Current Issues Surrounding the Utilization of Genetically Modified Organisms:

Andrea F. Huberty

Initiated in 1993 by George Kennedy and Fred Gould and now sponsored by the ESA Student Affairs Committee, the Formal Conference on Student Affairs: Student Debates encourages students to research assigned topics, synthesize relevant entomological information, and debate the issues from a broad public perspective. For the 2001 Student Debates, we focused on issues concerning genetically modified organisms (GMOs). Two graduate student teams also debated a GMO topic during the Plenary Session of the ESA Annual Meeting in San Diego. We are grateful for the introductory notes presented by May Berenbaum at the Plenary Debate, and to the Program Chairs, Mike Gray and Ken Steffey, for the opportunity to showcase this student activity.

Each team that participates in the debates is assigned randomly to the pro or con position on a topic. Therefore, the opinions presented in the various papers are not necessarily the position of the student members or the university departments represented. At the debates, each topic begins with a 5-minute nonbiased introductory statement by a nonparticipating team. Each team then presents its 7-minute position statement followed by 3-minute rebuttals. Each topic is concluded by a question and answer session with the audience.

Participation in the debate is encouraged for all student members of the association. Debate topics are chosen, and letters for team recruitment are sent to entomology departments (and related disciplines) in early spring. Teams use the fall semester to organize and prepare for the debates with their faculty advisers. Many schools offer formal seminar credit for debate team participation, whereas other teams use informal seminars or journal clubs to prepare for the debates. Students interested in participating in future debates are encouraged to contact the Student Affairs Committee of ESA (http://www.entsoc.org/about_esa/committees/STUDENT_AFFAIRS_COMMITTEE.htm).

Acknowledgments

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■ TOPIC:

Resistance management protocols for genetically modified crops are adequate

Introduction

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University of Illinois

Agricultural revolutions come in all forms. Take the invention of the self-scouring plow as an example. John Deere's remarkable technological innovation, a highly polished moldboard plow that prevented thick prairie loam from adhering to its surface and stopping its progress through the furrow, allowed farmers for the first time to convert prairie to agricultural land quickly and efficiently. Within 10 years of producing the first plow, John Deere's company was manufacturing 1,000 plows a year, and these plows changed the face of the landscape; for example, the "Prairie State", Illinois, has less than 0.01% of original prairie remaining today.

We are experiencing another agricultural revolution, but it is subtler in its impacts. The landscape looks much as it always has. In fact, this revolution is essentially invisible to all but the most well-trained and technologically equipped observer. The ability to manipulate organisms genetically—to splice genes encoding proteins that confer protection against pests or that improve the appearance, nutritional value, or storage property of a crop plant—has not radically changed the appearance of the crop or the landscape in which it grows. What has changed, however, is the selective regime imposed on crop plants and their pest insects, along with the legal landscape within which the agricultural enterprise is carried out.

And here is where the problem arises. Understanding the changes that agriculture has undergone in the past two decades as a result of advances in genetic engineering is not easy. Adding to the challenge is that these changes have been spectacularly rapid.

The U.S. Environmental Protection Agency (EPA) permitted commercial use of transgenic insecticidal cultivars in 1996; among those released that year were so-called *Bacillus thuringiensis*–plant-incorporated protectants. These crops, engineered with a gene from the bacterium *Bacillus thuringiensis* Berliner (*Bt*) that confers resistance against insect pests, have enjoyed a meteoric rise in popularity. Genetically modified (GM) cotton, in 1996 comprised less than 2 million acres; by 2000 GM cotton was planted on almost 4.4 million acres. The increase in GM corn acreage has been even more dramatic. In 1996, GM corn was planted on less than 0.5 million acres, constituting 1% of total acreage; by 2000, 19.5 million acres were planted, constituting more than 25% of total acreage.

Rapid changes rightly elicit concerns; and, with respect to GM crops, questions were raised even before commercial release, largely on the basis of 50 years of experience with problems created by the use of synthetic organic insecticides. The possibility of resistance acquisition to pest-protected crops was a particularly acute concern, given the heavy reliance upon a single (or similar) insecticidal protein for engineering resistance: Cry1Ab in corn shares >90% amino acid identity with Cry1Ac in cotton.

Bt has been used as a microbial formulation or a spray for many years, and field-evolved resistance is well documented (it is reported in the United States, Costa Rica, Guatemala, China, Japan, Malaysia, and the Philippines, among other places). Resistance to the *Bt* protein engineered into crop plants thus seemed a likely possibility. Resistance to any single *Bt*-protected crop was seen as having the potential to alter the efficacy of other *Bt*-protected crops and to lead growers to shift to more toxic and less environmentally friendly alternatives. As well, *Bt* itself is among the few tools used by organic growers for pest control; loss of efficacy would leave organic growers, one of the most rapidly growing segments of the agricultural community, without any effective management tools.

The EPA views protection of insect susceptibility to *Bt* to be "in the public good", and the agency in 1998 mandated Insect Resistance Management (IRM) programs. These programs are based on a high dose–structured refuge approach: a high dose is defined as 25 times the concentration needed to kill susceptible insects and a structured refuge as "all suitable non-*Bt* host plants for a targeted pest planted and managed by people." This approach assumes that resistance is a recessive trait, controlled at a single locus, and initially rare in populations, with random mating between resistant and susceptible adults. Size and location of refuges vary with the GM crop and are set on the basis of mathematical models, grower acceptance, and logistical feasibility. Dose, too, is crop- and insect-dependent.

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Other elements in an IRM program include requirements for GM crop users to sign "grower agreements" imposing contractual obligations to comply with refuge requirements. For their part, registrants are required to develop, implement, and report to EPA about grower education efforts; to evaluate and promote grower compliance; to develop and implement programs to monitor insect susceptibility through such venues as grower reports of unexpected damage, field surveillance, bioassays, F2 screens, and sentinel plots; and to develop and implement, if needed, a "remedial action plan" if resistance is detected. Although resistance is known to evolve in response to almost any kind of selection pressure resulting in significant mortality (including nonchemical management techniques such as crop rotation), GM crops were the first pest management tools for which specific resistance management practices were mandated by federal law.

According to the EPA's Biopesticides Registration Action Document (BRAD) for *Bt* Plant–Incorporated Protectants, released October 15, 2001, "the issue of resistance management has generated more data, meetings, and public comment than all of the other sections covered in this BRAD," a 153-page document (EPA 2001a). Not inappropriately, then, this is the subject of the first of four student debates on genetically manipulated organisms in entomology. The topic "Resistance Management Protocols for GM Crops are Adequate" was debated at the ESA annual meeting by students from Texas A & M representing the pro side and students from Virginia Tech representing the con side.

▲ Pro Position

Roberto L. Gorena, Jason L. Mottern,
and Marcia K. Trostle
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Given today's understanding of insect behavior and genetics, we maintain that current insect resistant management (IRM) strategies in crops genetically modified to express *Bacillus thuringiensis* Berliner (*Bt*) toxins are adequate. These strategies consist of high-dose expression of the Cry toxin in genetically modified plants coupled with refuges of nontransgenic plants to ensure susceptible pest populations.

This strategy makes two assumptions: (1) random mating within the pest population and (2) recessiveness of resistance alleles. Random mating is addressed by the temporal and spatial refuge components of the strategy. Liu and Tabashnik (1997a) demonstrated the efficacy of a 10% refuge planting for delaying resistance. On the basis of this and other studies, current EPA requirements mandate that 20% of total corn acreage be planted with a non-*Bt* crop refuge (EPA 2001a). Additionally, refuge fields must be planted within 0.5 mile of transgenic fields. The EPA has also mandated refuge requirements for cotton, ranging from 5 to 25% non-*Bt* refuge, depending on the relative placement of *Bt* and nontransgenic crops (EPA 2001a).

Resistance is usually conferred by rare recessive alleles (Gould et al. 1997, Tabashnik et al. 1997, Gahan et al. 2001), although dominant alleles have been identified (Gould et al. 1997, Liu and Tabashnik 1997b, Tabashnik et al. 1997). Therefore, the assumption of recessiveness is typically valid, and new technologies such as inserting multiple insecticidal genes in a transgenic cultivar (gene stacking) can address the rare cases of dominance.

In the unlikely event that resistance does occur, the EPA has outlined remedial action plans to minimize the potential for resistant populations to persist. In cases of suspected resistance, alternative control measures (e.g., chemical insecticides) are used immediately to control pests. Furthermore, all crop residues in the affected region are immediately destroyed to prevent overwintering of resistant pests. If resistance is verified, additional measures are taken to modify cropping techniques to prevent future resistance from developing (EPA 2001a).

Despite the approximately 175-million ha of *Bt*-transformed crops planted globally since 1996 (James 2001), only the diamondback moth [*Plutella xylostella* (L.)] has become resistant to *Bt* toxins in the field (Frutos et al. 1999). Furthermore, this resistance occurred before EPA-mandated IRM guidelines were in place. Given the track record and basis of current IRM plans in science, we maintain that current IRM strategies are adequate to address resistance issues in transgenic cultivars.

Acknowledgments

We thank Craig Coates for serving as our faculty adviser for the debates, Marvin Harris and the anonymous reviewers for helpful comments about the debate summary, and Andrea Huberty for organizing all components of the debate process.

▼ Con Position

Corey D. Broeckling, Michelle E. McClanan, Sarah
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Exercising caution in resistance management for *Bt* crops is more than justified because of *Bt*'s valuable insecticidal properties, as well as the prospect of imminent *Bt* resistance occurring in various damaging insect pests. Only one generation was necessary for a lab-reared strain of cotton bollworm [*Helicoverpa zea* (Boddie)] to become resistant to *Bt* (EPA 2001b), demonstrating the possibility of rapid resistance for many insect pests.

The high dose–refuge strategy for delaying *Bt* resistance can be effective, but only under the following four assumptions: (1) resistant individuals are rare, (2) resistant alleles are recessive, (3) random mating occurs among individuals in *Bt* crops and refuges, and (4) high dose is expressed in *Bt* crops (EPA 1998). Simulation models have confirmed the effectiveness of the high dose–refuge strategy under these assumptions (Onstad et al. 2001). However, exceptions to these assumptions have been found in the field. The following are exceptions to each of the four assumptions:

(1) Resistant individuals are not always rare. There is a relatively high initial frequency of resistant alleles, 0.16 compared with the benchmark of 0.0030, for some strains of pink bollworm [*Pectinophora gossypiella* (Saunders)] (Tabashnik et al. 2000).

(2) Resistant alleles are not always recessive. Pink bollworm resistance was found to be codominant at low concentrations of *Bt* toxin, and

recessive only at very high doses (Bourguet et al. 2000).

(3) Random mating may not occur. *Bt* delays Colorado potato beetle [*Leptinotarsa decemlineata* (Say)] development, thus emergence times, between *Bt* and refuge crops are not synchronized (Nault et al. 2000).

(4) High doses are not always expressed. None of the *Bt* cultivars of cotton or corn produces a high dose for cotton bollworm (EPA 2001b).

Resistance can develop faster if one of the above assumptions fails, so procedures must be available to monitor and remediate resistance. However, current techniques for monitoring *Bt* resistance are difficult and time-consuming (Andow et al. 1998, Bailey et al. 2001). Monitoring techniques are too slow for the remediation of resistance to be effective, even when a remedial action plan exists (i.e. Arizona Rapid Response Team) (EPA 2001b). Currently, there is no remedial action plan for cotton bollworm or tobacco budworm [*Helicoverpa virescens* (F.)] (EPA 2001b).

Adjustments must be made to resistance simulation models to account for any failings of the assumptions for each pest system. There must also be viable resistance monitoring procedures and remedial action plans in place. Until then, we argue that resistance management in *Bt* crops is inadequate.

Acknowledgments

We thank our faculty adviser, Scott Salom, and the Department of Entomology at Virginia Tech.

■ TOPIC:

The use of genetically modified organisms in agriculture will lead to increased levels of biological diversity in agro-ecosystems

Introduction

Boris A. Castro, Jeffrey Gore,
Kelly Tindall, and Erin Watson
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The introduction and commercialization of genetically modified organisms (GMOs) in agriculture have raised interests among producers, the scientific community, and society. These technological advances have encouraged a refocusing of scientific efforts into new areas of research and commercial development. However, the rapid increase in deployment of GMOs for U.S. agriculture also has initiated a controversial debate among scientists about the potential negative effects of GMOs on biological diversity in agro-ecosystems.

Some studies indicate that the protein produced by *Bacillus thuringiensis* Berliner (*Bt*) and expressed by genetically engineered insect-resistant crops does not adversely affect honey bees, *Apis mellifera* L., and other beneficial insects directly (Pilcher et al. 1997, Halford and Shewry 2000). In addition, Halford and Shewry (2000) suggest that the protein is not toxic to fish, birds, and mammals. However, GMOs may reduce certain herbivore or omnivore populations dramatically, thereby limiting the availability of food sources at subsequent levels in the food chain. Reduced food supplies could lower populations at higher trophic levels and ultimately lead to local species extinctions (Watkinson et al. 2000).

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Toxic effects of *Bt* corn pollen on the monarch butterfly, *Danaus plexippus* (L.), (Losey et al. 1999) and *Chrysoperla carnea* (Stephens) (Hilbeck et al. 1998) have been reported. However, additional studies report negligible toxic effects of *Bt* corn pollen from current commercial corn hybrids on the monarch butterfly (Hellmich et al. 2001, Sears et al. 2001, Zangerl et al. 2001), with only a minor localized concern under specific environmental conditions (Pleasants et al. 2001, Zangerl et al. 2001). Also important have been observations of nontoxic effects of *Bt* corn pollen on the black swallowtail, *Papilio polyxenes asterius* Stoll, (Wraight et al. 2000), and on coccinellid, anthocorid, and chrysopid natural enemies (Pilcher et al. 1997).

Genetically engineered herbicide-tolerant crops may result in the intensified use of glyphosate, which is toxic to some nontarget organisms (Paoletti and Pimentel 1996). However, Halford and Shewry (2000) argue that glyphosate is a safe and rapidly degrading herbicide compared with more hazardous, persistent, and highly mobile herbicides commonly used in agriculture.

Biodiversity is the essential ingredient for all life, as well as a source of discoveries for the advancement and understanding of life processes and human interactions on earth (Lovejoy 1997). Therefore, it is important to make a conscious effort to reduce the negative impacts of agricultural pest control on biodiversity in agro-ecosystems as well as on the nonagricultural environment. The following arguments review current information and identify areas of impact that GMOs could have on environmental biodiversity. This, in turn, will help to characterize and understand the advantages and/or disadvantages of transgenic technology in contrast to other pest control strategies for agricultural production.

Acknowledgments

We thank the LSU advisers for the 2001 debate team, T. E. Reagan, Professor of Entomology (IPM and sugarcane insects), Tom Riley, Professor Emeritus of Entomology (corn IPM), and Roger Leonard, Professor of Entomology (cotton IPM).

Pro Position

Jon C. Bedick, Laura A. Campbell, Diana K. Londoño, Rodney A. Madsen, and Raj K. Saran
University of Nebraska

We do not dispute the contention that GM crops affect biodiversity. The more important question is whether transgenics can have a positive effect on diversity in agro-ecosystems. The potential risks and benefits of genetically modified crops must be compared with traditional pest management practices that involve nonselective pesticides or augmentative release of biocontrol agents, both of which have been shown to negatively effect biodiversity (Peterson et al. 2000).

Pro Position

Society cannot afford to lose this powerful tool that may in the future offer even greater protection of our environment and increase biodiversity in agro-ecosystems.

The possible positive effects on biodiversity in agro-ecosystems are exemplified by three specific situations.

Reduced Pesticide Use. Depending on their specific uses, GM crops could decrease the amount of nonselective insecticides used to control insect pests and therefore enhance biodiversity in agro-ecosystems. Transgenic crops, such as *Bt* cotton, have been shown to replace conventional neurotoxin insecticides that are widely known to negatively affect nontarget organisms (Betz et al. 2000). Relative to traditional synthetic insecticides, the technology is likely to have positive effects (Stanley-Horn et al. 2001).

Conservation Tillage. GM crops tolerant of specific herbicides allow farmers to use conservation tillage systems (Betz et al. 2000). As a consequence, soil and weed cover are undisturbed; soil erosion and water runoff are reduced; and soil nutrients are retained. Nutrient retention would result in less fertilizer use, reducing leaching (nitrate) into waterways and lowering production costs. Undisturbed ground cover during winter provides habitat for insects and other animals, helping to sustain and promote biodiversity (Gruissem 1999). Compared with cultivated fields, for a parallel comparison, conservation tillage minimizes carbon dioxide release because more carbon remains in the soil, thereby helping to slow global warming (Robertson et al. 2000).

Environmental Reclamation. GM plants that tolerate soils contaminated with salts and metals may provide an opportunity to reclaim arable lands lost through environmental mismanagement. Such reclamation could take several forms. Transgenes that prevent the uptake of harmful materials by plants allow for immediate and safe use of the contaminated land (Zhu et al. 1999). Additionally, tolerance and sequestration of contaminants by genetically altered plants would allow concentration of metals and possible remediation of contaminated soil (Lopez-Bucio et al. 2000, Schmohl et al. 2000). Using transgenics to reclaim contaminated areas would allow species to recolonize these former habitats.

In summary, GM crops provide an alternative to conventional pesticides and may help to reclaim lost arable lands. Society cannot afford to lose this powerful tool that may in the future offer even greater protection of our environment and increase biodiversity in agro-ecosystems.

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Con Position

Shannon Sked, Clayton Myers, Abid Kazi, Tim Tomon, and Patrick Tobin
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Biodiversity is not well understood at any level, nor is there a consensus on how to measure it. This problem is particularly acute in the study of microbes and other components of soil communities that are very important in agriculture (O'Donnell et al. 1994). Nevertheless, the implementation of GMOs continues to increase, despite several studies demonstrating their inimical effects on agro-ecosystem biodiversity. Our objective is to summarize some of these studies.

Plants that produce toxins with insecticidal properties (e.g., *Bt*-corn) are the most controversial GMOs with respect to biodiversity in agricultural systems. The use of these crop plants has resulted in several direct effects on agro-ecosystem biodiversity. For example, Jesse and Obrycki (2000) reported increased mortality in monarch butterflies, *Danaus plexippus* (L.), that fed on milkweed with *Bt*-corn pollen. Flexner et al. (1986) observed that *Bt* toxins caused >40% mortality across several nontarget insect taxa, including honeybees, ladybird beetles, lacewings, and parasitoids.

There also have been reports of indirect effects of GMOs on agro-ecosystem biodiversity. For example, several studies have shown increased mortality in *Chrysoperla carnea* (Stephens) (Neuroptera: Chrysopidae) when they were reared on prey species that had been reared on diet or host plants containing *Bt* toxins (e.g., Hilbeck et al. 1999). *Macrocentrus cingula* Reinhardt (Hymenoptera: Braconidae), which attacks European corn borer, *Ostrinia nubilalis* (Hübner) (Lepidoptera: Pyralidae), was less abundant in fields of *Bt*-corn than in those with traditional hybrids (Pilcher 1999). Also, Birch et al. (1999) observed reductions in fecundity, egg survivorship, and longevity of two-spotted lady beetle, *Adalia bipunctata* (L.) (Coleoptera: Coccinellidae), when fed green peach aphid, *Myzus persicae* Sulzer (Heteroptera: Aphididae), that were reared on transgenic potato.

Another area of concern is the use of crop plants that are engineered to be resistant to the toxic effects of herbicides (e.g., Round-up Ready soybean). Increased herbicide use results in a decrease in plant floral biodiversity, with cascading effects in agro-ecosystem communities. For example, Watkinson et al. (2000) contended that the use of herbicide-resistant crops drastically reduced the abundance of weed seeds and, therefore, threatened bird populations that depended on these seeds for food.

The use of GMOs may also reduce genetic diversity, and the high adaptation rate of GM crops can lead to regional crop homogeneity. Adoption of single genotypes of GM crops over polycultures, particularly in developing countries, is of great concern. Introgression of transgenic material from crops into other plants may further reduce biodiversity as weeds that incorporate these genes may competitively exclude those that cannot. Also, landraces and wild relatives may be contaminated with transgenic material (Quist and Chapela 2001).

We have highlighted some of studies that showed adverse effects of GMOs on agro-ecosystem biodiversity. We submit that these negative effects of GMOs outweigh their benefits. Nevertheless, the use of GMOs is advancing faster than our knowledge of biodiversity, resulting in losses to agro-ecosystem biodiversity before we even have an opportunity to study it.

Acknowledgments

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■ TOPIC:

Crops that are genetically modified using transgenic approaches require stricter regulations than crops modified by conventional crop breeding approaches

Introduction

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and Amanda C. Staley
University of Kentucky

As the human population increases, food yields also must increase. New varieties of crops are needed that improve nutritional quality, disease and insect resistance (Kareiva 1999), and adaptability to marginal areas (Vasil 1999).

Historically, the most practiced method for crop improvement was artificial selection wherein the farmer–breeder chose plants with characteristics that could enhance yield and quality. Recently, the more structured practices of hybridization and mutagenesis were developed (Agrawal 1998). Modern recombinant DNA and PCR (polymerase chain reaction) techniques make it possible to engineer plants by silencing or inserting genes regardless of phylogenetic relatedness. This modification can be done in several ways; for example, new DNA fragments conferring desired traits could be incorporated into a target plant genome through vector-mediated transformation, ballistic impregnation, or by electroporation. Inserting or deleting a gene fragment can apply antisense technology to silence or neutralize undesirable genes. The end product of such technologies is known as a transgenic or genetically modified organism (GMO) (Murray 1991).

Unlike conventionally developed crops, GMOs must receive governmental approval before commercial release in the United States. Studies are required to evaluate environmental and food safety risks of the GMO crop. The EPA assesses the risks to the environment of releasing genetically modified crops that incorporate genes to produce toxins for pest control (EPA 2001c). Three branches of the U.S. Department of Agriculture (USDA) determine whether it is safe to release GMO crops into the environment. The Animal Health and Plant Inspection Service oversees field tests and issues permits to grow new cultivars. The Agricultural Research Service runs in-house tests, and the Cooperative State Research, Education, and Extension Service oversees the USDA risk assessment program (EPA 2001c). The Food and Drug Administration (FDA) decides whether the GMO crop is safe for human and animal consumption; FDA laws only regulate the safety of GMOs for processed food (FDA 2001).

Current GMOs can reduce pest-related crop loss and allow greater flexibility for weed control (Le Buanec 1996). When economically favorable, GMOs have been adopted very quickly. At the same time, public concern about the regulation and safety of biotechnology is increasing. This controversy is compounded as countries implement different regulatory policies to protect their own economic interests (BCPC 1998).

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▲ Pro Position

Jeffrey Gore, Boris A. Castro, Kelly Tindall,
and Erin Watson
Louisiana State University Agricultural Center

The United States has been the global leader in the development and commercialization of transgenic crops; therefore, an effective regulatory process in the United States should set the regulatory standards for transgenic crops. Several differences between transgenic and conventional crops should be addressed before genetically engineered crops are integrated into agriculture. With transgenic crop breeding techniques, genetic material often is derived from distantly related species (in many cases from different Kingdoms), whereas, with conventional breeding, the genetic material comes from the same or closely related species (NRC 2000). Another important difference, in terms of insect-resistant crops, is how the trait is expressed. A single gene generally controls the trait in a transgenic crop. In contrast, multiple genes are often involved in regulating insect resistance traits with conventional crops (NRC 2000).

Transgenic crops pose several concerns that are not typically considered with conventional crops; for example, potential allergenicity (Nordlee et al. 1996), gene flow of nonplant genes (Quist and Chapela 2001), and resistance management (Mellon and Rissler 1998). Foreign genes in transgenic crops result in the introduction of novel products into the food supply with potential adverse effects on human health. Also, introduced traits in transgenic crops could be transferred to closely related wild species and disrupt native ecosystems. Organic farmers often rely on formulated *Bacillus thuringiensis* Berliner (*Bt*) products in their production systems (Mellon and Rissler 1998). The development of resistant arthropod strains could result in a total loss of insect control in those systems. Therefore, resistance management plans should remain an important component in the registration process of transgenic crops.

Much of the publicity about transgenic crops has focused on negative aspects of the commercialization process. The 'Starlink' corn incident (Kuiper et al. 2001) and *Bt*-corn pollen toxicity to monarch butterflies (Shelton and Sears 2001) highlighted problems with the regulatory process and reduced public confidence in the technology. Regulatory laws should bolster public confidence; however, public confidence should not shape those laws (Jasanoff et al. 1995).

Con Position

Processes and regulations currently in place to screen for potential allergens and toxins in conventional crops should be equally effective in detecting health risks that arise with GMOs.

Transgenic crops are an important component of a holistic integrated pest management (IPM) system. However, in keeping with the principals of IPM, this technology must be a safe and environmentally friendly alternative to synthetic pesticides for economical pest management. The only way to ensure that this technology remains a sustainable component of IPM practices without adverse effects on human health or the environment is through proper regulation. Regulatory policies that go beyond those for conventional crops will minimize negative publicity and ensure local, national, and international consumer confidence in transgenic technologies.

Acknowledgments

Members of the Louisiana State University team express appreciation to their faculty advisers, Gene Reagan, Roger Leonard, and Tom Riley, for advice in preparing the argument.

Con Position

Kelly Cook, Jonathan Lundgren, Timothy Mabry, and Christopher Pierce
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More than a decade of safety evaluation and experience with genetically modified plants has provided evidence and assurance that risks pertaining to allergenicity and human health, gene transfers to endemic crop relatives, and effects of transgenic plants on nontarget organisms are no different from risks posed by plants bred with traditional methods (NRC 2000).

There is no difference between the health risks posed by GMOs and conventionally produced plants. Many conventionally produced plants contain compounds that are hazardous to human health. For example, conventionally bred varieties of potato and celery that contained unacceptable levels of toxins were identified as harmful before serious human health effects occurred (Diawara and Trumble 1997, Friedman and McDonald 1997). Processes and regulations currently in place to screen for potential allergens and toxins in conventional crops should be equally effective in detecting health risks that arise with GMOs.

More information should be gathered on the effects of gene flow from crop plants to wild relatives and the effects of crop plants on nontarget organisms. Regulations should be established for all crop varieties, regardless of how they are produced. Scientists have documented gene transfers from crop plants to wild relatives for decades (Small 1984, NRC 2000), and these genes have altered endemic plant species and promoted weedy traits in some species [i.e., Johnson grass, *Sorghum halepense* (L.) (NRC 2000) and wild sugar beets, *Beta vulgaris L.* (Boudry et al. 1993)]. The genomes of conventionally produced crops undergo manipulation and selection as intensively as the genomes of GMOs, through exposure to mutagens, interspecies hybridizations, and somatic cell fusion; and currently no federal regulations monitor the development of new varieties.

Changes in structure and the chemistry of conventionally produced crops have had direct and indirect negative effects on nontarget species (NRC 2000). For example, crops bred with leaf hairs and leaf hair exudates, trichomes, or increased leaf glossiness can adversely affect insect natural enemies (Bottrell et al. 1998). Also, increasing plant secondary compounds such as cucurbitacins (Tallamy et al. 1998) or nicotines (Thorpe and

Barbosa 1986) can decrease the survival and efficacy of natural enemies.

Ultimately, dissemination of accurate information about GMOs is the best way to preserve this valuable technology, and excessive regulation of GMOs will only serve to raise the level of concern among a public that is largely unfamiliar with biotechnology.

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■ TOPIC:

Releasing insects that have been genetically modified to be incapable of vectoring human diseases is safe and ethical

Introduction

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University of Nebraska

Malaria may be the best known of the insect-vectored diseases, but insects vector many other diseases. Such diseases are often fatal or cause extreme hardships, especially in developing countries, which lack sufficient resources for effective treatment or vector control (Beaty 2000). It has been reported that some insect-vectored diseases, such as malaria, are resurging, and other diseases, such as West Nile encephalitis and yellow fever, are expanding beyond their original ranges (Gratz 1999, Beaty 2000, Hoffman 2000, Kokoza et al. 2000). Examples from efforts to combat malaria illustrate the difficulty in effectively managing insect-vectored diseases. Of all the control methods available, antimalarial drugs have been the most successful when followed by insecticidal treatment of the vector population. However, the ability of the disease and vector to develop resistance to drugs and to insecticides, respectively, has outpaced the development of new treatments or pesticides that are effective and safe (Gratz 1999, Coates 2000, Osei-Atweneboana et al. 2001).

A novel approach to managing malaria has been to genetically modify the vector itself so that the disease organism cannot survive in the insect or so that the insect is incapable of transmitting the disease. One approach is to identify antimalarial genes associated with malaria resistance and then introduce those genes into receptive strains of vectors (Aldhous 1993). Such transgenic insects could be released into wild populations to produce more malaria-resistant individuals. A second approach is to introduce foreign genes into *Anopheles gambiae* Giles/*A. stephensi* Liston, the principal vectors of the disease-causing agent, to make the mosquitoes resistant to malaria parasites.

Genetically modifying insects offers the potential to control many insect-transmitted diseases. As with any other genetically modified organism (GMO), concerns about effects on the environment persist. In addition, modifying vectors of human diseases requires testing on human subjects, with implications for human health (Beard et al. 2002). Although these insects would be released with community approval, their release could affect entire regions; government regulation will be more complicated and crucial.

It has been reported that some insect-vectored diseases, such as malaria, are resurging, and other diseases, such as West Nile encephalitis and yellow fever, are expanding beyond their original ranges

Some people question whether it is even ethical to do these manipulations in the first place. Will the GMOs create new problems as harmful as those they were meant to control? This new technology has great promise, but the question remains: do the risks or potential risks of introducing genetically modified insect outweigh the benefits?

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▲ Pro Position

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Insect-vectored diseases affect millions of people. Uncontrollable infection rates not only cause sickness and death, but also compromise the economies and political stability of countries where these diseases are epidemic. Preventive medicine may be more cost effective than treatment.

Insecticides can have negative impacts because of persistence and nontarget effects. Rising costs of new insecticides and reduced efficacy of older compounds may make effective control less accessible (Pettigrew and O'Neill 1997). Disease control has been hindered by development of insecticide resistance and the emergence of drug resistance in parasites (Coates 2000). Using modern technologies to genetically modify insects can reduce or eliminate their ability to transmit human pathogens (James et al. 1999). Although this approach is not appropriate for every disease (Spielman 1994, Curtis et al. 1999), we argue that it is a promising tool when used in conjunction with current methods.

Numerous ethical and safety concerns are associated with the release of genetically modified vectors (GMV) (Aultman et al. 2000). Individuals, as well as entire countries, may have general concerns about genetic modification that can be alleviated through public awareness and international cooperation. Because the establishment of the new GMVs requires the release and protection of many insects, it has been suggested that current vector management programs must be relaxed, which would create confusion or harm the human population directly involved. Instead of relaxing control programs, alternative hosts or prefeeding of GMVs could alleviate this concern.

Gene escape, nontarget effects, and additional safety issues are concerns that warrant adequate funding for extensive prerelease research and ongoing surveillance to assess risks and determine reliability. In all forms of disease treatment and prevention, a small amount of managed risk is perceived as acceptable, provided the benefits greatly outweigh those risks. No vaccine, drug, or pesticide is completely safe and effective.

▲ **Pro Position**

In all forms of disease treatment and prevention, a small amount of managed risk is perceived as acceptable, provided the benefits greatly outweigh those risks.

The etiological agent of Chagas' disease, *Trypanosoma cruzi* (Chagas) has been eliminated from reduviid vectors in the laboratory by transforming the obligate gut endosymbiont *Rhodococcus rhodnii* Goodfellow and Alderson (Beard et al. 1998). This system could be applied to other insect vectors harboring obligate endosymbionts. In Dengue type-2 virus, the expression of antisense RNA blocks replication of the virus in the salivary glands of *Aedes aegypti* (L.) (Olson et al. 1996). This technology is potentially applicable to other arboviruses. The use of thoroughly studied GMVs for disease control, in conjunction with current control practices and international cooperation, will aid in the management of insect-borne diseases.

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▼ Con Position

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Releasing arthropod vectors that are genetically modified for refractoriness to a pathogen is neither safe nor ethical. Of greatest concern is the horizontal transmission of the modified gene to nontarget species. Numerous studies have demonstrated horizontal transmission in the lab and field (Jehle et al. 1998, Imase et al. 2000, Leaver 2001). Although horizontal transmission occurs infrequently, the high fecundity of most insects markedly increases its likelihood. No mechanism has been established to reliably mitigate the accidental release of a GMO, and it is impossible to predict potentially deleterious effects of modified genes on nontarget organisms.

Numerous other safety issues exist. Long-term effects and safety issues of a GMO release are not well studied. Considering the required scale of mass rearing, the accidental release of GMOs into nontarget areas is likely and poses an unacceptable risk because of the impossibility of recapture. Other issues include the ecological impact of introducing a GMO into the environment; the high expense required to maintain the project; the loss of innate immunity among the local human population originally gained by repeated exposure to the parasite that could result in a future epidemic if the disease were not completely suppressed; and the possibility of other parasites filling the vacuum created by the eradicated disease organism. These questions need to be addressed before any large-scale release is considered.

Even more important are the ethical concerns arising from a large-scale GMO release. The primary ethical concern surrounding a GMO release is exposing unknowing individuals to a large-scale experiment. According to the Nuremberg Code, Directives for Human Experimentation, "informed consent of human subjects is mandatory" (USGPO 1949). For the duration of the experiment, human subjects should have the option to withdraw, and the experimenter must be prepared and able to terminate the experiment at the participant's request. When one considers the reproductive capacity and dispersal ability of arthropod vectors, obtaining informed consent from all potential subjects becomes logistically impossible. Other concerns include reduced biodiversity, the ethics of introducing a foreign gene into a natural population, the necessity of nurturing a released pest species; and determination of whether the cost of release results in a significant gain in public health and quality of life compared with conventional control methods.

Again these issues must be addressed before a release could proceed. With our limited knowledge of vector and parasite biology, vector ecology, horizontal transmission, and ethical concerns including informed consent, it is neither safe nor ethical to release GMOs to combat disease.

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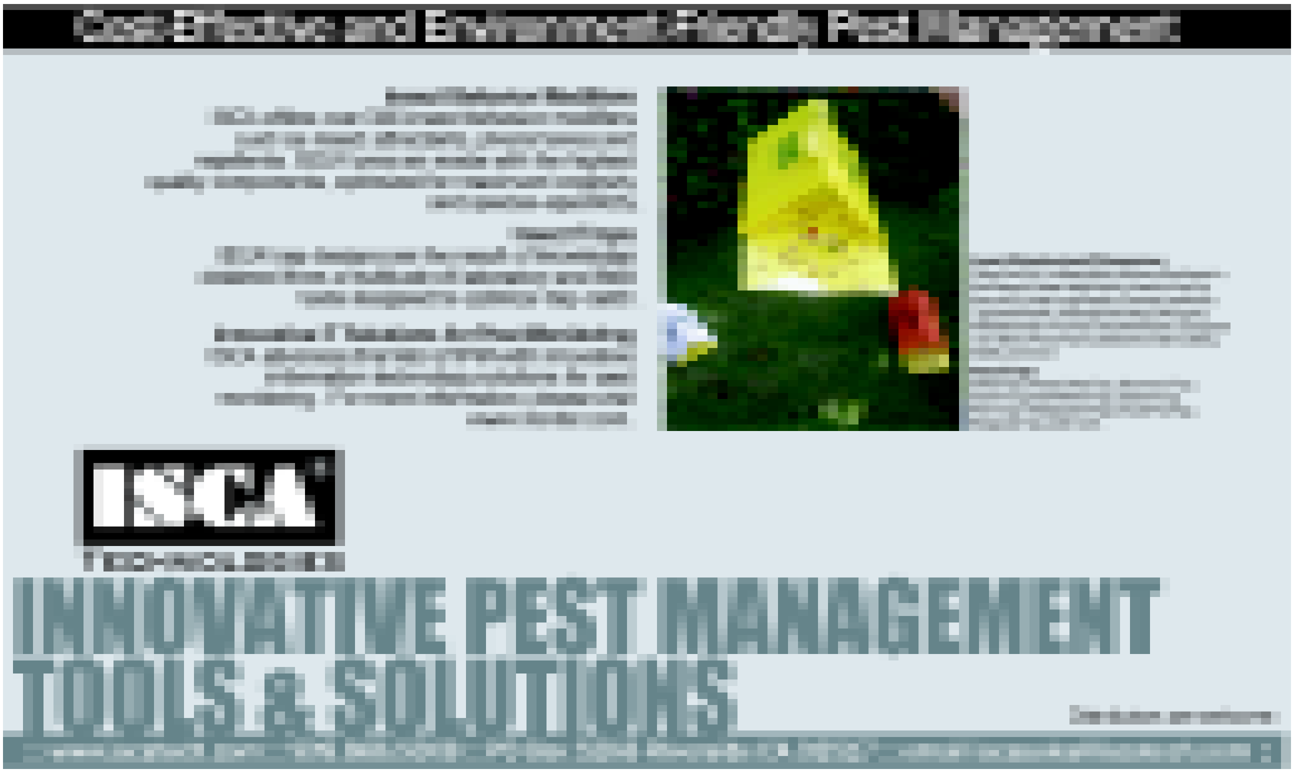

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