1998

NATIONAL AGRICULTURAL BIOTECHNOLOGY COUNCIL REPORT

NABC REPORT 10

Agricultural Biotechnology and Environmental Quality: Gene Escape and Pest Resistance

Edited by Ralph W.F. Hardy and Jane Baker Segelken

Published by the
National Agricultural Biotechnology Council
Ithaca, New York 14853

NABC Report 10

Agricultural Biotechnology and Environmental Quality: Gene Escape and Pest Resistance

The National Agricultural Biotechnology Council provides an open forum for the discussion of issues related to the impact of biotechnology on agriculture. The views presented and positions taken by individual participants in this report are their own and do not necessarily reflect the views or policies of the NABC.

The National Agricultural Biotechnology Council grants permission to copy the overview and workshop texts. Permission to copy individual presentations is retained by the authors.

Copying of this report or its parts for resale is expressly prohibited.

The photo on the cover is courtesy of Monsanto Company.

Additional copies of NABC Report 10 are available for $5.
Please make checks or purchase orders payable to:

NABC / BTI
419 Boyce Thompson Institute
Tower Road
Ithaca, NY 14853

© 1998 NABC All rights reserved.

ISBN: 0-9730907-6-3
Library of Congress Catalog Card Number 97-075428

♲ Printed on recycled paper

National Agricultural Biotechnology Council

Providing an open forum
for exploring issues in
agricultural biotechnology

The NABC, established in 1988, is a consortium of not-for-profit agricultural research, extension and educational institutions.

Member Institutions

Association of Research Directors, Inc.
Boyce Thompson Institute
Clemson University
Cornell University
Iowa State University
Michigan State University
Mississippi State University
North Carolina State University
The Ohio State University
Oklahoma State University
Oregon State University
The Pennsylvania State University
Purdue University
Texas A&M University
University of Arizona
University of California System
University of Florida
University of Georgia
University of Hawaii
University of Illinois at Urbana-Champaign
University of Minnesota
University of Missouri-Columbia
University of Nebraska-Lincoln
University of Saskatchewan
University of Wisconsin-Madison
Washington State University

Other NABC Reports Available:

NABC Report 3, *Agricultural Biotechnology at the Crossroads: Biological, Social and Institutional Concerns* (1991)

NABC Report 4, *Animal Biotechnology: Opportunities & Challenges* (1992)

NABC Report 5, *Agricultural Biotechnology: A Public Conversation About Risk* (1993)

NABC Report 6, *Agricultural Biotechnology & The Public Good* (1994)

NABC Report 7, *Genes for the Future: Discovery, Ownership, Access* (1995)

NABC Report 8, *Agricultural Biotechnology: Novel Products and New Partnerships* (1996)

NABC Report 9, *Resource Management in Challenged Environments* (1997)

ACKNOWLEDGMENTS

On behalf of the National Agricultural Biotechnology Council, we express our appreciation to the many people who successfully planned and hosted the 10th annual meeting. Their thoughtful programming and careful attention to detail afforded more than 100 attendees the opportunity to listen in plenary sessions to some of the most knowledgeable experts on gene escape and pest resistance, and to dialogue with others in workshop discussions.

First and foremost, we gratefully acknowledge James R. Fischer and Joe Dickerson at Clemson University for their tireless efforts to ensure the success of this meeting from concept to completion. We would also like to recognize the valuable guidance by the Clemson University planning committee, including John W. Kelly, Gary McMahan, Susan Barefoot, David Howle, William Marcotte, Dalphene Jameson, and Debbie Dalhouse.

Second, our sincere thanks go to the speakers whose professional expertise provided for lively exchange, the moderators who helped keep the discussions focused, and the workshop co-chairs without whom the topical deliberations and conclusions would not have occurred.

Special thanks go to Barbara Kneen Avery, NABC Associate Coordinator, for her technical assistance and her production efforts on the NABC Vision Statement, and to Eugene Sander, 1997-98 NABC Chair, for his leadership.

To the many others who worked on the meeting and this Report whom we have not mentioned by name, please accept our sincere thanks.

Ralph W.F. Hardy
NABC President

Jane Baker Segelken
NABC Executive Coordinator

December 1998

PREFACE

The National Agricultural Biotechnology Council (NABC) was established in 1988 with funding from the Joyce Foundation to promote dialogue on the emerging issues of agricultural biotechnology. The Boyce Thompson Institute, Cornell University, Iowa State University, and the University of California were the initial members. Today, the NABC has grown to include 26 of the leading not-for-profit research and educational institutions in North America. Representatives to the Council include senior management of these institutions.

The goal of the NABC was, and still is, the early identification of agricultural biotechnology issues and their discussion in an open forum; the safe, efficacious and equitable development of the products and processes of agricultural biotechnology; and the development of public policy recommendations.

The NABC has a record of early identification and broad consideration of the major issues, and provides all stakeholders — including representatives from academe, government, industry, public interest, farming, and others — the opportunity to speak, to listen, and to learn about the key issues. Through its meetings, the NABC has addressed many major issues: sustainable agriculture in 1989; food safety and nutritional quality in 1990; social issues in 1991; animal biotechnology in 1992; risk in 1993; public good in 1994; discovery, access, and ownership of genes in 1995; novel products and new partnerships in 1996; and challenged environments in 1997. More than 50,000 NABC reports of its annual conferences have been freely distributed worldwide.

Environmental quality was the focus of NABC 10. “Agricultural Biotechnology and Environmental Quality: Gene Escape and Pest Resistance” was hosted May 31 - June 2, 1998 by NABC member institution Clemson University and was held in Greenville, SC. The two key environmental issues for transgenic plants — gene escape to wild and weedy relatives and the development of pest resistance to pesticidal transgenes — were considered. The expanding experience base — about 70 million acres of transgenic crops were grown in 1998 — has not yet revealed problems in either of these risk areas but they will probably occur in time (e.g., pests have developed resistance to most pesticides). Can management systems like those being implemented by governmental agencies, seed companies, and growers effectively minimize the extent and delay the appearance of these problems? The encouraging factor is that discussion of these concerns, such as occurred at NABC 10, is coinciding with transgene seed use and the development of science-based management techniques.

However, there are still individuals, especially outside the United States, who express strong opposition or concerns to anything that is transgenic. The major issues in the US for transgenic crops appears to be moving from environmental risks to the risks from the consolidation of the input and end-user industries of crop production (e.g., how consolidation affects food security and sustainability). Within the last year, a few US chemical companies have spent more than $10 billion in consolidation and vertical integration. The consolidation into the end-user area is less developed than the input side, but considering the value on the end-user side investments could be substantially greater. The 1999 NABC annual meeting — “World Food Security and Sustainability: The Impacts of Biotechnology and Industrial Consolidation” — will be held June 6-8, 1999 at the University of Nebraska-Lincoln.

Candid forums such as NABC10 help to promote better understanding of the many diverse viewpoints, and provide an opportunity for addressing concerns about agricultural biotechnology. We believe that the NABC has helped contribute to the informed and relatively favorable environment for transgenics in the US in contrast to the disarray regarding transgenics in Europe where there appears to have been no equivalent organization to NABC.

In 1998, the NABC took a leadership role in generating a concise, comprehensive, and compelling vision statement on agricultural research and development for the 21st century. This statement, supported by the member institutions, projects that not only improved feed, food, and fiber from the agricultural research of the 21st century, but agriculture’s key role in securing our future through the biobased production of energy, chemicals, and materials. The statement is included as an appendix of this NABC Report.

Ralph W.F. Hardy
NABC President

Jane Baker Segelken
NABC Executive Coordinator

CONTENTS

PART I

AGRICULTURAL BIOTECHNOLOGY AND ENVIRONMENTAL QUALITY: GENE ESCAPE AND PEST RESISTANCE

Photo courtesy of Pioneer Hi-Bred International, Inc.

NABC 10: An Overview

James R. Fischer
Chair, NABC 10 Planning Committee
Dean and Director, South Carolina Agricultural and Forestry Research System
Clemson University
Clemson, SC

Concerns about the risks of altered genes migrating into non-crop plants and the risks of pests, such as insects and viruses, developing a resistance to genetically modified plant pesticides are of critical concern to people opposed to genetic engineering, such as Britain's Prince Charles and the Greenpeace organization.

Yet, with more than 67 million acres of transgenic crops in the world today, just 25 years after the discovery of gene splicing technology, we cannot turn back the clock. If anything, the demand for genetically modified food and fiber crops is accelerating.

To address the concerns about gene escape, the National Agricultural Biotechnology Council's 10th annual meeting, *Agricultural Biotechnology and Environmental Quality: Gene Escape and Pest Resistance*, hosted by Clemson University, debated the research and development, regulatory and public policy, and industrial and economic issues surrounding genetic engineering. More than 130 participants from 30 states and three foreign countries, representing consumer groups, industry, government and academia, attended the conference. In addition, news media representatives, from CNN television, *Progressive Farmer*, *Chemical and Engineering News*, and *Southeast Farm Press* served as moderators for the plenary sessions.

Conference participants heard presentations by nine authorities representing the full spectrum of viewpoints on biotechnology, from strongly supportive to strongly opposed. In keeping with the tradition of NABC conferences, all exchanges were conducted in an open forum, respectful of diverse opinions.

Contrasting the general acceptance of agricultural biotechnology by growers with the public's fears was Carl B. Loop, Jr., president of the American Farm Bureau Federation. "Biotechnology is here to stay and will be the future of agriculture," Loop said. "Farmers have seen plants produced on land that couldn't produce crops before biotechnology provided plants that are resistant to drought and disease, and require less pesticides and herbicides. Biotechnology is traditional plant breeding speeded up. If we had continued to call it plant breeding instead of biotechnology, it would have been more acceptable to the public. We must be aware that there is fear in some people, so we must find a happy medium between 'full speed ahead' and doing nothing because of fear."

Public opinion is not always based on scientific research, agreed Frederick H. Buttel, professor of rural sociology at the University of Wisconsin. "The public is not aware of the benefits of agricultural research because there is widespread ignorance of biotechnology and of science in general, and because the groups opposed to biotechnology question the validity of scientific research," Buttel said. "Agricultural biotechnology has remained controversial for the past 25 years; but there are other areas of more immediate concern to the public than biotechnology, such as food quality and safety, and the impact of chemicals and livestock waste."

Fred Gould, professor of ecology at North Carolina State University, pointed out the importance of providing refuge areas to prevent insects from developing resistance to Bt (*Bacillus thuringiensis*) crops. "The tobacco budworm that attacks cotton is resistant to traditional pesticides so it would be difficult to come up with a suitable alternative to Bt," Gould said. "To avoid the possibility of insects becoming resistant to Bt, the US Environmental Protection Agency (EPA) recommends that four percent of the cotton crop be left as a refuge where no insecticide — neither Bt nor chemicals — is used. This strategy was developed for American farming practices. It could have a different effect in developing countries where US regulations are not enforced."

New genetic engineering strategies are being developed to produce plants that resist viral infections, explained Roger Beachy, head of plant biology at The Scripps Research Institute in California. "The tobacco mosaic virus resistant genes have proven very stable and durable over the past 25 years," Beachy said. "We can change the interaction of viruses and plants by changing a single amino acid so it does not act as a virus. But not all viruses are the same and not all risks are the same. The question becomes: Can we minimize risk to where it is more favorably accepted? The challenge for molecular biologists is whether we develop a resistance gene that is effective against multiple viruses since there are more than 2,000 plant viruses.

Public opinion varies widely from one country to another, observed Thomas J. Hoban, professor of sociology at North Carolina State University. "Consumers in Canada, the United States, and Japan have a higher acceptance of biotechnology than consumers in Europe," Hoban said. "The lowest acceptance levels are in Austria and Germany where about one-third of consumers find biotechnology acceptable. This compares to acceptance by two-thirds of consumers surveyed in North America and Japan. This is because of the early strength of opposition groups in Europe, such as Greenpeace, which held dramatic public demonstrations against genetically modified soybeans and corn. However, there are widespread misperceptions in all countries because people do not understand food processing, much less agriculture. Results clearly show the need for much greater education of consumers and opinion leaders."

Biotechnology is one of many techniques that can be used to increase food production in a sustainable manner, pointed out Thomas E. Nickson, a scientist with Monsanto Company. "The world's human population is projected to double in the next 40 years, and the demand for food is projected to triple because of the growing middle class," he said. "Currently, an area the size of North America is under agricultural cultivation, and we cannot significantly increase that without destroying the world's wildernesses, deserts, and rain forests. No single technology can address these issues; but we have many tools available now, including genomics, marker-assisted plant breeding, new agrochemicals, biological controls, improved farm management practices, and biotechnology. We must apply science-based risk assessments to the products from biotechnology, and develop appropriate risk management strategies founded in stewardship."

Sounding a strong cautionary note was Mae-Wan Ho, a senior research fellow at Open University in England who warned of moving too far too fast with biotechnology. "Scientists should not ignore sociological and economic issues," Ho said. "Big business and science are run by selfish individuals who see nature as objects to be exploited. A few major corporations are poised to take over food production and distribution throughout the world, and internalize the profits while they externalize the risks and costs. This will turn farmers into hired laborers and concentrate farming into giant corporations that are accountable to no one. Europeans are calling for a five-year moratorium on genetic engineering and a return to traditional agriculture because they feel biotechnology today is unethical, unnecessary, unsound, and unsafe."

There are strict safety regulations for plant-produced pesticides in the United States, explained Sharlene R. Matten, a biologist with the EPA. "Plant pesticides have been regulated by the EPA since 1994," Matten explained. "The EPA does not regulate the plant, but the pesticidal substance in the plant (*Bacillus thuringiensis*) and the genetic material used to produce it. The EPA reviews the possible effects on humans, birds, fish, beneficial insects, other plants, and the environment. The Science Advisory Panel of outside experts reviews the EPA's findings and makes recommendations for Bt crops. The EPA also receives input on pesticide regulations from many other groups, including growers, the US Department of Agriculture, the Union of Concerned Scientists, the International Life Sciences Institute, and Greenpeace."

Biotechnology developments should be guided by scientific research and a close association with regulatory agencies such as the EPA and the USDA, agreed Murray Robinson, president of Delta and Pine Land Company. "I'm not a scientist, I'm a businessman," Robinson said. "Our customers have found that Bt crops are good for business and the environment. One customer reduced costs by $100 per acre and increased production by one bale per acre with Bt cotton. The beneficial insects thrived because he did not use any chemical insecticides. Bt cotton also eliminates pesticide exposure for farm workers and surrounding property. There are also significant advantages with Roundup Ready® soybeans and cotton for growers plagued with weed problems. These crops allow growers to use conservation practices, such as reduced tillage, to preserve the topsoil and reduce erosion."

Workshop Recommendations

This year's workshops focused on three areas: research and development, regulatory and public policy, and industrial and economic perspectives. Participants weighed the many sides of the issues, from profitability to social acceptance, and came to the following conclusions:

- Research and Development Perspectives

  (See page 15 for the full workshop report.)

  - Educate growers so they understand and practice resistance management techniques.
  - Enhance basic research to prevent gene escape into non-target organisms.
  - Develop better monitoring techniques.
  - Form a new, independent agency for agricultural biotechnology that would be a coalition of private industry, growers, and government agencies, similar to the National Institutes of Health.

- Regulatory and Public Policy Perspectives

  (See page 23 for the full workshop report.)

  - Seek scientific input on all levels of biotechnology development and regulation, and take action to guarantee that this input is free from bias.
  - Develop regional pest management plans.
  - Create a separately funded agency to fill in the gaps in regulatory policy and work to keep this policy scientifically and socially sound.
  - Form a network of product/technology stewardship involving government, industry, and growers to monitor and manage the development of pest resistance.
  - Build trust among growers, industry, consumers, and environmentalists.
  - Include sociological and value considerations in biotechnology development, such as in the Human Genome Project.

- Industrial and Economic Perspectives
  (See page 33 for the full workshop report.)
  - Encourage cooperation between industry and university scientists to develop a standard method for monitoring genetically engineered crops.
  - Rekindle and strengthen industry-university research efforts.
  - Impose a penalty for growers who do not comply with biotechnology regulations, similar to the penalties imposed for misuse of chemical pesticides.
  - Create an independent oversight committee to set standards and decide research priorities.
  - Develop plain-language information for policy makers, news media, civic groups, school children, and the general public.
  - Designate land-grant universities to take the lead in disseminating plain-language information to the public.

PART II

WORKSHOP PAPERS AND REPORTS

Photo courtesy of Monsanto Company

Paper Presented to the Research and Development Perspectives Workshop

Daniel Jones
National Program Leader, Biochemistry/Biotechnology
US Department of Agriculture
Washington, DC

This workshop is on research and development perspectives on genetically modified crops containing pesticidal substances, and the possible development of pest resistance to those substances through biological selection.

Modern biotechnology has the potential to provide highly specific biopesticides for protection of agricultural crops from the ravages of pests that were formerly controlled by conventional chemical pesticides. The use of chemical pesticides can result in negative outcomes such as: 1) toxic residues in soil, water, and food; 2) emergence of secondary pests; 3) development of pest resistance; and 4) pest resurgence following the development of resistance. In addition, certain uses of some chemical pesticides may be discontinued as a result of the Food Quality Protection Act enacted by Congress in 1996.

Whether these same problems will plague the use of biopesticides will depend on the nature of the biopesticide, and may depend on how it is used. For example, should biopesticides be expressed in plants at high levels to maximize killing of pests, or at low levels to minimize selective pressures for the development of pest resistance?

The most widely used biopesticides at the present time are those derived from insecticidal proteins of a soil bacterium called *Bacillus thuringiensis* (Bt). These insecticidal proteins act by binding to receptors in the insect gut thereby disrupting digestion and leading to the insect's death within a few days. There are more than 50 different Bt proteins with differing toxicities for caterpillars, beetles, flies, and nematodes. Bt insecticidal protein can be applied to plants either as an external spray, as it has been for about 40 years, or inserted into the genetic blueprint of crops by the newer transgenic techniques.

The growing acreage planted to Bt crops has caused some scientists and interest groups to express concern about the development of pest resistance to Bt insecticidal proteins. In 1997, for example, there were close to four million acres of Bt corn, two million acres of Bt cotton, and 25,000 acres of Bt potatoes. In the next few years, alfalfa, canola, soy, sorghum, and wheat containing Bt genes are expected to reach the market.

The economic costs of losing Bt as a viable biopesticide due to the emergence of resistance in large populations of insects would be enormous. Organic farmers would be particularly hard hit. Resistance to Bt insecticidal proteins has been reported in insect populations that are exposed extensively or continuously to the toxins. Resistance to Bt in the diamondback moth has been documented in field populations in Asia, Central America, and the United States (Hawaii, Florida, and New York). Researchers from the US Department of Agriculture (USDA) have shown that the Indianmeal moth can become resistant to Bt if it lacks a key enzyme needed to activate Bt toxins.

There are a number of strategies to minimize or delay the development of pest resistance. In general, limited use and rapid degradation of biopesticides after release decreases selection pressures for the development of pest resistance. Specific strategies to delay the development of pest resistance include:

- Multiple toxins
- Low expression levels
- Partial resistance
- Timed expression
- Tissue-specific expression
- Mixtures of resistant/susceptible seed
- Provision of refuges

To protect the continued use of Bt-based biopesticides, the US Environmental Protection Agency (EPA) currently requires companies developing transgenic crops to submit and implement pest resistance management (PRM) plans as a condition of product registration. The major components of the current PRM plans are a high dose of the insecticidal protein to kill as many insects as possible, and the mandate of refuge areas where nonresistant insects can grow and breed with any resistant ones that might arise.

Some interest groups and scientists have taken issue with the EPA-approved PRM plans. They contend that some insects are not getting sufficiently high doses of insecticidal protein in the field to be killed, and that the refuge areas provided are not large enough relative to the area planted with transgenic crops. These interest groups have asked the EPA to suspend current transgenic plant registrations, and stop new ones on the basis of their belief that the transgenic plant varieties will worsen the pest-resistance problem.

There is an apparent lack of consensus among academic, government, and other scientists about many aspects of PRM. Knowledge gaps in basic pest ecology clearly exist, but there is also disagreement about:

- How the knowledge gaps should be filled
- What assumptions can be made now
- How quickly resistance will develop
- What regulatory and farming practices should be followed in the meantime

One solution for pest resistance to Bt is to develop a more diverse array of insecticidal proteins for agricultural use. In addition to Bt, there are a number of insecticidal proteins being studied, but they are not as far along commercially. These include lectins, antibodies, protease inhibitors, insect peptide hormones, vegetative insecticidal proteins, and wasp and spider toxins.

The USDA has funded research that transfers insecticidal genes from soybeans to corn to combat crop damage from corn rootworm. This research identified a whole series of inhibitor genes with different modes of action that are available for use in case the corn rootworm acquires resistance to the original inhibitor now in the field. The USDA National Research Initiative has a major research area entitled Pest Biology and Management. This includes a subarea on Biologically Based Pest Management that solicits proposals for a variety of biological pest management research including resistance management studies.

We at the USDA are open and receptive to suggestions developed at this workshop on directions that future research on pest resistance management could take.

Workshop Report: Research and Development Perspectives

Co-Chairs

Vicki Bowman Vance
University of South Carolina
Columbia, SC

Tom Brown
Clemson University
Clemson, SC

Pest resistance has evolved against every form of pest control applied in agriculture to date. There are more than 600 species of insects resistant to insecticides, nearly 200 weed species resistant to herbicides, and more than 100 plant pathogens resistant to fungicides and bacteriocides. It is expected that pests will eventually evolve resistance to new transgenic technologies including plant pesticides (such as insect resistant, *Bacillus thuringiensis* [Bt] transgene crops now in use), herbicides combined with herbicide resistant crops, and transgenic crops with resistance to plant pathogens. Delaying the evolution of resistance will depend on carefully constructed and thoroughly implemented pest resistance management strategies. The US Environmental Protection Agency (EPA) has required such a plan for registration of plants and pesticides. The current approach is a combination of high doses of insecticidal protein and provision of refuge areas. *(Note: A refuge is a set-aside part of a field that is planted to maintain a population of insects that is sensitive to Bt, i.e., non-Bt transgenic crops not protected against insects.)* This plan, which marks the first such regulatory requirement in the pesticide registration process, appears to be working. However experience with the effectiveness of this plan is limited, and flexibility in modifying it may be required if resistance begins to evolve.

A similar situation may occur with the use of herbicide-resistant transgenic crops where increased herbicide use may accelerate the evolution of weeds with resistance to the herbicide. Transgenic plants resistant to attack by plant pathogens are under development. Proteins introduced via transgenes for this protective trait will be considered as plant pesticides, thereby requiring resistant pest management plans for EPA registration. Research experts and concerted efforts by professional societies will be needed to assist in developing these strategies. Such was the case for use of viral coat proteins to confer resistance to viral pathogens where the EPA, with input from experts in the field, has granted an exemption from plant pesticide regulation.

In general, it is most important that transgenic tools be viewed as only one aspect in the overall scheme of integrated pest management in agriculture. Furthermore, it is important to continue to improve the transgenic approaches to pest management to maintain the benefits for the future.

Environmental Impact of Gene Escape

The workshop groups were asked to discuss several issues concerning the long-term ramifications of gene escape, and the existing or potential natural and artificial barriers to gene escape. The first issue involved the potential benefits of transgenic technologies in plant systems. In general, this technology allows improved yields from a variety of crops with reduced environmental impact from use of toxic chemicals. Probably the best example is the use of transgenic Bt plants that provide resistance to insect pests with no toxicity to humans, wildlife, or most beneficial insects, while reducing the need for toxic and expensive chemical pesticides. A similar situation occurs for transgenic resistance to viruses that allow protection against devastating viral diseases and reduces the need for toxic–pesticides commonly used to eliminate the insect vectors of many viruses. Finally, the use of transgenic resistance to herbicides allows the use of relatively benign herbicides for weed reduction.

The second issue concerned the potential risks associated with this technology. Ironically, the first and perhaps the greatest, risk identified is the potential loss of the benefits conferred by the technology. For example, the potential loss of Bt insect resistance in plants and the development of Bt resistant pests due to misuse or overuse. Another potential risk is the possibility of escape of the transgene into non-target organisms, in particular wild relatives of the transgenic crop. An example is the acquisition of herbicide resistance by weeds or by non-weed plants that then become a weed.

Do the benefits of the technology justify the risks? Can the risks associated with this technology be reduced? The technology provides great benefits to society, to the economy, and to the environment. To preserve these benefits an effort should be made to reduce the risks (or perceived risks) associated with the technology.

A number of proposed strategies for risk reduction centered around an influx of money into research that would focus on attaining a basic understanding of the biology of the targeted plant/pest interactions. It is crucial that efforts to develop more sophisticated biocontrol begin immediately. This development depends on an understanding of the basic science of the particular system. For example, basic research into the nature of the interaction between Bt toxin and the insect receptor for the toxin could lead to designer toxins that provide better resistance. Thus, the second generation of transgenics could be in hand in time to supplement the expected failing resistance of first generation transgenics. It is unfortunate for everyone involved that this type of innovative basic science is currently woefully under-funded, and that many opportunities to preserve this beneficial technology are being lost.

A second proposed method to reduce risks is the development of programs designed to educate the users of biotechnology. The education would focus on the importance of implementing current pest resistance management principles to slow down development of resistance in the pests, and on integration of transgenic technology with other management techniques.

RECOMMENDATIONS

1. *Enhance basic research to develop effective resistance-management plans. The focus of the research should be towards development of a second (more sophisticated) generation of plant pesticides to supplement the first generation. An understanding of the molecular mechanisms that lead to transgenic resistance will facilitate the development of more sophisticated approaches.*
2. *Take steps necessary to slow down the development of resistance to current biocontrol while developing the second generation of pesticides.*
    - *Educate growers, crop consultants, extension agents, salespersons and international users on current pest-resistance management principles.*
    - *Incorporate biocontrol strategies as a component of integrative pest management.*
3. *There is a critical need to create a source of funding for research into innovative approaches for the safe and effective use of biotechnology in agriculture. It is important that these efforts take place in a timely manner so that the new transgenics become available before the first generation has failed. The group suggests an alliance between the private sector and the government to provide funding for a new government agency (National Institute for Agricultural Biotechnology?), or a free-standing research institute, co-funded by industry and government.*

Paper presented to the Regulatory and Public Policy Perspectives Workshop

ANDREW JORDAN
Director
National Cotton Council
Memphis, TN

Agricultural biotechnology represents a new range of tools for production and processing, and for numerous new agriculturally based products. This year's conference — *Agricultural Biotechnology and Environmental Quality: Gene Escape and Pest Resistance* — is on a topic of great importance to all. This workshops deals with public policy and regulations. Collectively you represent diverse interests, ranging from state and federal regulators, agribusiness providers, public scientists, educators, and farmers and other users. Interests as diverse as these typically generate healthy debate. We can expect that a discussion about regulating environmental impacts of gene escape and pest resistance will be no exception.

Discussion during the first workshop session has to do with pest-derived resistance to transgenic plants; the second session will consider gene escape. I have been asked to set the stage for both.

REGULATORY AND PUBLIC POLICY

As one who represents cotton farmers and processors, I am sensitive to the specter of unnecessary regulations. Having said that, I will concede the necessity for more regulations in cases where there is a clear inadequacy for protection of health, safety, environment, and economic well being.

The cotton industry has firsthand experience dealing with costly regulations. Most recently we supported the sound principles of the new Food Quality Protection Act (FQPA) because we agreed that reform of pesticide and food safety regulations was essential because the old regulations were archaic and unreasonable, and made little sense from a risk-avoidance standpoint. The act eliminated the Delaney Clause, an eccentric provision in the old law whose origin was driven by emotion rather than scientific merit. We embraced the basic proposition that pledged a more sensible and more holistic approach to decisions about pesticides and food safety.

Given assurances that the new act would be better for all of us, we were disappointed to discover that execution appeared to differ markedly from expectation. In our view many regulatory decisions in implementing the new act were arbitrary and without merit. Furthermore, there was no clear plan for implementing the new law.

Confusion abounded. This chaos proved to be burdensome to farmers. It was expensive in terms of denied access to important agricultural chemicals, costly due to untimely decisions (sometimes after crops had been planted and materials purchased), and unsettling with respect to the cloud of uncertainty for planning a year-long pest management strategy. It was clear the decisions were not based on improving diet and reducing risk to human health but instead were made to fulfill the passionate needs of some individuals.

Of course, there are those who disagree with me because of a different experience, agenda, bias, emotion, or understanding of risks and benefits. There are those who consider theirs a noble cause and are immovable in their conviction that some products should be regulated out of existence.

While I seem to belabor the point of regulation, it is for the following purpose: We will be discussing public policy and regulations affecting transgenic plants. I foresee a path that potentially could parallel development of pesticide regulations in complexity, and in emotional attachments to positions. No doubt, decisions of federal agencies regulating real or perceived hazards become bitterly controversial. One person's passion for purity will be pitted against another's desire to provide basic human needs. Economic benefits will be challenged by perceived risks, and interpretation of one expert's facts will go against another's interpretation.

Goals

We will have made a major contribution if we succeed in providing early enlightenment to the debate on regulation of transgenic plants. We need to strive for reliability and objectivity in the scientific assessment of pest resistance and the environmental effects of gene escape. In our hearts we may desire to be impartial, but there is no escaping the fact that by necessity there invariably will be subjective evaluations.

Another of our goals should be to identify those institutional mechanisms that best form a constructive partnership between science and government. We should consider whether we could create alternative public policy mechanisms to support the goal of acceptable risk demanded by society. Rhetorically, can this technology be used without the burden of over-regulation? Can it be done with no regulation? Perhaps not. So if regulations are deemed necessary, let's ensure that the rules are based on the best available scientific knowledge.

The public policy-setting task is complicated even further by the unavoidable collision of conflicting interests that impact most important regulatory decisions. The fact that costs and benefits of regulatory policies fall unequally on different groups makes the task a daunting one.

Resistance and Gene Escape

The plenary speakers presented interesting ideas. They set the stage for discussion if not debate. While each of us has a notion as to our level of agreement with the speakers, our aim is to discuss these topics in the context of public policy.

Dr. Gould made a good case as to why he thinks that alternative protein toxins will be hard to identify. He also discussed the alternative refuge/high dose approach endorsed by many scientists. I will want those of you from industry and academia to help elucidate whether you think Dr. Gould's theories are sound. If I understood Gould correctly, he said (to paraphrase) that we will be wasting effort looking for alternative *Bacillus thuringiensis* (Bt) proteins.

Dr. Beachy discussed resistance to virus infections in transgenic plants. He cited studies that suggest that specific transgenes may be more likely than others to develop pathogen-derived resistance. In that light, I will want to hear your opinions as to the significance of those studies.

The afternoon plenary speakers presented interesting but disparate views. Dr. Nickson asserted that biotechnology could be an environmentally responsible way to meet increasing requirements for feeding a hungry world. On the other hand Dr. Ho presented an entirely different view. While the title is long, it appropriately captures Dr. Ho's emotion. While we individually may disagree with Dr. Ho, we must recognize that hers is an opinion shared by many around the world. Those beliefs represent issues that must be considered and responded to in an appropriate and science-based manner as we debate public policy.

Drs. Gould and Beachy suggested uncertainties in our knowledge gap about resistance. Drs. Nickson and Ho, while not corroborating deficiencies in information, clearly disagreed on whether biotechnology would help feed and clothe the world or whether the gains from biotechnology are only short term. If we are to believe any or all of our plenary speakers, we must accept the fact that there are uncertainties. In the absence of good research to sort out answers to these questions, a cloud of doubt and mistrust will shadow this new technology. Good sound research is key to addressing the risks and benefits of transgenic plant technology.

In the meantime we must decide in the context of public policy how to deal with uncertainty with the information now available. Agreeing that there is no such thing as zero risk, our challenge will be to help set a framework of decision making to establish a level of acceptable uncertainty. Given that the best of scientists don't always agree, we must decide which science is dependable and how to generate acceptable risk models.

Questions for Discussion

- What potential risks do resistant pests pose to society? Are they real or perceived?
- What are the social costs of the wrong decision or the wrong regulation?
- By what mechanisms do we weigh consequences of over-regulation vs. under-regulation? Are they social, economic or political? All of the above?
- Whose best interest are we regulating for — how do farmers fit into the equation? Do they really have a say?
- What conditions would warrant a regulatory strategy that is as permissible as possible early on, monitored for effect, and then adjusted to respond to the expanding experience base?
- Conversely, what conditions would warrant a strategy that is “highly restrictive early on, followed by strict laboratory research, and then loosening of regulations if new information dictates”?
- What are the consequences of wrong decisions? Are they catastrophic, or can eco-systems recover?
- The EPA convened a Scientific Advisory Panel for Bt products. They agreed that BT is an important IPM tool and that we need to protect the technology. Can we make an informed recommendation as to the proper ratio of transgenic crop to that left for refugia? What’s magic about four percent, 20 percent, or even 50 percent?
- As we are dealing with resistance or gene escape, who is responsible for monitoring? Is this a public responsibility? An industry responsibility? A farmer responsibility?
- Is our reliance on population models appropriate?
- In absence of definitive field data, can we appropriately extrapolate laboratory data to the real world? Under what circumstances should these data be extrapolated, and where should they not?
- I would like to hear discussion on how to best quantify benefits of transgenic technologies compared with the risks. In doing so, we need to answer the questions as to how benefits and risks are measured and assessed. Can risks identified with this technology be reduced to levels acceptable to the public?
- Finally the last question: Who should be responsible for deciding the future of plant biotechnology, and how does the public participate in this decision-making process?

In conclusion, there is no doubt that the task facing this technology is awesome. Plainly, there are questions; some more important than others are. We will not have the last say, but what we do at this conference will make a difference. If I were to summarize all our goals into a single objective, it would be to promote understanding of the issues.

Workshop Report: Regulatory and Public Policy Perspectives

Co-Chairs

Daniel E. Wueste
Clemson University
Clemson, SC

John Gentry
Clemson University
Clemson, SC

Calvin Schoulties
Clemson University
Clemson, SC

This workshop broadly discussed the issues of transgenic crops and the environmental concerns of gene escape and development of pests resistant to the transgenic pesticide. Risks of resistant pests, resistance management, benefits and risks, food safety, and communication were examined. Several key recommendations were proposed.

Risks to the Environment and Society posed by Resistant Pests

Many general questions and observations were made concerning the risk of pests, especially insect pests to a crop containing a transgenic pesticide, e.g., the *Bacillus thuringiensis* (Bt) toxin. If pests cannot be controlled, food and fiber crops will be jeopardized and may negatively impact society throughout the world. As a result, farmers may choose to plant crops that require an increased use of fertilizers and pesticides, which may negatively impact soil conservation and water use by increasing the amount of chemical runoff. In addition, the hazards associated with mixing and loading pesticides should be considered.

For example, if pests develop resistance to the Bt toxin transgenic crops, Bt microbial sprays will lose their effectiveness and Bt could be lost as a control measure. Growers faced with pests resistant to Bt would likely increase or return to the use of higher risk synthetic chemical pesticides. That will entail higher costs to growers, which would be passed on to consumers. A return to chemical pesticides is likely to be unfavorable to the environment and society in comparison to the use of Bt.

COMMUNICATION

We must improve communication among the variety of groups concerned with or impacted by agricultural biotechnology, including academics, environmentalists, consumers, industry representatives, farmers, and others who use biotechnology. Many distinguish between the use of biotechnology to improve food and fiber production. However some crops, e.g., cotton, are both food and fiber crops making such a distinction difficult to impossible.

It is important to remember that the development of a pest-management system is an ongoing task; it requires constant adaptation to changes in pest-control technologies as well as response to the development of resistance on the part of pests. The problem of pest resistance is not new nor is it widely understood. Pests developed resistance to chemical pesticides before the use of biotechnology in agriculture. Communication is the linchpin to understanding.

Some people are worried that agricultural biotechnology will create super-pests. Are their worries unfounded? If so, this needs to be made clear because fear of this sort impedes progress. One participant stressed that not all fears are ungrounded. Those that are ungrounded should be identified as such and addressed through education and communication. Those fears that are based in reality must be responded to with safeguards. Sometimes we do not have adequate information to determine if the fears are legitimate and work should continue to define their legitimacy. Are there cases where public fear is based in reality and use continues anyway, or are there cases where public fear is not based on reality and the use is stopped? The alar scare may be an example of the latter.

Public perception is very important. It should be made clear that agricultural biotechnology is not the field of the proverbial mad scientist or of scientists driven by greed or other improper motives who ignore real dangers. With this last point in mind, it was stressed that research and development activities need to be monitored with the interests of public health and welfare and good science in mind. The system of monitoring these activities must be responsive to the changing needs of the public as well as to changes in scientific knowledge. In addition, the design of this system must include appropriate incentives.

RESISTANCE MANAGEMENT

The major focus to minimize/delay the development of pest insects resistant to Bt toxin in transgenic crops is management of the planting patterns of the crops and monitoring for appearance of resistant insects. The group raised many questions: Who is monitoring for pest resistance to Bt and what is being monitored? Are farmers complying with regulation and licensing agreements? Is the development of resistance being observed? Are both being watched and if so, by whom? In this connection, the workshop participants expressed deep concern about the role of state regulatory agencies in terms of statutory authority and capability. Another question raised was whether the size of refuge set-asides will eliminate the participation of small farmers.

The answer to the first question was immediately provided: the US Environmental Protection Agency (EPA), the US Department of Agriculture (USDA), and industry are following up on the licensing agreement. Yet it was questioned whether auditing procedures and the enforcement tools are sufficient, and whether industry can adequately enforce its agreements with users. Currently, industry monitors efficacy by means of field sampling and comparing field susceptibility to baseline susceptibility levels. However, detecting resistance proactively is very difficult for large-crop acreage. There are at least two sources of difficulty here — field sampling itself and the sensitivity of the monitoring technique. Moreover, monitoring of this sort will not provide all of the information that is needed.

Education of growers of Bt transgenic crops is very important. If farmers know that the rules are not arbitrary or capricious, they are more likely to comply with them. The big picture — the whole-system— needs to be laid out for the users. It is important to develop close connections between public officials and private parties for the purpose of monitoring. Protocols for resistance detection should be revisited, reviewed, and revised as appropriate.

What degree of change in the level of resistance or level of crop loss is acceptable and how long should it be before additional control measures are taken? Should genes be re-engineered? Should crop insurance, which might prevent farmers from taking steps that are unwise or illegal in an effort to save a crop, be mandatory? These matters are of concern to all entities involved with the system, and action is required by all.

Farmers and industry should be willing to undertake monitoring because it is in their own best interest. Government involvement is important for the purposes of promoting trust and communicating to the public that what needs to be done is being done honestly, carefully, and in accordance with objectively rational standards. Government can be an honest referee. On the other hand, overly severe regulation based on misinformation may seriously hamper effective agricultural biotechnology.

A key concept here is product/technology stewardship involving all the stakeholders so as to establish trust and legitimacy.

Benefits and Risks of Transgenic Plants

Clearly, there are economic benefits for the producer and the end user, including the fact that a decreased use of conventional pesticides will result in substantial health benefits for farm workers. Others, both human and non-human, will benefit through enhanced air and water quality. Herbicide tolerant plants have a positive impact on crop management practices and soil conservation. In addition, production and equipment costs go down and control systems are simplified (mixing of chemicals for example, is less of a problem).

One area of risk is the creation of herbicide resistance in weedy relatives of the transgenic herbicide crop. The herbicide-resistance gene is transferred by the pollen of the transgenic crop to a cross-pollinating relative (weeds) in the area (gene escape). A similar problem could occur with insect resistance. There is a general concern about unintended effects of biotechnology as a result of gene flow or gene escape.

If out-crossing occurs, does it have negative environmental or social results, for example, in the form of super pests — new weeds, new viruses, new insects, and new and dangerous species? We need to know more than we do. The group agreed that there is a need to develop methodologies for measuring the probability of out-crossing and assessing its potential impact on the ecosystem, and defining an acceptable level of risk. In making these evaluations, one would consider sexual compatibility, geography (centers of origin), presence of out-crossing plants in the area of production of transgenic crops, and mechanisms of pollination (e.g., wind, hummingbirds, bees, animals).

Good Science

Good science is key to the successful use of biotechnology in agriculture. Scientific input should be sought at all levels of the decision-making process. Such input is essential, and is needed to answer such questions as whether another host crop can constitute a refuge and whether the extensive use of a bioengineered genotype will limit biodiversity. It is also essential that scientific input be free from bias. In the effort to guarantee that we have good science it will be necessary to avoid even the appearance of impropriety.

Legitimacy is very important. Once trust is developed it has to be maintained by continuous effort. One way to insure that effort is the involvement of stakeholders — producers, users, government regulators, and academics — in the decision-making process. Another way is adherence to high standards of professional and moral ethics. The integrity of the parties (people and institutions) and the integrity of the processes have to be maintained.

We need to find ways to incorporate value considerations in the decision-making process by encouraging more research regarding the social issues surrounding agricultural biotechnology. Not all decisions in this area turn on empirical, scientific determinations. Not all of the questions that have to be answered are purely scientific questions. Of this we must not lose sight.

Other Issues/Concerns

Other issues and concerns came up during our discussions. Thinking that they are worthy of consideration in any case and may be topics for future conferences, we record them briefly here: What are the risks and benefits of food quality enhancement by biotechnology? What about the development of plants to produce pharmaceuticals, and the genetic engineering of plants to make or be sources for polymers and industrial products?

Food safety

Concern about the risks of consuming transgenic crops already exists in Europe. One participant noted that labeling of genetically engineered products in Europe is not a safety matter; it is done to facilitate informed choice. Are such concerns shared by those in the United States? US regulatory agencies (Food and Drug Administration [FDA] and EPA) assess biotechnology products and evaluate industry data. In the US there is a need for more objective data and more communication.

One reason that labeling of genetically engineered plants might be necessary is to inform consumers of potential allergens (e.g., if genes from peanuts or brazil nuts were inserted into other plants).

Recommendations

1. *There should be scientific input into decision-making at all levels. Because it is essential that input be free from bias, an independently funded research institute should be established. This institute would conduct scientific and social/value research to provide information to fill in the gaps of regulatory policy and ensure that regulations are thoroughly debated for scientific and social soundness. With respect to the research to be undertaken in the values area, it was suggested that the ELSI (Ethical, Legal and Social Impact) research program of the Human Genome Project could serve as a model.*
2. *The EPA should be encouraged to continue working with scientists and industry to define the safety parameters of transgenic plants and determine how these plants are to be regulated. Regulations should be based on the transgene and the crop, using validated scientific field data, model, and laboratory findings. Work on methodologies for measuring the probability of out-crossing and assessing its potential impact on the ecosystem should continue. It will be necessary to define acceptable levels of risk.*
3. *Efforts should be undertaken to develop an appropriate network of product/technology stewardship involving technology providers, users, government regulators, and other stakeholders. Protocols for resistance management and detection should be reviewed and refined as necessary. At the same time, efforts should continue to be made to define acceptable levels of resistance. Also, regional cooperation must be increased, specifically with respect to regional pest management plans.*
4. *In order to achieve legitimacy for the decisions that come from the decision-making process, we must find ways to involve the public, producers, government, academics, environmentalists, industry, and other stakeholders in that process. Close connections should be developed between public and private parties to monitor and manage resistance.*
5. *Communication is critical. Communication must be initiated and maintained in accessible ways with targeted audiences. As an example, farmers are on*

the front-line for resistance monitoring and management. It is critical that they are aware of the reasons for regulations and that they receive assistance in compliance. Similarly, it is important to communicate with the general public to address and put to rest ungrounded fears. To be effective communication must not be a one-sided affair. Rather, it must be in the form of dialogues among concerned and impacted parties. Related to communication is the idea of developing trust among technology users, providers, and regulators. Effective dialogue will be a valuable tool for the achievement of this goal.

6. *We must find a place for value considerations in the decision-making process, for after we answer the question as to whether it can be done the key question of whether it should be done remains.*

Paper Presented to the Industrial and Economic Perspectives Workshop

Anthony J. Cavalieri
Vice President and Director, Trait & Technology Development
Pioneer Hi-Bred International, Inc.
Johnston, IA

The adoption of the products of biotechnology has proceeded at a much faster rate than almost anyone anticipated. The potential of these products to deliver significant value and change agriculture has driven enormous research funding over the last 15 years. In the case of Pioneer Hi-Bred, we increased our research spending from three percent of sales to more than eight percent of sales at the same time that the total sales were increasing rapidly. The need for research funding to develop and apply the new technologies has driven considerable change in agrobusiness and the farm sector. In particular, it has sparked a wave of consolidation of agricultural chemical companies and seed companies. Along with the enormous promise of the technology, there are concerns related to the wide-scale use of this technology. This meeting deals with one of those concerns: the development of pests that are resistant to the genetically altered host. I have been asked to share my thoughts on the management of the new technology so as to minimize the risks as we explore practices that might mitigate the risks of development of pest resistance. Our workshop is to explore these issues from the perspective of industrial and economic concerns.

Resistance to synthetic agrochemicals or to gene products produced in crops can develop in insect, pathogen, or weed populations. The general mechanisms and basis of the development of resistance is well understood since it is a case of natural selection. However, the specific controlling factors and their management are much less clearly understood. Current models for minimizing selection pressure and maximizing efficacy of the transgenes is much more limited. Although there are only a few transgenic crops introduced into the market at this time, many more are at various stages of development. A few transgenes like Bt (*Bacillus thuringiensis* endotoxin) and various types of herbicide tolerance are finding broad acceptance and are being introduced across crop species. Transgenic crops with insect resistance and herbicide tolerance have significant value to farmers by replacing synthetic agrochemicals for insect control and expanding the ability to use broad spectrum and relatively environmentally safe herbicides in production systems. The farmers' desire to solve these problems using genetic solutions has resulted in rapid acceptance of the new technology. Meanwhile, our understanding of resistance management has been useful but has not been adequate to result in widely accepted management programs. Nor has the efficacy of implemented management plans been established. The need for resistance-management programs to function across geographical areas, crops, state and national borders, and different company products makes the development and implementation of compliance with management plans particularly challenging.

It is worthwhile to explore the nature of the participants in the industrial and economic arena, and consider the strengths and weaknesses they bring to resistance management. This exercise might suggest approaches that maximize the strengths of the participants and minimize the weaknesses.

Technology Providers

University programs, small companies, or the technology development efforts of large companies discover genes providing crop protection traits. The strength of the technology providers is that they are extremely aggressive in applying both basic and applied science to important problems. Their activities drive changes in competitive positions as new products with improved characteristics displace or reduce the use of existing products. An example is the transition from synthetic chemical control of pest insects to genetic control. These technology generators tend to move very rapidly and to focus narrowly on the technology. They are more likely to concentrate on their business and their technology, and not have the resources or time to devote to addressing larger societal issues. Some projects are done because they are possible technically, while a discussion of the broader social, economic, and environmental issues may lag the technology.

Crop Input Companies

Over the last 15 years there has been significant consolidation of the companies involved in providing crop production inputs. Recently there have been significant moves to consolidate crop-input companies and chemical/agrochemical/pharmaceutical companies. Many of the remaining players in this area are large "life sciences" companies that have activities in agricultural chemicals, seeds and other traditional inputs, as well as pharmaceutical, nutritional, and processing activities. These companies bring significant, positive capabilities. They are willing to spend large sums of money on research and to move new products quickly into the hands of farmers and consumers. They concentrate on selling products not traits, and have the resources and scope to address regulatory requirements and to move technologies around the globe. These companies, because of anti-trust concerns, are limited in their ability to cooperate with one another once they begin to compete in the marketplace. In the case of herbicide-tolerant soybeans, a number of companies are selling varieties across the entire soybean growing area and they are limited in their ability to plan among the companies for restrictions on acreage or usage of the products. Additionally, these companies are gaining benefit from moving quickly and being the first to introduce products, and would like to avoid multiple-year discussions of societal impacts. Their businesses may involve one or two crops, but not all the crops containing a trait like Bt for insect resistance. This means that resistance-management planning that goes across regions and crops may not be addressed by the same companies. Pioneer, for instance, sells Bt corn, but is not in the cotton business. In spite of this, a resistance-management plan in the southern United States must consider both crops.

Farmers

American farmers are the most efficient producers of grain in the world. They do this at a low cost, and have provided a reliable, inexpensive source of food for the US, and increasingly the world. They are in competition with farmers in other countries and tend to adopt technology quickly to optimize their own position. In dealing with questions of transgenic insect resistance, they recognize that in a low-margin commodity business there are significant benefits of new technology that accrue to the early adopters. Consequently their interests are not always in concert with those of their neighbors or those of the companies selling the products. This divergence tends to make coordinated planning for minimizing the development of pest resistance difficult.

Summary

The opportunity for an extended theoretical discussion of the issues surrounding the development of insect resistance to transgenes is well past. There are a number of new technologies and genes currently being developed that extend well beyond the Bt insect resistance or herbicide tolerance traits that are in the marketplace. These traits represent both alternate genes for insect resistance as well as other traits that have yet to be commercialized. The discussion of resistance management shouldn't be seen as being for or against a single technology. In the case of insect resistance, the replacement of chemical technologies by genetic technologies offers an additional approach. This transition offers many benefits to the environment and farm safety, but also raises questions. It is unlikely that the groups listed above will reach durable approaches to minimizing insect resistance without a dialog that ensures a representation of them all and that recognizes and minimizes their specific weakness.

It is in all our interests to manage the genes for insect resistance in a way that prolongs their useful lifetime. Increased understanding of the nature and efficiency of resistance management programs has significant value.

Workshop Report: Industrial and Economic Perspectives

Co-Chairs

Hortense Dodo
Alabama A&M University
Normal, AL

Allison Tally
Novartis Crop Protection
Greensboro, NC

The workshop on Industrial and Economic Perspectives was highly diverse in membership and included representatives from industry, academe, government, farmers, and others. Most of the discussion focused on transgenic crops containing the gene for biopesticidal toxin from Bt (*Bacillus thuringiensis*.) A major concern discussed in the plenary sessions, as well as in the workshops of the NABC conference, was the potential for insects to develop resistance to the Bt toxin. Although at the time of the workshop no cases of insect resistance to transgenic crops containing the Bt gene had been documented, there was great concern expressed about this possibility.

What Potential Risks Do Resistant Pests Pose to the Environment and Society?

The loss of the ability to control a plant pest via a biopesticide produced in a transgenic crop could result in crop losses to growers and the return to reliance on the use of chemical pesticides. However, this type of risk is not new. Resistant pests have always developed in response to conventional hybrid resistant varieties or use of chemical pesticides. Over the years various weeds, insects, and fungi have become resistant to a variety of chemicals. Yet with management plans that include cultural practices, alternative chemistries, and crop rotations, the pests have been controlled.

If pest resistance occurs with transgenic pesticidal plants, regulatory hurdles could be increased (especially with Bt) and become a liability in both the domestic and global arena. Even if the pest is ubiquitous in many crops (e.g. lepidopteran) and the gene for resistance is also in those crops, pest resistance may not develop if the exposure of the pest to the gene is seasonal and appropriate refuges are used.

Because Bt is a natural resource, care must be taken to ensure its usefulness is maintained. Resistance to Bt could lead to a negative perception of Bt crops by consumers and have a negative economic impact on producers and manufacturers. Meanwhile, industry (seed, agricultural, chemical, and biotechnology companies) is working to identify new genes as alternatives to Bt that target pests not controlled by Bt. Academic institutions and other credible groups can play a role in educating the public.

How is Development of Resistance Monitored and Who Is Responsible for Monitoring?

Both the companies that have commercialized the technology and the US Department of Agriculture (USDA) are monitoring for the development of pest resistance to transgenic Bt plants. However, the effectiveness of monitoring techniques is not yet clear. The US Environmental Protection Agency (EPA) requires that companies monitor for pest resistance. Industry has a vested interest in resistance and the proper use of its products. Concern was expressed that industry may be seen as ‘the fox guarding the chicken house’ and it was suggested that a third party should be involved. Such an approach could use universities, extension services, or private consultants under contracts to verify industry’s findings.

A European suggestion is to put in place an organization comprised of university and government personnel to oversee and monitor pest resistance in transgenic plants. There is a need to find a credible source for monitoring, for public disclosure, and for educating the legislature and all parties involved.

Is There an Acceptable Level of Resistance?

Pest resistance to control measures, per se, is not new. Future generations of transgenic plants will come with new variants of the Bt genes or other genes for insect control. There will also be new synthetic chemical pesticides to complement and assist the effectiveness of the transgenics. Resistance to a pest control agent is almost inevitable when the agent’s mode of action targets a single site. However, due to the effectiveness of the transgenics, the benefits to the growers, and the investment of industry, the goal is to minimize and/or delay pest resistance to biopesticides produced by transgenic plants by following recommendations for refuges and alternative chemistries. Guidelines should be developed with the following questions in mind:

- Breadth of pest resistance (e.g., is the resistance confined to a specific insect or many insects?)
- Alternatives (e.g., do safe and economic alternate methods of pest control exist?)

Responsibility for Enforcement and Penalties

Questions about the responsibility for enforcement and use and size of penalties for non-compliance have not been resolved. For example, what is the penalty to the grower who does not follow the guidelines? What should the size and location of the refuge be? How can this be implemented in third world countries where there are many farmers with very small acreage? Much more research is needed to generate real data to answer these questions. Matching grants from industry and government may provide the funds needed to conduct such research.

What Are the Potential Benefits of Transgenic Technology in Plant Systems?

There are many benefits projected from the use of transgenic crops:

- Decrease in the amount of crop protection chemicals used, which is better for the environment, water quality, and overall health and safety.
- Increase in food production in third world countries.
- Value-added crops for growers.
- Increase quality traits such as oils, proteins, etc.
- Allows crop yield to approach its potential.
- Less capital.

In addition, society may benefit from the use of transgenic plants in phytoremediation, and in the production of bio-based products such as plant vaccines, nutraceuticals, and industrial products.

What Are the Potential Risks of Transgenic Technology in Plant Systems?

While there are many benefits, there are also some risks that need to be managed. One threat is the potential for gene escape. For example, the pest resistance gene(s) may be transferred from the transgenic host plant to a native relative (weedy) plant in the field area. Further investigations need to be done on the probability of this happening. As with failures with conventional products, companies are liable when the product fails or causes a side effect. From an industry perspective, there is concern that the transgenic biopesticide product life will be shorter than that of a chemical product. In addition, inventory control is more difficult since the seeds for the next year's crop are grown during the current year. The demand for a mix of traits (e.g., Bt plus high oil) also make inventory management more difficult. With transgenic plants there is also the problem of increased regulation and trade barriers. The major consolidation in the agrochemical/biotechnology/seed industry suggests that there will be less diversity in the research of a few consolidated companies than the primary companies that pre-existed consolidation. Furthermore, large consolidated companies will have larger market share and more control of germplasm, and may have a monopoly in some markets.

To Decrease the Risks of Gene Escape:

- Develop technologies so that the transgene is not expressed in next generation.
- Avoid planting transgenic crops in their evolutionary center of crop origin where there may be wild and weedy relatives.
- Rotate crops so that other types of chemical or cultural pest control measures can be used.

How Should Responsibility for the Future of Plant Biotech Be Decided and How Does the Public Participate?

The EPA currently has regulations governing the registration of transgenic plants. Should there be additional standards for safety and efficacy? Should there be an equivalent of the Centers for Disease Control to oversee the use of transgenics? Industry might argue that the current regulations suffice and it is in their own best interest to ensure compliance with guidelines so their plant biotechnology products have a long life. Others could argue that a tool such as Bt should not be ruined by overuse for the sake of immediate rewards. While Bt is widely used by home gardeners and organic growers, other transgenic plants for pest management (herbicide- and virus-resistant) are more like conventional products and have similar regulatory and management issues. There is still a gap in research on the best way to avoid/delay development of pest resistance. In the end, the transgenic plant is just another tool for the grower to use in the quest for maximum yield and economic return.

While educating the public seems logical, we must be realistic about who is really interested and who is influencing public opinion. The land grant universities should take the lead in developing methods to deliver the information about biotechnology, genetically altered organisms and transgenics in "plain" language. This information should be presented to (but not limited to):

- Service groups (e.g. Kiwanis, Rotary).
- Influencers of public opinion (Note: the influencer is not always the leader but may have the leader's ear and trust).
- Classrooms.

RECOMMENDATIONS

1) To decrease the risk of development of pest resistance:

- *Maintain an integrated approach to pest management with diverse options.*
- *Maintain strong public and private research infrastructure to ensure diverse options.*
- *Encourage shared funding between industry and government.*

2) Resistance monitoring:

- *Registrant (industry) should conduct baseline monitoring starting with field trials and through commercialization.*
- *The strategy needs to be part of the registration package.*

3) Enforcing resistance management strategies:

- *Research is needed on how to delay/avoid pest resistance, and test such theories.*
- *Use existing groups (e.g. Crop Improvement Association) or new non-industry groups to monitor development of resistance and compliance with management strategies.*
- *Industry and universities need to develop "certified" methods for monitoring.*
- *Growers should keep crop records, including the field location of transgenic and non-transgenic crops.*
- *Penalty for non-compliance should be the same as for misuse of a chemical.*
- *Monitoring and penalties must be standardized across regions.*

4) To reduce the risk of gene escape into the environment:

- *Identify areas of particular concern (centers of origin).*
- *Develop a management plan (e.g., crop rotation).*
- *Express transgenes only in the current crop, not in the next generation.*
- *Create an oversight committee.*
- *Set standards for efficacy and safety.*
- *Identify needed research.*

5) To communicate/educate the public:

- *Land grant universities should take the lead to develop a plain language delivery method of information.*
- *Education is needed for influential leaders and policymakers, media, service groups (Rotary, Kiwanis, etc.), and teachers.*

PART III

KEYNOTE ADDRESSES

Photo courtesy of Monsanto Company

Biotechnology: Is It Defendable?

Carl B. Loop, Jr.
Vice President
American Farm Bureau Federation
Gainesville, FL

Biotechnology is defendable. It is here to stay, and it is going to grow at a faster pace. The questions now relate to its direction and boundaries. Let me state that I am making this presentation as an agricultural producer. I do not profess to be a scientist providing a lot of scientific data. I will leave that aspect to those of you in this room, for I recognize that you are some of the world's finest agricultural scientists.

I am a nurseryman. That was my training. That has been my life. Through the years, I have seen a great deal of genetic management in the materials we produce in our greenhouses. I have accepted those changes and adopted many of them. Doing so has helped me stay in business, improve our products, and stay competitive. By and large, I think that farmers and ranchers believe in science and research as applied to our industry. To them, it is an easy step to accepting and believing in the potential benefits of biotechnology. They recognize that older methods of genetic manipulation are too slow and not specific enough. They see biotechnology as the future.

For the past decade, agriculturalists have heard a lot about the promise of biotechnology. It has been only in the past several years that we have been seeing the results. So far, results have been everything we were led to believe. We have seen crops grown on ground where growth was not previously practical. There are plants that fight disease, drought, and destructive bugs. We have seen dairy animals become tremendously more efficient because of growth hormones. We have seen animals being developed to produce pharmaceuticals for use in humans. US farmers do not need any more convincing about new genetically altered plants. They know that:

- New soybeans are resistant to specific herbicides.
- Cotton repels caterpillars.
- Corn is either a new high-oil type, borer-resistant, or resistant to a specific herbicide.

Preliminary harvest data are extremely promising. Cotton designed to fight bollworms is yielding 15 to 17 percent more than cotton grown with applications of conventional pesticides. And this new cotton is getting a good test. Field inspections indicate bollworm infestations at 20 times the level that used to send farmers scurrying for their sprayers. But cotton carrying the anti-caterpillar bacterial toxin in its genes is doing a better-than-expected job. One southern state Extension director said that farmers with genetically altered crops took their sprayers into the fields one time compared with the traditional 20 to 30 passes.

Think of the cost savings. Think of the reduced soil compaction. Think of the reduced likelihood of run-off or drift. Cotton growers are enthusiastic, so are soybean farmers. Nine out of 10 producers of genetically altered soybeans say that they are getting the results they expected or better.

Corn growers are equally upbeat. The benefits of this new seed, genetically altered to repel corn borers, are obvious. Farmers get relatively easy borer control without the hassle of field scouting, calculating economic thresholds, determining whether or not to apply an insecticide, and then worrying about how the weather will affect the application. By planting this biotechnology corn, farmers will save money and time and still get top yields.

Farmers know that population growth means expanded markets for food and other products. However, the potential for conflict grows too. Farmers are blamed for many environmental issues. By using less pesticide, fertilizer, water, and other resources, the sustainability of agriculture will be greatly increased. Farmers believe in biotechnology, but they have concerns. I think those concerns are brought about not from absolute knowledge, but from a sense that the future is going to be greatly different from the past. And they sense that scientific projects sometimes become widely accepted before the research is complete. As I drive through the southeastern section of the United States, I sometimes think that Kudzu is the natural habitat. Of course, it isn't. Kudzu was introduced to control soil erosion, and it became a noxious weed.

In my own state of Florida, Malaleuca was introduced to help draw water out of the ground to lower the water table. I guess it does but that's not what it is known for today. It has become an invasive weed that has overrun the land, clogged ditches and canals, and in general has become an intolerable nightmare. The point I am trying to make is that all things that appear good do not always turn out that way. We must know how new products will react in the real world under real conditions and not just in the laboratory.

Farmers recognize that there is risk involved as we attempt to improve things. As scientists, you are also aware of that fact. We must be aware that in some people there is no fear. It is full speed ahead. In other people, there is too much fear. That certainly is the case in dealing with biotechnology.

As I look at biotechnology, there are five issues I'd like to address. They are changes to agriculture, competitiveness, ethics, public understanding, and public policy. Some people think of biotechnology and genetic engineering as simple modification of plants and animals. It is far more. It will lead to a completely changed agriculture. I'm not certain I can begin to comprehend all the changes, but let's think of a few. A crop that is engineered for mechanical harvesting, instead of hand harvesting, will be far more attractive production-wise. A crop made tolerant to colder weather or varying soil conditions will create expanded production areas. Products made healthier and more attractive will increase consumer demand, therefore affecting production and marketing.

Biotechnology may well change production areas, as well as who will grow a product and who will market that product. As these things become different, there will be waves of change in all aspects of management. The very structure of the agricultural industry will be affected. Biotechnology has already started to change agriculture. Its application is spreading faster than most people realize. It is estimated that more than one-half of all cotton, 40 percent of the soybeans, and 20 percent of the corn grown in this country in 1998 were genetically altered. And, acceptance is worldwide. Recently, a *Wall Street Journal* article estimated that one company alone would provide genetically engineered seed for 55 million acres worldwide. That's about equal to the farmland of Iowa and Illinois.

Who will control agriculture is of vital concern. If a farmer is limited to the available seeds or breeding stock, then control is exerted on him. If a company producing the seed indicated that products coming from that seed can only be marketed in a certain way, then more control is placed on farmers. Many people think that whoever controls the genetic input in seeds and animals also controls agriculture.

American agriculture has long had the reputation of being the wonder of the world. That reputation was brought about by a great public and private research system making information available. Our incentive system rewarded farmers for adopting new technology. This has always given us a competitive advantage. To let other nations move into the role of being the dominant agricultural producer would be a tragic error. Food supply is the key to security.

We now see biotechnology research being conducted in all parts of the world. We see technology being adopted worldwide as well. Will that make competition keener? American farmers must be able to sell products abroad. The efficiency of our agricultural system makes that possible by requiring exports. A concern that I have is that some nations are using the issue of biotechnology as an artificial trade barrier. They claim there is a problem in the safety of genetically engineered food.

We are hearing the same concerns here at home. A coalition of consumer groups has sued the US Food and Drug Administration (FDA) to remove 36 genetically engineered foods from store shelves until the items are tested and labeled. The suit, filed in US District Court, claims consumers are put at risk by eating foods that are genetically engineered. We must work for worldwide acceptance of scientific standards so that safe in one country also means safe in another. When the mainstream scientific community proclaims a product safe, the statement should mark agreement. If people choose not to buy, that's fine, but let them have a choice.

A problem exists in this area because the World Trade Organization has not yet identified any scientific body as the primary reference point for biotechnology. One such entity does exist for food safety and animal health. I understand that a working group is meeting and will recommend a protocol for testing genetically modified organisms. A major concern of many people is the matter of the ethics of the people who conduct biotechnology projects.

When research was being done on plants, no one seemed to think much about it. As work expanded to animals, there was more concern. With the public announcement of the cloning of Dolly, the sheep, voices have been raised about the role of biotechnology. I suspect there are even some who fear its future.

Certainly we will see the second wave of biotechnology progress. This will include the development of natural compounds to fight cancer and other diseases. There will be genetic modifications to create more nutritious, healthier food and, in addition, the development of compounds for improved human health.

I hope that the scientific community will take the lead in establishing bioethical guidelines and peer review procedures. If that is not done, then government will step in. I'm not at all sure that government would provide a set of sound ethical guidelines.

Some people fear that scientists will become financially greedy in their biotechnology efforts. There has always been that temptation. I believe that most scientists are dedicated to the development and application of science in the best interest of humanity. It seems to me that in most instances recognition of peers and scientific accomplishments is more important to these individuals than financial motivation.

I also recognize that a major fear on the part of some people is that of corporate greed. There is a belief that developers of biotechnology projects will be motivated only by money. The cost of developing new products is tremendous. Developers must be protected. Once these products are licensed and get into foreign hands can they be controlled? If they become obsolete, or a better product comes on the market in three to five years, a 17-year patent doesn't have much value.

I am a realist who knows that financial considerations do matter. Economics is a strong motivating force. But let me point out two things. If there is no incentive or reward, there will be no effort put into a project. Why should an individual or corporation risk capital on developing a product if there can be no gain. Secondly, we must remember that financial gain comes only after or through consumer acceptance. We cannot force individuals to use a product or service.

Yes, money will be made by those who are successful in the areas of biotechnology development and genetic transfer. That is the reward for contributions in serving society. A major concern to me is public attitude and acceptance of scientific advances generated by biotechnology. We all know that the public seems to live on the edge of fear regarding food supply. Just a little push throws many people off balance. Unfortunately, there are some scientists and others who, for their own reasons, seem willing to provide that little nudge. I certainly hope that scientists have a questioning attitude. That creates good science. It would seem, however, that a goal should be to establish criteria that would mean agreement on safety and acceptability.

It seems to me that the scientific community must become more active in an educational, public relations type of effort to create consumer understanding of biotechnology accomplishments. The public must understand that product safety is of major concern to scientists. Really, scientists and farmers do not want to produce products that harm consumers. To do so would be very shortsighted. Consumers must become aware that scientists are dedicated to actions that benefit consumers. At the same time, scientists are constrained by program safeguards established by government, the scientific community, and common sense.

The last issue I will mention is the establishment of public policy regarding biotechnology. This is an area where sound-thinking individuals of the scientific community must be active. You cannot let the extremist within your ranks become the alarmist voices that poison the work done in biotechnology. I hope scientists will discuss and disagree on issues. That causes progress. But I would hope that self-discipline and self-control would be a major behavior of scientists.

One thing is for certain — we must not turn over all the decision-making about biotechnology to the politicians. To do so would guarantee an ineffective program of biotechnology development, a costly boondoggled program, and would assure the success of our competitors in other countries.

In closing let me summarize several points:

- Biotechnology is accepted by most farmers, and they know that this is where the future lies.
- We must educate the consumers and bring them along as new products are being developed.
- Safe must mean safe, and there needs to be an international body that is respected and responsible to say so.

- Incentives must be in place to encourage development and use.
- If we are going to remain strong agriculturally, protect the environment, and be competitive in a world market, then in my view biotechnology is a must.

I believe in the future of this nation and in agriculture, its most important industry. I believe all parties will be better off in the future because of the efforts being made in biotechnology. And, I believe that biotechnology will provide better conditions for humans and the world. Therefore, biotechnology is defendable.

Assessing the Environmental Implications of Agricultural Biotechnologies: A Sociological Perspective

Frederick H. Buttel
Professor, Rural Sociology
University of Wisconsin
Madison, WI

Introduction

Lt. Governor Peeler closed his welcoming speech at this NABC meeting by stressing the importance of family farming to South Carolina, and the fact that much more needs to be done to help save family farms. I agree. Even so, when we discuss research, technology and so on in relation to family farming, there are often clashes among differing groups because competing social values relating to the importance of family farming strike many as being outside of the realm of science or empirical discourse, and difficult to choose between. It is thus ironic, but also instructive, if we recognize that debates over the environmental consequences of agricultural science and technology have been as or more perplexing and just as contested as the matter of the social implications of technology. In this paper I explore some of the reasons why this has been the case, and offer what some appropriate responses from the public agricultural research system should be.

The environmental implications of new agrofood biotechnology products arguably represent today the most socially-salient issue relating to agricultural biotechnology — and, for that matter, to agricultural technology in general. This is not to suggest that the structure of agriculture or the socioeconomic impacts of technology have ceased to be of concern to a good many people, or that there are no longer expectations that agricultural research will contribute to increased productivity, competitiveness, food safety, and so on. With the shift of our national political culture — and most of the rest of the world's — over the past two decades or so, the issue of the socioeconomic consequences of agricultural research and technological change is now on the margins of the political agenda of most governments and agencies. Many of these socioeconomic concerns, however, have been repackaged as environmental issues. In my part of the country, for example, there is a very significant level of resistance to the siting of large-scale, integrated confinement hog operations in rural communities. This issue is, at root, mainly a socioeconomic issue relating to agricultural technology and the structure of agriculture, but it is increasingly being played out on environmental grounds — odor, water quality, the risk of lagoon accidents and spills, and so on. In the developing world, landlessness and land tenure concerns have often been repackaged in the form of indigenous rights or sustainability movements.

Much of this paper will revolve around the symbolic or subjective aspects of environmental quality. Recognizing the fact that the environment is, in part, a matter of subjectivity, perception, and symbolism is not meant to trivialize the importance of the environmental implications of agriculture or agricultural technology. Environmental impacts and constraints are extremely high priority matters for agricultural researchers to address seriously. It is important to recognize that scientific evidence alone, no matter how compelling it might appear to the agricultural research community, will ultimately carry the day only if it is consistent with how various groups in society see their own lives and futures. There must also be societal trust in government, universities, and other institutions generating this evidence. Not only is there a tendency for agricultural scientists' calculations of risks to be different than those of nonscientists, but public environmental concerns do not always coincide well with data from environmental science research.

A Sociological Perspective on the Environment

The classical tradition in sociology and all the other major social sciences has revolved around stressing that the realm of the social can — and must — be understood apart from the natural world. Thus, for most of the nineteenth and twentieth centuries, social scientists thought that an explanation was satisfactory only if it was a social explanation (i.e., in terms of a social variable such as social class, culture, or power). There was deep suspicion and a lack of professional regard if social phenomena were explained in terms of physical or biological forces such as genetic heritage, climate, biophysical environment, and so on. In my discipline it is still the case today that scholars who study societal-environmental relationships, or who try to explain social phenomena by using biophysical variables, are considered more or less out of the mainstream (Harper, 1996).

When the environment rose to prominence as an issue nearly 30 years ago, some sociologists were of the view that their disciplinary tools needed to be dramatically changed if they were to be able to understand the significance of the environment. This has given rise to a substantial community of sociologists who take the environment seriously. There are now a goodly number of sociologists and other social scientists who are exploring the social significance of the natural world as a source of materials, resources, and (ecosystem) services as well as being a decisive constraint on human activities. But it is also very apparent to these environmental sociologists that the significance of the environment to human social life goes beyond the matter of the goods and services that humans obtain from nature, and the impacts that societies have on nature.

For example, the very notion of the environment can be seen as a Western cultural construct that is predicated on the distinction between society and the natural world. However, if we look at how humans have related to the natural world historically and cross-culturally, it becomes clear that the Western distinction between society and environment is by no means a universal one. The cultures (or "cosmologies") of many of the world's people today still involve seeing humanity as an integral and inseparable part of nature. For them, the notion that society or technology has "impacts" on "the environment" is unfamiliar or even nonsensical. Even so, the symbolic salience of the environment is still important in the Western world and in much of the remainder of the world that is undergoing Westernization and modernization. Widespread public concern about the environment is one of the defining features of social life in the late twentieth century.

Some sociologists believe that the essence of environmental concern is basically a response to the growing knowledge that the ecological/environmental sciences have been generating about how the expansion of human societies and modern technological practices are prejudicing the quality of the biophysical environment. Without denying that this process plays an important role, I believe that the significance of environmental concern is more social and symbolic (Hannigan, 1995). Matters such as personal security (particularly health), aesthetics, community livability, and the future quality of life for one's children tend to be the most enduring types of environmental concerns. Some movement leaders, however, have had a tendency to want to stress global environmental concerns that cannot be directly experienced by individuals and communities. One of the ways that environmental issues become socially salient is through the formation of public perceptions that there exist environmental risks that are unwarranted or unreasonable. This can occur when there is an environmental event that can be attributable to or blamed on an institution or organization in which there is a lack of trust. We, of course, live in a world where there is fairly widespread cynicism about major institutions, including both government and industry, creating fertile ground for cycles of concern about environmental and technological risks (Beck, 1992; Macnaghten and Jacobs, 1997).

Whether or not we define a particular social issue as an environmental one or not is therefore as much a process of social "framing" (Hannigan, 1995) and culture as it is a deduction from scientific research. I noted earlier that agricultural biotechnology has been contested increasingly on the grounds of whether this type of technology will or will not have adverse environmental implications. Thus, groups that for one reason or another have concerns about agricultural biotechnology are increasingly couching these concerns in environmental terms. Similarly, proponents of agricultural biotechnology, including many of the large private biotechnology firms, devote considerable effort to justifying these technologies on environmental grounds.

These debates about the environmental advantages and disadvantages of biotechnology occur not only in the media as direct or indirect attempts of various groups — including those of us at this conference — to influence the views of the public. They also occur in a variety of political, regulatory, and scholarly arenas. It is increasingly the case today that groups on opposite sides of a social policy issue will both actively use scientific arguments to bolster their case. In particular, it has increasingly been the case that social movements — including but not limited to environmental movements — will couch their arguments in science. This process, which I call the "scientization of social movements," is having significant impact on the work and practices of scientists (Yearley, 1991). This is particularly the case in the sciences whose processes or outcomes have potential environmental impacts. Agricultural biotechnology is a prime example of the "scientization" of public policy discourse. A parallel process that I find particularly significant as well is that professional and interest groups are increasingly conducting themselves more or less like social movements, in the sense that they actively hone ideological positions and claims in order to influence policymakers and the public. And in this process of the "social movementization" of professional and interest groups it is commonly the case that these groups rely on scientific arguments, and also make appeals to environmental concern or greenness.

The typical configuration of these policy debates and conflicts today is that environmental-type groups employ scientific reasoning about how technologies, policies, or other interventions will lead to environmental and other risks. Their opponents will typically respond with claims that in the reputable (or "sound") scientific literature there is no evidence that an adverse environmental impact necessarily will occur. And increasingly the response is complemented with uncertainty arguments. It is typically argued that the risks discussed by environmentalists are only hypothetical, that there is doubt in the scientific predictions and conjectures used to forecast risk, and that it would be imprudent to make costly responses to risks that are only hypothetical. Typically, both sides sincerely believe that "sound science" is on their side.
It should be stressed, though, that risk and uncertainty, while they are common words in our language that have several meanings (Thompson, 1997), are perfectly legitimate scientific concepts. But they are employed so often as rhetorical weapons that there is now a growing cynicism in policy circles about whether they are more-so political slogans or methods of scientific analysis.

The Environmental Impacts and Implications of Biotechnology: Some Observations

Why is there so much debate and concern about the environmental implications of agricultural biotechnology? My analysis thus far is that one dimension of this concern is socially constructed. One implication of this point is that scientific evidence and argument alone can play only a partial role in resolving policy conflicts whose origins have deep roots in society and social structure. But it is important to recognize that these conflicts are not merely symbolic — or, some might say, nonempirical or irrational — ones. The fact that agricultural biotechnology remains controversial nearly 20 years after the onset of large-scale public and private R&D suggests that concern about the technology is much more than an irrational obstacle or public resistance to change. Agricultural applications of biotechnology account for less than 15 percent of private biotechnology R&D investment, but perhaps 80 percent or more of the conflicts and controversies over the technology have been agriculturally related (Krimsky and Wrubel, 1995). In part, this is because many of the first generation of crop biotechnology products — particularly herbicide-tolerant and Bt (*Bacillus thuringiensis*) engineered crop varieties — have had environmental liabilities or vulnerabilities.

Second, agriculture in the US and elsewhere faces some considerable environmental and resource management challenges, and the nature of ongoing trends suggests that the path we are on is problematic for dealing with these challenges. Agricultural chemical use has increased, and since the late 1980s there has been a decisive reversal of the farm-crisis-induced decline of agrochemical usage (Goodman and Redclift, 1989). Nitrogen usage has never been higher. Despite much touting of integrated pest management (IPM) technology, agricultural pesticide usage (as measured by pounds of active ingredients) remains virtually unchanged from the levels of 15 years ago (GAO, 1995). Cultivation of highly erodible land is still widespread (ERS, 1995a, 1995b). Agriculture remains the most significant contributor to impairment of the quality of the nation's water resources. About 38 percent of the miles in lakes and streams, and 44 percent of the nation's lake acres, were estimated to be not fully supporting their intended uses, according to US Environmental Protection Agency (EPA) data for 1992 (GAO, 1995). Agriculture was the leading source of impairment of the quality of water in rivers, streams, and lakes. At some point over the next decade or two the national and world agricultural communities will need to address the interrelated problems of the excess of fixed nitrogen compounds in the global environment (Vitousek et al., 1997; Hellemans, 1998), and the impact of agricultural production on the quantity and quality of water resources. Add to these macro-level environmental constraints the more highly salient public concerns about food quality and safety, the odors and water quality impacts of animal wastes, and so on, and it becomes clear how important the environmental dimensions of agricultural technology will be in the future.

There have traditionally been two major ways in which the environmental implications of agricultural biotechnology have been analyzed and dealt with in policymaking. The first approach to assessing the environmental implications of biotechnology has been to undertake experimental field or laboratory assessment of whether a particular biotechnology, such as Bt-engineered corn or herbicide-tolerant soybean varieties, has definite, empirically verifiable adverse environmental consequences. Experimental assessment of a specific biotechnology product generates data that can be useful in regulatory arenas. There is, to be sure, more than a small amount of grumbling about the EPA, the US Food and Drug Administration (FDA), and the United States Department of Agriculture (USDA) regulation of agricultural biotechnology. But it has been very seldom that regulatory roadblocks have derailed an attractive agricultural technology. And a strong regulatory process serves a useful long-term purpose in building public trust and in discouraging scientists from bringing highly risky technologies to the market. Nonetheless, these experimental data, while they are of clear use in addressing what might be termed the population-ecological and ecotoxicological effects of agricultural biotechnology, do not exhaust the broader environmental issues that relate to agriculture.

The second approach has been to make assessments about whether biotechnology as a class of technologies is likely to be environmentally friendly or environmentally destructive. For example, many proponents argue that because biotechnology will make possible increased productivity and output, these technologies are environmentally friendly because they will enable food to be produced on smaller acreages than would otherwise be the case. There will, therefore, be less "pressure" on tropical rainforests, wetlands, marginal agricultural environments, and so on. This type of argument, however, has a good many fallacies. It is premised on the notion that biotechnology is the only possible way to increase the productivity and output of the world's croplands. The nature of technological change in the industrial countries, where biotechnology products will be most extensively used, are not likely to have much effect on land use in the tropics. This argument also ignores the fact that to the degree to which there is rapid technological change in the developing world and this technological change is of the capital-intensive type (as is the case with most biotechnology products), it is likely to exacerbate landlessness. All things being equal, landlessness will result in more rather than less of a tendency for the rural poor in the developing world to seek land for subsistence in rainforests and other ecologically significant zones. Similarly, some observers (including some opponents of biotechnology) argue that due to the nature of the technology it will lead to genetic uniformity and to risk of widespread incidence of pest and pathogen outbreaks. It is not clear, however, that biotechnological methods will lead to genetic uniformity of a magnitude greater than what conventional plant breeding makes possible.

I am not inclined to put very much stock in claims that agricultural biotechnology is environmentally friendly or not due to the methods that are used in research and development. In part, this is because of the fact that biotechnology is not a particularly meaningful term anymore. Granted, there is a certain coherence to biotechnology if we say that it involves cellular or subcellular manipulation of life forms. Recombinant DNA is the most significant — and controversial — technique in the cluster that is generally referred to as biotechnology, but relatively few agricultural scientists actually create transgenic organisms. Gene mapping is a central technique of biotechnology, but again gene mapping is not a common activity among agricultural scientists, and gene mapping can be useful in ways other than creating new organisms. Marker-assisted plant breeding is a tool of general utility. Thus, "biotechnology" is a diverse set of research methods. Further, as with most scientific methods, the implications of the technologies that derive from these methods are shaped more so by the research priorities that these methods are used to achieve than by the methods themselves. Thus, there is no inherent reason to either promote or disparage the technologies that can be developed through use of these methods on environmental or other grounds.

Nonetheless, if forced to make some overall judgment about the environmental implications of biotechnology, my guesses about plant biotechnology products would be as follows. The crop biotechnology products that have been commercialized or are in the pipeline are basically derivative technologies. By this I mean that these technologies are basically being derived from or being grafted onto an established trajectory, rather than defining or crystallizing a new one. This established trajectory in crop agriculture consists of a predominance of farm- and regional-level specialization — basically monoculture, continuous cropping, and spatial homogenization — along with incremental shifts toward labor-saving technology and larger scales of production. New technologies such as the first generation of biotechnology products basically provide some management options for dealing with the problems of large-scale, specialized crop agriculture. Herbicide-tolerant crop varieties, for example, may help to rationalize herbicide usage by expanding the scope of usage of less toxic and/or less persistent herbicides and enabling these crop protection chemicals to be used postemergence. Bt engineered varieties (and other biopesticide products) enable the large commercial producer to control pests without having to resort to crop rotations. Contemporary commercial biotechnology is essentially based on high-value, single-gene traits. We need to recognize that there is an economic-environmental contradiction of single-gene-trait biotechnology. The more valuable the trait the more widespread it will become, and the greater the selection pressures for resistance and other forms of environmental disruption. I would suggest that crop biotechnology products will basically nudge world and US agriculture a little farther along the trajectory of specialization, ecological homogeneity, and incremental increases in chemical use that was initiated earlier in this century. They are not likely to dramatically exacerbate these problems, nor will they do much to solve them.

The technological products derived from biotechnology (and of other combinations of research methods and research priorities) will need to be assessed in meaningful packages that avoid the limits of the two prevailing assessment methods. Meaningful clusters of biotechnology products are much smaller than that of biotechnologies as a whole, but larger than that of a specific biotechnology product. Most importantly, environmental assessment of meaningful clusters of biotechnologies must address the implications of these technologies for the degree to which they will make a significant contribution to addressing the overarching environmental problems of agriculture, such as global nitrogen overload, water quality and quantity, and maintenance of ecosystem services. However, these assessments must not be narrowly environmental or ecological in nature. For instance, the ecological impacts of technology often occur through socioeconomic processes. Hybrid corn, for example, historically led to soil erosion problems, but not because hybrid corn was intrinsically destructive of soil. Rather, the technology involved a high level of genetic uniformity, and was highly consistent with mechanization. The mechanization of tillage, and especially harvesting, led to incentives for monocultural production, and in many areas to soil erosion. Assessments of environmental implications and risks need to take into consideration the context of the use of technology — particularly the structure of the production sectors for which they are being developed (Kunkel et al., 1998).

Thus far I have not placed much emphasis on global environmental issues. This might seem to be a serious omission when we consider the fact that the major western environmental organizations have long tended to stress global climate change, stratospheric ozone depletion, loss of biodiversity, and so on. And in my own discussion of the agricultural environment I have stressed the importance of macro-level, if not global, environmental issues. The global surplus of fixed nitrogen is a particularly important example of a large-scale environmental issue in agriculture that we need to take into account as we think about the environmental implication of biotechnology.

Even if we grant that the matter of the global surplus of fixed nitrogen is a relatively new issue (National Research Council, 1997; Burns and Hardy, 1975), it is still worth noting that there is currently no organized movement oriented toward encouraging agricultural researchers and policymakers to address this matter, and there is not likely to be such a movement any time soon. If we think about why this has been the case it can tell us something very important about the often-imperfect alignment between public environmental concerns and global environmental issues. Most people are likely to care more about environmental problems that they can directly experience, that affect their quality of life, their sense of personal safety, or their community integrity. It is usually the case, however, that the typical citizen cannot directly experience global-scale environmental problems such as climate change or the rising level of fixed nitrogen in the environment. This is because these problems will generally not be fully apparent for decades, their impacts may be felt most strongly by others, or any solutions implemented now will mainly benefit future generations. Thus, it is not surprising that while environmental mobilizations around global issues such as atmospheric warming can grab headlines and attention for a while, these issues do not have much public staying power. Global climate change, for example, has now almost entirely disappeared as a major public issue.

Concluding Remarks

Is biotechnology a threat to the environment in some sociological or objective biophysical sense? I do not think this question has a meaningful answer. The technologies that will derive from cellular and subcellular manipulation of organisms will be a function of research priorities or public policy.

Will biotechnology, in and of itself, lead to solutions to the major environmental concerns that I distinguished between earlier? Probably not without some significant institutional changes such as ecological taxes. But if there are some institutional changes, biotechnological methods will have a lot to contribute. I have a strong feeling, however, that we will get the most out of biotechnology if we begin to invest a lot more in agroecological approaches to agricultural systems.

Should agricultural researchers pay attention to the public and the rank-and-file of their clienteles and respond to their environmental concerns? Or should the research system be attentive to the more macro environmental constraints? We need to do both. We always need to listen to our constituents — even the ones we disagree with — and strive to open new lines of communication. This is an integral part of the process of building public trust and being a responsive public institution. And this means more than getting in contact in order to convince them about our data and our views. But we also have an obligation to be forward looking and to anticipate the kinds of technologies that could be possible and desirable in the more environmentally constrained world that we'll meet up with in the next century.

Is the public essentially becoming anti-science or anti-biotechnology? There is no evidence at all that this is the case. There have been no major changes in public trust in science over the past two decades. The only key shifts are that minorities, and to a modest extent women, have declined in their trust in science (when education is controlled), and that today the very well educated are somewhat more polarized between very pro-science and anti-science views than in the 1970s. In general, though, there is no significant public opposition to biotechnology, or science in general, provided that we meet our obligations as scientists and universities of taking the public seriously. But you don't need a sociologist to tell you this. It basically involves doing what the Morrill Act and Hatch Act established the land-grant system to do.

Agriculture has some significant issues to address if it is to build this trust. Farm numbers are again declining rapidly, after a period of relative stability during the 1970s and early 1980s. Livestock industrialization is creating some very problematic public relations for agricultural research institutions, and food and agriculture in general. Many agricultural groups are active politically (in pursuit of "right to farm" and "food disparagement" legislation, in opposition to land use planning) in ways that many in the public find to be narrowly self-interested. Agriculture needs to reestablish itself as a public (rather than primarily a private) goods-generating set of institutions if it is to rebuild this trust.

References

Beck, U. 1992. The Risk Society. London: Sage

Burns, R.C., and Hardy, R.W.F. 1975. Nitrogen Fixation in Bacteria and Higher Plants. New York: Springer-Verlag

______. 1995a. "1994 Nutrient Use and Practices on Major Field Crops." AREI Updates, No 2, Washington, DC: Economic Research Service, US Department of Agriculture

______. 1995b. "Tillage and Cropping Systems on Highly Erodible Land." AREI Updates, No 6, September. Washington, DC: Economic Research Service, US Department of Agriculture

______. 1995. US Agriculture: Status of the Farm Sector. GAO/RCED-95-104FS. Washington, DC: General Accounting Office

Goodman, D., and Redclift, M. (eds.). 1989. The International Farm Crisis. London: Macmillan

Hannigan, J. 1995. Environmental Sociology. London: Routledge

Harper, C. L. 1996. Environment and Society. Upper Saddle River, NJ: Prentice-Hall

Hellemans, A. 1998. "Global nitrogen overload problem grows critical." *Science* 279:988-989

Krimsky, S., and Wrubel, R. 1996. Agricultural Biotechnology and the Environment. Urbana: University of Illinois Press

Kunkel, H. O., Thompson, P. B., Miller, B. A., and Skaggs, C. L. 1998. "Use of competing conceptions of risk in animal agriculture." *American Journal of Animal Science* 76:706-713

Macnaghten, P., and Jacobs, M. 1997. "Public identification with sustainable development: investigating cultural barriers to participation." *Global Environmental Change* 7:5-24

National Research Council. 1994. Biological Nitrogen Fixation — Research Challenges. Washington, DC: National Academy Press

Thompson, P. B. 1997. Food Biotechnology in Ethical Perspective. London: Blackie Academic
Vitousek, P.M., Aber, J. D., Howarth, R. W., Likens, G. E., Matson, P. A., Schindler, D. W., Schlesinger, W. H., and Tilman, D. G. 1997. “Human alteration of the global nitrogen cycle: sources and consequences.” *Ecological Applications* 7:737-750
Yearley, S. 1991. The Green Case. London: HarperCollins

International Acceptance of Agricultural Biotechnology

THOMAS J. HOBAN
Professor, Department of Sociology and Anthropology
North Carolina State University
Raleigh, NC

The promises of agricultural biotechnology are becoming reality. It is exciting to watch this field develop. Farmer acceptance of transgenic crops has been phenomenal. It took hybrid corn about fifteen years in Iowa to become completely accepted. Anything takes time, but the use of biotechnology crops has been limited mostly by seed availability.

We have recognized for a number of years that consumer acceptance is really the ultimate determinant of the success of these products (Hoban and Kendall, 1993). We also now realize that the products must be acceptable in the international marketplace. In some European countries, interest groups have expressed opposition to the products of biotechnology.

Education is very important, but it must be based on an in-depth understanding of public knowledge and public attitudes. This paper will review some of the trends of public perception or consumer acceptance of biotechnology as we have tracked it for almost a decade (Hoban, 1996; Hoban and Katic, 1998). It will also present some very new information about consumer attitudes and awareness around the world (Einsiedel, 1997; European Commission, 1997; Hoban and Miller, 1998).

OVERVIEW OF RESEARCH PROJECTS

The US Department of Agriculture (USDA) sponsored our first study in 1992 (Hoban and Kendall, 1992). We did a national telephone survey of more than 1,200 people in the US. A couple of years later I followed up with a study focusing on the then hot topic of bovine somatotropin (BST) (Hoban, 1994). I also have worked over the years with another group in Washington, DC — the Food Marketing Institute (FMI). They included some questions on biotechnology in their US surveys (Food Marketing Institute, 1996) and the same questions on their 1995 European survey.

I conducted a national study of Japanese consumers in 1995 and in 1998 (Hoban, 1996a). In March of 1997, I worked with the International Food Information Council (IFIC) on a study of American consumers' attitudes (Hoban and Katic, 1998). The objective of that project was to determine any impact from the report of cloning sheep and the related issues. Some very new information is just becoming available from an international team of scientists. A contingent of European researchers conducted a survey in Europe of more than 16,000 consumers (European Commission, 1997), as part of a periodic Euro-barometer study. A Canadian researcher conducted the same survey in Canada with 1,000 consumers (Einsiedel, 1997). Jon Miller, a colleague of mine, and I recently conducted a US survey of more than 1,000 consumers (Hoban and Miller, 1998). Some very interesting information was obtained, particularly country comparisons since there were many common questions.

CONSUMER ATTITUDES ABOUT BIOTECHNOLOGY

It is important to compare results from surveys of consumers in the US over a fairly long time period. Throughout the past decade there has been remarkable stability of people's opinions on biotechnology in the US. These results are as close to identical as you can find from a series of surveys. In all three years we asked towards the end of each interview, as a summary comment: "Tell me whether you support or oppose the use of biotechnology in agriculture and food production." In 1992, 70 percent said they supported it, a few did not know, and less than twenty percent were opposed. In 1994, during the height of the controversy over BST, 72 percent said they were supportive of it. In 1998, we again found 72 percent supportive.

We wanted to determine if there were demographic differences among groups. Two key ones stand out. Men are clearly more positive than women are in their evaluation of biotechnology, and this has occurred over the years in response to a variety of questions. There is a narrowing of this gender gap in 1998. This difference is important because women set the family food policy. They serve as food gatekeepers in our society as far as what is acceptable food for the family.

There are also significant differences based on formal educational level. In all three surveys from 1992 to 1998, respondents with a college degree were much more likely to support biotechnology than those with only a high school degree. College tends to provide an opportunity to be exposed to a variety of different ideas. However, not all college graduates have a good understanding of science.

Two FMI studies and the 1997 IFIC survey provide additional data over time in the US. Three out of four people would be willing to buy potatoes or tomatoes developed through biotechnology to require fewer pesticides and be protected from insect damage. This finding is remarkably consistent over time. A majority of consumers would also be willing to buy produce that tasted fresher and better through biotechnology.

There is a comparison of three questions in 1995 across the countries in Europe, as well as the US, Canada, and Japan (Figure 1). The vast majority of European countries were above 50 percent in terms of consumers' willingness to buy insect-protected produce. There are only two countries where acceptance is very low: Austria with only 22 percent consumer acceptance, and Germany with about 30 percent. Europe is not a homogeneous market. The European willingness to buy fresher and better tasting produce follows the same basic pattern, but is a bit lower in all countries than for insect protection.

The recently completed surveys in Europe, Canada, and the US asked consumers to evaluate six different applications of biotechnology. Two of them related to food, two to animals, and two to human health care. As you might imagine, human health care is acceptable and seen as valuable to about 85 percent of people around the world. The insect-protected crop plants were seen as third most acceptable, right after human medicine. Canada is very positive, as is the Netherlands, Italy, the UK, and Finland. The only country that is quite negative is Austria. They have a lot more organic farmers and low government support for biotechnology.

Figure 2 provides a summary to whether or not consumers agreed or disagreed that insect-protected crops developed through biotechnology should be encouraged. The results are generally positive. Support among Canadian and US consumers is very strong. Consumers in Finland, France, Italy, the Netherlands, and a number of other countries are also quite positive about plant biotechnology. Half the German citizens felt these products should be encouraged. That is a very different story from the perception that all of Europe is negative on biotechnology. In fact, the data show that only Austria is very negative. There certainly are groups within some European countries that are negative, but these results are a random sampling of citizens, not the opponents who get all the media attention.

It is important to put attitudes about biotechnology in perspective. Figure 3 shows US consumers' relative perceptions of whether biotechnology is a risk to their health compared to other concerns. The one that gets the most attention in the media (and probably the one most consumers ought to worry about) is microbial contamination that was identified by three out of four people as a serious hazard. Consumers then identified pesticide residues, which actually declined in recent years as a risk. Antibiotics and hormones, irradiated foods, additives, and preservatives were identified next in decreasing risk. Foods developed through biotechnology are lowest on the list of potential health risks perceived by the US public.

European consumers have similar perceptions (Figure 4). They see "genetic engineering" as slightly more risky than artificial coloring, nitrites, cholesterol, and fat, and well below the others that are of more concern to them. These issues need to be kept in perspective. Greenpeace would make you think that genetic engineering is the biggest food concern of European consumers; it is not.

There are some striking country-by-country differences (Figure 5) with Sweden, Austria, and Germany having the higher levels of concern. In most other countries, less than half the consumers saw biotechnology as a serious hazard. Portugal is an unusual case with very high acceptance and very high perceived risk.

[redacted]

[redacted]

Biotechnology Awareness

Our surveys in the United States have tracked public awareness over time. Respondents were asked “How much have you heard or read about biotechnology?” Two thirds of US consumers (Figure 6) had heard only little or nothing about biotechnology between 1992 and 1996. In fact, awareness seemed to have gone down slightly in recent times. Then, in March of 1997, almost half of all respondents reported “a lot” or “some” awareness. Awareness in the US increased substantially with all the news on cloning the sheep, but as shown previously, attitudes about plant biotechnology had not changed, with willingness to buy foods from biotechnology remaining high.

Respondents to the most recent surveys in the United States, Canada, and Europe were asked “Have you heard or read anything about biotechnology in the past three months?” In the US and Canada just over half the respondents said they had. Awareness was higher in Austria, Finland, Sweden, and Germany. Other countries tended to be relatively low in terms of awareness and media coverage. This does reflect the extent to which biotechnology is an issue. If people are really interested in a subject they will talk to somebody about it.

That may be a family member, friend, physician, or even a scientist. Figure 7 reports how many claimed to have ever talked to someone about biotechnology in each of the countries. If they have not discussed it, they are not very concerned or interested in it. There are some major differences. Germany is the highest, followed by Sweden, Austria, and Finland. When something is controversial, there is a tendency to talk about it more. Some of the countries (such as Ireland and Spain) have not had much discussion about biotechnology.

European awareness reveals some interesting contradictions. The two countries that were lowest in their willingness to buy biotechnology produce were Germany and Austria (Figure 1) yet a relatively high awareness was also reported. This observation does not, however, mean that education doesn't work. It depends to a large extent on what people have heard or read. People who have done media analysis in Germany and Austria have found mostly negative reports. The opponents had the chance to tell their story in 1996 without much balance. So, consumers read a whole lot more about it in those countries, but what they had heard or read was very negative. There is some evidence that this has changed in the last year with more positive media coverage.

Several knowledge questions were asked on the recent European, Canadian, and US surveys. These also reflect the types of impressions people have of biotechnology. Consumers need a basic understanding of how food is produced.

Respondents were asked if it was true that “Yeast for brewing beer consists of living organisms.” Results are shown in Figure 8. Remember, this is a random sample of consumers not scientists. In the US and Canada, three out of four people gave the correct answer. A number of people admitted they did not know. About 10 percent actually said it is false (that yeast is not a living organism). There is some variation in Europe, (e.g., in Spain, less than half of the people recognized this as true). Consumers in Sweden and the UK tend to be among the highest in terms of their understanding of basic biological principle.

The questions got more difficult, and more specific to biotechnology. Consumers were asked whether or not the following statement was true or false: “Ordinary tomatoes do not contain genes, while genetically modified ones do.” As shown in Figure 9, there is a lot of uncertainty on this question. Not many people gave the right answer, and many people, including almost half the Americans, did not know. This has important implications because if consumers think that genetically modified tomatoes have something “different” in them, concerns will be raised. We have to be sure to educate consumers about the basic principles of biology at an early stage. There are major differences between European countries in knowledge.

Another question asked if eating genetically modified food would change a person's genes. Figure 10 shows a great amount of variation in responses to this statement. There is a better understanding in some countries (like the Netherlands, Canada, and the US). On the other hand, 40 percent of Austrians believe it to be true. This false impression may explain some of the perceived risks and fears.

One to the key issues for education is to identify and use sources of information that consumers trust. We asked US consumers whom they would trust as sources of information about biotechnology. The American Medical Association (AMA), the National Institutes of Health (NIH), the Food and Drug Administration (FDA), the American Dietetics Association, and university scientists (which are third party scientific groups) tend to be the most trusted (Figure 11). Groups like TV news reporters, biotechnology companies, packaged food manufacturers, chefs, activist groups, and grocery stores tend to have lower credibility. The lowest three are also the ones who have been most negative on biotechnology. In the European countries, this is basically reversed. Environmental and consumer groups are at the top of the list. Government and industry are both quite low in credibility. This is not surprising in light of the "mad cow" controversy and other recent problems.

Hoban

Labeling Issues

The last set of findings seeks to determine whether or not consumers want foods developed through biotechnology to carry special labels. When surveys have simply asked "Should foods be labeled?" the majority say "yes." But, we get a very different answer if we ask about support for the FDA policy. In this case we describe the FDA policy in a shorthand way (i.e., that foods will be labeled if they have been changed in a material way, otherwise no special labels will be required.) In the 1997 IFIC survey, almost 80 percent supported the FDA position on labeling. We believe the approach of explaining the FDA policy to consumers and then asking if they support it provides a more valid answer on the need for labeling.

In 1992 we conducted eight focus groups where a lot of time was spent talking to consumers about labeling issues. Consumers started out by saying they wanted information about everything. But then we learned that they only expect a label if the food has been changed in some way. In response to the example of recombinant chymosin, which is essentially the same as the rennet traditionally used to produce cheese, consumers said there was no need for special labels. The labels just say "enzyme," not how the enzyme is made.

We found an interesting difference in whole versus processed foods. A consumer would want to differentiate a whole, fresh tomato so they can pick out the genetically enhanced ones. This becomes important if they are being charged a premium for that particular product. Next we asked about the case where processors blend together a range of different tomatoes to produce ketchup. The first thing a consumer would generally ask is "What do you mean that they blend together different kinds of tomatoes to make ketchup?" There is not a clear understanding that some varieties are higher in solids or some are sweeter. Processors blend them together to get the taste or consistency they want. Consumers would agree there wasn't much need to label such processed food. Then we asked "What about tomato paste used on a frozen pizza." By that time, consumers said they didn't care if the tomato had been genetically modified because it is already processed.

The other thing we found was that consumers don't place much value on labeling. We asked if they would be willing to pay more if it cost extra to keep the food segregated. People generally said, "No, we should not have to pay, just let the food companies pay for it." However these costs would be passed on to the consumer. Labeling is not education. The recent Nutritional Labeling and Education Act (NLEA) states that information on a label should be clear, meaningful, and consistent. All labeling should start with this premise.

Conclusions and Implications

Labeling is still the "hot button" issue for activist groups. The FDA requires labeling when there is a significant change. For most consumers, that is all that's really meaningful. The costs and logistical problems with segregating commodities are considerable. If there is no real benefit for a consumer, it will be very hard to recover these additional costs. A label on a processed food that says it contains genetically modified organism (GMO) ingredients is not going to be helpful to consumers. It will raise anxiety and confusion about what the statement means. There will be niche producers of non-biotech crops if there is a premium market.

The majority of US consumers have positive attitudes about biotechnology. They perceive benefits and will buy the products. The NatureMark™ potato did quite well in market tests when they were labeled and put next to others. Consumers perceived a benefit of the reduced use of pesticides. There was a very clear preference among British consumers for tomato paste from genetically modified tomatoes. Biotechnology is not a high priority issue for consumers. When studies ask “What is the major problem facing our country?” no one says “biotechnology.” Maybe one percent will say “the environment.” Nobody even says “food.” The biggest concerns are crime, the economy, and breakdown of moral values. We have conferences like this where everybody is interested in the subject. However, the average consumer is just not interested or concerned.

Consumers’ attitudes about biotechnology are closely related to their general beliefs about science, technology, and food. In the US, there is a strong public support for and appreciation of science. People recognize that they have received major benefits from science and technology. The public may feel there is a potential down side, but overall they are very supportive of new developments. People are pragmatic about food. With any food product, consumers mainly want to know about taste, nutrition, safety, convenience, and price. Those are the main questions a consumer will want answered about food produced through biotechnology or any other means.

The future prospects in Europe are less certain, at least in the short term. Seed companies, farmers, and suppliers in the US and Canada want to make sure the European controversy is short lived. The US government is not going to accept mandatory segregation of crops. That would be a logistical nightmare. The Europeans had a chance to buy elsewhere in 1996 when the transgenic crops were introduced. Now, South American farmers and others are starting to raise crops developed through biotechnology. In fact, more products are going to arrive on the market from around the world. Europe will soon have few options except to pay more for food certified as “GMO-free.” European leaders also have concerns about lost jobs, increased food prices, and other economic costs that are going to result from rejection of biotechnology.

Educational efforts will continue to be very important in Europe. Such efforts are starting to take hold among European leaders and consumers. A meeting sponsored by the Georgetown Center for Food and Nutrition Policy in Washington, DC, a little over a year ago invited leaders from the European Union. They were hungry for information. These were some of the top

European officials, but most of what they had heard about biotechnology up to that point had come from Greenpeace.

Statistical analysis has helped evaluate what influences people's acceptance of biotechnology (Hoban et al., 1993). At the top of the list is awareness and knowledge. People need to have some level of knowledge about biotechnology. They also need to recognize a societal benefit or feel there is something in it for them personally. They need to view it as ethically acceptable. Ultimately acceptance comes down to confidence in government and trust in the information sources.

The educational opportunities and challenges are very important. There still is a lot of work to do in Europe. In the US, we've been able to effectively reach consumers by educating opinion leaders, including scientists and government officials. The media in the US have had ample opportunity to learn about biotechnology. Through groups like the NABC and the IFIC, they are provided with the latest factual information on biotechnology. Finally, farmers and the food industry need more education. It is very important that food retailers and others who have direct contact with consumers have enough information to answer any questions.

Through education, we need to talk about the benefits and the uses of biotechnology. This will give people a reason to accept the products. We must address consumer concerns, including labeling, allergens, and other questions that are on people's minds. It is also important to tell consumers about third-party oversight and regulations. Consumers want to know that the government is regulating biotechnology. In the US, the FDA and the USDA have done a good job of keeping the public confidence high. Europe has been a much different story.

Finally, it is important to put biotechnology into a historical context. We need to tell people that we have been breeding plants for years. Some consumers seem surprised to learn that scientists have already changed plants. Overall, we need to increase consumer understanding of food production and processing. Most consumers simply think that food comes from the grocery store or, increasingly, from restaurants. These are all part of the educational challenges and opportunities with biotechnology.

References

Einsiedel, E. 1997. Biotechnology and Canadian Public. Calgary, Alberta: University of Calgary

_____. 1997. European Opinions on Modern Biotechnology. Luxembourg: European Commission

_____. 1995. Trends in Europe. Washington, DC: Food Marketing Institute, pp. 96

_____. 1996. Trends in the United States, Consumer Attitudes and the Supermarket. Washington, DC: Food Marketing Institute, pp. 88

_____. 1997. Trends in the United States, Consumer Attitudes and the Supermarket. Washington, DC: Food Marketing Institute, pp. 88

Hoban, T.J., Woodrum, E., and Czaja, R. 1992. "Public Opposition to Genetic Engineering *Rural Sociology*." 57:476-493

Hoban, T.J., and Kendall, P.A. 1993. Consumer Attitudes about Food Biotechnology. Raleigh, NC: North Carolina Cooperative Extension Service

Hoban, T.J. 1994. Consumer Awareness and Acceptance of Bovine Somatotropin. Conducted for the Grocery Manufacturers of America

Hoban, T.J. 1996a. "How Japanese Consumers View Biotechnology." *Food Technology* 50:85-88

Hoban, T. J. 1996b. "Trends in Consumer Attitudes about Biotechnology." *Journal of Food Distribution Research* 27(1):1-10

Hoban, T.J. 1997."Consumer Acceptance of Biotechnology: An International Perspective." *Nature Biotechnology* 15:232-234

Hoban, T.J., and Miller, J.D. 1998. Consumer Images and Impressions. Paper presented at the annual meetings of the American Academy for the Advancement of Sciences. Philadelphia, PA

Hoban, T.J.. and Katic, L. 1998. "American Consumers' Views on Biotechnology." *Cereal Foods World* 43 (1): 20-22

PART IV

PLENARY LECTURES

Photo courtesy of Pioneer Hi-Bred International, Inc.

Sustaining the Efficacy of Bt Toxins

FRED GOULD
Professor, Department of Entomology
North Carolina State University
Raleigh, NC

INTRODUCTION

In 1997 corn, cotton and potato cultivars that produce insecticidal proteins were grown on more than five million acres of US farmland. The acreage dedicated to these cultivars is likely to increase dramatically in the next two-to-five years. The use of these cultivars decreases the use of broad spectrum insecticides, especially in cotton and potato production. The toxin gene is derived from the bacterium, *Bacillus thuringiensis* (Bt), which has been naturally fermented and used as an organic pest control tool for decades. The toxin breaks down rapidly in the environment and is harmless to humans, vertebrates, and even most beneficial insects. In almost all ways this is the natural insecticide that you might expect environmentalists to dream about.

So why have Bt toxin-producing crops been met with so much concern from the environmental and academic community? The issue is sustainability. Until recently, all formulations of fermented Bt had incredibly short insecticidal half lives in the field. The toxic action of the bacteria all but disappeared within two days after exposure to sunlight. Organic and conventional farmers who relied on Bt had to carefully time their spraying of the spore/crystal formulations to make sure that the bacteria were in the right place at the right time. This was difficult, but the positive side to this was that the pest population was typically exposed to the toxin only at times of peak pest densities. (Farmers would be wasting money if they sprayed pests when densities were low.) From an evolutionary perspective, this meant that the majority of insects in the pest population were never exposed to the toxin. These unexposed insects served as an “evolutionary buffer” to the development of resistance in the pest population.

Currently available Bt toxin-producing cultivars have the potential to almost completely eliminate this evolutionary buffer because they typically produce the toxin in all plant parts throughout the growing season. This means that if the engineered cultivars were widely adopted, almost all of the insects in the targeted population would be exposed to the toxin. We have learned the lesson over and over again with persistent synthetic pesticides that when an insect population is put under relentless exposure to a pesticide, it typically responds with genetic changes that make it resistant to the pesticide. Rapid pest adaptation is not limited to synthetic insecticides. Insect pests have adapted to cultural controls and biological control agents when the selection pressure is intense (Gould, 1991). There is no reason to think that the situation will be dramatically different with engineered crops.

There are two general types of responses to the potential problem of pest adaptation to Bt crops:

1) We can search for novel Bt toxins and other insecticidal proteins. Gene coding for these toxins could be engineered into crop plants when the efficacy of the currently used Bt toxins is lost to pest resistance.
2) We can develop approaches for using Bt toxin-producing plants that maintain evolutionary buffers that slow the rate at which resistance evolves.

I think it would be economically and ecologically prudent to take both approaches. There would be economic benefits for certain groups if resistance to Bt evolves quickly, because they already own the replacements. These could either be producers of the next generation of transgenic insecticidal cultivars, or producers of the conventional insecticides that may replace Bt cultivars. For all the other stakeholders, a longer life for Bt crops would seem to be economically beneficial.

On the environmental side, Bt toxins appear to be exceptionally benign to non-target organisms. It is feasible that other proteins (or more novel resistance factors) will be found that are equally benign, but this is far from assured. It is likely that searches for environmentally friendly but pesticidal proteins will be of benefit to society at large. Even with the best resistance management program, some pest species are likely to adapt to Bt toxins, and there is always the problem that there are some pests for which no effective Bt toxins have yet been found. Perhaps the novel proteins found in broad surveys of microbial proteins will fill pest control niches that Bt toxins can’t fill. Basic studies of pest and plant biochemistry might also reveal some new approaches for developing insect resistant cultivars that don’t involve the use of toxins at all.

Unfortunately, today we have no clear replacements for Bt toxins. There has been a lot of talk about replacements but we lack human toxicology studies, environmental fate studies, and data on the impact of novel Bt replacements on crop productivity. I have and will continue to emphasize insecticidal cultivars in this paper because I am familiar with them and because they are currently the most widely used transgenic pest control tools (herbicide tolerant crops do not offer direct crop protection). Of course, there are other transgenic pest control tools such as virus resistant plants. Little is known about the potential for viruses to adapt to these plants, but it is certainly not outside the realm of possibilities. Viruses and other plant pathogens have always presented plant breeders with a formidable challenge because of their ability to adapt to resistant cultivars (Gould, 1991). There is no special reason to expect that these organisms will not be able to adapt to transgenic, pathogen-resistant cultivars.

For the rest of this paper I will focus on the potential of slowing down the evolution of pest resistance to Bt crops. Slowing the evolution of such resistance could be useful to society, and from a more pragmatic perspective it is useful to understand how and why the EPA is proceeding to use regulations to help enforce resistance management in Bt crops.

GENERAL RESISTANCE MANAGEMENT TECHNIQUES FOR TRANSGENIC INSECTICIDAL CULTIVARS

Resistance management is based on general principles of population genetics. A number of reviews are available that discuss details of applying these principles to engineered crops (Roush, 1996, 1997; Tabashnik, 1994; Gould, 1991, 1998). Below I will give a general overview of principles of resistance management techniques in engineered crops. I will sacrifice some precision in hopes of making the presentation more accessible. Readers can obtain more details from the references in the bibliography.

Resistance management techniques take advantage of two factors in population genetics that can impact the rate of evolution. The first factor is the difference in fitness between resistant and susceptible genotypes. Fitness is defined as the number of offspring contributed to the next generation by a single female. It is approximately equal to the probability of survival multiplied by the average number of offspring expected from each survivor. (We typically express fitness as a relative value, setting the fitness of the most fit genotype to 1.0. The fitness of the other genotype then become a proportion of the fitness of the most fit genotype.) Because it is very hard to estimate fecundity, many studies only measure survival and assume that all survivors have the same fecundity. Any approach to engineering or deploying toxic cultivars that decreases the difference in fitness between resistant and susceptible insects slows the rate of evolution.

The second factor used in resistance management is manipulation of the inheritance of fitness. When resistance is inherited as a dominant trait, the heterozygotes (RS) are just as fit as homozygous resistant insects (RR). Because the RS heterozygotes are initially much more common than resistant RR homozygous insects, dominant expression of the resistance in these RS heterozygotes speeds up evolution of resistance. Conversely, when resistance is inherited as a recessive trait the RS heterozygote is no more fit than the susceptible homozygote, so any change in the number of resistant individuals is based on high fitness of the rare RR resistant homozygotes. This typically slows the rate of evolution.

An example may help to clarify this point. If the initial frequency of resistance genes is one in one thousand (0.001), and each individual carries two genes, we expect there to be about 0.002 (or two in one thousand) RS heterozygotes, 0.998 SS susceptible homozygotes, and only 0.000001 RR homozygote resistant insects. If resistance was recessive and both the RS and SS insects had a fitness of 0.01 (1 percent) compared to the RR fitness of 1.0, the frequency of resistance genes would increase to about 0.002 in the next generation. This happens because the one in a million RR insects each produce 100 times more offspring than the other genotypes. In a rough approximation, the decimal point moves two places to the right (0.000001 to 0.0001) but that still is very few individuals. If resistance is dominant, then the fitness of the RR and RS insects would be 1.0, while the fitness of the SS insects would be 0.01. This causes the frequency of resistance genes to increase from 0.001 to 0.0835 in the next generation. This much faster rate of change is due to the fact that RS heterozygotes start at 0.002 and move to 0.2. The point is that RR homozygotes are so rare, initially, that they can't cause a rapid change in the overall proportion of resistance genes, even if they were a thousand times more fit than the other genotypes.

A resistance management strategy that can cause inheritance of resistance to be recessive will typically slow down resistance evolution in the population. How can this be done? One way is to have plants produce a very high concentration of the Bt toxin. The US Environmental Protection Agency's (EPA) Science Advisory Panel (EPA, 1998) recently defined this high dose as 25 times the amount of Bt toxin needed to kill 99 percent of the SS insects. They came up with this definition because genetic studies of insects with resistance genes have shown that RS insects can not survive when the concentration of the Bt is 25 times higher than the concentration that kills SS insects. This basically means that the high dose kills almost all SS and RS insects, making their fitness almost equal (i.e., almost recessive). The approach of building a plant with this high dose has also been the goal of industry (Fischoff, 1996).

The EPA Science Advisory Panel concurred with findings of other scientists in concluding that the high dose by itself wasn't sufficient because even with this recessive inheritance resistant pest populations would still evolve too quickly. They recommended that the first population genetics principle described above be added to any resistance-management strategy. This is the idea of decreasing the difference in fitness between RR, RS, and SS insects. They recommended providing refuges for susceptible insects to achieve this. How does this decrease the fitness difference? Again, an example is useful. If the RR fitness is 100 times that of SS insects when they are on Bt plants, but their fitness are equal on non-Bt plants, a small refuge of non-Bt plants can have a dramatic effect on the fitness difference. When 10 percent of the plants are non-Bt, the fitness of the RR insects is 1.0 times 0.9 (i. e., the frequency of Bt plants) plus 1.0 times 0.1 (i. e., the frequency of non-Bt plants). The total is 1.0, no surprise. For the SS insects fitness is 0.01 times 0.9 plus 1.0 times 0.1. The total is 0.109. So without a refuge the difference in fitness between the RR and SS insects is 100-fold. With the 10 percent refuge it is a little less than 10 fold. This small refuge slows the rate of resistance development dramatically.

The refuge serves another essential function. It ensures that the RR insects will likely mate with SS insects coming from the refuge. This will produce RS insects that will be killed by the high dose of Bt toxin. If the refuge is placed relatively far away from the Bt plants compared to the insects ability to move before mating, the refuge is less beneficial because RR insects will mate with each other instead of with the SS insects.

Combining the refuge and high dose is widely accepted as the most feasible way of slowing the rate of resistance development at this time. Other approaches have been discussed (Gould, 1998; Roush, 1996), but they have not gained acceptance or are not feasible with today's technology. These other approaches should not be ignored, but in the next few years we will need to concentrate on the refuge/high dose approach. Most scientists agree that the refuge/high dose approach has one theoretical Achilles' heel. This is the possibility that a resistance mechanism is present in some insects which confers more than 25 fold resistance on the RS insects. If this happens the effectiveness of the high dose decreases dramatically.

Implementing the refuge/high dose approach

Most applied entomologists regard the theoretical Achilles' heel of the refuge/high dose approach as much less troublesome than the problems associated with implementing this approach.

A number of reports have recently been published that evaluate current attempts at implementing the refuge/high dose approach and make recommendations (Ostlie et al., 1997; Forrester and Pyke, 1997; EPA, 1998; Andow and Hutchison, 1998; Gould and Tabashnik, 1998; Whalon and Ferro, 1998). Most of these reports are crop specific because the implementation problems are highly dependent on the biology of the pests and the agricultural practices associated with the crop. I will try to summarize some of the issues that have arisen regarding Bt corn, cotton, and potato.

Corn

Of the three Bt crops, corn is grown on the largest acreage. The most often discussed target pest is the European corn borer (ECB), which can feed on many plants, but feeds primarily on corn in large agricultural areas. Relatively little insecticide is used to control the ECB because the larvae feed inside the plant where they are hard to reach with sprays and where they cause damage that is hard to notice. Bt corn can increase yields by around 10 percent in many areas. If the Bt genes were placed in cultivars that were also best in agronomic performance there could be incentive for farmers to plant wall to wall Bt cultivars and forget about refuges. The EPA did not initially mandate refuges because it was assumed that Bt cultivars would initially be limited. The EPA is now revisiting this issue (EPA, 1998). It was also expected that all Bt cultivars would provide a high dose for ECB throughout the summer. It is now clear that some cultivars do not provide such a dose (Ostlie et al., 1997; Andow and Hutchison, 1998).

In revisiting the refuge issue it has become apparent that the ECB moths don't typically move long distances before mating. Although there is certainly a need for more research in this area, we already know enough to recommend that refuges be placed adjacent to the Bt crop.

Because ECB mostly feeds on corn, the refuge must be composed of non-Bt corn. The current recommendations are between 20 and 50 percent of corn acreage in non-Bt corn depending at least in part on whether the farmer sprays the non-Bt corn for ECB control. Any time a farmer sprays a non-Bt field its refuge status is diminished. The more effective the spray the more the refuge is diminished.

Can farmers and society accept a 25 percent unsprayed refuge? The first year this is implemented there could certainly be economic damage to the refuge corn. But, consider the fact that with a 25 percent refuge only one out of four eggs lands on a non-Bt corn plant. We must ask if an ECB population whose fitness has been diminished from 1.0 to 0.25 will remain a major corn pest. An economic analysis (Hurley et al., 1998) has indicated that over a long period of years farmers may gain more by having a 20 percent refuge than by maintaining no refuge at all, even if resistance does not evolve.

ECB is only one major corn pest affected by Bt. In some areas, the Southwestern corn borer (SWCB) is a major pest. Because it is naturally more tolerant of Bt toxins there is some question about whether current corn cultivars provide a high dose (Ostlie et al., 1997; EPA 1998). There is definitely a need for more research in this area. The corn earworm (also known as the cotton bollworm) attacks corn but is not generally considered a major pest of corn. The impact of Bt corn on this pest will be discussed in the cotton section.

Cotton

Unlike corn, cotton is typically sprayed to control the target pests of Bt cultivars. Left unchecked, the cotton bollworm (also known as the corn earworm), the tobacco budworm, and the pink bollworm can each cause significant yield loss. The EPA and Monsanto, the producer of Bt cotton, developed a refuge/high dose plan before Bt cotton was commercialized. This plan gives farmers two refuge options. They can plant up to 96 percent Bt cotton if they leave a four percent refuge that is not treated with conventional insecticides that kill the target pests. Alternatively, they can plant up to 80 percent of their cotton acreage in Bt cultivars and manage insects in the 20 percent non-Bt cotton with all registered insecticides except Bt sprays. It is assumed that the conventional controls kill about 80 percent of the insects in the non-Bt cotton. This mortality reduces the 20 percent refuge to about four percent in terms of SS moths produced.

Gould and Tabashnik (1998) pointed out a number of problems with this plan, as did the EPA (1998). One striking problem was the assumption that there was a high dose. Although a high dose (by EPA 1998 standards) is achieved for the tobacco budworm, and may be achieved for the pink bollworm, it is certainly not achieved for the cotton bollworm. With this pest species 20 percent or more of the larvae survive the dose of Bt in plants with the Monsanto gene. This creates a real dilemma. Industry and the EPA have set the refuge/high dose approach as the standard, but the current plants don't produce a high dose. Population genetic models indicate that without a high dose the refuge needs to be much larger than four percent. Gould and Tabashnik (1998) argue for a refuge of about 50 percent or 17 percent, depending on whether farmers are or are not allowed to use conventional insecticides in the non-Bt cotton.

It has been proposed that there is less need for a non-Bt cotton refuge in the case of the cotton bollworm because a large proportion of the larvae feed on corn. There are two problems with this proposal. One is that the corn only has a large proportion of cotton bollworms in one of the three to five generations of bollworms over the summer. The second problem is that companies are trying to get the EPA to allow them to plant Bt corn in areas where Bt cotton is grown. The Bt corn also produces less than a high dose for this insect, so if the two crops with moderate doses are planted near each other the risk for resistance becomes very high.

While we assume that there is a high dose for tobacco budworm and pink bollworm, field data from Australia indicates that this assumption requires more testing. In Australia, it has been found the environmental factors can significantly decrease the production of Bt-toxin in cotton plants (Forrester and Pyke, 1997).

Another problem with the current resistance management plan is the lack of limits on the distance between the refuge and the Bt crop. The tobacco budworm moths appear to move long distances early in the spring, but in the summer they tend to move very little. The pink bollworm often stays in the same field for a number of generations. This has prompted recommendations for keeping the Bt and non-Bt cotton plants within 0.5 miles of each other whenever the tobacco budworm is a pest, and to interplant Bt and non-Bt cotton as blocks within fields when the pink bollworm is present.

It is not recommended to plant a seed mixture of Bt and non-Bt seeds, especially for the tobacco budworm because the larvae move from plant to plant. If Bt and non- Bt plants are within crawling distance, a RS larva might feed on a high dose plant for just long enough to get an intermediate dose and then could move onto a non-Bt plant. Lab and field studies have shown that larvae spend less time on Bt than non-Bt plants. This would ruin the high dose part of the resistance management plan.

Potato

The potato has only one target pest for Bt toxin in the US, the Colorado potato beetle (CPB). Fortunately, the plants produce a very high dose relative to the CPB's tolerance. The only real problems with Bt potatoes are the placement and maintenance of the refuge. Here, the CPB offers a real challenge. Unlike all the other pests mentioned above, the CPB is a beetle that feeds on plants as a larva and as an adult. Additionally, the adults often move short distances before mating. The problem is that seed piece mixes can't be recommended because the larvae and adults move between plants while feeding, and field to field mixtures are a problem because adults don't move far enough before they mate. Whalon and Ferro (1998) recommend that blocks of non-Bt potatoes be planted on the edges (or within) Bt potato fields.

Another problem is that potatoes are high value crops so farmers are reluctant to allow any CPB damage. A new insecticide, Imidicloprid, commonly used in potato, can kill almost 100 percent of the potato beetles. If this insecticide is used in a refuge, the refuge basically disappears. Whalon and Ferro (1998) recommend that farmers rotate fields to decrease CPB numbers and avoid use of this extremely toxic insecticide. In the appendix to the EPA (1998) document, a rough guide is given for how to determine if a refuge is producing enough insects to slow the development of resistance. The rule of thumb that emerges from this is that at least 500 insects should be produced in the refuge for every resistant insect produced in the Bt crop. This can be achieved with relatively small refuge size if the Bt crop, like Bt potato, produces a very high dose and insects in the refuge are not heavily sprayed.

Conclusions

Resistance management with Bt crops is far from simple. It has forced researchers to learn a lot more about the biology of the targeted insects. And, we still have a lot more to learn. It is pointed out in the EPA Science Advisory Panel Report (1998) that we should take a conservative approach in developing management plans until we know enough to make the plan requirements less stringent.

In the consensus statement of the EPA Science Advisory Panel it is recommended that:

1) A refuge/high dose strategy must be employed for target pests within the current understanding of the technology.

2) Regulatory strategies should serve to provide growers with a sustainable approach that encourages compliance for utilizing this valuable and environmentally friendly technology.

3) To the extent possible, feasibility should figure in the development of resistance management plans.

4) Needs of growers who rely on Bt sprays should be taken into consideration.

If the EPA follows the general guidance of the Science Advisory Panel, as well as more detailed recommendations by informed researchers (e.g., Andow and Hutchison, 1998), the use of Bt crops could probably be sustained until the next generation of environmentally benign transgenic cultivars are carefully tested and ready for commercialization.

References

Andow, D. and Hutchison, W. 1998. Major recommendations from the scientists' resistance management plans, p. 10. In M. Mellon and J. Rissler [eds.], "Now or never. Serious new plans to save a natural pest control." Union of Concerned Scientists, Cambridge, MA

_____. 1998. FIFRA Scientific Advisory Panel. Subpanel on *Bacillus thuringiensis* (Bt) plant pesticides and resistance management. US Environmental Protection Agency, Washington, DC

Fischoff, D. A. 1996. Insect-resistant crop plants, pp. 214-227. In G. J. Persley [ed.], Biotechnology and integrated pest management. CAB Int., Oxon, UK

Forrester, N. and Pyke, B. 1997. The researchers' view. *Aust. Cottongrower* 18: 23-30 (Publ. no. 405518/00026)

Gould, F. 1991. The evolutionary potential of crop pests. *Am. Sci.* 79: 496-507

Gould, F. 1998. Sustainability of transgenic insecticidal cultivars: integrating pest genetics and ecology. *Annu. Rev. Entomol.* 43: 701-726

Gould, F. and Tabashnik, B. E. 1998. Bt cotton, pp. 10-11. In M. Mellon and J. Rissler, "Now or never. Serious new plans to save a natural pest control. Union of Concerned Scientists, Cambridge, MA

Hurley, T. M., Babcock, B.A., and Hellmich, R. L. 1998. Biotechnology and pest resistance: an economic assessment of refuges. Working Paper 97-WP 183, Center for Agric. & Rural Develop., Iowa State University, Ames, IA

Ostlie, K. R., Hutchison, W. D., and Hellmich, R. L. [eds.]. Bt corn and European corn borer. North Central Reg. Ext. Publ., Univ. Minn. Ext. Serv., St. Paul, MN

Roush, R. T. 1996. Can we slow adaptation by pests to insect transgenic crops?, pp. 242-263. In G. J. Persley [ed.], Biotechnology and integrated pest management. CAB Int., Oxon, UK

Roush, R. T. 1997. Managing resistance to transgenic crops, pp. 271-294. In N. Carozzi and M. Koziel [eds.], Advances in insect control: the role of transgenic plants. Taylor & Francis, London

Tabashnik, B. E. 1994. Delaying insect adaptation to transgenic plants: seed mixtures and refugia reconsidered. Proc. R. Soc. London Ser. B 255: 7-12

Whalon, M. and Ferro, D. 1998. Bt potato, p. 11. In M. Mellon and J. Rissler [eds.], Now or never. "Serious new plans to save a natural pest control." Union of Concerned Scientists, Cambridge, MA

Pathogen Derived Resistance and Reducing the Potential to Select Viruses with Increased Virulence

ROGER N. BEACHY,* *Professor, Scripps Family Chair, and Division Head*
MOHAMMED BENDAHMANE, *Research Associate*
The Scripps Research Institute, Division of Plant Biology
La Jolla, CA

INTRODUCTION

Pathogen derived resistance (PDR) refers to using sequences from a pathogen to protect the host from the effects of the pathogen (Sanford and Johnson, 1985). Following the first example of coat protein (CP)-mediated resistance, a type of PDR, to protect transgenic tobacco plants from infection by tobacco mosaic virus (TMV) (Powell-Abel et al., 1986) there have been many reports of different types of PDR. Genes that produce virus-derived antisense RNAs, (+) sense RNAs that do not encode proteins, modified and wild type replicases, and wild type and mutant cell-cell movement proteins have been used to confer resistance. Certain gene strategies appear to be more effective than others depending upon the virus and host. Likewise, certain strategies are anticipated to be more useful in agricultural settings than others. To date, the most common type of PDR in advanced stages of development is CP-mediated resistance; furthermore, government regulatory agencies have approved the use of CP genes to protect plants in agriculture. Other types of genes are being reviewed for similar status.

During the technical stage of development and applications of PDR, a variety of questions have been raised related to the relative safety of transgenic plants that contain virus-derived gene sequences. Some of the concerns are based upon lack of understanding of the methods used to develop resistance, or the biology of virus infection and disease, while certain concerns have some degree of validity. This short paper highlights several of the arguments offered to restrict the use of PDR and those presented to promote its use. This is followed by a summary of recent results that show that knowledge of mechanisms of resistance can lead to increased efficacy of PDR and can reduce concerns about safety and durability of PDR in agriculture.

*Roger Beachy is now president of Donald Danforth Plant Science Center, St. Louis, MO.

STRATEGIES FOR PATHOGEN DERIVED RESISTANCE AND REDUCING BIOSAFETY ISSUES

A) Replicase-*mediated* and *RNA-mediated resistance.* The first report of resistance in transgenic plants that resulted from expression of virus gene sequences involved in virus replication (e.g. replicase, helicase and methyl-transferase) was reported by Golemboski et al. (1990). In this work, the sequence of the TMV 54-kDa open-reading frame conferred high levels of resistance to TMV in transgenic tobacco plants. Subsequent papers reported resistance that was conferred by genes that produce complete, or partial, virus proteins that were either wild type or mutated to eliminate function of the replication protein (Beachy, 1997; Palukaitis and Zaitlin, 1997). In some cases, resistance was due to what is referred to as RNA-mediated resistance (Beachy, 1997). In some examples of replicase-mediated resistance, transgenic plants are highly resistant to infection, and in some cases, are essentially not infected by the virus from which the replicase gene is derived. However, such plants are usually susceptible to closely related viruses and virus strains (Palukaitis and Zaitlin, 1997).

The objection most often raised in relation to use of replicase-mediated resistance is based upon the possibility that recombination may occur between the virus that infects the transgenic plants and the mRNA produced by the transgene. In this situation, mRNA sequences produced by the transgene are 'captured' during replication by the second virus. Capture may occur if replicase jumps, or switches, from the viral genome to mRNA (template switching) produced by the transgene. Template switching may result in chimeric viral RNA that increases the host range or virulence of the resulting virus. Template switching has been observed to occur in plants infected by several viruses that are closely related to each other (Simon and Bujarski, 1994). Transgene caputure was detected in transgenic plants that were challenge-infected by a mutant virus that would survive only if a recombinant virus was produced (Greene and Allison, 1994; Allison et al., 1996). In another case, recombination was observed under conditions that are considered to be less stringent to the selection of recombinant virus (Wintermantel and Schoelz, 1996; Király et al., 1998).

It is now known that template switching or other types of intergenomic recombination occurs more frequently with certain groups of viruses than with others (Simon and Bujarski, 1994). For example, it has been documented to occur with certain potyviruses (Cervera et al., 1993), tobravirus (Robinson et al., 1987; Angenent et al., 1989), bromoviruses (Allison et al., 1989) and geminiviruses (Liu et al., 1998), but apparently occurs at much lower frequency for other viruses (e.g. tobamoviruses) (Fraile et al., 1997).

In considering the potential impact of recombination between viruses and host mRNAs, it is important to recall the biological nature of virus infection. Viruses survive in nature because their replication is ensured by their genetic composition, and viruses that cannot replicate cannot survive. Thus, the likelihood that a virus that lacks a replicase would cause an infection in transgenic plants that contains a replicase gene sequence, and subsequently acquire a functional replicase gene, is very remote. It is theoretically possible (though unlikely) that defective viruses that lack a replicase would be co-transferred during insect or other transmission from plants that are infected by multiple viruses. Such virus may, under very selective and as yet unknown conditions, gain competitive advantage for recombination. It is important to gain a more complete understanding of virus replication and recombination, and, if possible, to reduce or eliminate the likelihood of recombination in pathogen derived resistance. For example, if the "hot spots" for virus recombination are known, it may be possible to develop transgenes that lack such sequences. Indeed, when sequences that are involved in strand switching/recombination were removed from a transgene, the frequency of sequence capture by challenge virus was substantially reduced or eliminated (Greene and Allison, 1996; Allison et al., 1996). Similar results were found when the sequences involved in recombination between RNAs associated with turnip crinkle virus (TCV) were modified (Cascone et al., 1993).

B) *Movement protein (MP)-mediated resistance.* Cell-cell and long distance spread of virus infection requires one or more viral proteins (Hull, 1991; Séron and Haenni, 1996; Nelson and van Bel, 1998). In certain cases virus host range and pathogenicity are determined by movement protein(s). Therefore, there is legitimate concern about the use of movement proteins to confer pathogen-derived resistance. On the other hand, because many viruses accomplish spread in the host via common, intercellular channels known as plasmodesmata, there is a strong likelihood that durable and broad resistance to multiple viruses could be achieved if cell-cell and long distance spread could be blocked by expression of a transgene (Deom et al., 1992). Several research groups have demonstrated moderate levels of virus resistance in transgenic plants that express non-functional mutants of movement proteins. Such proteins presumably act as dominant negative mutants for one or more functions of movement proteins that are produced during virus infection [i.e. defective movement protein of TMV expressed in transgenic plants confers protection against multiple viruses from different groups (Cooper et al., 1995)].

Based upon the role of movement proteins in virus disease it is easy to understand the concerns about using wild type movement proteins as resistance genes in transgenic plants. However, the fact that sequences of movement proteins are vastly different between different viruses dramatically lowers the likelihood that movement protein sequences will be captured during infection by non-related viruses. Such differences make it highly unlikely that 'functional domains' could be reconstructed in the event that MP sequences are captured by virus infection. Using movement proteins that are made non-functional by directed mutagenesis further reduces potential risk.

C) *Coat Protein (CP) mediated resistance.* Coat, or capsid proteins, protect the viral nucleic acid from degradation. CP can also be important in several stages in virus infection, including acquisition and transmission of virus by insect vectors, cell-cell and long distance spread in the host, and for some viruses, CP regulates one or more steps of virus replication. It has been argued that transgenic plants that exhibit CP-mediated resistances represent a biosafety risk because the CP may encapsidate the genome of unrelated viruses that infect the transgenic plant, and that such viruses may be acquired and spread to non-hosts by the insect vector. In addition, it is known that certain CPs can encapsidate non-related RNAs (Robinson, 1996). In mixed infections of zucchini yellow mosaic potyviruses strain ZYMV-NAT (non-aphid-transmissible) with papaya ringspot potyvirus (aphid transmissible) their CP molecules can co-assemble. As a result, aphids can acquire and transmit ZYMV-NAT by virtue of mixed encapsidation by both CPs (Bourdin and Lecoq, 1991).

Likewise, it was shown that in transgenic plants heterologous encapsidation of RNA of the challenge virus by the transgenic CP could occur. For example, in transgenic plants that contain CP of the strain N of Potato virus Y (PVY^N), and infected by strain O of PVY (PVY^O), the transgenic CP can co-assemble with the challenge virus (Farinelli et al., 1992). Similarly, it was shown that transgenic plants that contain CP of the aphid transmissible plum pox potyvirus (PPV), and infected by the non-aphid-transmissible strain NAT of ZYMV, transgenic CP could co-assemble with the challenge virus. As a result of the co-assembly, ZYMV can be transmitted by aphids (Lecoq et al., 1993).

DOES *TRANS*-ENCAPSIDATION REPRESENT A SIGNIFICANT RISK TO THE ENVIRONMENT?

Since virus replication is determined by the viral genome rather than the capsid, it is unlikely that *trans*-encapsidation *per se* will lead to permanently expanded host range of a particular virus. Furthermore, since multiple viruses infect many plants, including viruses that are in the same taxonomic group, it is likely that *trans*-encapsidation that may occur in transgenic plants poses no greater risk than *trans*-encapsidation that occurs in mixed virus infections.

It is possible to reduce the risk of *trans*-encapsidation by using CP that is incapable of assembly or insect transmission. Recently, we constructed mutants of TMV CP that are incapable of forming viable virus particles but confer CP-mediated resistance against TMV (Clark et al., 1995; Bendahmane et al., 1997). Similarly, the amino acid sequences on CP molecules that are required for insect acquisition and/or transmission are known for potyviruses (Atreya et al., 1990; Gal-on et al., 1992; Blanc et al., 1997) and cucumber mosaic cucumovirus (Perry et al., 1998). As such sequences are identified they can be removed from

CP genes that are used for CP-mediated resistance (Stark and Beachy, 1989; Jacquet et al., 1998). Taking steps to reduce insect acquisition and virus assembly of CP molecules used in CP-mediated resistance will reduce some of the concerns regarding possible insect transmission of *trans*-encapsidated virus.

Improving the Efficacy of Coat Protein-Mediated Resistance

Based on a series of studies, we proposed that CP-mediated resistance to TMV resulted when CP in the transgenic plant formed an appropriate interaction with CP of the challenge virus to prevent disassembly and virus replication (reviewed by Fitchen and Beachy, 1993). In more recent studies to clarify the molecular mechanisms of CP-mediated resistance, we developed mutants of TMV CP, determined the effect of the mutation on virus assembly, and, whether or not transgenic plants that produced the mutant CPs were resistant to TMV.

Mutants were created, based upon the known structure of the CP and the virus, that were predicted to increase or decrease interactions between CP molecules. In published studies, changes were made to CP codons 28 to encode isoleucine rather than threonine (Clark et al, 1995) or CP codon 28, 42, and 89, to encode tryptophan rather than threonine (Bendahmane et al., 1997). In these cases the volume of the amino acid side chains was increased. None of the mutant CP molecules was capable of assembly with viral RNA, and the proteins were therefore unable to form infectious virus. However, all but one of the mutants was capable of self-assembly and formed various types of aggregates, some of which were virus-like while other mutants produced paracrystalline arrays of CP. Mutant CP that failed to assemble (i.e., did not form virus-like particles or other aggregates) did not confer CP-mediated resistance. Mutants that produced highly stable aggregates conferred high levels of CP-mediated resistance while aggregates with intermediate levels of stability conferred intermediate levels of resistance. Interestingly, the CP mutants that formed virus-like particles that were more stable than those produced by wild type CP conferred a higher level of CP-mediated resistance than did the wild type (Bendahmane et al., 1997). We suggest that increased resistance resulted from increased H-bonds between transgenic CP and challenge virus, which decreased virus disassembly and virus infection.

Conclusions

Pathogen derived resistance can be used to develop transgenic plants that are resistant to virus infection. It is possible to reduce both potential and perceived risks associated with the transgenes by constructing transgenes that reduce potential for trans-capsidation, insect transmission, and sequence capture (recombination). The recent studies of TMV coat protein that resulted in high levels of CP-mediated resistance demonstrate that knowledge of the structural and cellular mechanisms of resistance can lead to the development of a 'second generation' of transgenes that have both increased efficacy and greater environmental safely.

References

Allison, R.F., Janda, M., and Ahlquist, P. 1989. “Sequence of cowpea chlorotic mottle virus RNAs 2 and 3 and evidence of a recombination event during bromovirus evolution.” *Virology* 172:321-330

Allison, R.F., Schneider, W.L. and Greene, A.E. 1996. “Recombination in plants expressing viral transgenes.” *Sem. Virol.* 7:417-422

Angenent, G.C., Posthumus, E., Brederode, F.T., and Bol, J.F. 1989. “Genome structure of tobacco rattle virus strain PLB: further evidence on the occurrence of RNA recombination among tobraviruses.” *Virology* 171:271-274

Atreya, C.D., Raccah, B., and Pirone, T.P. 1990. “A point mutation in the coat protein abolishes aphid transmissibility of a potyvirus.” *Virology*, 178:161-165

Beachy, R.N. 1997. “Mechanisms and applications of pathogen-derived resistance in transgenic plants.” *Curr. Opin. Biotech.* 8:215-220

Bendahmane, M., Fitchen, J. H., Zang G.H., and Beachy, R. N. 1997. “Studies of Coat Protein Mediated Resistance to TMV: Correlation between assembly of mutant coat proteins and resistance.” *J. Virol.* 71:7942-7950

Blanc, S., Lopez -Moya, J.J., Wang, R., Garcia-Lampasona, S., Thornbury, D.W., and Pirone T.P. 1997. “A specific interaction between coat protein and the helper component correlates with aphid transmission of a potyvirus. ”*Virology* 231:141-147

Bourdin, D., and Lecoq, H. 1991. “Evidence that heteroencapsidation between two potyviruses is involved in aphid transmission of a non-aphid-transmissible isolate from mixed infections.” *Phytopathology*, 81:1459-1464

Cascone, P.J., Hadar, T.F., and Simon, A.E. 1993. “Sequences and structures required for recombination between virus-associated RNAs.” *Science* 260:801-805

Cervera, M.T., Riechmann, J.L., Martin, M.T., and Garcia, J.A. 1993. “3’-terminal sequence of plum pox virus PS and O6 isolates: evidence for RNA recombination within the potyvirus group.” *J. Gen. Virol.* 74:329-334

Clark, W. G., Fitchen, J. H., and Beachy, R. N. 1995a. “Studies of coat protein-mediated resistance to TMV: i. the PM2 assembly defective mutant confers resistance to TMV.” *Virology* 208:485-491

Cooper, B., Lapidot, M., Heick, J.A., Dodds, A.J., and Beachy, R.N. 1995. “A defective movement protein of TMV in transgenic plants confers resistance to multiple viruses whereas the functional analog increases susceptibility.” *Virology* 206:307-313

Deom, C.M., Lapido, M., and Beachy, R.N. 1992. “Plant virus movement proteins.” *Cell* 69:221-224

Farinelli, L., Malnoë, P., and Collet, G.F. 1992. “Heterologous encapsidation of potato virus Y strain O (PVY^O) with the transgenic coat protein of PVY strain N (PVY^N) in *Solanum tuberosum* cv Bintje.” *Bio/Technology*, 10:1020-1025

Fitchen, J. H., and R. N. Beachy. 1993. “Genetically engineered protection against viruses in transgenic plants.” *Annu. Rev. Microbiol*. 47:739-763
Fraile, A., Escriu, F., Aranda, M.A., Malpica, J.M., Gibbs, A.J., and Garcia-Arenal, F. 1997. “A century of tobamovirus evolution in an Australian population of *Nicotiana glauca*..” *J. Virol.* 71:8316-8320
Gal-on, A., Antignus, Y., Rosner, A., and Raccah, B. 1992. “A zucchini yellow mosaic virus coat protein gene mutation restores aphid transmissibility but has no effect on multiplication.” *J. Gen. Virol*. 73:2183-2187
Golemboski, B.D., Lomonossoff, G.P., and Zaitlin, M. 1990. “Plants transformed with a tobacco mosaic virus non structural gene sequence are resistant to the virus.” *Proc. Natl. Acad. Sci. USA* 87:6311-6315
Greene, A.E., and Allison, R.F. 1994. “Recombination between viral RNA and transgenic transcripts.” *Science* 263:1423-1425
Greene, A.E., and Allison, R.F. 1996. “Deletions in the 3' untranslated region of cowpea chlorotic mottle virus transgene reduce recovery of recombinant viruses in transgenic plants.” *Virology* 225:231-234
Jacquet, C., Decolle, B., Raccah, B., Lecoq, H., Dunez, J., and Ravelonandro, M. 1998. “Use of modified plum pox virus coat protein genes developed to limit heteroencapsidation-associated risks in transgenic plants.” *J. Gen. Virol*. 79:1509-1517
Király, L., Bourque, J.E., and Schoelz, J.E. 1998. “Temporal and spatial appearance of recombinant viruses formed between cauliflower mosaic virus (CaMV) and CaMV sequences present in transgenic *Nicotiana Bigelovii*..” *Mol. Plant-Microbe Interact.* 11:309-316
Lecoq, H., Ravelonandro, M., Wipf-Scheibel, C., Monsion, M., Raccah, B., and Dunez, J. 1993. “Aphid transmission of a non-aphid-transmissible strain of zucchini yellow mosaic potyvirus from transgenic plants expressing the capsid protein of plum pox potyvirus.” *Mol. Plant-Microbe interact*. 6:403-406
Liu, Y., Robinson, D.J., and Harrison, B.D. 1998. “Defective forms of cotton leaf curl virus DNA-A that have different recombinations of sequence deletion, duplication, inversion and rearrangement.” *J. Gen. Virol.* 79:1501-1508
Nelson, R.S., and van Bel, A.J.E. 1998. “The mystery of virus trafficking into, trough and out of vascular tissue.” *Prog. Bot.* 59:476-533
Palukaitis, P. and Zaitlin, M. 1997. “Replicase-mediated resistance to plant viruses.” *Adv. Virus Res.* 48:349-377
Perry, K.L., Hang, L., and Palukaitis, P. 1998. “Amino acid changes in the coat protein of cucumber mosaic virus differentially affect transmission by the aphids *Myzus persicae* and *Aphis gossipii*..”*Virology* 242:204-210
Powell-Abel, P., Nelson, R. S., De, B., Hoffmann, N., Rogers, S. G., Fraley, R. T., and R. N. Beachy. 1986. “Delay of disease development in transgenic plants that express the tobacco mosaic virus coat protein gene.” *Science*. 232:738-743

Robinson, D.J., Hamilton, W.D.O., Harrison, B.D., and Baulcombe, D.C. 1987. "Two anomalous tobravirus isolates:evidence for RNA recombination in nature." *J. Gen. Virol*. 68:2551-2561

Robinson, D.J. 1996. "Environmental risk assessment of releases of transgenic plants containing virus-derived inserts." *Transgenic Research* 5:359-362

Sanford, J. C., and Johnston, S. A. 1985. "The concept of parasite-derived resistance. Deriving resistance genes from the parasite's own genome." *J. Theor. Biol.* 113:395-405

Seron, K., and Haenni, A.L. 1996. "Vascular movement of plant viruses." *Mol. Plant-Microbe Interact.* 9:435-442

Simon, A.E., and Bujarski J.J. 1994. "RNA-RNA recombination and evolution in virus-infected plants." *Annu. Rev. Phytopathol.* 32:337-362

Stark, D.M., and Beachy, R.N. 1989. "Protection against potyvirus infection in transgenic plants: evidence for broad spectrum resistance." *Bio/Technology* 7:1257-1262

Wintermantel, W.M., and Schoelz, J.E. 1996. "Isolation of recombinant viruses between cauliflower mosaic virus and viral gene in transgenic plants under conditions of moderate selection pressure."*Virology* 223:156-164

Ecological Aspects of Genetically Modified Crops

THOMAS E. NICKSON, *Co-Director*
MICHAEL J. MCKEE, *Co-Director*
Ecological Technology Center, Monsanto Company
St. Louis, MO

ABSTRACT

It is evident from many recent analyses that the world's population will increase significantly in the near future. As a result, the demand for healthy, affordable food will also grow. Given that the area of available arable land required to produce food will not expand, new and environmentally sound technologies allowing farmers to produce more on the same amount of land must be developed. The development of genetically modified crops through biotechnology is one of several technologies now available to help address the world's increasing future demand for food. The first products from genetic engineering have been introduced recently into the market. Genetically modified plants tolerant to herbicides with superior environmental properties, along with crops that are protected from insect predation while posing negligible risks to beneficial insects, are now commercial realities. Unlike their traditionally bred counterparts, genetically modified crops have been studied in great detail to assure their food, feed and environmental safety. For the genetically modified crops currently on the market, the risk has been assessed in relationship to the benefits. An overview of ecological risk assessment is presented below along with an example of the environmental impact of Roundup Ready® Canola where attention was given to the potential for and impact of outcrossing.

THE NEED FOR NEW TECHNOLOGY IN FOOD PRODUCTION

One of the most important questions confronting society today is how will we produce food in a sustainable manner for a growing world population? Certain facts must be considered in the context of this discussion. Firstly, the world population will significantly increase to some level over the next 30 years. Global population estimates range from around eight billion people to much higher values. The exact value is almost irrelevant if we simply accept the fact that population increases will be greatest among the poorest people in the world. Secondly, the world's landmass is essentially fixed and only a small portion of this land is suitable for producing food. Almost all of the world's food is produced in an area about the size of North America. Were the population to double, given current agricultural productivity, the land used to produce the food for these people would have to increase substantially. The simple fact is that this "extra" land does not exist. Furthermore, the world's most significant ecological and environmental problems are being created by the conversion of forest and desert areas temporarily suitable for food production. Shortsighted strategies to address the economic, social and environmental problems of a growing population will not be sustainable. Several technologies and new strategies are being developed and implemented to address the need for sustainable food production. A short list of these approaches is given in Table 1.

TABLE 1. TECHNOLOGIES AND STRATEGIES TO ADDRESS THE NEED FOR SUSTAINABLE FOOD PRODUCTION

- Genomics
- Marker Assisted Breeding
- Agrochemical Discovery
- Biocontrol
- New Farm Management Practices
- Biotechnology

Advances in genomics (mapping genes and genetic combinations) are an exciting new area that will enhance the ability to develop new and more productive crops. Plant breeders are also using marker-assisted breeding to facilitate the development of new varieties and reduce the time required to bring these varieties to market. Agrochemical discovery remains an area of important research. Environmentally superior crop protection agents are needed immediately to control pests and promote the growth of crops. In addition to chemical agents, biocontrol offers the opportunity for enhancing safe and efficient agricultural productivity. Important improvements in farming practices such as precision farming, conservation tillage and water management will enable farmers to be better stewards of their land. These technologies combined with advances in biotechnology like genetic engineering of plants are the foundation upon which the important improvements in food production are currently based.

Monsanto scientists are committed to using the techniques of genetic engineering of plants to develop products for the sustainable production of abundant food. As such these products must enable farmers to produce food in a cost effective, socially acceptable, and environmentally sound manner. In other words, to be sustainable, an agricultural product must meet the economic and environmental needs of the increasing world population. The increasing concern and demand for sustainable agricultural products, particularly those derived through the techniques of modern biotechnology, has resulted in significantly more detailed assessments of the safety of new products. This paper discusses some of the potential ecological and environmental impacts of genetically modified crops with particular emphasis on the impact of outcrossing. The discussion begins with an overview of the principles and methods for conducting environmental risk assessment, and concludes with a specific example from a product that has a significant potential to outcross, Roundup Ready® Canola.

General Principles of Risk Assessment

We have completed detailed environmental risk assessments on our Roundup Ready® and Insect Protected products according to scientific principles developed and accepted internationally (Kjellsson, 1997; OECD, 1992). The basic concepts of risk assessment applied to genetically modified crops are similar to those used for chemical pesticides where the risk is equal to the product of the exposure and the hazard.

Risk = Exposure x Hazard

In this model, exposure is the probability that something could happen that might potentially be harmful, while the hazard is the degree to which the occurrence is harmful. As a purely mathematical formulation, no exposure or no hazard (exposure = 0, or hazard =0) equate to no risk. However, in science and society there is no situation of zero risk since the potential for exposure and hazard can always be estimated to be greater than zero. This leads us to the concept of acceptable risk that is much more complicated, defies scientific definition and is culturally grounded.

Several principles have been developed to provide general direction to assessing the safety of products derived from modern biotechnology. These principles have been applied to assessing the food, feed, and environmental safety of modified crop plants. Firstly, products developed through genetic engineering using plant transformation technology require a complete risk assessment that is reviewed by regulatory authorities. Secondly, the risk assessment will be conducted on a case-by-case basis. Broad conclusions such as all “genetically modified crops are environmentally safe” can not be made, and the long and short-term effects of each unique product must be examined. Thirdly, the information requested in a risk assessment must be science-based.

Experiments have to be designed to give clearly interpretable results concerning the environmental and ecological risks presented by the release of a genetically engineered plant. The safety factors imposed on modified plants will be modified based on increased information and experience (NRC, 1989). Taken as a whole, these principles establish a rational and cautious approach to assessing the safety of a product.

Environmental Risk Assessment Procedure

The first step in conducting an environmental risk assessment is that one must start with the most obvious potential environmental hazard posed by any product, its potential toxic effect. Genetically modified plants often, but not always, express novel proteins responsible for the improved phenotype and selection of transformed plants. If, as has been the case with Roundup Ready®, the potential toxicity of these proteins has been shown to be negligible, the risk assessment focuses on the properties of the modified plant. In the case of products modified to express a protein such as the *Bacillus thuringiensis* (Bt) protein, an assessment of potential effects on nontarget organisms is conducted in addition to an evaluation of the modified plant. The focus of this paper is on the risk assessment of the modified plant. A separate safety assessment of the Bt protein is conducted and will not be discussed further.

Procedurally, risk assessment is an iterative four-phase process including:

- Problem Formulation
- Risk Analysis
- Risk Characterization
- Risk Management

In the first phase, the risk manager assesses the problem using available information about the plant, the trait, and experimental endpoints. The risk analysis phase can also be termed the data collection phase where all the planning during problem formulation is reduced to data gathering. Thirdly is risk characterization, or data analysis. Based on the information gathered, the risk is characterized and the likelihood of an effect assessed. Lastly is risk management where the acceptability or unacceptability of the risk is determined. Very importantly in the risk management phase decisions are made as to future steps and conditions, if any, that must be imposed. The process is repeated until the risk manager is satisfied that all the relevant factors have been considered. In the process of gaining regulatory approval for a modified plant, the conclusions of the risk manager will be reviewed and questioned by scientists in the regulatory or reviewing bodies. It is also important to note that the risk assessment process does not stop after a product has gained regulatory approval or commercial acceptance.

Problem Formulation

Much information is available in the literature about the biology, use and agronomic characteristics of plants that have been genetically modified. To date over 25,000 field releases have occurred. The experience and information gained from these releases as well as other data from the literature serve as the basis for determining the important measurements to be taken and the accepted range of experimental results. In formulating the appropriate questions for Roundup Ready® and Insect Protected products, we thoroughly reviewed the literature of the host crop (the traditional unmodified counterpart) looking closely at the agronomic, ecological and environmental properties of the plant. In addition, key academics were requested to provide expert input concerning the biology of the crop plant. Perhaps one of the greatest challenges in the problem formulation was assessing the acceptable variability present in the risk assessment experiments. This variation occurs from genetic and environmental sources, and is present due to the natural complexity of biological systems. Choice of the appropriate control and reference samples is key to developing a valid risk analysis. Information concerning interactions with other organisms, especially beneficial organisms, is often reviewed. The weediness potential and invasiveness properties, as well as the potential for gene flow through volunteers or to wild relatives (outcrossing) are also essential components. Since some crops like canola and sugarbeet have high potential for outcrossing, the necessary management strategies had to be formulated prior to release of the modified plant.

Other important factors related to the potential routes of exposure and hazard were considered in the risk assessments we have conducted on our Roundup Ready® and Insect Protected products. Special attention was given to end use and dissemination. A detailed understanding of how the modified crop would be produced, handled and transported was completed for each product. Since the Roundup Ready® and Insect Protected traits effect an agronomic advantage, it was assumed that their use would not change the production uses of the modified crop. Careful analysis was also given to the nature of the trait, its potential to confer a selective advantage and to produce harmful effect to a species other than the target. The potential for enhanced toxicity of the modified plant was determined by measuring levels of known toxicants (e.g., glucosinolates in canola and gossypol in cotton). Also, as stated earlier, all gene products, as well as the marker proteins used to produce Roundup Ready® and Insect Protected crops, were thoroughly evaluated and shown to be safe.

Because unintended effects are remotely possible, consideration is given to the potential impact of our products on biodiversity. In addition, the experimental strategy takes into account secondary genetic effects such as gene instability and pleiotropic effects. Genetic instability would be clearly evident in a loss or sudden change in the plant phenotype. Lastly, based on the factors considered during the problem formulation phase, experimental design and endpoints are determined. The process is repeated when new information and knowledge gained from experimental results obtained during risk analysis.

Risk Analysis

We have used a tiered approach to the risk assessment of Roundup Ready® and Insect Protected crops based on the results of our problem formulation. The Tier I data is summarized in Table 2. We have assessed that these data are sufficient to thoroughly assess the risk associated with genetically modified crops. However, a second tier has been included for the situation where more data are needed.

Table 2. Tier I Risk Analysis for Roundup Ready® and Insect Protected Crops

- germination / emergence
- growth assessments
- reproductive potential
- seedbank longevity
- volunteer potential
- susceptibility to pests and management
- field observations and monitoring

In Tier I, data related to the emergence and germination, plant growth, reproductive potential, weediness, and susceptibility to pests were collected. In addition, fields were monitored for effects on subsequent rotations and any evidence for gene flow / outcrossing. When detected, volunteers were assessed for their quantity and tolerance to management practices. Most importantly, all field data and observations were made using a control that was a nonmodified counterpart of the genetically modified plant. For the Roundup Ready® and Insect Protected crops, these data provide a detailed picture of the potential ecological impact present.

If the risk presented by a genetically modified crop were characterized to be significant after Tier I analysis, or if the Risk Manager concludes that more data are required, some or all Tier II analyses could be conducted. Some of the analyses listed in Table 3 are very detailed and may necessitate multiple years to complete.

The results of our risk analysis using Tier I data have been sufficient to conclude environmental safety for all Roundup Ready® and Insect Protected crops. Nevertheless, we have facilitated Tier II analyses of some of our products. For example we supported an outcrossing study with Roundup Ready® canola (Bing, 1991). We also purposely made hybrids between Roundup Ready® sugarbeet and wild beet to study the effect of the trait in the weed (unpub-

TABLE 3. TIER II RISK ANALYSIS

- Hybridization studies
- Outcrossing studies
- Tier I analysis of hybrids
- Allele persistence
- Morphological character analysis
- Multiple crossing experiments

lished). Monsanto will continue to conduct more than the minimum risk analysis as well as make improvements to our risk assessment procedures as a part of our commitment to product safety and overall stewardship.

It is interesting to highlight that outcrossing studies are not a component of Tier I experiments. This is due to the fact that much is usually known about outcrossing to wild relatives from breeding and the scientific literature. Furthermore, as will be discussed later, the inherent ecological risks associated with gene flow from modified crops are not related to the phenomenon of outcrossing (Jorgenson et al., 1997; Hancock et al., 1997).

RISK CHARACTERIZATION

In the third phase of the risk assessment process, all experimental data and observational information are submitted to risk characterization. For the Roundup Ready® and Insect Protected products, the basis for characterization of the modified plant is founded in the concept of substantial equivalence. Though originally developed for assessing the safety of foods and feeds derived from modified plants (OECD, 1990), the basic premise is also appropriate for assessing the ecological and environmental safety of modified crops. The null hypothesis for genetically modified crops with agronomic traits such as Roundup Ready® and Bt is that the modified plant is substantially equivalent to the traditional counterpart. In other words, the modified plant has not been changed in any substantive way in terms of its impact on the environment allowing for the presence of the novel trait. Furthermore, the trait is assessed separately for its potential ecological and environmental impact. Once the experimental data confirm that the plant is unchanged in its ecological and environmental properties (allowing for the presence of the novel trait which is assessed separately) it can be concluded that the modified plant is as safe as the traditional plant.

This method is widely accepted as scientifically valid because of the extensive experience with large-scale environmental releases of the traditional plant. Furthermore, as products with improved environmental properties are developed and introduced, the principle of substantial equivalence and use of appropriate controls will serve as the reference point for future improvements and sustainable products. However, there is probably a need to differentiate substantial equivalence in the context of food and feed safety from ecological and environmental safety. As such we propose using a term like biological equivalence which defines that the modified plant is biologically (ecologically and agronomically) equivalent to the nonmodified plant in the absence of the target of the intended modification, i.e., the herbicide or insects.

In addition to the risk characterization of substantially (biologically) equivalent, it is possible to conclude that the plant is not substantially (biologically) equivalent. If this were the case, one would proceed appropriately in the risk management phase (*vide infra*).

As mentioned above, the risk of the introduced trait must be thoroughly characterized. For the Roundup Ready® and Insect Protected traits, the most significant potential impacts have been characterized as resistance management to glyphosate and Bt protein, respectively. These characterizations serve as the focus for the risk management phase of the risk assessment for these crops. Appropriate risk management procedures will define the overall impact of the release of a modified plant and the introduced trait.

Risk Management

The philosophical basis for risk management must be founded in product stewardship. Products developed under a strict philosophy of stewardship where the quality, integrity and benefits of the product are viewed against the risk they present will meet the requirements of the stakeholders (customers, consumers, and society in general). Roundup Ready® and Insect Protected products from Monsanto must afford environmental and economic benefit as mentioned earlier, and must enhance the ability to produce a crop in a sustainable manner. The safety of products derived through genetic engineering are assessed by independent regulatory agencies and determined to be at least as safe as existing agricultural technologies. This review is one assurance that appropriate stewardship policies and practices are being utilized. Other assurances are risk management and product support practices after commercialization.

Upon completion of risk characterization, the risk manager must weigh the risk presented by the product against the benefit gained. Clearly, such analyses assume that no action (or inaction) has zero risk. It is this balance between risk and benefit that form the concept of acceptable risk. When the benefits outweigh the risk, the risk is acceptable. All Roundup Ready® and Insect Protected products on the market today have exceeded these criteria. In addition and because our risk management is based on product stewardship principles, appropriate monitoring and resistant management procedures have been developed. These post market surveillance practices are continually being refined based on input from the leading experts in the fields of insect and weed resistance and knowledge gained after release of the modified plant.

Conversely, when the benefits are inadequate compared to the risk, the risk is unacceptable. In both situations, secondary steps must be taken as a part of appropriate risk management. The risk manager may wish to conduct additional tests (eg. Tier II) or propose post marketing management procedures that will manage the risk. In this situation, one additional option available is to consult regulatory, industry and academic experts regarding appropriate management strategies.

THE ENVIRONMENTAL IMPACT OF THE RELEASE OF ROUNDUP READY® CANOLA

Since the focus of this meeting is the impact of outcrossing from genetically modified crops, I will address this issue specifically. Risk assessment experts around the world have shown that introduced genes are inherited in the same manner as endogenous genes (Jorgenson et. al., 1997, Hancock et. al., 1997). Furthermore, outcrossing is not a new phenomenon created through genetic engineering. Plant breeders have been using these principles for years to modify and improve crops. Thus, the impact of outcrossing is not dependent on the phenomenon. Rather, it is related to the nature of the introduced trait. Since the environmental properties of the trait are thoroughly evaluated in the risk assessment, one can gain insight into the impact of outcrossing based on the selective advantage observed in field tests. If the trait confers a selective advantage to the modified plant, it is reasonable to conclude that any hybrids resulting from outcrossing of the trait will also possess the selective advantage.

A real life example of a highly outcrossing plant that also tends to volunteer that has shown no environmental impact is Roundup Ready® Canola (*Brassica napus* var. *oleifera*). This product contains the genes for two proteins, CP4 5-enolpyruylshikimate-3-phosphate synthase (CP4 EPSPS) and Glyphosate Oxidoreductase (GOX) which confer tolerance to glyphosate the active ingredient in Roundup® herbicide. The commercial line was first field tested in 1991 and ultimately received environmental regulatory approval in Canada in 1995. In their decision, Agriculture and Agrifood Canada looked very closely at the issue of outcrossing because *B. napus* is sexually compatible with two common weeds *B. rapa* and *B. juncea*. They concluded that outcrossing to weedy relatives is likely to occur at some low frequency, but that the presence of the herbicide tolerance trait in the weeds confers no greater fitness either in managed or unmanaged situations. They could state this because the plant had not undergone any fundamental changes in its biology, and currently accepted weed management measures were still applicable to control weedy relatives and volunteers. In 1998 the potential exists to plant approximately three million acres of Roundup Ready® Canola in Canada.

Based on farmer experience over the last 3 years, we can confidently conclude that the impact of outcrossing from Roundup Ready® Canola has been negligible. Furthermore, the issue of control of Roundup Ready® Canola volunteer plants has been manageable.

CONCLUSIONS

In conclusion, the ecological and environmental impact of genetically modified crops can be estimated through a rigorous science-based risk assessment. Furthermore, the impact of outcrossing will be assessed in the course of this experimental work. Based on our experience and information to date, the Roundup Ready® and Insect Protected products are at least as safe as their nonmodified counterparts. These new products offer benefits and fit better with sustainable agricultural practices. Most importantly however, risk assessment does not stop once a product receives regulatory approval and commercial acceptance. Superior risk management must be grounded in product stewardship which includes post market surveillance, resistance management, customer service and feedback and other appropriate monitoring practices. One of the critical challenges facing industry and academia today is to design appropriate post-commercialization monitoring activities that will ensure that these and future products contribute to sustainable agriculture.

REFERENCES

Bing, D.J. 1991. Potential of Gene Transfer among Oilseed *Brassica* and Their Weedy Relatives. Thesis M.Sc. Department of Crop Science and Plant Ecology. University of Saskatchewan, Saskatoon, Saskatchewan, Canada

Hancock, J. F., Grumet, R., Hokanson, S. C. 1996. "The Opportunity for Escape of Engineered Genes from Transgenic Crops" *HortScience*, 31:1080-1085

Jorgensen, R-B., Hauser, T. Mikkelsen,T., Ostergård, H. 1996. "Transfer of engineered genes from crop to wild plants." *Trends in Plant Sciences*, 1996, 1:356-358

Kjellsson, G. 1997, in "Methods for Risk Assessment of Transgenic Plants, II." Pollination, Gene-Transfer and Population Impacts. Kjellsson, G., Simonsen, V., and Ammann, K. eds. Birkhauser Verlag, pps. 221-236

______. 1989. Field testing genetically modified organisms: Framework for decisions. Committee on scientific evaluation of the introduction of genetically modified microorganisms and plants into the environment. Board on Biology, Commission on Life Sciences, National Research Council, National Academy Press, Washington, 170 pp

______. 1992. Safety considerations for biotechnology. Washington, DC: Organization for Economic Cooperation and Development Publications

______. 1993. Food safety and Biotechnology: Concepts and Principles. In "Safety evaluations of foods derived by modern biotechnology: Concepts and Principles." Washington, DC: Organization for Economic Cooperation and Development Publications

Dangerous Liaison–Deadly Gamble

Mae-Wan Ho
Professor, Biology Department
Open University, Milton Keynes, UK

The rule of bad science and big business

Genetic engineering biotechnology is hailed as the solution to all the problems facing humanity. It promises food for the starving billions in the Third World, greener agriculture, miracle cures and vaccines for cancer and other diseases, genetic diagnosis, gene therapy, genetic enhancements and even cloning of human beings. It threatens to change every aspect of our lives, not the least of which, our value system as human beings. Why is there so little debate?

In particular, why is almost no one questioning the science, which is taken to be unadulterated good not just by spokespersons for the industry, but also by our government representatives, by scientists, and the mainstream media? It is the latest offering in a reductionist tradition that has already brought us radioactive and toxic wastes, greenhouse gases, holes in the ozone layer, agrochemicals, environmental degradation, and other legacies of the Green Revolution. Can it really solve problems that reductionist science has created in the first place? Or are we facing dangers of a different order than anything that reductionist science has given us so far? I shall confine discussions to agriculture, although many of the main arguments are relevant to human genetics where major moral issues are raised in genetic discrimination, eugenics, and human cloning. A more comprehensive treatment can be found in my book: *Genetic Engineering: Dream or Nightmare? The Brave New World of Bad Science and Big Business* (Ho, 1998).

The reality, in my view, is that bad science and big business, both out of control, have formed a dangerous liaison that is gambling with our food security, biodiversity, and health, and at the same time tearing at the fabric of civilized society. The liaison is reinforced by a shared mindset that claims to be objective and neutral, but in reality, starts from some pretty simplistic and immoral assumptions. They see the world in bits and pieces, as selfish genes and selfish individuals instead of organisms, societies, and ecosystems. All of nature, including human beings and their genes, are objects to be manipulated and exploited for gain. Life and business are both in a competitive Darwinian struggle for the survival of the fittest.

The corporations are getting bigger and more competitive all the time. Just six agrochemical giants are poised to take control of world food production and distribution: Monsanto, Novartis, AgrEvo, DuPont, Zeneca and Dow (Vidal and Milner, 1997). In international financial organizations such as the World Trade Organization (WTO) and the Multilateral Agreement on Investment (MAI), legislation is being rewritten to remove all real or perceived barriers to trade and investment to enable corporations to better exploit the poor and the weak, to maximally internalize profit, and to externalize risks and costs with impunity (unpublished manuscript). At the same time, restrictive "trade related intellectual property rights" are to be protected, the most immoral of which are the patents on life that include seed varieties and knowledge stolen from Third World countries, as well as genes and cell lines taken from indigenous peoples under false pretext (Baumann, et al., 1996).

Patents on transgenic crops and other organisms will turn farmers everywhere into contracted laborers, and drastically reduce agricultural biodiversity as farmers will no longer be free to grow non-certified varieties. Farming will concentrate into fewer hands, displacing millions of small farmers or throwing them out of work by destroying export markets. Patents on human genes and cell lines will compromise healthcare for ordinary people who cannot afford to pay royalties or license fees. Basic scientific and medical research will also suffer. Most of all, these patents effectively grant monopolistic ownership of living organisms, including human beings and their genes, to powerful corporations that cannot be held accountable. Unfortunately, intense lobbying by the biotechnology corporations has persuaded the European Parliament to vote in favor of a directive that will make these patents legal. Patents that violate basic human rights are being legitimized by the dominant reductionist science that purports to set standards of propriety and probity.

This same science is also setting standards of what is safe, as we are repeatedly told by expert scientific committees at the United Nations, the European Union, and many national governments that have approved nearly all the genetically engineered products to date. The key concept is the "principle of substantial equivalence" on which all risk assessment is to be based. This principle is elaborated in a report issued jointly in 1996 by the Food and Agricultural Organization (FAO) and the World Health Organization (WHO), whose Codex Alimentarius sets world safety standards. It would be deemed illegal for countries to ban imports of any genetically engineered products so long as the Codex considers them safe. The principle is validated by the science, which pronounces that there is no essential difference between transgenic lines and conventional varieties produced by selective breeding. A product assessed to be substantially equivalent is regarded as safe and fit for human consumption.

However, substantial equivalence can be claimed in advance, in which case subsequent risk assessment is most perfunctory. Furthermore, "substantial equivalence" does not mean equivalence to the unengineered plant or animal variety. The genetically engineered food could be compared to any and all varieties within the species. It could have the worst characteristics of all the varieties and still be considered substantially equivalent. It could even be compared to a product from a totally unrelated species or collection of species. Worse still, there are no defined tests that products have to go through to establish substantial equivalence. The tests are so undiscriminating that unintended changes, such as toxins and allergens, could easily escape detection. For example, a grossly altered genetically engineered potato with deformed tubers was tested and passed as substantially equivalent (Conner, 1995). Risk assessment based on the principle of substantial equivalence, in my view, is the stuff of farce. It is a case of "don't need - don't look - don't see." Biotechnology corporations are effectively given *carte blanche* to do as they please, while regulators are serving to diffuse and allay legitimate public fears and opposition (Ho and Steinbrecher, 1998).

It is significant that a lawsuit challenging the United States Food and Drug Administration (FDA) policy on genetically engineered foods has just been filed by a coalition of scientists, health professionals, religious leaders, and chefs demanding adequate safety testing and mandatory labeling. According to a press release issued by the International Center for Technology Assessment, the FDA policy is scientifically unsound and ignores significant health risks.

NOT FEEDING THE WORLD

It is clear that no one needs genetically engineered foods, least of all peasant farmers in the Third World. "World hunger" is usually blamed exclusively on population increases in the Third World (Kendall et al., 1997; Food and Drink Federation, 1995; and Brown, 1998). Not mentioned are the large dam projects that continue to be supported by the World Bank. A total of 40,000 large dams already took 400,000 square kilometers of the best agricultural land out of production displacing 60 million farmers and further ruining vast areas of arable land by unsustainable irrigation practices that result in salination, waterlogging, drought and erosion (Goldsmith and Hilyard, 1984-92). At the same time, the policies of trade liberalization (WTO) enable corporations operating in the Third World to divert food-growing lands to non-food crops such as flowers and other luxury commodities, and to leisure complexes such as golf courses, turning traditionally food-exporting countries into importers (Cainglet, 1998). Over the past two years, 65 golf courses have been constructed in the Philippines alone, and the Government's own projections reveal that 1.5 million hectares of rice lands are to be converted into cash crops and golf courses. This is a country where 70 percent of the population are farmers, but the majority is landless, and less than one percent of the population controls more than 50 percent of all agricultural land. Those peasants still fortunate enough to own land have no more than two hectares. The Philippines has become a net importer of rice as a result, and the volume of import is set to grow. The same story is repeated all over the Third World, in Mexico, and in Russia.

Corporate interests are now offering genetic engineering agriculture to the Third World, with the World Bank as a major player (Kendall, et al., 1997). Far from feeding the world, genetic engineering agriculture, operating under the patents on life regime, will reinforce and intensify corporate control of food production and distribution, swelling the masses of displaced farmers, making the poor even poorer and hungrier.

Furthermore, in my view, it poses serious threats to food security, biodiversity, and human and animal health, and has the potential to unleash uncontrollable epidemics of drug and antibiotic-resistant infectious diseases. Those hazards are not teething problems, but inherent to the reductionist mindset of a bad science misguiding a hit-or-miss technology.

THE BAD SCIENCE OF GENETIC DETERMINISM

Genetic engineering is a set of techniques for cutting, joining, modifying, and multiplying genes, especially for transferring genes from one species to another, most of which would never interbreed in nature. Thus, human genes are transferred to pig, mouse, fish, plants, and bacteria. And genes of all species can be recombined, cloned, and modified in any and every way. Genetic engineering is a new departure from conventional breeding techniques, and introduces new problems and dangers. But let us look first at the science motivating the technology.

This is what the public is told: "Research scientists can now precisely identify the individual gene that governs a desired trait, extract it, copy it, and insert the copy into another organism. That organism (and its offspring) will then have the desired trait" (Food and Drink Federation, 1995). This description is typical of literature supposedly promoting public understanding, and neatly encapsulates the bad science of genetic determinism. It gives the highly misleading impression of a precise technology, implying that:

- Genes determine characters in linear causal chains, one gene giving rise to one character;
- Genes are not subject to influence from the environment;
- Genes remain stable and constant;
- Genes remain in organisms and stay where they are put.

This is the most extreme version of the classical genetics that has dominated biology roughly from the 1930s up to the 1970s when genetic engineering began. It is so extreme that no biologist would admit to actually subscribing to it. But, why else would they suggest that by manipulating genes, practically all the problems of the world can be solved?

Genetic determinism goes counter to all the scientific evidence accumulated especially within the past 20 years, which gives us the new genetics. What is the new genetics of the present day really like (Ho, 1998)?

- No gene ever works in isolation, but in an extremely complicated genetic network where the function of each gene is dependent on the context of all the other genes in the genome. So, the same gene will have very different effects from individual to individual, because other genes are different. There is so much genetic diversity within any outbreeding population, such as human beings, that each individual is genetically unique. And, especially if the gene is transferred to another species, it is most likely, in my view, to have new and unpredictable effects.
- The genetic network, in turn, is subject to layers of feedback regulation from the physiology of the organism and its relationship to the external environment.
- These layers of feedback regulation not only change the function of genes but can rearrange them, multiply copies of them, mutate them to order, or make them move around.
- And, genes can even travel outside the original organism to infect another—this is referred to as horizontal gene transfer.

The new picture of the gene is diametrically opposite to the old static, reductionist view. The gene has a very complicated ecology consisting of the interconnected levels of the genome, the physiology of the organism and its external environment (Ho, 1998; Ho et al., 1998). Putting a new gene into an organism will create disturbances that can propagate out to the external environment. Conversely, changes in the environment will be transmitted inwards and may alter the genes themselves. Genetic engineering profoundly disturbs the ecology of genes at all levels, and that is where the problems and dangers arise.

Genetic engineering is a crude, imprecise operation

First of all, I must dispel the myth that genetic engineering is a precise operation. It is not. The insertion of foreign genes into the host cell genome is a random process not under the control of the genetic engineer. It is done by means of artificial vectors for horizontal gene transfer. Horizontal gene transfer is naturally done by infectious agents such as viruses and virus-like elements (plasmids and transposons) that are passed from cell to cell and from organism to organism, sometimes causing diseases including cancer, and spreading drug and antibiotic-resistance genes. The gene(s) to be transferred are usually integrated into the genetic material of the vector; viruses can also transfer genes that are not integrated but are merely packaged within the protein coat that envelops the genetic material.

Species barriers limit natural agents, and all cells have mechanisms that break down or inactivate foreign genes. However, genetic engineers make artificial vectors for transferring genes by joining together parts of the most aggressive agents to overcome all species barriers. Most of the genes causing diseases are removed, but the antibiotic-resistance genes are left in. The gene to be transferred (transgene) is inserted into an artificial vector containing one or more antibiotic-resistance marker genes, which makes it possible to select for cells that have taken up the vector carrying the transgene. The vector carrying the transgene and marker gene(s) can either be replicated many times in the cell or become integrated into the genome, resulting in a transgenic cell from which a transgenic organism may be regenerated. The integration of the vector is random and not controllable by the genetic engineer (Walden et al., 1991).

This gives rise to correspondingly random genetic effects: inappropriate activation or inactivation of host genes, including, in my opinion, cancer (Doerfler et al., 1997). Recent studies document genetic disturbances that propagate far from the site of insertion of the foreign genes into the host genome (Parr, 1997). Furthermore, the foreign genes are equipped with very strong signals, most often from viruses, called promoters or enhancers, that force the organism to express the foreign genes at rates 10 to 100 times greater than its own genes. In other words, the genetic engineering process, both by design and otherwise, completely upsets the first two levels in the ecology of genes — the genome and the physiology — with dire consequences. It is my belief that the lines produced are unstable and are a threat to food security.

For every product that reaches the market, there are perhaps 20 or more others that have failed. However, even products that reach the market are failing:

- The FlavrSavr™ tomato was a commercial disaster and has disappeared (Fox, 1997).
- Monsanto's Bt-cotton, engineered with an insecticide from the soil bacterium *Bacillus thuringiensis*, failed to perform in the field in both US and Australia in 1996, and suffered excessive damages from Bt-resistant pests (Fox, 1997).
- Monsanto's 1997 Roundup Ready® cotton crops fared no better. The cotton bolls drop off when sprayed with Roundup and farmers in seven states in the US are seeking compensation for losses.
- The transgenic Innovator herbicide-tolerant canola failed to perform consistently in Canada. This has led the Saskatchewan Canola Growers Association to call for an official seed vigor test.

- Monsanto's entire Canadian genetically engineered rapeseed crop had to be recalled in 1997 because of "technical difficulties" (Monsanto Monitor, 1998).

Because genes respond to the environment; plants that perform in greenhouses may well fail in the field. But transgenic plants have additional problems.

There is widespread instability of transgenic lines, not only do they fail to perform consistently in the field, they generally do not breed true. In my opinion, transgenic lines are unstable because of the way they are made (see below).

Transgenic instability

Traditional breeding methods involve crossing closely related varieties or species containing different forms of the same genes. Selection is practiced over many generations under field conditions so that the desired characteristics and the genes influencing those characteristics, in the appropriate environment, are tested and harmonized for stable expression over a range of genetic backgrounds. Different genetic combinations moreover will vary in performance in different environments. This "genotype-environment" interaction is well known in traditional breeding so it is not possible to predict how a new variety will perform in untested environments. In many cases, new varieties will lose their characteristics in later generations as genes become shuffled and recombined, or as they respond to environmental changes.

This problem is greatly exacerbated in genetic engineering. First of all, completely exotic genes are often introduced into organisms. Secondly, the procedures for creating transgenic organisms inherently generate increased genetic instability, In plants, the genes are often introduced into cells in tissue culture, and transgenic plants are regenerated from the cells after selection in culture.

- The tissue culture technique itself introduces new genetic variations at high frequencies; these are known as *somaclonal variations* (Cooking, 1989). In my view, that is because the cells are removed from the internal, physiological environment of the plant which, together with the ecological environment, keep gene expression, genes, and genome structure stable in the cells and the organism as a whole (Ho, 1998). Unilever used tissue culture techniques to regenerate oil palms for planting in Malaysia several years ago. This has now been abandoned as many plants aborted in the field or failed to flower (Perlas, 1995).
- The process of gene insertion is random and many secondary genetic effects can result, as mentioned earlier.
- The extra DNA integrated into the transgenic organism's genome disrupts the structure of its chromosome, and can itself cause chromosomal rearrangement (Wahl et al., 1984), further affecting gene function.

- The integrated vector containing the transgene(s) and marker gene(s) has the potential to move out again or reinsert into another site, causing further genetic disturbances (Ho, 1998; Ho and Steinbrecher, 1998; Walden et al., 1991; Doerfler et al., 1997).
- The highly mosaic character of most vector constructs make them structurally unstable and prone to recombination (Ho et al., 1998). This may be why viral-resistant transgenic plants generate recombinant viruses more readily than non-transgenic plants (see below).
- The use of aggressive promoters and enhancers to boost expression of transgenes stress and unbalance the physiological system and increases instability, as already stated.
- All cells have mechanisms that silence foreign genes (Finnegan and McElroy, 1994). One common mechanism is methylation — a chemical reaction that adds a methyl group to the base adenine or cytosine in the DNA (there are four bases in DNA, adenine, cytosine, guanine and thymine) — as the result of which, the gene is no longer expressed.

Transgene instability occurs both in farm animals (Colman, 1996) and plants (Lee et al., 1995). The transgenic sheep Tracy, engineered to produce human alpha-antitrypsin at high levels in her milk, failed to reproduce female offspring that match her performance. That is why cloning techniques that resulted in Dolly the sheep were contemplated. Much more is known about instability in plants. In tobacco, 64 to 92 percent of the first generation of transgenic plants become unstable. The frequency of transgene loss in *Arabidopsis* ranges between 50 and 90 percent. Instability arises during the production of germ cells and in cell division during plant growth. It can be triggered by transplantation or mild trauma (Parr, 1997).

Transgenic lines, therefore, often do not breed true. A typical case is the supposedly non-allergenic rice produced in Japan (Tada et al., 1996), which turned out to be both ineffective and unstable. The transgenic plants of the second and third generations showed only a 20 to 30 percent reduction of the allergens. The project has been abandoned (Devlen et al., 1995).

There is, in fact, no data documenting the stability of any transgenic line in gene expression, or in structure and location of the insert in the genome. Such data must include the level of gene expression, as well as a genetic map and DNA base sequence of the insert and its site of insertion in the host genome in each successive generation. No such data has ever been provided by industry, nor requested by regulatory authorities.

The instability of transgenic lines creates difficulties in quality control and traceability. It also raises serious safety concerns. A transgenic variety with a certain gene insert may be assessed safe, and completely change in characteristics when the insert moves to another position in the genome. Furthermore, one does not have to be prescient to see that transgenic instability makes biotechnology unsustainable. It is my belief that it may ruin our agriculture and food supply just by being widely planted in place of nongenetically engineered and traditional, well-tried varieties. Small farmers in Third World countries will be especially vulnerable.

DANGERS FROM NOVEL GENE PRODUCTS BOTH INTENDED AND UNINTENDED

Genetic engineering introduced new genes and gene products into our food chain, many from viruses and bacteria, which we have never eaten before and certainly not in such quantities. The viral "promoters" or "enhancers" that boost the expression of introduced genes continuously at a high rate essentially places them outside normal control. These promoters may also have further affects on host genes. As no gene in a normal organism is on at full blast all the time, the genetically engineered organism is under permanent metabolic stress which, in my opinion, makes it an unwholesome food.

More importantly, because no gene functions in isolation, the introduced genes are bound to interact with the host genes to give unintended effects, among which are, I believe, likely to be toxins and allergens. The most notorious case of unintended toxin is a batch of genetically engineered tryptophan, an amino acid widely sold in health-food stores. It killed 37 and made thousands ill. Graphic illustrations of "unintended effects" are failures in transgenic animals, which is disastrous for animal welfare (Mayeno and Gleich, 1994).

- The superpig engineered with human growth hormone gene turned out arthritic, ulcerous, blind and impotent (Cox, 1996).
- The supersalmon engineered to grow as fast as possible ended up with big monstrous heads and died from not being able to breathe or feed properly (*GenEthics News*; Devlen et al., 1995a).
- The latest clones of the sheep Polly are abnormal and eight times as likely to die at birth compared with ordinary lambs (Devlen et al., 1995b).

And it is possible that the carcasses of failed transgenic experiments and xenotransplant pigs could turn up as meat on our dinner table. They have already been approved for sale by the US Department of Agriculture (USDA) in 1994, without being labelled as such. They will all pass as "substantially equivalent". And if not, then GRAS, Generally Regarded As Safe, according to the standards set by the FAO/WHO food safety report (FAO/WHO, 1996)

THREATS TO BIODIVERSITY

Agricultural biotechnology is already posing unacceptable threats to biodiversity, not surprisingly because wider ecological impacts are ignored by the reductionist science.

- Broad-spectrum herbicides used with herbicide-tolerant transgenic crops, such as glufosinate (Mendelson, 1998) (Novartis' Basta) and glyphosate (Cox, 1996) (Monsanto's Roundup) destroy plants indiscriminately, many of which are habitats for wildlife. They are toxic to animals and human beings. Glufosinate also causes birth defects and glyphosate is mutagenic (Cox, 1995).
- Transgenic plants with insecticidal transgenes not only harm beneficial species directly, but also indirectly down the food chain, such as lacewings and ladybirds feeding on prey species that have eaten transgenic plants (Kale, et al., 1995) and Birch, et al., 1997). In a field trial of Bt-cotton in Thailand, 30 percent of the bees around the test fields died (Hilbeck et al., 1997).
- Transgenic crops with insecticidal genes or herbicide tolerant genes actually favour the widespread mutation to resistance (Ho, 1998). In other words, they exacerbate the problem they are supposed to solve.

Pesticide resistance and herbicide tolerance are not due to the natural selection of pre-existing, rare random mutations, as we have been told in textbooks for years. They are due to genetic mutations that can occur in not all of the individuals in the populations in response to sublethal levels of the pesticide or herbicide. So, just as pesticidal transgenic plants, in my opinion, lead to rapid evolution of resistance among pests, the use of herbicide-tolerant transgenic plants will, I believe, also result in the widespread evolution of herbicide tolerance among weeds, even in the absence of cross-pollination. (The spread of transgenes by cross-pollination has already been demonstrated.) This has been known more than 10 years (Hyrien and Buttin, 1986). The genetic changes are part and parcel of the physiological mechanisms common to all cells and organisms challenged with toxic substances, not only pesticides and herbicides (Mikkelson, et al., 1996), but also anti-cancer drugs in mammalian cells and most dangerously, antibiotics in bacteria (Ho, 1998; Ho et al., 1998).

The use and abuse of antibiotics in intensive agriculture and conventional medicine have been responsible for the evolution of antibiotic resistances in pathogens. But, here is the final straw. Genes do not stay where they are put, but can travel horizontally between species that do not naturally interbreed.

Genetic engineering organisms contribute to drug and antibiotic-resistant infectious diseases

As previously mentioned, genetic engineering involves transferring genes horizontally between species that do not interbreed. While natural agents are limited by species barriers, genetic engineers make artificial vectors for transferring genes by joining together parts of the most aggressive agents to overcome all species barriers.

Artificial vectors and the genes they carry have the potential to spread horizontally to a wide range of species, to recombine with their genes to generate new viral and bacterial pathogens. This very danger had made the first molecular geneticists impose a moratorium on genetic engineering in the Asilomar Declaration of 1975 (Hyrien and Buttin, 1986). But commercial pressures soon intervened. Activities resumed after regulatory guidelines were put in place and commercial production began. Were those guidelines adequate? No, not in the light of recent scientific evidence as eight scientists including myself argue in a new report (Ho et al., 1998).

There has been a resurgence of infectious diseases within the past 20 years, diseases that are resistant to treatment by drugs and antibiotics. A public health crisis is looming worldwide. Infectious diseases are responsible for one-third of the 52 million deaths from all causes. Multi-drug-resistant tuberculosis is now estimated to affect 10 million each year with 3 million deaths. At least 50 new viruses attacking humans emerged between 1988 and 1996. Between 1986 and 1996, *E. coli* O157:H7 infections increased by 10-fold in England and Wales and 100-fold in Scotland. Vancomycin resistance rose from 3 percent to 95 percent in San Francisco hospitals in the four years between 1993 and 1997. And strains of dangerous bacteria including *Staphyloccocus aureus* (toxic shock syndrome), *Enterococcus faecalis* (blood poisoning and wound infection), *Pseudomonas aeruginosa* (blood poisoning and pneumonia) and *Mycobacterium tuberculosis* (TB) are invulnerable to all known antibiotics (Walden et al., 1991; Dobson, 1998).

Over the past three to four years, geneticists have discovered how horizontal gene transfer and recombination are responsible for generating the new viral and bacterial pathogens and spreading drug and antibiotic resistance genes (Ho, 1998; Ho et al., 1998). Are we unleashing widespread, cross-species epidemics that will be impossible to control? The signs are that the worst case scenario, predicted by the Asilomar Declaration, may already be with us as the result of 20 years of commercial gene technology.

Can transgenic plants and animals contribute to such processes? Yes. They can. Transgenic plants have been found to transfer their transgenes and antibiotic resistance marker genes to soil fungi and bacteria (Gainglet, 1998; Hoffman et al.; Schluter et al., 1995). Plants engineered with a viral gene, supposed to resist virus attack, actually have increased propensity to generate new, superinfectious viruses by recombination (Gebhard and Smalla, 1998; Vaden and Melcher, 1990; Lommel and Ziong, 1991; Greene and Allison, 1994; Wintermantel and Schoelz, 1996). Genetic engineering, by enhancing horizontal gene transfer and recombination, may, I believe, be greatly multiplying the odds for generating new viral and bacterial pathogens and spreading drug and antibiotic resistance genes.

The regulatory guidelines set up after Asilomar were based largely on assumptions, practically every one of which has been overturned by recent scientific findings (Ho, 1998; Ho et al., 1998).

- Biologically "crippled" laboratory strains of bacteria can often survive in the environment, or go dormant but continue to exchange genes with other organisms (Jager and Tappeser, 1996).
- Routine chemical inactivation methods may leave up to 10 percent of viruses and other pathogens in an infective state (Coghlan, 1997).
- Legal limits of "tolerated releases" from contained use vastly exceed the minimum infective dose of some pathogens: 10,000 colony-forming units/ml in air or water (Novo Nordisk) versus a minimum infective dose of 50 bacteria for *E. coli* O157:H7 (Smith, 1997)
- Antibiotics increase the frequency of horizontal gene transfer 10 to 10,000-fold (Lorenz and Wackernagel, 1994; Davies, 1994).
- DNA released from dead and living cells persist in the environment and transfer to other organisms (Sandaa and Enger, 1994; Yin and Stotzky, 1997).
- Naked viral and vector DNA may be more infectious, and have a wider host range than the virus (Traavik, 1995).
- Viral DNA resists digestion in the gut of mice; enters the blood stream to infect white blood cells, spleen and liver cells; and integrates into the mouse cell genome (Ho et al., 1998; Schubbert et al., 1994; Schubbert et al., 1997).

CONCLUSION

In conclusion, genetically engineering agriculture is unnecessary and unethical. It is based on science that is unsound, and the foods produced are, in my opinion, unwholesome. It is unsustainable because the technology is hit or miss. Most of all I believe it is inherently unsafe.

Erwin Chargaff, a founding father of molecular biology, warned that all innovation does not result in "progress." He once referred to genetic engineering as "a molecular Auschwitz" and warned that the technology of genetic engineering poses a greater threat to the world than the advent of nuclear technology. "I have the feeling that science has transgressed a barrier that should have remained inviolate," he wrote in his autobiography, *Herculean Fire*, ". . . you cannot recall a new form of life . . . It will survive you and your children and your children's children. An irreversible attack on the biosphere is something so unheard of, so unthinkable to previous generations, that I could only wish that mine had not been guilty of it."

In the face of the wealth of existing scientific evidence and the precautionary principle, the least our governments could do is to impose a five-year moratorium and to support independent scientists to go back to basic research on the legitimate, sustainable, and safe uses of the technology. At the same time, there should be a major public inquiry in which the scientific, social, and moral issues are considered together and openly debated. Most of all, we need to seriously rethink where the priorities are, and the sort of life we want as a civil society.

References

"And the cow jumped over the moon". 1994. *GenEthics News.* Issue 3. pp. 6-7

Baumann, M., Bell, J., Koechlin, F., and Pimbert, M. 1996. The Life Industry, Biodiversity, People and Profits. London: Intermediate Technology Publications

Berg, P. 1974. Potential biohazards of recombinant DNA molecules.*Science*. 185:303

Birch, A.N.E., Geoghegan, I.I., Majerus, M.E.N., Hackett, C., and Allen, J. 1997. Interaction between plant resistance genes, pest aphid-population and beneficial aphid predators. *Soft Fruit and Perennial Crops.* October. pp. 68-79

Brown, L. R. 1998. Struggling to raise cropland productivity. In "State of the World 1998". London: Worldwatch Institute Report, Earthscan Publications. pp. 79-95

Cainglet, J. 1998. The politics of GE agriculture — a Filipino perspective. In "Global Genes". London: Farmer's World Publications

Goldsmith, E. and Hilyard, N. 1984-1992. The Social and Environmental Effects of Large Dams. Vol.1-3, Wadebridge: Wadebridge Ecological Center

Coghlan, A. 1997. "Jetsetters send festering faces round the world". *New Scientist.* May 7. p. 7

Colman, A. 1996. "Production of proteins in the milk of transgenic livestock: problems, solutions and successes". *American Journal of Clinical Nutrition.* 63:639S-645S

Conner, A.J. 1995. Case study: Food safety evaluation of transgenic potato. In "Application of the Principles of Substantial Equivalence to the Safety Evaluation of Foods or Food Components from Plants Derived by Modern Biotechnology". WHO/FNU/FOS/95:1. pp. 23-25

Cooking, E.C. 1989. Plant cell and tissue culture. In "A Revolution in Biotechnology". Cambridge: Cambridge University Press. pp. 119-129

Cox, C. 1996. Herbicide Factsheet: Glufosinate. *J. Pesticide Reform* 16:15

Cox, C. 1995. Glyphosate, Part 2: Human exposure and ecological effects. *Journal of Pesticide Reform* 15:4

Davies, J. 1994. "Inactivation of antibiotics and the dissemination of resistance genes". *Science* 264:275-82

Devlen, R.H., Yesaki, T.Y., Donaldson, E.M. Du, S.J., and Hew, C.L. 1995a. "Production of germline transgenic Pacific salmon with dramatically increased growth-performance". *Canad. J. Fishery and Aquatic Science* 52, 1376-84

Devlen, R.H., Yesaki, T.Y., Donaldson, E.M., and Hew, C.L. 1995b. "Transmission and phenotypic effects of an antifreeze GH gene construct in coho salmon (*oncorhynchus-Kisutch*)". *Aquaculture* 137:161-9

Doerfler, W., Schubbert, R., Heller, H., Kammer, C., Hilger-Eversheim, K., Knoblauch, M., and Remus, R. 1997. "Integration of foreign DNA and its consequences in mammalian systems". *Tibtech* 15:297-301

Finnegan, H. and McELroy, A. 1994. Transgene inactivation plants fight back! *Bio/Techology* 12:883-888

_____. 1995. Food for Our Future: Food and Biotechnology. London: Food and Drink Federation. p. 5

Fox, J.L. 1997. EPA seeks refuge from Bt resistance. *Nature Biotechnology* 15:209

Gebhard, F. and Smalla, K. 1998. Transformation of *Acinetobacter* sp. strain BD413 by transgenic sugar beet DNA. *Applied Environ. Microbiol.* 64:1550-1554

Greene, A.E. and Allison, R.F. 1994. Recombination between viral RNA and transgenic plant transcripts. *Science* 263:1423-1425

Hilbeck, A., Baumgartner, M., Fried, P.M., and Bigler, F. 1998. Effects of transgenic *Bacillus thuringiensis* corn-fed prey on mortality and development time of immature Chrysoperla carnea Neuroptera: Chrysopidae. *Environmental Entomology* 27:480-488.

Ho, M.W. 1998. Genetic Engineering Dream or Nightmare? The Brave New World of Bad Science and Big Business. UK: Gateway Books; Malaysia: Third World Network

Ho, M.W. and Steinbrecher, R. 1998. Fatal Flaws in Food Safety Assessment: Critique of The Joint FAO/WHO Biotechnology and Food Safety Report. Malaysia: Third World Network

Ho, M.W., Traavik, T., Olsvik, R., Midtvedt, T., Tappeser, B., Howard, V., von Weizsacker, C., and McGavin, G. 1998. Gene Technology and Gene Ecology of Infectious Diseases. Malaysia: Third World Network

Hoffman, T., Golz, C., and Schieder, O. 1994. Foreign DNA sequences are received by a wild-type strain of Aspergillus niger after co-culture with transgenic higher plants. *Current Genetics* 27: 70-6

Hyrien, O. and Buttin, G. 1986. Gene amplification in pesticide resistant insects. Trends in Genetics 2, pp. 275-276

Jager, M.J. and Tappeser, B. 1996. Politics and Sciences in Risk Assessment. In "Coping with Deliberate Release. The Limits of Risk Assessment" International Centre for Human and Public Affairs, Tilburg. pp. 63-72

_____. 1996. Joint FAO/WHO Expert Consultation on Biotechnology and Food Safety. Rome

Kale, P.G., Petty, B.T. Jr., Walker, S., Ford, J.B., Dehkordi, N., Tarasia, S., Tasie, B.O., Kale, R., and Sohni, Y.R. 1995. Mutagenicity testing of nine herbicides and pesticides currently used in agriculture. *Environ Mol Mutagen* 25:148-53

Kendall, H.W., Beachy, R., Eisner, T., Gould, F., Herdt, R., Ragen, P.H., Schell, J.S., and Swaminathan, M.S. 1997. Bioenergineering of Crops Report of the World Bank Panel on Transgenic Crops. Washington: The World Bank

Kendrew, J. ed. 1995. The Encyclopedia of Molecular Biology. Oxford: Blackwell Science

Lee, H.S., Kim, S.W., Lee, K.W., Ericksson, T., and Liu, J.R. 1995. Agrobacterium-mediated transformation of ginseng *(Panax-ginseng*) and mitotic stability of the inserted beta-glucuronidase gene in regenerants from isolated protoplasts. *Plant Cell Reports* 14:545-549

Lommel, S.A. and Xiong, Z. 1991. Recombination of a functional red clover necrotic mosaic virus by recombination rescue of the cell-to-cell movement gene expressed in a transgenic plant. *J. Cell Biochem*. 15A:151

Lorenz, M.G. and Wackernagel, W. 1994. Bacterial gene transfer by natural genetic transformation in the environment. *Microbiological Reviews* 58:563-602

Mayeno, A.N. and Gleich, G.J. 1994. Eosinophilia-myalgia syndrome and tryptophan production: a cautionary tale. *Tibtech* 12:346-352

Mendelson III, J. 1998. Lax labeling policies betray public trust. *GeneWATCH* 11:4-5

Mikkelson, T.R., Andersen, B., and Jorgensen, R.B. 1996. The risk of crop transgene spread. *Nature* 380:31

Monsanto Monitor: an ongoing report on the activities of the corporate giant. 1998. *The Ecologist Campaign & News*, May/June. p.4

______. Environmental Report. 1996. Denmark: Novo Nordisk

Parr, D. 1997. Genetic Engineering: Too Good to go Wrong? London: Greenpeace

Perlas, N. 1995. Dangerous trends in agricultural biotechnology *Third World Resurgence* 38:15-16

Sandaa, R.A. and Enger, O. 1994. Transfer in marine sediments of the naturally occurring plasmid pRAS1 encoding multiple antibiotic resistance. *Applied and Environmental Microbiology* 60:4243-58

Schluter, K., Futterer, J., and Potrykus, I. 1995. Horizontal gene-transfer from a transgenic potato line to a bacterial pathogen (*Erwinia-chrysanthem*) occurs, if at all, at an extremely low frequency. *Bio/Techology* 13:1094-8

Schubbert, R., Lettmann, C., and Doerfler, W. 1994. Ingested foreign (phage M13) DNA survives transiently in the gastrointestinal tract and enters the bloodstream of mice. *Mol. Gen. Genet.* 242:495-504

Schubbert, R., Renz, D., Schmitz, B., and Doerfler, W. 1997, Foreign (phage M13) DNA ingested by mice reaches peripheral leukocytes, spleen and liver via the intestinal wall mucosa and can be covalently linked to mouse DNA. *Proc. Natl. Acad. Sci. USA.* 94:961-66

Smith, H.R. 1997. Vero cytotoxin-producing Escherichia coli 0157: Cause for concern. *SGM Quarterly.* May. pp. 54-5

Tada, Y., Nakase, M., Adachi, T., Nakamura, R., Shimasda, H., Takahashi, M., Fujimura, T., and Matsuda, T. 1996. Reduction of 14-16 kDa allergenic proteins in transgenic rice plants by antisense gene. *FEBS Letters* 391:341-5

Traavik, T. 1995. Too Early May Be Too Late. Ecological Risks Associated with the Use of Naked DNA as a Biological Tool for Research, Production and Therapy (Norwegian), Report for the Directorate for Nature Research Tungasletta 2, 7005 Trondheim. English translation, 1998

Vaden V.S. and Melcher, U. 1990. Recombination sites in cauliflower mosaic virus DNAs: implications for mechanisms of recombination. *Virology* 177:717-26

Vidal, J. and Milner, M. 1997. Food: the £250 gamble. *The Guardian* Dec. 15

Wahl, G.M., de Saint Vincent, B.R., and DeRose, M.L. 1984. Effect of chromosomal position on amplification of transfected genes in animal cells. *Nature* 307:516-520

Walden, R., Hayashi, H., and Schell, J. 1991. T-DNA as a gene tag. *The Plant Journal* 1:281-8

Wintermantel, W.M. and Schoelz, J.E. 1996. Isolation of recombinant viruses between cauliflower mosaic virus and a viral gene in transgenic plants under conditions of moderate selection pressure. *Virology* 223:156-64

Yin, X. and Stotzky, G. 1997. Gene transfers among bacteria in natural environment. *Applied Microbiology* 45:153-212

EPA Regulation of Plant-Pesticides and Bt Plant-Pesticide Resistance Management

SHARLENE R. MATTEN*
Biologist, Biopesticides and Pollution Prevention Division
Office of Pesticide Programs
US Environmental Protection Agency
Washington, DC

OVERVIEW OF EPA REGULATIONS OF PESTICIDES

The US Environmental Protection Agency (EPA) regulates pesticides under two major statutory authorities: the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), and the Federal Food Drug and Cosmetic Act (FFDCA). Under FIFRA, the EPA has the authority to regulate the development, sale, distribution, use, storage, and disposal of pesticides. To be registered, FIFRA required that a pesticide will not cause "unreasonable adverse effects" to human health or the environment. The Federal Food Quality Protection Act of 1996 (FQPA) modified the test for "unreasonable adverse effects," effective August 3, 1996. The EPA determines if a pesticide would cause an unreasonable adverse effect by considering "the economic, social, and environmental costs [risks] and benefits" of the use of the pesticides. FIFRA generally prohibits the sale or distribution of a pesticide unless it is registered. A product may be registered either unconditionally (see FIFRA section 3(c)5) or conditionally(see FIFRA section 3(c)(7)).

FIFRA, amended by FQPA, defines the term "unreasonable adverse effects on the environment" to mean: "(1) any unreasonable risk to man or the environment, taking into account the economic, social, and environmental costs and benefits of the use of any pesticide, or (2) a human dietary risk from residues that result from a use of a pesticide in or on any food inconsistent with the standard under section 408 of the Federal Food, Drug, and Cosmetic Act" (7 U. S. C. 136(bb)). Before the FQPA amendments took effect on August 3,

*The views expressed in this article are those of the author and do not necessarily represent those of the United States government.

1996, FIFRA contained only the first definition of “unreasonable adverse effects on the environment.” FQPA added the second definition regarding consistency with the FFDCA section 408 standard.

FFDCA gives broad authority to protect human dietary risks that might be posed by the use of any pesticide in food for humans, or as feed for animals. Under FFDCA, the EPA is responsible for determining the amount of pesticide residue that is allowable in raw and processed agricultural commodities” and that may enter commerce. The EPA determines that “there is a reasonable certainty that no harm will result from complete exposure of the pesticide chemical residue, including all anticipated dietary exposures and all other exposures for which there is reliable information”(21 U. S. C. 346a(b)(2) and c(2)(A)).

TYPES OF PESTICIDES

There are two basic types of pesticides: conventional chemical pesticides and biopesticides. Biopesticides include: microbial, biochemical, and plant-pesticides. Microbial pesticides are living organisms used as pesticides, e. g, microorganisms, fungi, and viruses. Biochemical pesticides are naturally occurring or analogous to naturally occurring pesticidal substances with a non-toxic mode of action against the target pest e. g., pheromones and other semiochemicals used for mating disruption. Plant-pesticides are defined as a pesticidal substance(s) produced in a living plant and the genetic material necessary for the production of that pesticidal substance e. g., delta-endotoxins produced by Cry genes from the soil microorganism *Bacillus thuringiensis* (Bt), expressed in crop plants. These types of plant-pesticides are referred to as Bt plant-pesticides or more commonly as Bt crops.

REGULATION OF PLANT-PESTICIDES

Regulatory Development

As part of the agreement with the US Department of Agriculture (USDA) and the US Food and Drug Administration (FDA), stated in the Office of Science Technology and Policy’s 1986 Coordinated Framework for Biotechnology Products, the EPA proposed a rule on November 23, 1994 (59 FR 60496, 60519, 60535, 60542, and 60545 Nov. 23, 1994) for the regulation of plant-pesticides. In that proposal, the EPA describes what compounds it considers to be plant-pesticides and how these would be regulated both under FIFRA and FFDCA. In this proposed policy, the EPA makes clear that it would focus its regulatory authority on the pesticidal substances and the genetic material necessary for their production rather than on the plant, *per se*, and designates the pesticidal substances as plant-pesticides. In addition to the policy statement, the EPA issued proposed regulations that define certain categories of plant-pesticides that would be exempt from regulation under FIFRA and FFDCA. Plant-pesticides not exempt would be subject to regulation.

Even though there are no specific plant-pesticide guidelines for data supporting registration, there are regulations governing the registration of these pesticides and requiring the submission of data necessary to enable the Agency to make the requisite findings for registration under section 3(c)(5) and (7). In addition, there are draft guidance documents to aid registrants in their development of appropriate data. After the plant-pesticide rule and regulations are made final, the EPA will issue proposed data requirements for plant-pesticides (including Bt plant-pesticides) and go through a public notice and comment period including holding at least one FIFRA Scientific Advisory Panel meeting.

Proposed Plant-Pesticide Rule

The main features of the rule and its status are discussed below.

Definitions

In the proposed policy, plant-pesticides are defined in FIFRA as the pesticidal substance produced in a living plant and the genetic material necessary for the production of that pesticidal substance. This definition is intended to focus the safety assessment on the pesticidal substance itself, rather than the plant in which it was produced. Inclusion of the genetic material as part of the active ingredient of the plant-pesticide recognizes the biological reality that a pesticidal substance will not be produced in a plant without a gene to direct that production. In addition, inclusion of the genetic material provides a mechanism to address the escape of the gene into other plants and a consistent regulatory coverage for parts of a plant's life cycle when the pesticidal substance may not be actively produced.

FIFRA Scope and Exemptions

All plants produce secondary plant compounds that act as pesticidal substances to protect against or mitigate pests. Some plants even produce herbicidal compounds that aid in their colonization of a habitat. The broad definition of plant-pesticide under FIFRA and the extensive knowledge of plant science about certain pesticidal traits suggest that the EPA could easily exempt categories of plant-pesticides from regulation based on a history of exposure and/or safe consumption. A major focus of the rule is to describe these exempt categories of plant-pesticides and explain the triggers for regulatory oversight of other plant-pesticides. The trigger for closer examination under FIFRA focuses on plant-pesticides that have new exposures, either dietary or environmental. Pesticidal traits derived from sources that are not sexually compatible with the host plant would probably not have a history of expression in that host plant and would, as a result, be most likely to cause adverse dietary or environmental effects. Therefore, pesticidal substance originating from a sexually compatible plant species would be exempted from regulation. Also exempted from regulation would be plant-pathogenic virus coat proteins and traits that affect only the host plant such as physical barriers or some types of disease resistance genes.

Labeling

An important feature of the EPA's regulatory approach to plant-pesticides is that it will not register the plant, but rather the plant-pesticide active ingredient and the genetic material necessary for its production. The official FIFRA label is issued to the registrant. There will be no FIFRA-type label accompanying the seed sold in commerce, but rather informational material (referred to here as labeling information) that will instruct the grower on how to use the crop expressing the plant-pesticide (e.g. Bt). The registered label (the FIFRA label) may require that registrants put certain statements or guidance on all informational materials (e.g., technical bulletins, grower guides, Internet materials, videos etc.) that may accompany the Bt crop seed or other propagative material at the time of sale, similar to the information that accompanies seeds treated with conventional pesticides. For example, an informational label statement could tell growers that certain resistance management strategies should or must be followed.

FFDCA Scope and Exemptions

The EPA also has responsibilities under FFDCA to establish a safe level of pesticide residues allowed on food crops. For plant-pesticides, the EPA believes the major human exposure to pesticidal substances will be dietary. There are numerous plant species that have been safely consumed as food. Therefore, plant-pesticides that do not represent a novel dietary exposure in the new host plant would be exempt under the proposed regulations under FFDCA. The triggers for examination under FFDCA are if the pesticidal substance from a normally inedible portion of a food plant is found in the edible portion of the new plant, if the pesticidal substance is from a food plant normally processed before consumption and introduced into a food usually eaten without processing, and if the pesticidal substance has been altered from its original structure or function. The movement of known food allergens from one part of a plant to another part of a plant is being discouraged. The plant-pesticides that qualify for an exemption from the requirement for a food tolerance are those pesticidal substances from sexually compatible plants and viral coat proteins based on the history of safe consumption of these components in the current food supply. In addition, the EPA believes there probably is no dietary risk with the consumption of the small amount of additional genetic material coding for any plant-pesticide so the genetic material necessary for the production of a plant-pesticide is also exempt from a food tolerance.

Current Status

Since the November 1994 publication of the proposed policy in the Federal Register, the EPA has been reviewing the comments received and preparing for publication of the final rule. During the comment review period, Congress passed the Food Quality Protection Act (FQPA) in August 1996 that amended both FIFRA and the FFDCA. These amendments altered some aspects of the process for assessing the food safety of pesticide chemical residues. Therefore, the EPA recently published supplemental notices in the Federal Register to notify the public how the proposed tolerance exemptions for plant-pesticides met the new safety standards of the FFDCA as amended by the FQPA. The final rule for plant-pesticides under FIFRA and associated food tolerance exemptions under FFDCA should be published soon.

PUBLIC MEETINGS HELD ON BT PLANT-PESTICIDES

While there are no published plant-pesticide data guidelines, the Agency has sponsored, or cosponsored with other Federal agencies, four conferences dealing with plant-pesticides and the pertinent data needed to perform a risk assessment: 1) a "Transgenic Plant Conference" in Annapolis, Maryland, September 8-9, 1988; 2) a meeting on "Genetically Engineered Plants: Regulatory Considerations" at the Boyce Thompson Institute for Plant Research, Ithaca, New York, October 19-21, 1987; 3) a conference on "Pesticidal Transgenic Plants: Development, Risk Assessment, and Data Needs", November 6-7, 1990, and 4) a "Conference on Scientific Issues Related to Potential Allergenicity in Transgenic Food Crops" at Annapolis, Maryland, April 18-19, 1994. In addition, the Agency has requested the advice of four scientific advisory committees on FIFRA and FFDCA-related scientific issues. On December 18, 1992, a Subpanel of the FIFRA Science Advisory Panel (SAP) was convened to review a draft policy statement on plant-pesticides and respond to a series of scientific questions posed by the EPA's approach under FIFRA. On July 13, 1993, a Subcommittee of the EPA Biotechnology Science Advisory Committee (BSAC) was convened to address a series of scientific questions primarily on the EPA's approach under FFDCA. On January 21, 1994, a joint meeting of the SAP/BSAC Subpanel on plant-pesticides was held to discuss additional scientific questions. Information from these conferences and scientific advisory committees has been used by the Agency to develop a "points to consider" document as guidance for what data are required to support the registration of plant-pesticides and development of the draft plant-pesticide policy and regulations. The Agency has also provided guidance to registrants on the elements needed for a resistance management strategy for plant-pesticides. On March 1, 1995, a Subpanel of the FIFRA SAP was convened to review the Agency's risk assessment and resistance management analysis for Bt potato (CryIIIA).

Two independent Subpanels of the FIFRA SAP met, in part, to address resistance management of Bt crops. On December 18, 1992, a Subpanel of the FIFRA SAP addressed the issue of development of pest resistance to pesticidal substances produced by plants. The Subpanel felt that delaying the evolution of resistance was very important and urged the EPA to actively assess the problem of pesticide resistance, especially when the pesticide is part of the progression toward use of "safer" pesticides. A third independent SAP Subpanel met exclusively to discuss Bt plant-pesticide resistance management issues on February 9-10, 1998. The findings of this Subpanel are discussed below.

The March 1, 1995 SAP met to discuss in part, resistance management of Bt crops. This subpanel was in agreement with the Agency's review of the Monsanto plan for Bt CryIII(A) delta-endotoxin produced in potatoes and the general elements necessary for a resistance management plan to address resistance to Bt delta-endotoxins produced in potatoes. The Agency and the SAP agreed that Monsanto's resistance management strategy for the potato variety producing the Bt CryIII(A) delta endotoxin, although adequate for the present, should be further refined in the future as additional data become available. Many of the specific questions with respect to monitoring for resistance development and strategies to retard resistance development can best be addressed when use of the potatoes producing the Bt CryIII(A) delta endotoxin has reached commercial scale production over a period of several years throughout potato producing regions. Refinements of resistance management strategies are typically needed during the years of actual use of any pesticide. Monsanto agreed to voluntarily implement the resistance management plan for the Bt CryIII(A) delta endotoxin produced in potatoes and has agreed to continue to voluntarily work with the Agency on refinements to the resistance management plan as more information is gathered during wide-scale commercial use.

Although the 1995 SAP meeting focused primarily on the review of the risk assessment and resistance management issues for Bt potatoes, the FIFRA SAP Subpanel also generally discussed resistant management issues for Bt corn and Bt cotton. The Subpanel members recommended that in order to refine existing resistance management plans, large-scale use of these plant-pesticides was needed. The Agency agreed with this approach and is allowing such large-scale use, with appropriate safeguards to protect against the development of resistance, while requiring registrants to conduct research necessary to develop acceptable long-term resistance management plans.

The Agency has raised, in general, the issue of pesticide resistance management to its Pesticide Program Dialogue Committee (PPDC) in July 1996. The PPDC supports the EPA's continued efforts to protect the use of Bt foliar pesticides and plant-pesticides. The EPA has also held two public hearings, one on March 21, 1997 (in Washington D. C.) and the other on May 21, 1997 (College Station, Texas), to solicit comments on resistance management plans for plant pesticides. There were four issues open for comment: 1)the requirement for resistance management plans, 2) scientific needs for resistance management plans, 3) use of "public good" as a criterion for the requirement of resistance management plans, and 4) 1996 performance of Bt cotton.

Approximately 100 individuals/organizations submitted written comments and/or delivered presentations regarding the subject of Bt plant-pesticide resistance management and the four issues open for comment. Copies of the written comments are available in the Office of Pesticide Programs public docket, OPP-00470.

The EPA held an Office of Pesticide Programs FIFRA SAP meeting on February 9-10, 1998 to examine the resistance management strategies for Bt delta-endotoxins expressed in potatoes, field corn, and cotton. The Agency published a recent analysis of the current resistance management strategies for Bt potato, Bt field corn, and Bt cotton in a paper entitled "The Environmental Protection Agency's White Paper on Bt Plant-Pesticide Resistance Management" (January 14, 1998)-(EPA, 1998a). In this paper, the Agency summarized the findings from the March and May 1997 public hearings on Bt plant-pesticide resistance management (OPP Docket, OPP-00470), the 1996 growing season reports on resistance management activities for Bt potato, Bt field corn, and Bt cotton, and 1997 research efforts for resistance management strategies (EPA, 1998a). The Agency asked the SAP Subpanel to review specific questions posed by the EPA based on its "White Paper. "Oral and written statements were received from approximately 20 different groups representing industry, growers or grower groups, trade organizations, academia, and environmental groups. The Subpanel provided the Agency with a final report of the meeting on April 28, 1998 (SAP, 1998). Copies of the written statements and the Subpanel report can be obtained from the OPP Docket Office (OPPTS-00231). The EPA White Paper can also be obtained electronically from the EPA Home Page at: Federal Register—Environmental Documents—"Laws and Regulations" (http: //www. epa. gov/fedrgstr/). A summary of the key points made in the Subpanel report and in the White Paper will be discussed later in this article. Other SAP meetings are planned on Bt plant-pesticide resistance management in the next several years.

Registration of Bt Plant-pesticides: Scientific Data Considerations

Each registered Bt plant-pesticide has undergone a determination that the proposed use of the plant-pesticide poses no "unreasonable adverse effects", including a thorough review of the human health and environmental risks and a benefit assessment. Under FIFRA section 3(c)(7), time-limited conditional registrations have been registered during which time the company is addressing questions that were unanswered at the time of initial application. There have been two types of plant-pesticides approved by the EPA to date: delta-endotoxins derived from Bt and coat proteins from plant pathogenic viruses. In addition, five other genes termed marker genes, used to tag the desired trait during the trait development process and carried along with the plant pesticide genes, have been evaluated by the EPA for food safety. These products have had safety assessments done by the EPA for both human health and environmental effects. The basis of the assessment was an accurate characterization of the newly introduced trait, a description of the host plant biology, and adequate information to assess the toxicity of the expressed pesticidal compound to humans and exposed non-target species. A summary of all of the science review findings and regulatory management conclusions for each of the registered Bt plant-pesticides is found in the EPA Pesticide FACT sheets (EPA 1995a, b, c, 1996a, b, 1997, 1998b, c, d).

Characterization of the Active Ingredient

Fundamental to the EPA's risk assessment of the Bt plant-pesticides was a thorough description of these plant-pesticides including the source of the inserted sequences necessary to produce the pesticidal substance and any novel proteins encoded by this introduced genetic material. For the individual delta-endotoxins, a great deal of historical information was available to the EPA due to the numerous registered microbial products known to contain such endotoxins. However, the companies were required to verify that the inserted DNA did, in fact, code for the toxins claimed and that these plant-expressed toxins were similar to those found in the microbial products. This similarity analysis was done using standard protein biochemistry analyses such as amino acid sequencing, immunological recognition as well as biological activity against target pests. Additionally, the expression of the pesticidal substance was determined for various tissues at different maturities. Since the pesticidal substances and associated proteins were adequately characterized, a reasonable prediction of the type of data necessary to evaluate potential risks for mammalian and environmental effects was proposed.

Human Health Risk Assessment

Dietary consumption was determined to be the predominant route of exposure to humans and domestic animals for the crops engineered to express these pesticidal substances. For crops producing proteinaceous pesticidal substances, mammalian toxicology was assessed by acute oral studies in the rodent. If significant prior human dietary exposure to the plant-pesticide could be documented, some acute mammalian toxicology studies were waived. When required, these acute oral studies in rodents were done with high doses of a purified test material such as 2-5gm/kg bodyweight. No abnormalities were seen in any tests done with the plant-pesticidal substances or related compounds examined to date. The EPA also assessed information provided to indicate the introduced traits were not responsible for a food allergy. This information included a screen for amino acid homology to known food allergens and an in vitro digestibility assay in artificial digestive fluids to address the potential for a protein to persist in dietary exposure and possibly induce food allergy or other toxicity. For all the pesticidal traits seen to date, the lack of mammalian toxicity has justified an exemption from the requirement for a food tolerance as required by the EPA's responsibility under FFDCA.

Environmental Fate and Ecological Risk Assessment

Ecological nontarget data needs are driven by exposure to the plant-pesticide. The pesticidal active ingredient (e. g., the Bt delta-endotoxin and the genetic material necessary for its production) is contained only within certain plant parts of the crop plant into which it has been genetically engineered. This means that nontarget organisms will only have a minimal exposure to the pesticidal active ingredient. This type of exposure situation is quite different from that associated with spray applications of pesticides. Exposure of nontarget organisms to plant pesticides would occur primarily when wildlife feed on plants expressing the pesticidal substance or if sexual transfer of the new trait(s) to nontarget wild/weedy relatives occurs by cross-pollination.

Therefore, the ecological effects data are based on the expected exposure of non-target species to the plant-pesticide and by geographical use considerations based on the proximity to related cultivars or weedy relatives that can cross-pollinate with plants expressing the pesticidal substance. This amounts to a case-by-case analysis. Each risk assessment is made from an analysis of the properties of the engineered organism and its target environment, i.e. on the nature of the gene being introduced, the plant receiving the gene, the environment where the plant will be grown, and the species susceptible to the effects of the introduced gene. The degree of scrutiny depends on the type of gene product, i.e. the protein or the product of metabolic pathway more akin to conventional chemicals, and the intended mode of action. Protein products are not expected to pose much, if any, nontarget hazard outside of living plant tissue, while chemical compounds may be more resistant to degradation, more toxic, and have a broader exposure.

For environmental effects, the EPA has examined the toxicity of the plant-pesticidal traits in plant tissue to non-target organisms. The specific non-target organisms tested were chosen as indicators of potential environmental effects and are similar to those examined for microbial or biochemical pesticides. The choice of appropriate indicator organisms for testing was based on the potential exposure from data on plant-pesticide expression in the engineered plant. Trait expression data are used to predict exposures for target organisms that may impinge on resistance management decisions. For Bt plant-pesticides, the EPA has examined the toxicity of the pesticidal substance to birds, fish, honeybees and certain other beneficial insects. Among the beneficial species, data on Collembola and earthworm species may be required if crop residue exposure is a possibility. In the honeybee study, effect studies on immature individuals as well as adults may be required if exposure to the Bt delta-endotoxin in pollen is expected. The Agency has examined the environmental fate endpoints regarding the movement and expression of the gene trait in other plant species (biological fate) and persistence of the pesticidal product in the environment (chemical fate). Specifically the environmental fate endpoints are: a) gene product (chemical) persistence and movement in the environment, b) potential for the genetically engineered plant to survive outside of cultivation and become a weed (i.e. weediness potential), and c) potential for the introduced genetic trait to confer a selective advantage to a wild relative (i.e. outcrossing potential and ecosystem disruption). Data on the toxicity of the gene product to nontarget insects are required when the proposed use pattern indicates that insect predators and/or parasites may be exposed to the pesticide. Appropriate test species should be chosen based on the ecosystem where the plant-pesticide will be used.

THE EPA'S REVIEW OF BT-PLANT-PESTICIDE RESISTANCE MANAGEMENT

With a greater focus on pollution prevention and pesticide risk reduction, the EPA believes that it is important to implement effective resistance management strategies for pesticides such as Bt plant-pesticides. Bt plant-pesticides and Bt microbial pesticides are recognized as safer pest control resources and are part of the "public good."A great deal of Agency attention has focused on the potential development of resistance to the delta-endotoxins of Bt genetically-engineered into plants (Bt plant-pesticides). This is because Bt plant-pesticides produce the pesticidal active ingredient, the Bt delta-endotoxin(s), throughout the growing season. Long-term exposure to a pesticide is one of the factors that increases the potential selection pressures upon both the target pests and any other susceptible insects feeding on the transformed crop. The EPA recognizes the value of Bt plant-pesticides as effective and safer pest management tools and has determined it is appropriate to conserve this resource by requiring resistance management plans for certain transformed crops. In addition to Bt delta-endotoxins being used in plant-pesticides, they are also widely used in a variety of Bt microbial spray products on many crops. Because the high benefits of using Bt plant-pesticides could be diminished by the development of resistance to individual Bt plant-pesticides and the threat cross-resistance poses to Bt microbial pesticides, the Agency has requested that all registrants for Bt plant-pesticides voluntarily submit pesticide resistance management strategies as part of the registration submission.

The Agency identified seven elements that should be addressed in a Bt plant-pesticide resistance management plan (Matten and Lewis, 1995). These elements are: 1) knowledge of pest biology and ecology, 2) appropriate dose expression strategy, 3) appropriate refugia (primarily for insecticides), 4) monitoring and reporting of incidents of pesticide resistance development, 5) employment of IPM, 6) communication and educational strategies on use of the product, and 7) development of alternative modes of action. These elements were presented to the March 1, 1995 Federal Insecticide, Fungicide, and

Rodenticide Act (FIFRA) Science Advisory Panel (SAP) Subpanel on Plant-Pesticides. The SAP Subpanel approved of these seven factors (SAP, 1995; see Office of Pesticide Program (OPP) docket, OPP-00401). These elements are discussed in more detail in Matten et al. (1996) and EPA White Paper on Bt plant-pesticide resistance management (1998a). All registrants of Bt plant-pesticides voluntarily submitted Bt plant-pesticide insect resistance management strategies to the Agency for Bt delta-endotoxins produced in potato (Bt potato); field corn (Bt corn), sweet corn (Bt sweet corn), and popcorn (Bt popcorn); and cotton (Bt cotton). When necessary, the Agency made certain recommendations and requirements of registration for data to develop and implement long-term resistance management strategies as part of the registration decisions. The Agency's reviews of the resistance management strategies for registered Bt plant-pesticides are summarized in the EPA Pesticide FACT sheets (EPA 1995a, b, c, 1996 a, b, 1997, 1998 b, c, d).

In May 1995, the Agency registered the CryIIIA delta-endotoxin and the genetic material necessary for its production in potato (Bt potato). Following the advice of the March 1, 1995 SAP Subpanel, a resistance management plan for Monsanto/Naturemark's Bt potato was voluntary rather than mandatory. EPA and Monsanto/Naturemark have worked together on the development and implementation of appropriate long-term resistance management following the registration of Bt potatoes in 1995. Monsanto/Naturemark requires growers to sign a Grower Agreement to use the technology. The Grower Agreement specifies that each grower must follow a mandatory structured refuge. The original Bt potato resistance management strategy has been refined as more data became available.

The Agency mandated specific resistance management data requirements and mitigation measures with a resistance management strategy for all of the Bt corn and Bt cotton registrations. Registrations for Bt corn plant-pesticide products expire April 1, 2001 and the registration for Bt cotton plant-pesticide products expire January 1, 2001. These registrations were conditional to allow, in part, for completion of the studies related to resistance management. Collection of various data, e. g. , target pest biology and behavior, secondary pest biology and behavior, population dynamics, cross-resistance potential, refuge strategies, dose deployment adequacy, baseline susceptibility, discriminating concentration, monitoring, and reporting were made conditions of registration for the Bt corn and Bt cotton registrations. Refuge requirements were mandatory for Bt cotton. Development of draft refuge options by August 1998, a final refuges strategy by January 1999 with implementation by April 1, 2001were required of Bt corn registrations. As part of the terms and conditions of registration, the EPA will reevaluate the effectiveness of each registrant's resistance management plan before the expiration date and decide on whether to convert the registration to a non-expiring registration.

The Agency registered the use of CryIA(b) in sweet corn (Bt sweet corn) and popcorn (Bt popcorn) in March 1998. Specific monitoring and sales reporting were made requirements of the Bt sweet corn registration. No specific refuge requirements were mandated for Bt sweet corn (Event BT 11) because harvesting occurs before insects mature, approximately 21 days after silking. Growers are instructed in all labeling and technical material to destroy any CryIA(b) sweet corn silks that remain in the fields following harvest or within a short period of time (a maximum of one month) later in accordance with local production practices. Stalk destruction will help reduce the possibility of larvae surviving to the next generation. The Bt sweet corn registration expires April 1, 2001. The Agency mandated specific refuge requirements on the use of Bt popcorn (Event 176) based on the USDA NC-205 recommendations (Ostlie et al. , 1997). Specifically, a 20-30 percent unsprayed or 40 percent sprayed non-Bt corn structured refuge in close proximity to Bt corn is required. Spraying with pesticides reduces the effectiveness of the refuge. The refuge must be established within 0.5 miles of the Bt corn. Specific monitoring and sales reporting requirements were also made for the Bt popcorn registration.
All previous data required for Bt field corn were also required for Bt popcorn. The Bt (Event 176) field corn and popcorn registrations expire April 1, 2001.

The Agency registered the use of Cry9(c) field corn in May, 1998. This is a one-year registration for 120,000 acres for animal feed, industrial non-food, and seed increase uses expiring on May 30, 1999. EPA mandated specific refuge requirements based on the USDA NC-205 recommendations (Ostlie et al., 1997). Specifically, a 25 percent unsprayed or 40 percent sprayed non-Bt corn structured refuge must be planted within 1500-2000 feet of Bt corn. Because of the one-year duration of this registration, only sales reporting and grower education are required as part of this registration. Additional resistance management factors must be addressed for a full commercial registration.

All stakeholders are concerned with how the EPA regulates resistance management for Bt plant-pesticides. Scientifically sound long-term resistance management strategies are essential to the survival of Bt plant-pesticides, maintaining the effectiveness of Bt microbial pesticides, and reduction in the risks from the use of chemical pesticides. The EPA is continuing to evaluate and refine how it regulates resistance management of Bt plant-pesticides. The EPA has worked and is working with stakeholders (industry, extension and research entomologists and other academic scientists, USDA, individual growers, user groups, trade organization, public interest groups, and government agencies) to address long-term resistance management strategies for Bt plant-pesticides.

The EPA White Paper on Bt Plant-Pesticide Resistance Management

As noted earlier, the EPA published a recent analysis of the current resistance management strategies for Bt potato, Bt field corn, and Bt cotton in a paper

TABLE 1. REGISTERED BT PLANT-PESTICIDES AND ACTIONS PENDING

Events/ Products	Year Registered	Expiration Date	Toxin	Crop	Company(s)
New Leaf®	May 1995	None	Cry IIIA	Potato	NaturMark/ Monsanto
Bollgard™	October 1995	January 2001	Cry IA (c)	Cotton	Monsanto
Event 176	August 1995	April 2001	Cry I(A)b	Field Corn	Novartis Seeds and Mycogen Corporation
Event 176	March 1998	April 2001	Cry I(A)b	Popcorn	Novartis Seeds
BT11	October 1996	April 2001	Cry I(A)b	Field Corn	Novartis Seeds
BT11	March 1998	April 2001	Cry I(A)b	Sweet Corn	Novartis Seeds
MON810	December 1996	April 2001	Cry I(A)b	Field Corn	Monsanto
DBT-418	March 1997	April 2001	Cry IA (c)	Field Corn	DeKalb Genetics Corporation
CBH-351	May 1998	May 1999	Cry 9(c)	Field Corn	AgrEvo/PGS

entitled "The Environmental Protection Agency's White Paper on Bt Plant-Pesticide Resistance Management" (EPA, 1998a). A summary of the EPA's White Paper is provided below.

WHITE PAPER SUMMARY

Since Bt plant-pesticides became commercially available in 1996, growers have adopted this technology as part of their Integrated Pest Management (IPM) practices to control pests in potato, corn, and cotton. Based on industry reports sent to the EPA, the greatest adoption of Bt crop technology has been by cotton growers, especially in the southeastern United States in 1996, with about 13 percent of the cotton acreage, 1. 8 million acres, and an estimated 2.2 to 2.4 million acres in 1997 planted in Bt cotton. Corn growers planted about 400,000 acres of Bt corn in 30 states in 1996 and an estimated four million acres in

1997. Potato growers planted about 10,000 acres of Bt potato in 1996 and an estimated 25,000 acres in 1997. The differences in the rate of adoption of Bt potato, Bt corn, and Bt cotton are likely due, in part, to the availability of effective alternatives, the cost of the biotechnology crop, extent of regional pest problems, and familiarity and acceptance of the technology by growers. For example, there are several insecticide alternatives for control of Colorado potato beetle. The cost of and lack of familiarity with the technology and type of hybrids available may have discouraged a wider adoption by corn growers in the first years of commercialization. The adoption rate for Bt cotton was especially high for a new technology because few, if any, effective alternatives existed to control tobacco budworm (*Heliothis virescens* (Fabricius), TBW) in cotton especially where insect resistance to registered conventional pesticides was extremely high in states such as Mississippi and Alabama.

No evidence exists that resistance to Bt delta-endotoxins expressed in transgenic potato, corn, or cotton has developed in the 1996 or 1997 growing season. Monitoring for changes in susceptibility to the different registered Cry proteins, CryI(A)b, CryI(A)c, and CryIIIA, has been conducted for TBW, Colorado potato beetle (Leptinotarsa decemlineata (Say), CPB), European corn borer (*Orsinia nubilalis* (Habner), ECB), cotton bollworm (*Helicoverpa zea* (Boddie), CBW), and pink bollworm (*Pectinophora gossypiella* (Saunders), PBW). Baseline susceptibility studies show a wide-range of variability, so it is important to look at susceptibility changes in the context of the baseline range for a particular geographic location of the pest (i. e., different portions of a state). No changes in baseline susceptibility have been detected for any of the target insects exposed to the Bt delta-endotoxins expressed in Bt potato, Bt corn, and Bt cotton. This information indicates that there has been no measured increase in tolerance to date to the Bt delta-endotoxins expressed in potato, field corn, and cotton.

Toxin-tolerant colonies of CPB, ECB, TBW, CBW, and PBW have been created in the laboratory through selection against purified Cry proteins or mixtures of Cry proteins using Bt microbial pesticides. The ability of insects to develop high levels of tolerance to Bt in the laboratory indicates that these insects possess the genetic potential to develop resistance to Cry delta-endotoxins expressed as Bt plant-pesticides. Laboratory-tolerant colonies are useful to study the genetics and biochemistry of resistance of possible resistance mechanisms that may exist in the field. It is unlikely that laboratory selective procedures provide the identical selective conditions that exist in the field. The ability to select for tolerance to Cry proteins in the laboratory in different insect pests indicates that it is prudent to use appropriate resistance management strategies.

In 1996, cotton bollworm populations were the highest seen in ten years in parts of the Cotton belt (i. e., Brazos Valley, Texas, Mid-South and Southeast growing regions). Monsanto reported to the Agency the potential Bt cotton control failures as early as July, 1996, and followed up with a full analysis of these incidents in the fall of 1996. Monsanto performed studies in all Bt cotton areas affected by high CBW infestations to determine whether CBW susceptibility to the CryI(A)c toxin had changed, whether the Bt cotton was expressing the CryI(A)c, and whether the CryI(A)c expression levels and patterns had changed. Monsanto also provided the results of these studies in its 1996 annual report on resistance monitoring activities. Results of these studies indicate that there was no change in CBW susceptibility and no change in Bt expression in the Bt cotton areas affected by high cotton bollworm infestations. These studies indicated no detectable level of resistance in these populations. Unusually high infestation levels of CBW may have, in part, resulted from the dramatic increase in corn acreage in the South. In addition, CBW has a lower sensitivity (about 25-fold lower) to the CryI(A)c delta-endotoxin relative to TBW and PBW. Scouting detected CBW larvae lower in the plant canopy of Bt cotton than expected and, in some cases, supplemental chemical insecticides were used to control CBW. The fact that supplemental insecticides might be necessary to control unusually high CBW infestations was not unexpected and was considered in the Agency's review of the initial resistance management strategy for Bt cotton. Modifications to the CBW scouting program for Bt cotton were made for the 1997 season to improve detection of the CBW larvae which might escape the Bt delta-endotoxin by feeding on blooms and bloom tags that are lower in the cotton plant.

The vast majority of cotton growers complied with the structured refuge requirements. Cotton growers seem to prefer the 20 percent sprayed refuge option that allows them to treat the refuge with chemical insecticides normally used to control TBW, CBW, and PBW (except for Bt microbial pesticides). This option appears to provide a higher yield in the refuge acreage than the four percent unsprayed refuge option that often had higher management costs and lower yields. Most cotton researchers, who commented at the two public hearings held in March and May 1997, favored the 20 percent structured refuge as a better strategy for Bt cotton resistance management. They believed that this refuge option is more likely to provide a greater percentage of susceptible insects throughout the growing season to mate with any rare resistant individuals that might survive in the Bt cotton fields. The EPA received comments that the four percent unsprayed refuge was decimated early in the growing season so that there were few, if any, adult moths surviving to mate with any resistant insects that survived in the Bt cotton fields later in the growing season. The EPA believed that during the first five years following the first complete growing season in 1996, there would not be enough Bt corn acreage to provide substantial Bt selection pressure for the development of ECB resistance. Consequently, the EPA did not mandate specific refuge requirements for Bt corn, but the EPA has required research data on the size, structure, and deployment of a structured refuge. A combination of temporal and structured refuges is being studied. A draft refuge strategy must be submitted to the

Agency by August, 1998, and a final refuge strategy is required to be submitted by January, 1999. Implementation of an EPA-approved structured refuge plan or an EPA-approved alternative resistance plan is required no later than April 1, 2001. Monsanto and Dekalb are requiring structured refuges, either a five percent unsprayed or 20 percent sprayed structured refuge, as part of grower agreements. Beginning in the 1998 growing season, Novartis Seeds has adopted the NC-205 consortium's recommendations published in NCR-602 publication entitled "Bt Corn & European Corn Borer - Long Term Success Through Resistance Management" (Ostlie et al., 1997). As noted earlier, the NC-205 recommended a 20-30 percent structured non-Bt corn refuge to prevent Bt delta-endotoxin exposure to 20-30 percent of the larval populations. They also recommended that in continuous corn acreage sprayed with insecticides, the refuge size would be increased to 40 percent to compensate for larval mortality. In addition, a smaller refuge size may also be suitable if there are many alternate hosts providing adequate numbers of susceptible ECB. Mycogen has not made any specific refuge recommendations in its Grower Guide, but is supportive of the use of refuges and supportive of the NC-205 recommendations.

Monsanto/Naturemark requires a structured refuge as part of grower agreements for use of Bt potato. The EPA has required that Monsanto mandate specific refuge requirements as a condition of registration for Bt cotton, either a four- percent unsprayed or 20 percent sprayed structured refuge. Monsanto has implemented these refuge requirements through a grower agreement. Research is underway to study whether in-field narrow strip refuges or mixed Bt cotton/ non-Bt cotton seed mix options are viable for PBW resistance management because of the limited larval movement. Based on Monsanto's reports to the Agency, there has been a high level of compliance with a structured refuge in Bt cotton and Bt potato. The EPA is encouraged by reports of a tremendous reduction in the use of conventional insecticides that has resulted from adoption of Bt cotton (i.e., 250 thousand gallons of formulated product).

A great deal of research is underway to study the elements that are necessary for long- term resistance management strategies for Bt potato, Bt corn, and Bt cotton. Specific research data were required as part of the Bt corn and Bt cotton conditional registrations and was recommended for the Bt potato registration. These data included: the dosage effectiveness on the target pest(s), monitoring data including baseline susceptibility and validation of the diagnostic dose concentration, pest biology and ecology, influence of the Bt crop on secondary lepidopteran pests, the impact of CryIA(b)/CryIA(c) produced in Bt corn on the selection of CEW/CBW resistance in Bt corn and Bt cotton, impact of Bt on CEW overwintering survival and fecundity, effective refuges, alternate hosts as refuges, and cross-resistance potential. Additionally, alternative pest control strategies and integration into existing IPM programs are being examined for each of the Bt plant-pesticides. All of these data will provide the basis for specific improvements to the existing resistance management strategies. Future information is especially important for understanding the selection of CEW/CBW resistance in overlapping Bt corn and Bt cotton regions of the southern United States. This is because CEW/CBW usually moves from silking corn to cotton, has multiple generations per year, and overwinters in the South. Exposure to Cry delta-endotoxins produced in both Bt corn and Bt cotton in two or more generations per year could rapidly accelerate development of resistance. Research results and predictive models studying this situation are expected to be submitted to the Agency in 1998.

Science Advisory Panel Review of EPA's White Paper

The Agency asked the February 9-10, 1998 OPP FIFRA Science Advisory Panel Subpanel on Bt plant-pesticide resistance management to review specific questions posed by the EPA based on its "White Paper" (EPA, 1998a) on Bt plant-pesticide resistance management strategies for Bt potato, Bt corn, and Bt cotton. Oral and written statements were received from approximately 20 different groups representing industry, growers or grower groups, trade organizations, academia, and environmental groups. The Subpanel provided the Agency with a final report of the meeting on April 28, 1998 (SAP, 1998). Copies of the written statements and the Subpanel report can be obtained from the OPP Docket Office (OPPTS-00231). The Subpanel's report can also be obtained electronically. A brief summary of key points made in the Subpanel report is provided below. The Subpanel agreed with the EPA that the wide-spread use of crops that express Bt insecticides is in the public good by providing additional pest control options to producers and by reducing the use of conventional pesticides. The Subpanel also agreed with the EPA that appropriate resistance management is necessary to suppress the emergence of insect resistant to Bt toxins expressed in transgenic crop plants. The Subpanel recognized that resistance management programs should be based on the use of both high dose expression levels and structured refuges designed to provide sufficient numbers of susceptible adult insects with a minimum of economic impact on producers. Resistance management strategies should be sustainable and to the extent possible, strongly consider grower acceptable and logistical feasibility. The Subpanel made the following overall recommendations and conclusions: a) EPA should require the use of structured refuges in all registrations of Bt crops (unless proven to be harmful), b) a refuge/high dose strategy is needed to delay the development of resistance for targeted pests, c) precision of research models is good for evaluating refuge options, but is limited in establishing specific refuge options, d) the EPA should establish regional working groups for specific implementation of resistance management strategies for each of the major Bt crop producing regions, e)grower participation is the key factor for successful implementation of a resistance management strategy, and f) regulatory strategies should serve growers with a sustainable approach to resistance management that encourages compliance with a resistance management strategies. The Subpanel defined a high dose as 25 times the amount of Bt delta-endotoxin necessary to kill susceptible individuals. A cultivar could be considered to provide a high dose if verified by at least two of the following five approaches: 1) Serial dilution bioassay with artificial diet containing lyophilized tissues of Bt plants using tissues from non-Bt plants as controls; 2) bioassays using plant lines with expression levels approximately 25-fold lower than the commercial cultivar determined by quantitative ELISA or some more reliable technique; 3) survey large numbers of commercial plants in the field to make sure that the cultivar is at the LD99.9 or higher to assure that 95 percent of heterozygotes would be killed (see Andow and Hutchison, 1998); 4) similar to (3) above, but would use controlled infestation with a laboratory strain of the pest that had an LD50 value similar to field strains; and 5) determine if a later larval instar of the targeted pest could be found with an LD50 that was about 25-fold higher than that of the neonate larvae. If so, the stage could be tested on the Bt crop plants to determine if 95 percent or more of the later stage larvae were killed.

The Subpanel defined structured refuges to "include all suitable non-Bt host plants for a targeted pest that are planted and managed by people. These refuges could be planted to offer refuges at the same time when the Bt crops are available to the pests or at times when the Bt crops are not available. "The Subpanel stated that a good resistance management strategy should provide efficacy of the toxin(s) for more than 10 years. The Subpanel suggested that a production of 500 susceptible adults in the refuge that move into the transgenic fields for every adult in the transgenic crop area (assuming a resistance allele frequency of 5 $X10^{-2}$) would be a suitable goal. The placement and size of the structured refuge employed should be based on the current understanding of the pest biology data and the technology.

MONITORING FOR BT PLANT-PESTICIDE RESISTANCE

The EPA currently mandates that both baseline susceptibility and a discriminating concentration be developed for each labeled target pest for Bt corn and Bt cotton registrations (see EPA 1995b, c, 1996a, 1996b, 1997, 1998b, c, d).

Monsanto/Naturemark voluntarily instituted a monitoring program for Bt potato. If a discriminating concentration assay is unavailable then the registrant must proceed with efforts to develop discriminating concentrations assays for these target pests and ensure that monitoring studies are conducted annually to determine the susceptibility of all the labeled target pests to the Bt plant-pesticide. The resistance-monitoring program is being developed to measure increased tolerance to Bt plant-pesticides above regional/state/local baseline ranges. The results of the baseline susceptibility and monitoring studies must be communicated to the Agency on an annual basis, by January 31 of the year following the population collections for a given growing season. These annual reports must also describe progress towards development of a discriminating dose assay for each target pest. These current requirements provide the Agency with standardized information to determine whether resistance evolution is occurring. However, there are additional monitoring techniques, other than the discriminating concentration assay, which may be more aggressive to proactively determine whether resistance is developing such as a F2 screen (Andow and Alstad, 1998, Andow et al., 1998), in-field surveys including sentinel plots, screening against test stocks (see Gould et al., 1997). The SAP Subpanel report (SAP, 1998) provides a more detailed discussion of available monitoring techniques.

NEXT STEPS

The EPA is reviewing the Subpanel report and other materials submitted as a result of the February 9-10, 1998 SAP Subpanel Meeting. This information will contribute to how EPA continues to evaluate and refine its regulation of resistance management for Bt plant-pesticides.

The EPA will continue to work with stakeholders from industry, Extension and research entomologists and other academic scientists, user groups, trade organizations, public interest groups, and government agencies to address long-term resistance management for Bt plant-pesticides.

REFERENCES

Andow, D.A. and Alstad, D.N. 1998. The F2 screen for resistance alleles. *J. Econ. Entomol*. 91:572-578

Andow, D.A., Alstad, D.N., Pang, Y.H., Bolin, P.C., and Hutchison W.D. 1998. Using a F2 screen to search for resistance alleles to *Bacillus thuringiensis* toxin in European corn borer (Lepidoptera: Crambidae). *J. Econ. Entomol.* 91:577-584

Andow, D.A. and Hutchison, W.D. 1998. Bt corn resistance management. In "Now or never: Serious new plans to save a natural pest control" Mellon, M. and Rissler, J. [eds.]. Union of Concerned Scientists, Cambridge, MA

Gould, F.A., Anderson, A., Sumerford, D., Heckel, D.G., Lopez, J., Micinski, S., Leonard, R., and Laster, M. 1997. Initial frequency of alleles for resistance to *Bacillus thuringiensis* toxins in field populations of *Helioithis virescens*. Proc. Natl. Acad. Sci., USA. 94: 3519-3523

Matten, S.R. and Lewis, P.I. 1995. EPA and Bt Plant-Pesticide Resistance Management. NBIAP News Report. December, 1995

Matten, S.R., Lewis, P.I., Tomimatsu, G., Sutherland, D.W.S., Anderson, N., and Colvin-Snyder, T.L. 1996. The US Environmental Protection Agency's Role in Pesticide Resistance Management. In Molecular Genetics and Evolution of Pesticide Resistance. T.M. Brown (ed.) pp. 243-253. American Chemical Society Symposium Series No. 645, American Chemical Society, Washington DC

Ostlie, K.R., Hutchinson, W.D., and Hellmich, R.L. [eds.] 1997. North Central Regional Research Project (NC-205) Technical Committee. 1997. Bt-Corn & European Corn Borer: Long-Term Success Through Resistance Management. North Central Regional Extension Publication NCR 602. University of Minnesota, St. Paul, MN

Scientific Advisory Panel, Subpanel on Plant-Pesticides, March 1, 1995. 1995. A set of scientific issues were considered in connection with Monsanto Company's application for registration of a plant-pesticide containing the active ingredient *Bacillus thuringiensis* subsp. *tenebrionis* delta-endotoxins. (Docket Number: OPP-00401)

Scientific Advisory Panel, Subpanel on *Bacillus thuringiensis* (Bt) Plant-Pesticides, February 9- 10, 1998. 1998. Transmittal of the final report of the FIFRA Scientific Advisory Panel Subpanel on *Bacillus thuringiensis* (Bt) Plant-Pesticides and Resistance Management, Meeting held on February 9-10, 1998. (Docket Number: OPPTS-00231)

_____. 1994. Plant-pesticides subject to the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and the Federal Food, Drug, and Cosmetic Act (FFDCA); Proposed Policy, Federal Register 59: 60496, November 23, 1994. Washington, DC: US Environmental Protection Agency

_____. 1995a. Pesticide Fact Sheet for *Bacillus thuringiensis* subsp. *tenebrionis* CryIII(A) Delta-Endotoxin and the Genetic Material Necessary for Its production in Potato. Washington, DC: US Environmental Protection Agency

_____. 1995b. Pesticide Fact Sheet for *Bacillus thuringiensis* subsp. *kurstaki* CryI(A)b Delta-Endotoxin and the Genetic Material Necessary for Its Production (Plasmid Vector pCIB4431) in Corn. Washington, DC: US Environmental Protection Agency

_____. 1995c. Pesticide Fact Sheet for *Bacillus thuringiensis* subsp. *kurstaki* CryI(A)c Delta-Endotoxin and the Genetic Material Necessary for Its production in Cotton. Washington, DC: US Environmental Protection Agency

_____. 1996a. Pesticide Fact Sheet for *Bacillus thuringiensis* subsp. *kurstaki* CryI(A)b Delta-Endotoxin and the Genetic Material Necessary for Its Production(Plasmid Vector pZ01502) in Corn. Washington, DC: US Environmental Protection Agency

_____. 1996b. Pesticide Fact Sheet for *Bacillus thuringiensis* subsp. *kurstaki* CryI(A)b Delta-Endotoxin and the Genetic Material Necessary for Its Production in Corn. Washington, DC: US Environmental Protection Agency

_____. 1997. Pesticide Fact Sheet for *Bacillus thuringiensis* subsp. *kurstaki* CryI(A)c Delta-Endotoxin and the Genetic Material Necessary for Its Production in Corn. Washington, DC: US Environmental Protection Agency

_____. 1998a. The Environmental Protection Agency's White paper on Bt Plant-Pesticide Resistance Management. January 14, 1998. [EPA Publication 739-S-98-001]. Washington, DC: US Environmental Protection Agency, Biopesticides and Pollution Prevention Division

_____. 1998b. Pesticide Fact Sheet for *Bacillus thuringiensis* subsp. *kurstaki* CryI(A)b Delta-Endotoxin and the Genetic Material Necessary for Its Production(Plasmid Vector pZ01502) in Corn. Washington, DC: US Environmental Protection Agency

_____. 1998c. Pesticide Fact Sheet for *Bacillus thuringiensis* subsp. *kurstaki* CryI(A)b Delta-Endotoxin and the Genetic Material Necessary for Its Production (Plasmid Vector pCIB4431) in Corn. Washington, DC: US Environmental Protection Agency

_____. 1998d. Pesticide Fact Sheet for *Bacillus thuringiensis* subsp. *tolworthi* Cry9(c) Delta-Endotoxin and the Genetic Material Necessary for Its Production in Corn. Washington, DC: US Environmental Protection Agency

The Seed Industry and Agricultural Biotechnology

MURRAY ROBINSON
President, Delta and Pine Land Company
Scott, MS

When discussing matters of the environment, private industry is often falsely portrayed by some environmental groups as an enemy of our ecosystem. I am here today, as a representative of the agri-business industry, to address concerns of agricultural biotechnology and its impact on the environment, particularly the concerns surrounding the environmental impact of gene escape from transgenic plants to wild plants and the development of resistance by pests to genetically altered hosts.

For the past decade I have served as the president of Delta and Pine Land Company (D&PL). D&PL is a breeder, developer, and marketer of cotton and soybean planting seed. We're based in Scott, MS, which is in the heart of the Mississippi Delta. Our Company comprises three seed companies: Deltapine Seed, also based in Scott; Paymaster Cottonseed, based in Lubbock, TX, and Sure Grow Seed, based in Centre, AL. Our international division, D&PL International, is headquartered in Scott, as well. Through these divisions, D&PL provides seed varieties that currently plant more than 70 percent of US cotton acreage and 10 percent of Southern US soybean acreage.

Delta and Pine Land Company became a provider of biotechnology in 1996 when we, in conjunction with Monsanto, introduced one of the first successful transgenic crops to the United States and the world. The crop was a variety of cotton called NuCOTN 33B. This variety contains a Bt (*Bacillus thuringiensis*) gene that controls the bollworm and tobacco budworm, and pink bollworm pests that have historically plagued cotton farmers. Other seed companies have incorporated Bt genes into corn and potatoes.

In 1997, D&PL and Monsanto introduced Roundup Ready® cotton to the marketplace, and in 1998 we followed with our commercial introduction of

Roundup Ready® soybeans. Roundup Ready® has expanded farmers' options for weed control by allowing them to spray Roundup herbicide over the top of their crops, which does not damage the cotton or soybean plant when appropriately applied. This technology offers significant advantages to our farmers who experience weed problems.

As a participant in the delivery system for genetically enhanced crops, D&PL supports biotechnology as a means to better serve our customers and to improve farming practices that will benefit the farmer and the environment.

Environmental Benefits of Biotechnology

Bt "in-plant" pesticide is a highly effective product that enables our customers to lower their costs and improve the efficiency of their operations. By providing Bt cotton to our customers, we are enabling them to increase the success of their farming operations. Farmers have enthusiastically welcomed the introduction of insect-resistant cotton because of its effective pest control and its ability to reduce costs. In 1996, for example, an Arizona farmer planted 40 percent of his acreage to Bt cotton. This farmer described his experience as both outstanding and incredible. Not only were his costs $100 per acre less for Bt (including the technology fee) than for conventional cotton, but his yields averaged one bale more per acre for Bt than for conventional cotton.

In addition to having no pink bollworm or other bollworm activity in his Bt cotton, this Arizona grower did not need to spray for other pests. Neither the whitefly nor lygus reached levels that would trigger treatment according to University of Arizona guidelines. Beneficials, particularly spiders, were present in high numbers in this case and played an important role in reducing the numbers of insect pests.

Bt cotton offers cost saving benefits, and has been found by the Environmental Protection Agency (EPA) to be safe to humans and the environment and to offer many environmental benefits. Because the insect control agent is contained within the plant, traditional exposure of the environment and of workers to these pesticides during mixing, loading, and application is eliminated. The use of transgenic Bt crops can also reduce the environmental loading of conventional insecticides. Transgenic Bt also eliminates problems associated with the use of spray materials, including the exposure of nontarget sites.

In 1996, Bollgard cotton was planted on 42 percent of the Mississippi cotton acres. End of season surveys indicated Bollgard fields received an average of less than one pesticide treatment per field for bollworm and budworm control compared to 3.05 treatments per field for conventional cotton. In 1996, transgenic cotton reduced conventional pesticide application by 250,000 gallons. An additional environmental benefit is that the Bt protein does not persist in the plant residue and degrades rapidly, unlike conventional pesticides.

In 1996, 77 percent of Alabama's 560,000 cotton acres were planted to

Bollgard cotton. An Extension entomologist noted that Alabama went from the worst year on record for cotton insect losses (more than $41 million) in 1995, to in 1996, the lowest amount of insecticide applications and usage since the introduction of synthetic insecticide in the 1940s. Less than 20 percent of the total cotton acreage in Alabama received any foliar insecticides in 1996. Less than 10 percent of the Bt acreage was treated a single time. Most of this was in the Gulf Coast region where plant bug sprays had suppressed beneficials and fall armyworm populations were heaviest. By reducing the amount of pesticides applied to cotton acreage, biotechnology is providing immediate and ongoing benefits to the environment.

Roundup Ready®— Currently, Roundup Ready® herbicide tolerance genes are in approximately 35 percent of US cotton acreage with the potential to reach 95 percent of US cotton acreage. Herbicide-tolerant genes currently make up about 15 percent of US soybean acreage, with the potential to reach the same level of US market coverage as herbicide-tolerant cotton. As previously stated, Roundup Ready® cotton and soybeans have been popular with farmers because of the advantages they offer for weed control and crop management improvements. As with the environmental benefits of Bt, herbicide tolerance allows many farmers to use smaller amounts of chemicals in their crops. Therefore, a reduced amount of chemicals is introduced into the environment.

Roundup Ready® varieties also assist with conservation tillage in controlling soil erosion. Soil erosion due to wind and water create environmental and agricultural sustainability issues. When water runs off from agricultural land it carries soil and nutrients with it. This movement can “silt” streams, and nutrients support increased algae growth. Loss of topsoil from the land decreases its productivity. Conservation tillage leaves plant residue on the surface to protect soils from wind erosion and provides greater infiltration of rainwater thus decreasing runoff.

While conservator tillage has been a noble objective, adoption has been complicated by a lack of options for weed control. Herbicide tolerant varieties developed through molecular biology provide a tool that makes conservation tillage more feasible. In 1997, 109.8 million (37 percent) of US cropland acres were planted using conservation tillage. Experts expect the trend toward minimum-till and no-till farming to continue at an accelerated pace with the availability of herbicide tolerant cotton, soybeans, and corn.

According to scientific studies, Roundup should be a preferred herbicide in the environment for several reasons. It provides broad-spectrum, nonselective, postemergence effective weed control on a broad range of weeds. It does not move in water due to strong binding with soil. It produces no solid residues. It rapidly degrades to carbon dioxide, water and soil nutrients. It is essentially nontoxic to mammals, birds, fish, insects, and most bacteria. It has also had extensive use around the world since 1974, and has not induced Roundup herbicide-resistant weeds.

Environmental Risks of Biotechnology

Certain environmental groups are of the opinion that the biotechnology used by our industry is harmful to the environment. Delta and Pine Land Company, as well as our partners in biotechnology, disagree with this opinion. According to the American Crop Protection Association, there is no credible scientific evidence to date showing that Bt plant pesticides pose a risk of adverse effects to humans or other organisms, or that in-field uses have increased insect resistance. Nor can the mere potential for resistance development be equated with an "unreasonable adverse effect on the environment," as has been claimed.

As a provider of biotechnology to the marketplace, we accept the responsibilities that accompany this position. We follow the standards and regulations set forth by the EPA, the US Department of Agriculture (USDA), and the Food and Drug Administration (FDA) to regulate biotechnology. We cooperate fully with these organizations and trust them to set forth regulations that are based upon credible scientific evidence.

Pesticide Resistance — Members of the agri-business community are concerned about the potential for pests to eventually develop a resistance to Bt. We are following the EPA's recommendations regarding pest resistance management to help control this potential risk. The EPA has concluded that the use of resistance management programs is an effective means of deterring the development of resistance to transgenic Bt plant pesticides and that the potential for resistance to development is not a significant current threat to the environment. In *The Environmental Protection Agency's White Paper on Bt Plant-pesticide Resistance Management* published January 14, 1998, the EPA states that: "The EPA recognizes the value of Bt plant-pesticides as effective and safer pest management tools and has determined it is appropriate to conserve this resource by requiring resistance management plans for certain transformed crops." We agree with the EPA in that Bt plant pesticide products are likely to be beneficial by reducing the total pesticide burden on the environment and reducing the overall human and environmental exposure to pesticides. We also support the EPA's recommendation for pesticide resistance management, appropriate pesticide labeling, and education programs as a means to control possible environmental risks that could result from biotechnology being introduced to the environment.

Gene Escape — The probability of gene escape, meaning the escape of transgenic genes into wild plants, is another topic debated by industry, academics, and environmentalists. Again, we base our opinion on this issue on recommendations supported by scientific evidence.

Despite the commercial approval of 25 transgenic crops in the United States as of mid-1996, concern is still being expressed regarding the potential risks associated with genetically engineered crops. One recurring issue is the possibility of pollen-mediated escape of engineered genes into populations of wild relatives of the crop. To address this concern, the scientific community has depended on literature on pollen dispersal generated from non-transgenic organisms. Utilization of this information requires the assumption that the pollen mediated movement of native genes and transgenes is the same. Studies have indeed shown that dispersal of the native genes and transgene into non-contiguous plots was identical, and if gene flow were to occur that it would happen slowly and at a low probability under natural optimal conditions. Another study conducted in Australia found that only a remote possibility exists of transgenes from genetically engineered cultivars passing into natural populations. To date, studies such as these suggest gene escape is not currently the prevailing concern that many groups consider it to be. Industry members are cautious in our development and delivery of biotechnology, and we believe biotechnology to be a benefit to our customers and the environment.

Technology Protection System

Through biotechnology, we are developing tools to address the issue of management of gene movement. Transformation of the chloroplast DNA is one method being proposed. In most plant species, chloroplasts are maternally inherited and cannot be passed on through the pollen.

Delta and Pine Land Company, along with the USDA, has been awarded a patent for a Technology Protection System. The patent broadly covers all species of plants and seed, both transgenic and conventional, for a system designed to allow control of progeny seed viability without harming the crop. The principal application of this technology will be to control unauthorized planting of seed of proprietary varieties by making such practice non-economic. However, the system may have other benefits such as controlling pollen-mediated escape of engineered genes.

The system works as follows: Varieties developed incorporating this technology will produce a normal crop when planted in the first growing season. However, seed produced from this system in the second generation will not germinate and would be useless for planting. Therefore, if transgenic traits were to be transferred to a conventional plant, that plant would not reproduce as a result of this technology protection system.

Standards and Regulations

The agricultural industry participating in the biotechnology movement is faced with many responsibilities that accompany our voluntary position in the marketplace. The question we ask ourselves is not *if* we will accept these responsibilities but *how*. As I stated before, we work in full cooperation with the EPA and the USDA by following the regulations and abiding by the standards they establish. For example, the EPA has issued temporary approvals for pesticide-resistant and insecticidal genes with limitations on use coverage, and we support pesticide resistance management plans established by the EPA which benefit the American public by reducing the total pesticide burden on the environment and by reducing the overall human and environmental exposure to pesticides. We believe that it is industry's responsibility to not only abide by these plans but also to help ensure the successful development and implementation of these management strategies. In addition, we support the required isolations and movement procedures, labeling requirements, and reporting responsibilities set forth by these regulatory agencies.

We also initiated standards of quality in our transgenic products. For instance, D&PL 's varieties, both conventional and transgenic, must pass stringent tests to meet our quality assurance standards. These rigorous standards of D&PL provide our customers confidence that our seed is of consistent superior quality in all aspects. The results of these painstaking and expensive procedures are well recognized in the farming community. We have earned the trust of our customers, and it is our commitment to maintain this trust through responsible breeding, production, and marketing activities.

CONCLUSION

As we advance our knowledge of genetics through biotechnology, and as we advance our abilities to manipulate plant life, we must proceed with caution in these activities. We are breaking new ground. In doing so we must be prepared for the skepticism and criticism that accompany such activity. We listen with interest to those critics who support their hypotheses with credible science and sound evidence. We do not accept the pressures of groups who use unfounded statements and scare tactics to halt the progress of science and the advantages it offers.

As a provider of biotechnology, the agricultural industry is helping improve the success of its farmer customers. Our customers are an important gauge of the viability of these transgenic technologies and will support only those technologies that are truly advantageous to their business and to the environment. We will continue to work closely with regulatory agencies such as the EPA and the USDA to protect our environment and to follow responsible practices of biotechnology with regard to gene escape and insect resistance. In addition, we will continue to consider the risks associated with biotechnology and base our concerns and actions on credible scientific evidence. We will continue to provide biotechnology to our customers as long as it is a proven benefit to them, to agriculture, and to the environment.

PART V

LIST OF PARTICIPANTS

Photos courtesy of Debbie Dalhouse, Clemson University

Barbara K. Avery
National Agricultural Biotechnology Council
419 BTI, Tower Road
Ithaca, NY 14853

Paul Backman
Penn State College of Agricultural Sciences
217 Agricultural Administration Building
University Park, PA 16802

Susan Barefoot
Clemson University
A-203J Poole Food Science
Clemson, SC 29634

Roger Beachy
The Scripps Research Institute
Division Plant Biology, BCC 206
10550 N. Torrey Pines Road
La Jolla, CA 92037

Rebecca A. Bech
USDA/APHIS/PPQ/SS
4700 River Road, Unit 133
Riverdale, MD 20737

P.S. Benepal
Virginia State University
Central Stores Facility
Petersburg, VA 23806

Jim Boling
University of Kentucky
705 Brookhill Drive
Lexington, KY 40502

Bill Brown
University of Florida
P.O. Box 110200
Gainesville, Florida 32611

Thomas M. Brown
Clemson University
Box 340365
114 Long Hall
Clemson, SC 29634-0365

Michael J. Burke
Oregon State University
137 Stroud Hall
Corvallis, OR 97331

Frederick Buttel
University of Wisconsin
Department of Rural Sociology
1450 Linden Drive
Madison, WI 53706

Anthony J. Cavalieri
Pioneer Hi-Bred International, Inc.
7300 NW 62nd Ave.
Johnston, Iowa 50131-1004

Nancy M. Cox
Mississippi Agricultural & Forestry Experiment Station
Box 9740
Mississippi State, MS 39762

Charles Cubbage
Michigan Department of Agriculture
P.O. Box 30017
Lansing, MI 48909

Charles Curtis
Clemson University
264 Barre Hall
Clemson, SC 29634

Debbie Dalhouse
Clemson University
News Services, Trustee House
Clemson, SC 29634

Keith R. Davis
The Ohio State University
Plant Biotechnology Center
1060 Carmack Road
Columbus, OH 43210-1002

Ralph Dean
Clemson University
Department of Plant Pathology & Physiology
B04 Long Hall
Clemson, SC 29634

O.J. Dickerson
Clemson University
Department of Plant Pathology & Physiology
Box 340377
Clemson, SC 29634

William Dickinson, Jr.
Virginia Department of Agricultural & Consumer Services
1100 Bank St., Suite 210
Richmond, VA 23219

Natalie L. DiNicola
Monsanto Company
800 N. Lindbergh Blvd. (C2SB)
St. Louis, MO 63167

Hortense Dodo
Alabama A & M University
P.O. Box 266
Normal, AL 35762

Samuel Donald
Association of Research Directors
Room 1103 Early Childhood Research Center, IMES
Princess Anne, MD 21853

B. Allen Dunn
Clemson University
School of National Resources
132 Lehotsky Hall
Clemson, SC 29634-0303

Michael O. Ezekwe
Alcorn State University
1000 ASU Drive, #1374
Lorman MS 39096

Hal Farris, Jr.
Clemson University
Godley-Snell Research Center
Clemson, SC 29634

Jim Fischer
Clemson University, SCAFRS
104 Barre Hall
Clemson, SC 29634-0351

Frank FitzSimons, III
Clemson University
Cooperative Extension Service
223 N. Live Oak Drive
Moncks Corner, SC 29461

Vickie Forster
AgrEvo USA Company
Little Falls Centre One
2711 Centerville Road
Wilmington, DE 19808

Sheila Forsyth
National Agricultural Environmental Committee, Canada
Suite 1101, 75 Albert St.
Ottawa, Ontario, Canada K1P SE7

John R. Gentry
Clemson University
275 Oak Grove Road
Central, SC 29630

Jim Germida
University of Saskatchewan
51 Campus Drive
Saskatoon, SK, Canada S7N 5A8

Fred Gould
North Carolina State University
840 Method Road, Unit #1
Raleigh, NC 27607

W. Doyce Graham
Clemson University
Crop and Soil Environmental Science Department
Box 340359
Clemson, SC 29634

Ian Gray
Michigan State University
109 Agriculture Hall
East Lansing, MI 48824

Yang Guochen
North Carolina A&T State University
1601 E. Market St.
Greensboro, NC 27410

Dave Guyer
Norvartis Seeds
3054 Cornwallis Road
Research Triangle Park, NC 27709

Ralph W. F. Hardy
National Agricultural Biotechnology Council
P.O. Box 509
Clarence Center, NY 14032

Brian Harrison
Health Canada
22 Ross Ave., Tunney's Pasture
Ottawa, Ontario, Canada KIA OL2

Bryan Harvey
University of Saskatchewan
204 Kirk Hall, 117 Science Place
Saskatoon Saskatchewan, Canada S7N 5C8

Gregory Harvey
Clemson Extension Service
P.O. Box 2377
Sumter, SC 29151

David G. Heckel
Clemson University
Department of Biological Sciences
Clemson, SC 29634

Bette Hileman
Chemical & Engineering News
115 16th St., SW
Washington, DC 20036

Mae-Wan Ho
Open University
Biology Department
Walton Hall
Milton Keynes, UK MK7 6AA

J. Thomas Hoban, IV
North Carolina State University
Department of Sociology & Anthropology
Campus Box 8107
Raleigh, NC 27695

Donald Holt
College of ACES, University of Illinois
109 Mumford Hall
1301 W. Gregory Drive
Urbana, IL 61801

David S. Howle
Clemson University
511 Westinghouse Road,
Pendleton, SC 29670

Li-Chung Huang
AgrEvo USA Company
703 Nor-Am Road
Pikeville, NC 27863

Jim Hudson
Editor, Southeast Farm Press
136 Annapolis Drive
Raleigh, NC 27608

Mary Pat Huxley
Central Coast Biotechnology Center
4667 Telegraph Road
Ventura, CA 93003

Dalphene Jameson
Clemson University, SCAFRS
104 Barre Hall
Clemson, SC 29634

Patricia Jerman
Sustainable Universities Project - USC
School of the Environment
Suite 702H
Columbia, SC 29208

Daniel Jones
USDA Cooperative State Research
Education & Extension Service
Room 843, Aerospace Center
1400 Independence Ave., SW
Washington, DC 20250-2220

Andrew Jordan
National Cotton Council
1918 N. Parkway
Memphis, TN 38112-0285

Ann Kellan
CNN-TV
P.O. Box 105366
Atlanta, GA 30348

John W. Kelly
Clemson University
VP, Public Service & Agriculture
130 Lehotsky Hall
Clemson, SC 29634-5201

James W. King
University of Nebraska
300 Agriculture Hall
Lincoln, NE 68583-0709

Darrell L. Knight
Deltapine Seed
P.O. Box 8426
Dothan, AL 36304

Patrick Kohout
Clemson University
PSA-Development
Clemson, SC 29634

Britta Leverante
Clemson University
120 Long Hall,
Clemson, SC 29634

Philip Larsen
University of Minnesota
College of Agriculture, Food &
Environmental Science
St. Paul, MN 55108

Stephen A. Lewis
Clemson University
Department of Plant Pathology &
Physiology
118 Long Hall
Clemson, SC 29634-0377

David R. Lineback
University of Idaho
College of Agriculture
Moscow, ID 83844

John Long
SC Soybean Association
22858, US HWY 76
Newberry, SC 29108

Steven A. Lommel
NC State University
Department of Plant Pathology
Box 7616
Raleigh, NC 27695

Carl Loop, Jr.
Florida Farm Bureau Federation
P.O. Box 147030
Gainesville, FL 32614

Sharlene R. Matten
Biopesticides and Pollution
Prevention Division, EPA
Office of Pesticide Programs
US Environmental Protection Agency
401 M St. SW
Washington, DC 20460

William R. Marcotte, Jr.
Clemson University
132 Long Hall
Clemson, SC 29634

Marshall Martin
Purdue University
Krannert Building
West Lafayette, IN 47907

Martin Massengale
University of Nebraska-Lincoln
Rm. 220 Keim Hall
Lincoln, NE 68583

Bill F McCutchen
DuPont Agricultural Products
S-H Res. Center, P.O. Box 30
Newark, DE 19714

Gary L. McMahan
Clemson University
104 Barre Hall
Clemson, SC 29634

F. Blaine Metting
Pacific Northwest National Laboratory
902 Battelle Blvd. PF-54
Richmond, WA 99352

Walker Miller
Clemson University
Plant Pathology and Physiology
206 Long Hall
Clemson, SC 29634

Robert Morrison
American Cyanamid Company
Agricultural Research Division
P.O. Box 400
Princeton, NJ 08543

John E. Mullet
Texas A&M University
Crop Biotechnology Center
Texas Agricultural Experiment Station
College Station, TX 77843

Ron T. Nagao
University of Georgia
Department of Botany
Athens, GA 30602

Darrell W. Nelson
University of Nebraska-Lincoln
207 Agricultural Hall
Lincoln, NE 68583

Tom Nickson
Monsanto Company
700 Chesterfield Parkway, North
St. Louis, MO 63017

Margaret W. O'Brien
North Carolina Biotechnology Center
15 TW Alexander Drive
P.O. Box 13547
Research Triangle Park, NC 27709

Jack Odle
The Progressive Farmer
2100 Lakeshore Drive
P.O. Box 2581
Birmingham, AL 35202

Ed Page
Clemson University
300 Brackett Hall
Clemson, SC 29634

James H. Palmer
Clemson University
Department of Crop & Soil
Environmental Sciences
Box 340359
Clemson, SC 29634

Beverly Peterson
US General Accounting Office
Room 2T23, 441 G St. NW
Washington, DC 20548

Deborah Petrik
Westvaco Corporation
180 Westvaco Road
Summerville, SC 29407

Jochen Pfeiffer
Ministry for Food, Agriculture &
Forestry
State Brandenburg, Germany
Heinrich-Mann-Alle 103
Potsdam, Germany 14473

Michael T. Phillips
National Research Council
Board of Agriculture
2101 Constitution Ave., NW
Washington, DC 20418

Kees Planqu
Scientific Office
Netherlands Embassy
4200 Linnean Ave., NW
Washington, DC 20008

Verena Rappaport
Post Graduate FE DE RA C
Research Center for Agriculture and
Forestry
Kleine Weinmeister Strasse 12
14463 Potsdam Germany

Murray Robinson
Delta and Pine Land Company
P.O. Box 217
Scott, MS 38772

Bill Rhodes
Clemson University
E-142 Poole Agriculture Center
Clemson, SC 29634

Eugene G. Sander
University of Arizona
College of Agriculture
Forbes 306, P.O. Box 210036
Tucson, AZ 95721

Calvin Schoulties
Clemson University
111 Poole Agricultural Science Center
Clemson, SC 29634

Tom Scott
Clemson University
School of Animal, Biomedical &
Biological Sciences
128 Long Hall
Clemson, SC 29634

Jane Baker Segelken
National Agricultural Biotechnology
Council
419 BTI Tower Road
Ithaca, NY 14850

Shantharam Sivramiah
USDA/APHIS/PPQ/SS
4700 River Road Unit 133
Riverdale, MD 20737

Daniel Smith
Clemson University
103 Barre Hall
Clemson, SC 29634

Powell Smith
Clemson Extension Service
Lexington County
158 Thedo Bush Road
Gilbert, SC 29054

Garth Sundeen
Canadian Federation of Agriculture
Suite 1101 - 75 Albert Street
Ottawa, Ontario, Canada KIP 5E7

Cecil Stushnoff
Colorado State University
Department of Horticulture &
Landscape Architecture
133B Shepardson Building
Fort Collins, Co. 80523

Patricia Swan
Iowa State University
211 Beardshear Hall
Ames, IA 5001

Allison Tally
Novartis Crop Protection
410 Swing Road
Greensboro, NC 27419

David L. Tompkins
South Carolina Department of
Agriculture
P.O. Box 11280
Columbia, SC 29211

Tom Trantham
South Carolina Farmer
330 McKalvay Dr.
Pelzer, SC 29609

Andreas Ulrich
Center for Agricultural Landscape &
Land Use Research
Muncheberg Eberswalder Str. 04
Munchebert, D-15374 Germany

Vicki B. Vance
University of South Carolina
Department of Biological Sciences
Columbia, SC 29208

Brenda VanderMey
Clemson University
132 Brackett Hall, Box 341513
Clemson, SC 29634

Roger R. Vega
Idaho State University
2270 Old Penitentiary Road
Boise, ID 83712

Jerry Walker
Virginia Department of Agriculture & Consumer Services
1100 Bank St., Suite 210
Richmond, VA 23219

Don Weeks
University of Nebraska
Room N300, Beadle Center
Lincoln, NE 68588

Mark E. Whalon
Michigan State University
Department of Entomology & Pesticide Research
107 Pesticide Research Center
Wilson Road
East Lansing, MI 48824

David Winkles
South Carolina Farm Bureau
P.O. Box 754
Columbia, SC 29202

H.J. Wolf
Ministry for Food Agriculture and Forestry
Heinrich-Mann - Allee 103
Polsdam, Germany, 14474

Daniel E. Wueste
Clemson University
139 Briar Lane
Central, SC 29630

Johnny Wynne
North Carolina Agricultural Research Service
Box 7643 NCSU
Raleigh, NC 27695

PART VI

APPENDIX

Vision for Agricultural Research and Development in the 21st Century

Biobased Products Will Provide Security and Sustainability
in Food, Health, Energy, Environment, and Economy

Prepared by the National Agricultural Biotechnology Council

National Agricultural Biotechnology Council
419 Boyce Thompson Institute, Tower Road, Ithaca, NY 14853
Tel: 607-254-4856 Fax: 607-254-1242 E-mail: NABC@cornell.edu
http://www.cals.cornell.edu/extension/nabc

December 14, 1998

The National Agricultural Biotechnology Council (NABC), a consortium of 26 major agricultural research and education institutions in the U.S. and Canada, has formulated the attached “Vision for Agricultural Research and Development in the 21st Century”.

The role of agriculture in the 21st century will see major expansion beyond food, feed, and fiber. It will be the basis for the emerging biobased industrial products era. In the 21st century we will not only continue to have food security but will see improved nutritional quality and food safety. In addition, the new biobased economy will bring increased security in energy, materials, environment, and health. Agricultural R&D will be the driving force for the new biobased economy.

We are excited about this opportunity and hope that this vision also inspires you. Please contact us if you have questions or would like further details on this vision of agricultural R&D and a sustainable economy. We encourage you to share this vision with others.

Sincerely,

James R. Fischer
Chair, NABC
Dean and Director, South Carolina
Agriculture and Forestry Research System
Clemson University

Ralph W. F. Hardy
President, NABC

Vision for Agricultural Research and Development in the 21st Century

BIOBASED PRODUCTS WILL PROVIDE SECURITY AND SUSTAINABILITY IN FOOD, HEALTH, ENERGY, ENVIRONMENT, AND ECONOMY

Prepared by the National Agricultural Biotechnology Council, 1998

Agricultural research and development (AR&D) will take the lead in providing the technology for a biobased economy in the 21st century. In contrast with our present fossil-based economy, the biobased economy will use renewable resources such as plants instead of non-renewable fossil sources. With the biobased industry now emerging, AR&D has a greatly expanded role beyond the traditional areas of food, feed, and fiber. The 21st century biobased economy will:

- be rooted in life-science, the dominant science as we enter the new millennium, coupled with bio-engineering processes;
- reduce our vulnerability in access to and supply of petroleum for energy and industrial products;
- make our industries more sustainable by utilizing domestically-produced renewable plant resources;
- be driven by AR&D to improve cost-competitiveness of biobased vs. fossil-based energy and products
- lessen projected global climate change by reducing the build up of carbon dioxide, the major greenhouse gas;
- create rural and urban job opportunities in the agricultural and industrial sectors;
- improve the quality of our air, water, and soil;
- improve the healthfulness of food;
- produce human health-related products in plants, microbes, and animals;
- produce value-added biobased products (fuels, chemicals, and materials) for domestic use and export;
- impact favorably our balance of payments by reducing or potentially eliminating our need for petroleum imports;
- be broadly distributed across the US; and
- make optimal use and improve sustainability of our agricultural land growing food, feed, fiber, and bio-industrial crops.

Thus, the biobased economy will be a major contributor to improved US security in energy, industrial chemicals and materials, the environment, human health, and our economy as well as maintaining the security of and improving the quality of our food supply.

20th Century AR&D has enabled the US to have a secure, low-cost food supply and to export surplus food to the rest of the world. 21st Century AR&D will maintain this food security while improving nutritional quality and food safety. Food will be modified to be more healthful with, for example, improved levels of antioxidants and balance of oil types. Transgenic plants and animals will produce health-related products such as pharmaceuticals and vaccines.

The energy resources and industrial chemicals of the 20th century are mainly fossil-based, as are a growing portion of materials, such as synthetic fibers. The dominant sources of energy and industrial products will become biobased, at prices that are economically competitive with those that are fossil-based. With AR&D investment, bio-industrial crops and novel biobased processes are being developed to produce liquid fuels at approximately half the current cost of producing ethanol thereby making it cost competitive with gasoline. Plants will be modified genetically to make bio-polymers or be processed into chemicals, polymers, and fibers. In the long term, the need for imported fossil fuel, e.g. petroleum, could be eliminated, making the US self-secure in energy, chemicals, and materials.

The fossil-based economy at the end of the 20th century is a major cause of global, regional, and local environmental problems. The biobased economy will minimize net carbon dioxide accumulation into the environment, thereby significantly reducing the problem of global warming and improving sustainability and global environmental security. Fossil-based products, both in their manufacture and use, contaminate our air, water, and soil resulting in numerous environmental and health concerns. The growth, processing, and utilization of biobased products are less contaminating, thereby improving the quality of our air, water, and soil, and thus, our health security.

Biobased industrial products will be a major US economic growth area in the next century as fossil-based industrial products, such as synthetic chemicals and liquid fuels, were in the 20th century. Biobased industrial products will improve economic security through use of domestic versus imported resources, optimal use of currently unused or underused land, and geographically widespread production and manufacture across the US.

Investment in AR&D to develop the biobased industry of the 21st century will enable the US to be the world leader in this major emerging industry while expanding US security in food, energy, environment, health, and the economy. The National Research Council Report on Biobased Industrial Products, issued in 1998, outlines in some detail the opportunities of the biobased economy and the need for an expanded AR&D.

We, the representatives to the National Agricultural Biotechnology Council (NABC), support the

Vision for Agricultural Research and Development in the 21st Century

ASSOCIATION of RESEARCH DIRECTORS
Kenneth W. Bell,
Dean and Research Director,

OKLAHOMA STATE UNIVERSITY
Sam E. Curl,
Dean and Director, Division of Agricultural Sciences & Natural Resources

BOYCE THOMPSON INSTITUTE
Charles J. Arntzen,
President and CEO

CLEMSON UNIVERSITY
James R. Fischer,
Dean and Director, South Carolina Agriculture & Forestry Research System

OREGON STATE UNIVERSITY
Thayne R. Dutson,
Dean, College of Agricultural Sciences; Director, Agricultural Experiment Station

IOWA STATE UNIVERSITY
Patricia B. Swan,
Vice Provost for Research & Advanced Studies

CORNELL UNIVERSITY
W. Ronnie Coffman,
Associate Dean for Research, College of Agriculture & Life Sci

THE PENNSYLVANIA STATE UNIVERSITY
Robert D. Steele,
Dean, College of Agricultural Sciences

MICHIGAN STATE UNIVERSITY
J. Ian Gray,
Director, Michigan Agricultural Experiment Station

PURDUE UNIVERSITY
William R. Woodson,
Assoc. Dean of Agriculture and Dire of Agricultural Research Programs

NORTH CAROLINA STATE UNIVERSITY
Johnny C. Wynne,
Assoc. Dean & Director, Agricultural Research Service, College of Agriculture & Life Sciences

TEXAS A&M UNIVERSITY SYSTEM
Edward A. Hiler, *Vice Chancellor & Dean,*
Agriculture & Life Sciences; Director, Agricultural Experiment Sta

OHIO STATE UNIVERSITY
Bobby D. Moser,
Vice President for Agriculture Administration

UNIVERSITY of NEBRASKA-LINCOLN
Darrell Nelson,
Dean, Agricultural Research Division

UNIVERSITY of ARIZONA
Eugene G. Sander,
Vice Provost and Dean, College of Agriculture

UNIVERSITY of CALIFORNIA-DAVIS
Alan Bennett,
Associate Dean, Plant Sciences

UNIVERSITY of FLORIDA
Richard L. Jones,
Dean for Research; Director, Florida Agricultural Experiment Station

UNIVERSITY of SASKATCHEWAN
Bryan Harvey,
Coordinator, Agricultural Research

UNIVERSITY of GEORGIA
Joe L. Key,
Vice President for Research

UNIVERSITY of WISCONSIN-MADISON
Elton Aberle,
Dean and Director, College of Agricultural & Life Sciences

UNIVERSITY of HAWAII
H. Michael Harrington,
Interim Director, College of Tropical Agriculture & Human Resources

UNIVERSITY of ILLINOIS at CHAMPAIGN-URBANA
Steven Pueppke,
Associate Dean for Research,
College of Agricultural, Consumer & Environmental Scienc

UNIVERSITY of MINNESOTA
Michael Martin,
Dean, College of Agricultural, Food &Environmental Sciences

WASHINGTON STATE UNIVERSITY
James R. Carlson,
Associate Dean, Agriculture & Home Economics and Associate Director, Ag Research Center

NATIONAL AGRICULTURAL BIOTECHNOLOGY COUNCIL
Ralph W. F. Hardy,
President

UNIVERSITY of MISSOURI-COLUMBIA
William C. Stringer,
Interim Dean, College of Agriculture, Food & Natural Resources; Director, Missouri Agricultural Experiment Station