corn hybrids, with use peaking in 1999 at about 26% of corn acreage (USDA–ERS 2003). Certain counties in the United States have adoption rates as high as 70 and 80%. In 2003, corn hybrids that code for the Cry 3B(b) protein were released commercially to protect against corn rootworm.

Bt corn hybrids designed to protect against ECB feeding have resulted in an average yield advantage of between 20 to 30 bushels per hectare over their near isolines. This value or yield protection varies greatly, however, between studies and across hybrids (Dillehay 2003). Hyde and colleagues (1999) provided an economic assessment of the *Bt* corn technology for European corn borer protection for several states based on published yield impacts of the pest. Little yield information currently is available for the corn rootworm material, but it is likely to provide significant yield protection.

The adoption rates of the *Bt* corn for ECB protection currently are being driven by both the perceived and actual value of the technology at a given geographic location. The actual value is determined by climatic factors that influence the synchrony of crop growth stage and timing of stalk tunneling by third instars (Bode and Calvin 1990; Calvin et al. 1988). The synchrony is a function of planting date, relative maturity group of a hybrid, and weather conditions during a year. Other factors that contribute to impact on value include hybrid sensitivity to the pest and frequency of an infestation level. Geographically, the value of the technology can vary from negative net returns to significant positive returns for farmers (unpublished simulations for Risk Assessment and Mitigation Program project [RAMP] (Figure 7.4.1).

The first objective of this paper is to report on the design and capability of a high-resolution landscape ECB management model to predict average net returns to a technology and the frequency of fields that can economically benefit from the same technology. The model provides a mechanism to assess the local need for *Bt* corn technology. Limiting the use of *Bt* corn or any other technology use only to fields that will economically benefit from the technology is the first line of defense in a resistance management program.

Effective Resistance Management Programs

The second line of defense is the implementation of an effective resistance management program, particularly in high-adoption regions. Genetic models suggest that at least 20% of corn acreage should be

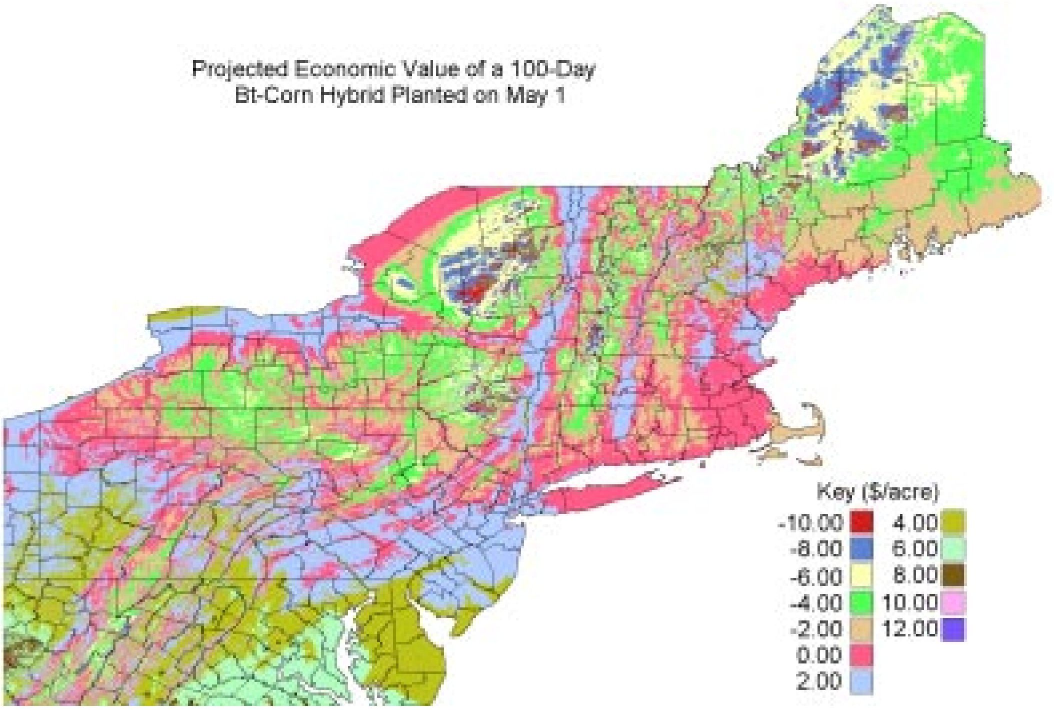

Figure 7.4.1. High-resolution landscape map of projected economic value of a 100-day *Bt* corn hybrid planted on May 1, 2002 using the European corn borer management model (map created by ZedX, Inc., Bellefonte, Pennsylvania).

planted to a non-*Bt* corn refuge to maintain susceptibility of ECB in the population. These fields also must be planted within 0.5 mile of the *Bt* corn field to assure close to random mating, and the field preferably should be planted on about the same date and be of the same relative maturity. Resistance management programs for transgenic crops represent the first time that the U.S. Environmental Protection Agency (EPA) has made resistance management a mandatory requirement for using a technology. Although the rules may change in the near future, traditional pesticide technologies have not had mandatory resistance management programs. Resistance management was adopted in an attempt to preserve new products for insects that are known to develop resistance rapidly. The EPA rules to minimize the evolution of resistance when using *Bt* hybrids are the culmination of discussion among research scientists, government, industry, special interest groups, and the general public. The rules are based in part on science, but also on compromise. For instance, it is not known scientifically whether 0.5 mile is the appropriate maximum distance for the resistance management program. This is because scientific methods to quantify insect movement are crude and typically are based on mark/recapture studies that only recover 1 to 5% of the released individuals. The researchers do not know the fate of the remaining 95 to 99% of the population.

Regardless of the scientific understanding behind the resistance management requirements, they will not be effective unless growers adopt them. Lack of adoption or improper adoption will lead to rapid evolution of resistance and the loss of a highly effective pest management tactic. Therefore, it is imperative that growers do the best they can to accomplish the mandatory resistance management requirements when using the technology. The second objective of this paper is to illustrate how information technology can assist growers, crop consultants, seed industry personnel, and government agencies in planning and implementing resistance management plans.

Predicting the Value of a Technology

The High-Resolution European Corn Borer Management Model has four major components: (1) weather, (2) corn development,(3) ECB phenology, and (4) economic analysis. The weather component is provided by ZedX, Inc. of Bellefonte, Pennsylvania in the form of spatially interpolated 1-hour temperature predictions at a 1-km^2 resolution. These temperature predictions are fed into both the corn development and

ECB phenology components of the model. The temperature predictions can be 30-year historic values, individual year, or real-time predictions (current year). Additional inputs for the corn development model are planting date and relative maturity of a hybrid. The output of this component is a day-by-day prediction of the proportion of corn development remaining to physiological maturity. The ECB phenology component is driven by the weather inputs, and it outputs the proportion of the population entering a particular life stage on a given day. By overlaying the predicted proportion of corn development remaining to physiological maturity with the predicted proportion of the ECB population entering the third instar, the daily contribution of the ECB population to yield loss per larva is calculated. By summing the daily contributions to loss per larva, the weighted average loss per ECB larva is calculated for each geographic grid. For a given geographic grid (1 km^2), the weighted average loss per ECB larva is calculated for each planting date by relative maturity group grown at the location for 30 years of individual weather profiles. This provides a probability distribution of possible losses per ECB larva for each relative maturity and planting date combination to feed into the economic analysis component.

The basic structure of the economic analysis component is a cost/benefit ratio. Benefit of a technology is calculated using the following formula:

$$\text{Benefit of the Technology} = \text{MV X EY X NIPP X PLPI X PC}$$

where MV = expected market value of the crop; EY = expected yield of the crop; NIPP = number of insects per plant; PLPI = predicted loss per larvae per plant; and PC = expected proportional control from the technology.

The cost of the technology is calculated using the following formula:

$$\text{Cost of Control} = \text{NA (MC X AC)}$$

where NA = number of applications; MC = material cost; and AC = application cost. For transgenic corn hybrids, the cost of control simply is the technology fee because it is applied only once a season at the time of planting. Therefore, a second trip across the field is not needed. The outputs of the model are colored maps of the average net return of *Bt* corn for each 1 km^2 across North America and the frequency of cornfields likely to benefit from the technology.

The high-resolution ECB management model is an information technology that integrates all relevant biological knowledge necessary for an economic assessment of a technology to manage the pest. These maps will provide growers and their crop advisors with an on-line tool to assess the value of *Bt* corn on their farm. It also will provide an interactive interface that will allow growers to modify values in the economic equations to better reflect their individual field or farm conditions. The major advantage of this information technology is that it is the first tool for farmers and crop advisors to assess whether *Bt* corn should be grown in a field or on a specific farm. In locations where the frequency of fields that will benefit from the technology is low, there is little need for high levels of technology adoption. If the model's predictions are followed, then there also will be a decreased likelihood of resistance evolution there. In locations where the model predicts that a high percentage of fields will benefit from the technology, then adoption of a resistance management program will be essential to prevent resistance evolution.

Information Technology Tools for Refuge Compliance

A web-based crop management database system has been developed by ZedX, Inc. that allows consultants to input directly Global Positioning System (GPS) coordinated field-specific information for pest and crop management (Figure 7.4.2). The consultants collect and input field data from a remote setting onto the ZedX, Inc. server in Bellefonte, Pennsylvania. There the GPS data can be analyzed and a report returned to the consultants to help their clientele plan crop management. This system offers a mechanism to provide growers with assistance in developing a resistance management program for their farm and to help the seed industry and the EPA monitor compliance.

Currently, farmers provide to their consultant information on corn hybrids that includes planting date, maturity group, and GPS position. The GPS position may be for a field or a subfield location where the hybrid was planted. Using these GPS locations, mathematical formulas can be employed to measure location and distances between the *Bt* corn and its non-*Bt* refuge. The database system can be used to calculate whether individual fields are in compliance and the degree to which a farm is in compliance. If adequate numbers of farms within a county or region are in the database, then the percentage of compliance for the region can be calculated and made available to industry or to the EPA (with permission of the consultant's farmer clientele). The key, however, is cooperation of the farmers with industry and the EPA. The technology is available to check compliance, but

Figure 7.4.2. Example of how fields, bounded with GPS coordinates, can be used for hybrid location and the calculation of resistance management compliance (screen shot provided by ZedX, Inc., Bellefonte, Pennsylvania). The map background is a U.S. Geographical Survey orthodigital quarter quad.

it will require trust among farmers, industry, and the EPA. Without this trust and cooperation, the only mechanisms are to help farmers with planning refuge compliance and to implement an educational program through crop consultants and extension. No matter what the mechanism for monitoring compliance, the industry still is responsible for assuring that farmers who purchase their seed comply with mandatory resistance management.

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7.5 Resistance Management Education and Communication: Weeds in Vegetable Crops

Michael D. Orzolek

Introduction

Weed management in vegetable crops, and in horticultural crops generally, presents many challenges, the least of which is that vegetables are classified as minor crops and have few labeled herbicides compared with agronomic crops. Also, there are no weed-resistant vegetable varieties like there are disease-resistant and, to some extent, insect-resistant varieties. Out of necessity vegetable growers have had to practice integrated weed management, but many have adopted only a partial list of integrated pest management (IPM) practices, assuming that weed resistance to current herbicides will not occur in their fields or during their lifetime (growers in the age group over 50).

Weed Management Programs

All vegetable weed management presentations in Pennsylvania have emphasized an IPM approach. The presentation is divided into two segments: cultural controls and chemical controls. Cultural controls include tillage methods, liming and soil pH management, banding fertilizer, crop rotation, cultivation, crop density, identifying and treating hot spots of weeds in the field with nonselective herbicides, eliminating weed seed production in the crop, and using plastic mulch, raised beds, and drip irrigation. Chemical control methods include proper identification of the problem weed, treatment of actively growing weed(s), correct choice of herbicide and rate, correct application technique, and uniform application in the field.

A Resistance Management Education program has been part of my Integrated Weed Management Extension program for the last 10 years in Pennsylvania. Weed resistance is a critical concern to both educators and regulators in Pennsylvania because there are currently two widespread weeds resistant to atrazine: common lambsquarters and redroot pigweed. Because atrazine is an inexpensive herbicide to apply, controls a large number of grass and broadleaf weeds, and can be applied either pre- or postemergence, almost all corn growers (those raising field, sweet, pop, and ornamental corn) in Pennsylvania make one application/acre/year. Thus, the challenge for Extension is to provide viable, efficient method(s) of controlling weeds in vegetables by chemical and/or cultural means and to encourage the decrease or elimination of atrazine use in the state while using IPM methods for weed control in vegetables.

Cultural Controls

Cultural controls can help to decrease problem populations and resistant weed populations in many fields by at least 50% a year. Monitoring fields and identifying the different type of weeds and population changes that take place each year will help growers decide what crop(s) to plant in each of the fields, depending on weed demographics. In addition, some vegetable crops, when grown in a no-till system, are more competitive than the weeds and compete rather effectively from establishment through harvest.

- Crop rotation. Use of legume cover crops (hairy vetch, clovers, etc.) or small grain in a crop rotation program will provide effective weed control of most annual broadleaf weeds such as ragweed, jimsonweed, and galinsoga. Because most minor crops have few labeled herbicides, rotating minor crops (horticultural crops) with corn and soybeans will increase the number of labeled herbicides available that will control both annual and perennial weeds. This practice also will enable the grower to choose from more herbicide families and to decrease the potential for resistance in weed populations.
- Tillage. The use of a moldboard plow in alternate years or at least every third year will provide generally better perennial weed control (for weeds such as Canada thistle and horsenettle) than chisel plowing. Moldboard plowing will bring to the soil surface and expose the large storage organ (root) of many weeds so that over time the

storage root desiccates and/or rots.

- Cultivation. Timely cultivation can control many annual weeds effectively, especially weed populations that have acquired resistance to herbicide(s) or have a very narrow genetic base or variation. Generally, cultivating several times during the growing season in specific crops grown in fields with low weed seed populations will provide effective weed management during the entire growing season. The one drawback of relying solely on cultivation for weed control during the growing season, however, is rainfall and wet soils. Extended wet periods can eliminate the use of a cultivator in the production field for several weeks while young weeds still are growing actively.
- Banding or injecting fertilizer. Application of fertilizer as a band next to the crop provides nutrients to the crop but not to the weeds, especially between crop rows. Likewise, injecting fertilizer in drip irrigation tapes will provide nutrients for the crop but not for the weeds. Banding also helps to decrease the total cost of nutrient application for a vegetable crop.
- Plant populations. The higher the plant population per acre, the greater the canopy of the vegetable crop and the decrease in the number of weeds that are competitive with the crop due to lack of or decrease in photosynthetic active radiation. Plant populations can be increased within limits to enhance canopy development of the crop without compromising crop yield or quality.
- Eliminating weed seed production. This is the most significant cultural practice that will reap rewards for years. The elimination of viable weed seed and/or reproductive structures by either mechanical or chemical means will, over time, result in much smaller weed seed populations in the soil bank that can actively compete with vegetable crops in the future. Simply mowing weeds and eliminating immature flowers on the weeds is very effective. Some weeds when mature can supply thousands of weed seeds per plant back into the soil bank and be problems for many years to come.
- Treating hot spots. Many weed problems originate in fencerows near the field with only a few plants or even one. Treating and eliminating weeds, even if only one or two that seem insignificant at the time, in fencerows will help to eliminate future problem weeds in the field. Also, eliminating hot spots in a production field as they become apparent will prevent future large-scale populations of a weed.
- Use of plasticulture systems for vegetable production. Many vegetables benefit from being grown on raised beds covered with plastic mulch and drip irrigation tape buried beneath it in the bed. The plastic film generally is black but can be other colors; it not only eliminates weed growth in the 28" to 30"-wide top of the 6" to 8"-tall bed but also increases soil temperature, maintains higher soil moisture levels, decreases leaching of nutrients and other pesticides applied to the bed, and retains soil structure throughout the growing season.

If populations of volunteer weeds are still growing after the grower has used several of the cultural controls available for weed management in vegetables, then the use of herbicides should be considered. Before applying the herbicide on the problem weed(s), however, the grower needs to make several decisions: (a) is the herbicide labeled for that particular crop use? (b) will the herbicide provide effective control of the problem weed in the crop? (c) what rate should be applied and what method of application should be used? (d) are there any sensitive crops being grown near the field where the herbicide will be applied? and (e) what is the half-life of the herbicide and how long will it last in the field after application? If a grower has answered all these questions to his or her satisfaction, then applying a specific herbicide to a specific vegetable crop to control specific weeds should be the choice that is made. Of course, it is assumed that (1) there is negligible wind during application, (2) the sprayer has been calibrated correctly, (3) all nozzles tips and screens have been checked for wear and blockage, and (4) both the crop and weed populations are actively growing and not under stress.

After presenting this material to grower/producer clientele at local and statewide meetings during the winter, I am amazed, even after 29 years as an Extension Educator, at the number of growers who contact me during the growing season to ask why there are still volunteer weeds in their vegetable crop or why their vegetable crop appears stunted, discolored, or necrotic. Even though the information on herbicide application presented to the growers is current and up-to-date, as growers become busier tilling their fields, planting crops, and monitoring pests in the field, they invariably will take short cuts to use their time more efficiently and to maintain a production plan for the year. But short cuts lead to mistakes and mistakes can result in the decrease of both yield and quality of most vegetable crops.

Sweet Corn: A Case Study

Weed control in the 9,700 hectares of sweet corn in Pennsylvania is important to ensure timely harvest, maximum yield, and quality of the sweet corn crop. Early weed infestation in sweet corn decreases both early and total marketable yield and quality because of competition for both water and nutrients and may serve as a reservoir for other sweet corn insect pests. Although there are several herbicide options for use in sweet corn, maturity of the variety, production system, and date planted will influence the choice of herbicide and other weed management practices. Soil temperature will generally determine when sweet corn is planted (minimum soil temperature for sweet corn germination and emergence is 50°F) throughout the state. For very early sweet corn (before July 4), most growers will plant sweet corn seed in furrows and cover the double rows with clear polyethylene mulch in mid- to late April. The clear polyethylene mulch will warm the soil and maintain a higher level of soil moisture compared with bare ground. Plastic is not selective, however, so weed seed will have the same advantage as sweet corn seed for early germination and soil emergence. Weed management in this instance could be as simple as field selection and crop rotation or as intense as preplant-incorporated and preemergence herbicide applications. Currently there are only 3 labeled herbicides for preplant-incorporated or preemergence weed control in sweet corn: atrazine, metoachlor, and alachlor. One immediate concern for continued use of these materials, especially atrazine, is the development of weed resistance. Currently, both atrazine-resistant pigweed and lambsquarters can be found in Pennsylvania. In addition, many vegetable crops are extremely sensitive to atrazine residues, especially from application rates in excess of 1.4 kilograms/hectare from the previous year. Because sweet corn can be planted continually from April through August, application of atrazine can result in buildup of atrazine residue in soil and the potential for additional weed resistance development. How can this problem with atrazine and other herbicides be avoided in the future? The answer may be using more cultural weed management techniques including (a) scouting the field in which sweet corn will be planted the following year, (b) avoiding fields with serious weed problems, especially high populations of perennial weeds, (c) effective crop rotations programs including the use of cover crops, (d) use of higher plant population programs (39,500 vs. 54,300 plants per hectare), and (e) using different families of herbicides to control weeds in sweet corn.

7.6 The *Resistant Pest Management Newsletter* and Resistant Arthropods Database

Mark E. Whalon and Erin Gould

Introduction

The *Resistant Pest Management Newsletter* (*RPM News*) is international in scope with worldwide circulation to approximately 3,000 resistance workers in academia, industry, and government. The newsletter provides information on the ongoing changes and advances in the field of resistance management. The *RPM News* is a biannual publication of the Center for Integrated Plant Systems (CIPS) in cooperation with the Insecticide Resistance Action Committee (IRAC) and the Western Regional Coordinating Committee (WRCC-60). We are proud to introduce the first electronic version of the *RPM News* during this, the tenth year of publication. With the new electronic format, the *RPM News* endeavors to provide an accurate, informative, and useful resource to our readers while enhancing the communication of ideas among colleagues worldwide.

The electronic format allows us greater facility to serve our readers through the rapid publication of breaking events in resistance development and management. Our hope is that there will be decreased time between the availability of issues as well as increased access, leading to a more informative and complete reporting process for resistant pest management globally. In addition, we intend to publish updated lists and other relevant information from our sister website, the Resistant Arthropod Database. We trust that you will find many of the articles, abstracts, and other information in our newsletter useful and informative.

RPM News

The editorial staff of *RPM News* is excited about our new web venue and hope that it will serve readers' resistance information needs effectively. The website is available at <http://whalonlab.msu.edu/rpmnews>. The *RPM News* is a versatile means for communicating information on resistance to all types of pesticides. We are interested in research and news about resistance from around the world, and we readily accept submissions.

Features of the *RPM News* include the following:

- Letter from the Editors / Editorials
- Resistance Management Reviews: Summaries and analyses of important resistance management topics geared toward a general reader audience
- Resistance Management from Around the World: Articles highlighting resistance issues from global localities
- Research in Resistance Management: The feature article—an exhibition of research in the field that leads toward an advanced understanding of issues while providing practical applications
- Resistance Management News: Briefings (new findings, recommendation, etc.) and industry news (new products, label changes, etc.)
- Abstracts
- Symposia Information: Meetings, forums, conferences of interest
- Readers' Response: Letters and comments from our readers
- Announcements and Submission Information: Corrections, reminders, calls for papers
- E-mail Notification of New Issues
- A Link to the Resistant Arthropods Database
- An Archive of Past Issues
- Ask an Expert: A listserv of international professionals in various fields willing to give expert advice related to resistance management.

The Resistant Arthropods Database is the accumulation of resistance data published on the Internet as a public service, for use by resistance management practitioners around the world. This database reports instance of resistance from 1914, when resistance was first discovered for a specific time and place, to the present. Pesticide resistance is a dynamic, evolutionary phenomenon and a record in this database may or may not be indicative of your field or specialty. Similarly, the absence of a record in this database does not indicate absence of resistance.

Resistance Database

There is a worldwide need for accurate, easily accessible pest resistance information—information that will be used by numerous stakeholders in agriculture, human health, and animal protection as well as those in structural, ornamental, and other pest management arenas. In addition, regulatory, structural, and evolutionary pressures surrounding resistance development illustrate the need to document, understand, and manage resistance more effectively. In order to manage resistance effectively there is a clear need for access by decision makers to appropriate and critical information. Our goal in implementing a resistance database is to help address arthropod resistance by evolving an integrated, cooperative system to deliver resistance information efficiently. Currently, our information resides in an electronic database at Mark Whalon's laboratory at Michigan State University's Center for Integrated Plant Systems and is available through the Internet at <http://www.cips.msu.edu/ resistance/rmdb/>. The database design features a central table of "resistance" records with five key pieces of information: the arthropod, the pesticide, the location (country), the year, and a reference to the document reporting the instance. There are secondary tables that elaborate on these five key informational groups, as well as auxiliary tables to help refine the information further or link to external data sources. The database is, in essence, a historical snapshot of resistant arthropod detection and monitoring. The primary outputs are counts of compounds, species, regions, and documents over time. Currently we are developing an electronic input interface available over the World Wide Web. Anyone interested in participating in this experimental process may contact the *RPM News* coordinator (<rpmnews@msu.edu>) or Mark Whalon (<whalon@msu.edu>). This database was made possible by a grant from the U.S. Department of Agriculture's Cooperative State Research, Education, and Extension Service, Pest Management Alternatives Program, and the IRAC.

7.7 Resistance Management Education and Communication

Ronald E. Stinner

Introduction

By way of introduction, a brief description of the Center for IPM (CIPM) and our focus is needed to put our efforts with resistance management information in context. The Center for IPM is a National Science Foundation-founded Industry/University/Government Cooperative Research Center that both funds projects throughout the United States with membership fees and competes for funding in the sectors of information dissemination and cooperative management of integrated pest management (IPM) programs. The Center was started in 1991. To avoid potential conflict of interest, the Center engages in no proprietary research and all programs are approved, and results shared, by the Center members through an Industry Advisory Board.

Because many of our members are national and international companies and organizations, the CIPM has maintained a national and international focus. With the geographic diversity in our membership and the nature of IPM, we were forced early on to invest heavily in information systems. With the public advent of the World Wide Web in 1993, one of our primary tasks became the dissemination of current, accurate, and unbiased information needed in the IPM community. Because we have been a member-based organization, we have focused on cooperative efforts with many diverse organizations to provide IPM information electronically.

Four Cooperators

In this paper, I would like to describe our efforts with four cooperators. Two are funded through our membership account; one is a funded U.S. Department of Agriculture–Cooperative State Research, Education, and Extension Service (USDA–CSREES) program (USDA Pest Management Centers); and one is not funded, but supported internally, simply because the information needed to be made available and we could provide the technology (Herbicide Resistance Action Committee [HRAC]).

- Insecticide Resistance Action Committee (IRAC) website. Approximately 5 years ago, the CIPM was approached by the IRAC to see if we would be willing to set up a small website for IRAC, consisting primarily of a PowerPoint presentation explaining the issue of Insecticide Resistance and the role of IRAC. The site has expanded greatly since then in size, types of content, and technology. The site is now a complex, database-driven, international source of information from IRAC. It includes information on resources, education, current events, and news. It also has project funding reports and a members' section for internal use. News is maintained in a database and shown dynamically on the first page. Current literature citations are available along with a calendar of events. Of course, the site maintains the original educational slide shows and knowledge quiz for students. A unique feature is that all of the site's content is written and controlled from the United Kingdom through a secure back-end database that allows immediate updating.
- HRAC website. The CIPM also has maintained the HRAC website for several years. The site features a number of reports and the Mode of Action (MOA) Classification, including downloads of large posters displaying the chemical structures involved. The HRAC also has developed a number of their documents in Spanish and these are available on the site. This is a more traditional site, with updates e-mailed from the chairman of the communications committee in Germany, but to a CIPM employee now living in Kansas for posting on the server located in North Carolina.
- Insecticide Resistance Management (IRM) training website. The third site provides on-the-ground information to consultants and farmers on their choices for IRM with genetically modified crops, specifically *Bacillus thuringiensis (Bt)* cotton and corn. The site has been funded from our Center membership account, at the request of Monsanto, but with the approval and review of our full Industry Advisory Board. With the U.S. Environmental Protection Agency (EPA)

requirements for management plans, the use of online training and management plan explanations makes both components easy and accessible. For these management plans to work, growers, extension personnel, crop consultants, and industry all must use the same information. Community plans can be complex and the rules can change, as we have already seen with *Bt* cotton. Where numerous choices in refuge design exist, as is the case with *Bt* corn, graphics of the choices make choice selection easier. With a web format, updates in information are easy and downloadable agreement forms can even be provided. The site is relatively small, easy to navigate, and provides the essentials needed for planning decisions.

- PM Centers. The CIPM is the management entity for the National Information System of the USDA Regional IPM Centers. Much of the focus of this system deals with pesticides and pesticide use in the context of PM. To that end, the CIPM currently maintains databases for the National Agricultural Statistics Service (NASS) pesticide use data, IR–4 and Office of Pest Management Policy (OPMP) new technology data, and the EPA crop activity timelines. We also maintain dynamic searching and links among some of these databases as well as with the EPA Pesticide Label System. At present we do not have resistance data, but we see some new technologies as the key to integrating the information we maintain with that available or being developed by others. There is a crucial need for this integration. The MOA classifications change, new resistance problems emerge, the EPA continues to require more planning and data, and much of the information is text-based rather than part of a formal database structure.

Because of this, the CIPM has been drawn into the mysterious world of Extensible Markup Language (XML), or data-sharing on the Web. Without a dissertation on XML, suffice it to say that this technology for data sharing requires a formal set of standards that define terminologies and structure called a DTD (Data Type Definition). Groups such as RAPID and C&P Press already have developed Pesticide DTDs, but these are proprietary and not available in the public domain. The CIPM, through the USDA Regional Pest Management Centers and cooperating with representatives from IR–4, NASS, OPMP, and the EPA, has begun the process of developing and publishing a DTD. We would welcome involvement from industry and other organizations that have an interest in public exchange of data.

In closing, I would expand on the CIPM's desire to cooperate with other organizations, both public and private. The CIPM has national and international information dissemination as a core function. We have the infrastructure in terms of personnel and commercial servers, and we have public interest—with more than 2.5 million hits per month. If you have valid and current IRM data, and you want to share it, we will work with you.

7.8 A Producer's View of Managing *Bacillus thuringiensis* Technology

Thomas Slunecka

Introduction

In the practice of producing high-quality corn at minimum expense, each percentage increase is crucial. *Bacillus thuringiensis (Bt)* corn has proved to be an important technology to help corn growers control damaging insect pests and produce higher yields and better-quality grain. For many producers, the consistency of control far outweighs up-front seed purchase costs. But the cost/benefit ratio of the technology is not calculated easily. Complications in this calculation result from added production costs of planting to meet insect resistance management (IRM) requirements and variations of hybrid maturity. In addition to these agronomic differences, we need to add management costs of hybrid selection and marketing restriction.

According to a survey of growers who planted *Bt* corn in the 2002 season, the majority of *Bt* corn growers understand the importance of IRM; awareness has risen to 81% in 2002 from 58% 2 years earlier (Agricultural Biotechnology Technical Committee 2002). Compliance to IRM requirements still is not at 100%, however. According to that same survey, the majority of *Bt* corn growers (86%) planted at least the minimum required refuge size in 2002, remaining fairly constant over the previous year. From the National Corn Growers Association's (NCGA) perspective, reasons for noncompliance include several economic factors; yield concerns; convenience factors; available hybrid selection; information flow; and the key messages being presented to producers, the media, and influencers.

Insect Resistance Management Requirements

The *Bt* corn industry has been operating under the "unified plan" for IRM since it was accepted by the U.S. Environmental Protection Agency (EPA) in 2000. The unified plan was developed by the Agricultural Biotechnology Stewardship Technical Committee (ABSTC) in cooperation with the NCGA. In 2003, the Compliance Assurance Program (CAP) was expanded, outlining how registrants of *Bt* corn are required to monitor, assist, and deal with growers who do not follow IRM requirements.

With the advent of rootworm-resistant corn, the rules are changing. Insect resistance management requires corn borer-resistant-corn growers to plant at least 20% of their acreage to a non-*Bt* corn refuge. In certain cotton-growing regions where both *Bt* corn and *Bt* cotton are planted, growers must plant a 50% non-*Bt* corn refuge. The *Bt* corn must be located within 0.5 mile of the refuge (0.25 mile is preferred). When using strip methods, the refuge must be at least four rows wide. Rootworm-resistant corn has the same refuge requirements; however, those refuges must be adjacent and at least six rows wide. The differences in product IRM requirements can create confusion, which further illustrates the need for a consistent source of information for all stakeholders.

Role of the National Corn Growers Association

One of the NCGA's main roles is to serve as the leading voice for corn growers in the promotion of IRM to U.S. corn growers. The NCGA advocates the continued availability of federally regulated and approved seed and crops produced through biotechnology. The NCGA supports the science-based regulatory process and stands behind the system that approves these new tools for agriculture and food protection.

Through its educational program, the NCGA has instituted a multifaceted approach that includes the following:

- Insect Resistance Management Logo. The NCGA was instrumental in the development of the IRM logo, which has been adopted by government and industry in IRM awareness campaigns.
- "Know Before You Grow" Program. This program includes a comprehensive, dynamic database of commercially available hybrids as well as their

approval status, allowing growers to make informed decisions that will affect them not only at planting, but also at harvest when the grain is to be marketed. This database is accessible at the NCGA's website, <www.ncga.com>, and is linked to "Know Where to Go," the American Seed Trade Association's (ASTA) grain handler's database. "Know Before You Grow" also is linked to the industry's Market Choices Program.

- Insect Resistance Management Learning Center. New product registrations will bring new regulations. The NCGA is in the process of developing an IRM learning system to create greater IRM awareness through education and partnership. As the EPA becomes increasingly more thorough in its efforts to monitor compliance with *Bt* corn IRM regulations, the NCGA recognizes the need to create a higher level of awareness in terms of the benefits of a sound IRM plan and consequences of noncompliance. The Learning Center would be designed to meet the following objectives:
  - Provide a third-party facilitator to ensure IRM compliance
  - Provide an electronic system that growers could use to monitor their own compliance efforts
  - Allow tech providers and regional seed companies a platform of uniform IRM education
  - Provide a simple, cost-effective source of information regarding changes in regulations with new product additions

The challenge to the *Bt* corn industry will be to use this recognition of value as a means of improving growers' appreciation for the importance of IRM as the best way to preserve the technology over the long term. Certain elements of the CAP, such as the phased compliance approach, combined with the industry's ongoing educational plan, should strengthen growers' stewardship of this technology in the future.

Producers understand and take very seriously their role in the technology community. This is a steep learning curve, but U.S. farmers have proved time after time their willingness to do the right thing for the environment, their trade, and their own well-being.

Literature Cited

Agricultural Biotechnology Technical Committee. 2002. Insect Resistance Management Grower Survey for *Bt* Field Corn, <www.ncga.com/biotechnology/pdfs/IRM_exec_summary.pdf> (15 August 2003)

Conclusions and Recommendations

Conclusions

The Council for Agricultural Science and Technology's Pest Resistance Management Symposium was the first U.S.-based multidisciplinary stakeholder meeting on pest resistance management (PRM) since the 1995 American Chemical Society meeting on mechanisms of pest resistance and the 1984 National Research Council meeting on pest resistance. The Symposium provided the opportunity for all stakeholders involved in insect, weed, and pathogen pest management to come together in a fruitful discussion of the issues, laying the foundation for future collaborations addressing PRM.

The coverage of different classes of pesticides (herbicides, fungicides, and insecticides) made evident the important differences among and within these classes in terms of resistance management (RM) needs and highlighted the necessity of addressing these needs on a case-by-case basis. At the same time, a number of general conclusions emerged.

The overall conclusion of the meeting was that PRM is very important to the sustainability of agricultural production systems. Achieving proactive or preventive RM is a desirable goal, but how to achieve it is a complex process that requires extensive input and commitment by all stakeholders. The keys to effective RM are strong science; environmentally benign, feasible, and cost-effective strategies; and education about the benefits of implementation. In addition, multiple pest control tactics, including cultural practices, biological control, transgenic plants producing pesticidal substances (such as *Bacillus thuringiensis [Bt]* insecticidal endotoxins), and chemical pesticides (with different modes of action), can help decrease selection pressure for the evolution of pest resistance. That is, to most effectively curtail resistance, nonchemical pest control practices should be augmented with different pesticide modes of action including biological control. Lastly, further research into the development, implementation, and adoption of RM is necessary.

Several specific conclusions were identified from the presentations, papers, and discussions during the symposium.

- Pest resistance is a genetically based decrease in susceptibility in a pest species.
- Pest resistance results in control failures and can lead to disrupted pest management systems, higher costs of pest control, and use of more pesticides that may pose higher risks to human health and the environment. (Even organic production can be affected by pest adaptation to management practices, although pest resistance is not considered to be a major issue.) Therefore, pest resistance is identified as a growing challenge to sustainable agriculture both in the United States and in other countries throughout the world.
- Understanding the scientific basis for why a strategy will work is fundamental to the success of effective, preventive RM strategies.
- Resistance management is a key component of integrated pest management (IPM).
- Successful RM requires a long-term vision.
- Proactive or preventative RM generally is preferable to reactive RM, but is more complex. If preventative measures are expensive and of uncertain value, and the evolution of resistance does not impact the value of the product significantly, then preventative management may not be cost effective. It is desirable to formulate RM plans before commercialization of a new chemical active ingredient.
- Successful RM requires input and collaboration by all stakeholders. The goals and objectives of RM must be clear, and support should be sought from all parties.
- Education and training are fundamental to the implementation and adoption of RM strategies.
- Resistance management benefits must be demonstrated to growers. Successful RM should be profitable, sustainable, and environmentally beneficial.
- Federally funded RM research is important to the successful development and implementation of

effective RM strategies and should be a component of federally funded IPM grant programs.

- The U.S. Department of Agriculture (USDA) and the U.S. Environmental Protection Agency (EPA) play important roles in PRM and pesticide regulation. The Interregional Research Project–4 (IR–4) plays a particularly important role in registering new pesticide uses and biopesticides, especially for minor crops. The USDA–Natural Resources Conservation Service (NRCS) could be engaged by identifying RM programs as conservation practices within the Farm Bill Environmental Quality Incentives Program (EQIP) and Conservation Security Program (CSP) titles.
- Central and permanent databases of pest and pesticide resistance information are important and need continued funding. Two such databases exist: one for herbicides and resistant weed biotypes (WeedScience 2003) and one for insecticides and resistant insects (Michigan State University–Center for Integrated Plant Systems 2003).
- Dissemination of pest and pesticide resistance information is necessary to determine the extent of resistance. Such information also is needed to develop RM strategies in locations where resistance to the same or related mode of action has not occurred but is likely to occur in the future.
- Agricultural information technology provides a mechanism for disseminating forecast tools to know where and when to use a pest control technology. Use of this information may decrease the selection pressure on any one pest control tactic and increase its efficiency and effectiveness.
- Barriers that impede the development of effective RM strategies do exist and include the following:
    - limited understanding of the factors affecting resistance evolution,
    - limited product availability,
    - economic factors,
    - short-term solutions,
    - focus on individual crops/pests rather than a holistic-systems approach for the agroecosystem,
    - lack of clear goals and objectives,
    - lack of clear RM regulatory policy,
    - limited federally funded and industry-funded RM research, and
    - competitive marketing practices within industry that discourage proactive, preventive RM.

- Predictive models are useful for comparing RM options and identifying key data gaps, but they offer a simplified reality.
- Resistance monitoring plays an important role in surveillance and detection of resistance prior to field failure where suitable tools are available (e.g., many insecticides). It can be an expensive proposition to find a rare event, however. New developments using biotechnology and high-throughput engineering could increase significantly the effectiveness and timeliness of monitoring, while decreasing the cost. Homeland Security funding may be appropriate both in resistance detection/monitoring and resistance remediation to enhance food security.
- Plant breeding can be an important component in successful implementation of effective RM and should be encouraged in this context.
- In organic production of short-term annuals, pest resistance has not been a big issue because of the extensive focus on crop rotation and other cultural management practices, soil management, and the use of biological pesticides. Organic production of perennial crops, however, has not always successfully managed resistance (e.g., diamondback moth resistance to *Bt* microbial pesticides used in Hawaiian watercress production, and tetranychid mite, *Bryobia* sp., resistance to sulfur).

Recommendations and Suggestions

Participants made several RM recommendations and suggestions in a discussion held at the end of the symposium. These recommendations focused on four areas: (1) Science, (2) Research and Extension, (3) Education, and (4) Policy.

Science Recommendations

- Resistance management strategies should be developed on a case-by-case basis, considering characteristics of the chemistry, the target pests, and the management system using certain guiding principles.
- Guidance and direction are needed in developing resistance monitoring programs for new technologies including establishment of baseline susceptibility, detection techniques, and sampling strategies.
- Resistance management strategies should be flexible to allow changes over time due to the temporal and spatial variation in the pest/crop/pesticide situation. Databases can be used to measure the extent of resistance both temporally and

spatially. Further funding of resistance databases is recommended.

- Standard definitions of resistance should exist for pest/pesticide combinations and methods of documentation and validation (e.g., field failure, bioassay [dose response, discriminating or diagnostic dose concentration], tenfold LD_{50}, DNA markers, change in resistance allele frequency).
- Economic benefits and costs of effective RM should be developed, identified, and described better. One suggestion was to develop an issue paper on the economic impacts of resistance and RM.

Research and Extension Recommendations

- There should be explicit RM priorities within the federal government.
    - ◦ One suggestion was to create a new competitive grants program to focus on RM.
    - ◦ Other suggestions involved strengthening existing USDA competitive grants research programs to provide more explicit priorities within the Request for Applications (RFAs) to fund RM research. These include the National Research Initiative programs and the following Section 406 programs: Risk Avoidance Mitigation Program, Crops at Risk, Extension Integrated Pest Management Implementation, Methyl Bromide Transition Program, Organic Transitions Program, Pesticide Safety Education Program, and the Biotechnology Risk Assessment Research Program. For all programs cited here (or others to be developed), research efforts should be prioritized to make best use of available resources. This process should involve all stakeholders in the RFA development.
    - ◦ IR–4 funding should include RM research for minor crops.
    - ◦ Resistance management research should be part of the mission of the Regional Integrated Pest Management Centers.
    - ◦ Research efforts should be multidisciplinary and collaborative.

- One suggestion was to create an RM research initiative supported jointly by funds from a user fee associated with pesticide sales and funds from the federal government. Some grower groups noted that this could be a significant burden on growers.

Education Recommendations

- Resistance management education programs should continue to be developed and implemented as part of ongoing pesticide education programs. The support of the EPA and the USDA for RM, as part of a pesticide education program, is important. More educational materials are needed in relation to PR Notice 2001-5, including voluntary RM labeling based on mode of action. The USDA/Cooperative State Research, Education, and Extension Service should improve their coordination of education programs.
- Consumer education programs should include the cost of producing “blemish-free” food in the marketplace and the use of reduced-risk pesticides.

Policy Recommendations

- The USDA grading (marketing) standards and the marketing of food internationally should be examined for their impact on RM.
- Although all stakeholders noted the EPA’s role in RM as important, there was disagreement about the scope and regulatory nature of this role.
    - ◦ Some participants recommended a mandatory role for the EPA in RM, but consensus was not achieved in the limited time available.
    - ◦ Others noted that the rigid nature of mandatory regulations could impact negatively the effectiveness of RM, as well as industry investment in product development and the diversity of control options available.
    - ◦ The Fungicide Resistance Action Committee recommended that the mode of action guidelines described in PR Notice 2001-5 (EPA) and DIR 99-06 (Canada) become mandatory to provide uniformity within fungicide classes. The other Resistance Action Committees (herbicides and insecticides) did not support such a move.
    - ◦ The EPA’s regulatory process for RM should be more transparent and be made clearer (e.g., what constitutes a “public good” or pesticides deserving of regulation).
    - ◦ The EPA’s Section 18 (Emergency Exemption) process should allow for the use of reduced-risk pesticides with alternative modes of action in crops and on pests where resistance has been a chronic problem.
    - ◦ There should be mechanisms to provide incentives and/or rewards for good RM and environmental stewardship by industry and pest managers.

- Several suggestions were made that Farm Bill priorities should be changed to better fund RM research and education. Specifically, The NRCS should recognize RM as a conservation practice under the EQIP and CSP Titles.

Literature Cited

Michigan State University–Center for Integrated Plant Systems. 2003. The Database of Arthropods Resistant to Pesticides, <http://www.cips.msu.edu/resistance/rmdb> (4 September 2003)

WeedScience. 2003. International Survey of Herbicide Resistant Weeds, <http://www.weedscience.org/in.asp> (4 September 2003)

Appendix A: Abbreviations and Acronyms

µg	microgram
a.	acre
AAFC	Agriculture and Agri Food Canada
ABSTC	Agricultural Biotechnology Stewardship Technical Committee
ACCase	acetyl-CoA carboxylase
AHAS	acetohydroxyacid synthase
ALS	acetolactate synthase
ARS	Agricultural Research Service
ASTA	American Seed Trade Association
BRARGP	Biotechnology Risk Assessment Research Grant Program
Bt	*Bacillus thuringiensis*
BW	bollworm
CAP	Compliance Assurance Program
CAR	Crops at Risk
CAST	Council for Agricultural Science and Technology
CBI	Council for Biotechnology Information
CIPM	Center for Integrated Pest Management
CRW	corn rootworm
CSP	Conservation Security Program
CSREES	Cooperative State Research, Education, and Extension Service
DBM	diamondback moth
DMI	dimethylation inhibitor
DPE	diphenyl ethers
DSMA	disodium methanearsonate
DTD	Data Type Definition
EBDC	ethylenebisdithiocarbamates
ECB	European corn borer
ED	effective dose
EPA	U.S. Environmental Protection Agency
EPPO	European and Mediterranean Plant Protection Organization
EPSPS	5-enolpyruvylshikimate-3-phosphate synthase
EQIP	Environmental Quality Incentives Program
ERS	Economic Research Service
EU	European Union
EUP	Experimental Use Permit
FAOSTAT	Food and Agricultural Organization of the United Nations, Statistical Database
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
FQPA	Food Quality Protection Act
FRAC	Fungicide Resistance Action Committee
ft	feet
FTE	full time equivalent
FY	fiscal year
GE	genetically engineered
GMO	genetically modified organism
GPS	Global Positioning System
ha	hectare
HPPD	hydroxyphenyl-pyruvate-dioxygenase
HRAC	Herbicide Resistance Action Committee
ICM	integrated crop management
IGR	insect growth regulator
IMI	imidazolinones
IPM	integrated pest management
IR–4	Interregional Research Project Number 4
IRAC	Insecticide Resistance Action Committee
IRM	insect resistance management
IWM	integrated weed management
KD_{50}	median knockdown
LC_{50}	median lethal concentration
LD_{50}	median lethal doses
LGU	Land-Grant Universities
LT_{50}	median lethal time
MBT	Methyl Bromide Transitions Program
ml	milliliter
MOA	mode of action
MSMA	monosodium methanearsonate
MSU	Michigan State University
MSU–CIPS	Michigan State University–Center for Integrated Plant Systems
NA-FRAC	North American Fungicide Resistance Action Committee

NAFTA	North American Free Trade Agreement
NASS	National Agricultural Statistics Service
NCC	National Cotton Council
NCGA	National Corn Growers Association
NPC	National Potato Council
NRI	National Research Initiative
OECD	Organisation for Economic Co-Operation and Development
OP	organophosphate
OPMP	Office of Pest Management Policy
OTP	Organic Transitions Program
PAMS	prevention, avoidance, monitoring, suppression
PEP	phosphoenolpyruvate
PESP	Pesticide Environmental Stewardship Program
PSEP	Pesticide Safety Education Program
PIP	plant-incorporated protectant
PM	pest management
PMAP	Pest Management Alternatives Program
PMRA	Pest Management Regulatory Agency
PPDC	Pesticide Program Dialogue Committee
PPO	protoporphyrinogen oxidase
PRM	pesticide resistance management
PSEP	Pesticide Safety Education Program
PTB	pyrimidinyl-thio-benzoates
QoI	Quinone outside Inhibitor
RAC	Resistance Action Committee
RAMP	Risk Avoidance and Mitigation Program
RFA	Request for Application
RM	resistance management
RMP	resistance management plan
RPS	resistant pest management
RR	resistance ratio
SCN	soybean cyst nematode
SCT	sulfonylamino-carbonyl-triazolinones
SIMRU	Southern Insect Management Research Unit
SLA	state lead agency
SRI	Stanford Research Institute
SU	sulfonylurea
TBW	tobacco budworm
TP	triazolopyrimidines
UN FAO	United Nations Food and Agriculture Organization
USDA	U.S. Department of Agriculture
USDA–ARS	U.S. Department of Agriculture–Agricultural Research Service
USDA–ERS	U.S. Department of Agriculture–Economic Research Service
WCRW	Western corn rootworm
WHO	World Health Organization
WSSA	Weed Science Society of America
XML	Extensible Markup Language

Appendix B: Glossary

ALS inhibitor. Herbicides designed to inhibit the plant (weed) enzyme, acetolactate synthase (ALS).

Bacillus thuringiensis (Bt). A naturally occurring bacterium found worldwide in soil and on the surfaces of plants. *Bt* produces proteins toxic to certain insect groups (e.g., caterpillars, beetles, and blackfly and mosquito larvae). Different strains of *Bt* have been registered as insecticides but have had limited use. Genes from *Bt* have been genetically engineered into crop plants (*Bt* plants) to protect the plants from certain insect species.

Baseline population. A pest population that has not been exposed to a particular selective agent, such as a pesticide, and thus can be used as representative of unselected pest populations.

Biointensive IPM. A range of preventative tactics, such as cultural practices and biological controls, used to confine pest populations below economically damaging limits.

Biopesticide. A living organism, or a product derived from a living organism, that functions as a pesticide. Examples are parasites, microorganisms, plant metabolites, and plant-incorporated protectants.

***Bt* crops.** Crops that have been genetically engineered to express proteins from the soil bacterium, *Bacillus thuringiensis (Bt)* to control insect pests.

Cross-resistance. A situation in which a single resistance mechanism confers resistance to two or more pesticides. A pest with that resistance may be resistant to multiple chemistries without being exposed to all of them.

Dose-mortality. The mortality of a pest strain at a specific dose of the toxin, often expressed as the LD_{50}, which means the lethal dose required to kill 50% of the population.

Environmentalism. Advocacy for the preservation or improvement of the natural environment.

Evolved capacity. Resistance caused by a heritable change (mutation) in the genetic makeup of the pest that confers the ability to withstand a pesticide.

Fitness. A measure of the behavior, developmental time, fecundity, and fertility of an individual or group of individuals within a population. A decline in any of these heritable traits can result in a reproductive disadvantage and is termed a fitness cost.

Fungicide. An agent that destroys fungi or inhibits their growth.

Fungicide resistance. The evolved capacity of a previously fungicide-susceptible fungal population to survive a fungicide.

Genetically engineered crop. *See* **Transgenic crop.**

Herbicide. An agent used to kill plants or inhibit plant growth.

Herbicide mixtures. A combination of herbicides with different modes of action used to control a set of weed species.

Herbicide resistance. The evolved capacity of a previously herbicide-susceptible weed population to survive an herbicide application.

Herbicide rotation. Rotating between herbicide modes of action from year to year or within a season. This technique is used to delay resistance development.

Insecticide. An agent that kills, repels, or otherwise controls insects.

Insecticide resistance. The evolved capacity of a previously insecticide-susceptible insect population to survive an insecticide.

Integrated pest management. A strategy that uses combinations of biological, chemical, and cultural practices (including crop rotation and host-plant resistance) for the satisfactory control of pests and to keep pests below economically damaging levels.

Mode of action. The biochemical mechanism by which a pesticide kills a pest.

Multiple resistance. A situation in which more than one resistance mechanism is present within the same individuals of a pest population.

Organically grown food. Food grown under a set of standards set by the National Organic Program governed by the United States Department of Agriculture, Agricultural Marketing Service (Final Rule, 7 CFR Part 205, *Federal Register*, Vol. 65, No. 246, Dec. 21, 2000).

Organophosphate. A chemical class of insecticides that operates by blocking the enzyme acetylcholinesterase, interrupting the transmission of nerve impulses and leading to insect death.

Pest. Any insect, mite, fungi, bacteria, virus, weed, nematode, or mammal that poses a threat to human activities such as agriculture.

Pest complex. A combination of diseases, insects, or weeds targeted by pest control practices.

Pesticide resistance. The evolved capacity of a pest population to withstand exposure to a pesticide. The evolution of resistance occurs through a process of natural selection whereby a population becomes less sensitive to a pesticide. Resistance may develop in insects, weeds, or pathogens.

Pyrethroid. A chemical class of insecticides that affects sodium channels in both the peripheral and central nervous system of insects, stimulating repetitive nervous discharges leading to insect paralysis and death.

Quinone outside inhibitor. A chemical class of fungicides that acts at the Quinone “outside” (Qo) binding site of the cytochrome bc1 complex.

Reduced-risk pesticide. An EPA definition used to designate certain lower-risk pesticides (as compared with the registered alternatives) that pass a reduced-risk screening process (see Pesticide Registration Notices 97-2 and 98-7). Reduced-risk pesticides also include all biopesticides.

Redundant killing. The use of two pesticides with different modes of action to effectively kill susceptible individuals more than once because each mode of action is lethal by itself.

Refuge. An area in which a pesticide is not applied against a pest population and hence susceptible alleles to the pesticide can remain abundant. In terms of insect resistance management for *Bt* crops, an area planted to non-*Bt* varieties or alternative hosts where susceptible pests can survive and produce a local population capable of mating with any possible *Bt*-resistant insects that developed on the *Bt* crop.

Resistance. The evolved capacity of an organism to survive exposure to a selective agent (e.g., pesticide).

Resistance management strategy. A strategy that can be employed to delay the onset of resistance. For insect resistance management, this may include the use of a “refuge” area.

Resistance ratio. A measure of resistance defined by the ratio of dose-mortality of the tested strain over the dose-mortality of the susceptibility strain.

Resistance Risk Profile. The likelihood of resistance evolving to a particular pesticide based on its use pattern, mode of action, the genetics of resistance (to the extent known), and field studies.

Selectivity. The breadth of species affected by the pesticide.

Single-site inhibitor. A pesticide that targets only one enzymatic site of action.

Spatial model. A mathematical simulation model that explicitly considers spatial variation.

Target site. The biochemical site of action of a pesticide (e.g., the specific enzyme that the pesticide affects).

Target-site specificity. The degree to which a pesticide targets only one specific site of action.

Tolerance. The ability of a pest to withstand exposure to a particular pesticide. This ability need not be heritable, or related to exposure to that pesticide.

Transgenic crop. A crop modified through genetic engineering to contain one or more genes from an unrelated species to provide the crop with a desired trait, such as pest resistance.

Transgenic technology. A set of technologies by which a plant, animal, or microorganism may be genetically introduced into an unrelated species (e.g., *Agrobacterium tumefaciens*-mediated transformation, biolistic bombardment).

Varietal selection. The genetic breeding process for selecting specific agronomic or genetic traits of interest in a plant, animal, or microorganism.

Appendix C: Symposium Agenda

CAST Symposium
Management of Pest Resistance:
Strategies Using Crop Management, Biotechnology, and Pesticides

April 10-11, 2003
Indianapolis, Indiana
AGENDA

Thursday, April 10, 2003

1:00 P.M. **Welcome and Introduction to the Workshop**
Teresa A. Gruber, Council for Agricultural Science and Technology (CAST) and
Barry J. Jacobsen, Montana State University

1:10 P.M. **Session I: Scope of North American Pest Resistance Problems in 2003**

Each speaker will summarize the scope and magnitude of pest/pesticide resistance problems in North America.

A. Overview: Mark E. Whalon, Michigan State University
B. Insects: Mark E. Whalon, Michigan State University
C. Weeds: Ian M. Heap, Weed Smart LLC
D. Pathogens: Wolfram Koeller, Cornell University

2:05 P.M. **Session II: Issues in Pest Resistance Management**
Moderator: Sharlene R. Matten, United States Environmental Protection Agency

For each crop/pest(s) situation, each speaker will address the following:

1. the pest/pesticide resistance issues.
2. what is/was done to manage the resistance problems (or potential problems).
3. the barriers to pest resistance management.

A. Fruits and vegetables: Charles Mellinger, Glades Crop Care
B. Cotton: Patricia F. O’Leary, Cotton Incorporated
C. Potato: John Keeling, National Potato Council
D. Corn/soybean cropping system: Kevin L. Steffey, University of Illinois
E. Turf/ornamental: Larry Stowell, PACE Turfgrass Research Institute
F. Organic cropping systems: Kevin Brussell, Midwest Organic Farmers Cooperative
G. Panel discussion/Q & A

3:45 P.M. **BREAK**

4:00 P.M. **Session III: Lessons Learned I: Balance between Industry, Academia, Users, and Regulators [Case Studies]**
Moderator: Tony Shelton, Cornell University

For each case study, each speaker will address the following:

1. the particular pest/pesticide resistance problem (scope and extent in the U.S. and worldwide).
2. what is/was done to manage the resistance problem (or potential).
3. the barriers to pest resistance management.

A. Triazine, Acetolactate synthase (ALS) inhibitor, Protoporphyrinogen oxidase (PPO) inhibitor resistance: Les Glasgow, Syngenta
B. Glyphosate resistance: David Heering, Monsanto Company
C. Cotton pest (insects, weeds, pathogen) resistance in the Midsouth: Ralph Bagwell, Louisiana State University
D. Fungicide resistance in fruit crops: Wayne F. Wilcox, Cornell University
E. Diamondback resistance in crucifers: Anthony M. Shelton, Cornell University
F. Cotton/vegetable crop insect resistance in the Southwest: Timothy J. Dennehy, University of Arizona
G. *Bt* Crop insect resistance management: Graham P. Head, Monsanto Company
H. Panel discussion/Q&A

5:30 P.M. **DINNER ON YOUR OWN**

7:30–9:30 P.M. **Session IV: Lessons Learned II: Have Models Helped?**
Moderator: Wolfram Koeller, Cornell University

For insect, weeds, and pathogens, each speaker will address the following:
1. the predictive role models have played in pest resistance management.
2. how models have been used to identify data gaps/needs.
3. the uncertainty associated with input parameters in various models.
4. the validation of models.

A. Insects: Nicholas P. Storer, Dow AgroSciences
B. Insects: Richard Roush, University of California–Davis
C. Weeds: Carol Mallory-Smith, Oregon State University
D. Pathogens: Hendrik L.Ypema, BASF
E. Panel discussion/Q & A

Friday, April 11, 2003

8:00 A.M. **Session V: Role of Stakeholders**
Moderator: Carol Mallory-Smith, Oregon State University

For each stakeholder, each speaker will address the following:
1. the goals of RM implementation.
2. the barriers/challenges to resistance management (RM) implementation.
3. the goals of others in pest resistance management.

Session V, Part I: Consumers, Producers, and Distributors

A. Consumer/public interest communities: Doug Gurian-Sherman, Center for Science in the Public Interest (CSPI)
B. Crop consultants: Roger Carter, National Alliance of Independent Crop Consultants (NAICC)
C. Grower organizations: Frank L. Carter, National Cotton Council
D. Pesticide manufacturers: Caydee Savinelli, Syngenta, Insecticide Resistance Action Committee (IRAC); Gilberto Olaya, Syngenta, Fungicide Resistance Action Committee (FRAC); and Marvin Schultz, Dow AgroSciences, Herbicide Resistance Action Committee (HRAC)
E. Pesticide dealers and distributors: Scott Pace, Helena Chemical Company, Chemical Producers and Distributors Association (CPDA)

Session V, Part II: Regulation, Research, Education, and Funding

F. Federal pesticide regulation: Sharlene R. Matten, USEPA and Pierre Beauchamp, Canada/Pest Management Regulatory Agency
G. Federal cooperative research: Eldon E. Ortman, U.S. Department of Agriculture (USDA), Cooperative State Research, Extension, and Education Service (CSREES)
H. Minor crops (IR–4 Project): Michael P. Braverman, Rutgers, The State University of New Jersey
I. Pesticide education and training programs: Monte P. Johnson, USDA/CSREES
J. State pesticide regulation: David Scott, Office of the Indiana State Chemist
K. Extension: Walter R. Stevenson, University of Wisconsin
L. Academic research: Thomas O. Holtzer, Colorado State University

10:15 A.M. **BREAK**

10:30 A.M. **Session VI: Lessons Learned III: How Can We Work to Alleviate Barriers to Comprehensive RM Implementation? How Can We Work Together Better?**
Moderator: Barry J. Jacobsen, Montana State University

Each speaker will address the following questions:
1. What are the possible tactics/solutions that can/should be used to alleviate barriers to comprehensive resistance management implementation?
2. How should organizations work together to address proactively potential resistance issues?

Session VI, Part I: Consumers, Producers, and Distributors
A. Pesticide manufacturers: Gary D. Thompson, Dow AgroSciences, IRAC; Roger P. Kaiser, Bayer, FRAC and Natalie DiNicola, Monsanto Company, HRAC
B. Crop consultants: Roger Carter, National Alliance of Independent Crop Consultants
C. Growers: John Keeling, National Potato Council
D. Public interest consultants: Charles Benbrook, Benbrook Consulting Services

Session VI, Part II: Regulation, Research, Education, and Funding
E. Academic research: Thomas O. Holtzer, Colorado State University
F. Federal research: Eldon E. Ortman, USDA/CSREES
G. State regulatory: David Scott, Office of the Indiana State Chemist
H. Plant breeding research: Margaret E. Smith, Cornell University
I. Federal pesticide regulation: Sharlene R. Matten, USEPA
J. Canadian pesticide regulation: Pierre Beauchamp, Canada/PMRA
K. Panel Discussion/Q & A

12:00 P.M. **LUNCH ON YOUR OWN**

1:00 P.M. **Session VII: Pest Resistance Management Goals**
Moderator: Cindy Lynn Richard, Council for Agricultural Science and Technology

Session VII, Part I: Resistance Management Strategies
Each speaker will address the following:
1. the goals of pest resistance management: proactive versus reactive resistance management.
2. the role of resistance monitoring in managing pest resistance.
3. the strategies/tactics that should be used to limit selection pressure (e.g., mode of action rotation, limiting number and frequency of applications, timing of application, high dose/refuge, crop rotation, biological control etc.).
4. the use of forecasting and diagnostic tools in aiding resistance management?

A. Weeds: Dale L. Shaner, USDA/Agricultural Research Service

B. Insects: D. D. Hardee, USDA/Agricultural Research Service
C. Pathogens: Barry J. Jacobsen, Montana State University
D. Agricultural information technology: Dennis D. Calvin, Pennsylvania State University (& ZedX)
E. Discussion/Q & A

Session VII, Part II: Resistance Management Education and Communication
Each speaker will describe the education and communication efforts used to improve the effectiveness of long-term pest resistance management.

A. Michael D. Orzolek: Pennsylvania State University
B. Mark E. Whalon: Michigan State University
C. Ronald E. Stinner: North Carolina State University
D. Thomas Slunecka: National Corn Growers Association
E. Discussion/Q & A

2:45 P.M. **BREAK**

3:00 P.M. **Session VIII: Symposium Recommendations for Pest Resistance Management—Where to Now?**
Moderator: Teresa A. Gruber, Council for Agricultural Science and Technology

4:00 P.M. **Symposium Adjourns**

Appendix D: Symposium Attendees

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