

[COMMITTEE PRINT 106-B]

**SEEDS OF OPPORTUNITY:
AN ASSESSMENT OF THE BENEFITS, SAFETY, AND
OVERSIGHT OF PLANT GENOMICS AND AGRICULTURAL
BIOTECHNOLOGY**

REPORT PREPARED BY

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OF THE

SUBCOMMITTEE ON BASIC RESEARCH

AND TRANSMITTED TO THE

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LETTER OF TRANSMITTAL

April 13, 2000

The Honorable James F. Sensenbrenner, Jr.
Chairman
Committee on Science
U.S. House of Representatives
Washington, DC 20515

Dear Mr. Chairman:

I am submitting herewith a Chairman's Report providing an assessment of the benefits, safety, and oversight of plant genomics and agricultural biotechnology. It is a summation of the findings of a series of three hearings held during the First Session of the 106th Congress by the Subcommittee on Basic Research entitled, "Plant Genome Science: From the Lab to the Field to the Market."

Agricultural biotechnology has come of age. It is referred to under different names—genetic engineering, gene splicing, bioengineering, recombinant DNA technology. But no matter the name used to describe it, this technology represents the latest tool in the continuum of techniques that plant breeders have developed and adopted over centuries. What is truly powerful about this technology is that it allows individual, well-characterized genes to be transferred from one organism to another, thus increasing the genetic diversity available to improve important commercial crop plants. The potential benefits to mankind are limited only by the resourcefulness of our scientists.

Biotechnology has been used safely for many years to develop new and useful products used in a variety of industries. More than a thousand products have now been approved for marketing, and many more are being developed. These products include dozens of therapeutics, including human insulin for diabetics, growth factors used in bone marrow transplants, products for treating heart attacks, hundreds of diagnostic tests for AIDS, hepatitis, and other infectious agents, enzymes used in food production, such as those used for cheese, and many others.

The Hon. F. James Sensenbrenner, Jr.

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And this is just the beginning. In agriculture, new plant varieties created with these techniques will offer foods with better taste, more nutrition, and longer shelf life, and farmers will be able to grow these improved varieties more efficiently, leading to lower costs for consumers and greater environmental protection. Soybeans that produce high oleic oil containing less saturated fat and requiring less processing, cotton plants that fight pests or produce naturally-colored cotton reducing the need for chemical dyes, and bananas that deliver vaccines to fight enteric diseases are just a few examples of what is in store.

While millions of lives all over the world have been protected and enriched by biotechnology, its application to agriculture has been coming under attack by well-financed activist groups. The controversy they have generated revolves around three basic questions: (1) are agricultural biotechnology and classical breeding methods conceptually the same; (2) are these products safe to eat; and (3) are they safe for the environment?

The testimony and other material made available to the Subcommittee lead me to conclude that the answer to all three questions is a resounding, "Yes." In fact, modern biotechnology is so precise, and so much more is known about the changes being made, that plants produced using this technology may be even safer than traditionally-bred plants.

This Report contains background information on the development and oversight of plant genetics and agricultural biotechnology, a summary of Subcommittee hearings and my findings and recommendations based on these hearings. I hope that it will be of use to you and to other Members of Congress, the Administration, States, and the general public interested in gaining a greater appreciation of the incredible potential of plant genomics and agricultural biotechnology.

Sincerely,

NICK SMITH

Chairman

Subcommittee on Basic Research

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SUMMARY

The Subcommittee on Basic Research of the Committee on Science held a series of three hearings entitled, “Plant Genome Research: From the Lab to the Field to the Market: Parts I-III,” to examine plant genomics, its application to commercially-important crop plants, and the benefits, safety, and oversight of plant varieties produced using biotechnology. The testimony and other information presented at these hearings and information gathered at various briefings provides the basis for the findings and recommendations in this report.

Almost without exception, the crop plants in use today have been genetically modified. The development of new plant varieties through selective breeding has been improving agriculture and food production for thousands of years. In the 19th century, the basic principles of heredity were discovered by Gregor Mendel, whose studies on inheritance in garden peas laid the foundation for the modern science of genetics. Subsequent investigations advanced our understanding of the location, composition, and function of genes, and a critical breakthrough revolutionized the field in 1953, when James Watson and Francis Crick described the double helix structure of deoxyribonucleic acid (DNA), the substance of heredity. This groundbreaking research set the stage for deciphering the genetic code and led to the rapid advances in practical application of genetics in medicine, animal science, and agriculture.

The development of the science of genetics in the 20th century was a tremendously important factor in the plant breeding programs that have produced the remarkable diversity of fruits, vegetables, and grains that we enjoy today and that provide food security for the poor nations of the world. Traditional cross-breeding has been very useful in improving crop plants, but it is a time consuming process that results in the uncontrolled recombination of tens of thousands of genes, commonly producing unwanted traits that must be eliminated through successive rounds of backcrossing. Improving crops through traditional methods also is subject to severe limitations because of the constraints imposed by sexual compatibility, which limit the diversity of useful genetic material.

With the arrival of biotechnology, plant breeders are now able to develop novel varieties of plants with a level of precision and range unheard of just two decades ago. Using this technology, breeders can introduce selected, useful genes into a plant to express a specific, desirable trait in a significantly more controlled process than afforded by traditional breeding methods.

U.S. farmers have been quick to adopt plants modified using new biotechnology, including commercial crops that resist biologically insect and viral pests and tolerate broad-spectrum herbicides used to control weeds. As our knowledge of plant genetics expands, new varieties of plants with improved nutrition, taste, or other characteristics desired by consumers will become available. The federally-funded plant genome program provides much of the essential basic research on plant genetics required to develop new varieties of commercially important crops through advanced breeding programs.

For over two decades, the application of biotechnology has been assessed for safety. Oversight of agricultural biotechnology includes both regulatory and nonregulatory mechanisms that have

been developed over the last five decades for all crop plants and conventional agricultural systems. Federal regulation of agricultural biotechnology is guided by the 1986 Coordinated Framework for Regulation of Biotechnology, which laid out the responsibilities for the different regulatory agencies, and the 1992 Statement on Scope, which established the principle that regulation should focus on the characteristics of the organism, not the method used to produce it. Three federal agencies are responsible for regulating agricultural biotechnology under existing statutes: the U.S. Department of Agriculture (USDA), which is responsible for ensuring that new varieties are safe to grow; the Environmental Protection Agency (EPA), which is responsible for ensuring that new pest-resistant varieties are safe to grow and consume; and the Food and Drug Administration (FDA), which is responsible for ensuring that new varieties are safe to consume.

Although biotechnology has had an uninterrupted record of safe use, political activists in Europe have waged well-funded campaigns to persuade the public that the products of high-tech agriculture may be harmful to human health and the environment. As a result of these efforts, public confidence in the safety of agricultural biotechnology has been seriously undermined in Europe. Many European countries have established new rules and procedures specifically designed to address “genetically-modified organisms,” and these have had a detrimental impact on international trade in agricultural products.

The controversy over agricultural biotechnology now has spread to the United States, the world's largest grower of plants and consumer of foods produced using this technology. At the core of the debate is food safety, particularly the possibility that unexpected genetic effects could introduce allergens or toxins into the food supply. The use of antibiotic resistance markers also has been criticized as dangerous to human health. As a result, there have been calls for both increased testing and labeling requirements for foods created using biotechnology.

Environmental concerns also have been raised. It has been suggested, for example, that widespread use of plants engineered with built-in protection against insect and viral pests could accelerate the development of pesticide-resistant insects or could have a negative impact on populations of beneficial insects, such as the Monarch butterfly. It also has been argued that the use of herbicide-tolerant plants could increase herbicide use and that “superweeds” could be developed through cross-pollination between these plants and nearby weedy relatives.

Extensive scientific evaluation worldwide has produced no evidence to support these claims. Far from causing environmental and health problems, agricultural biotechnology has tremendous potential to reduce the environmental impact of farming, provide better nutrition, and help feed a rapidly growing world population. Crops designed to resist pests and to tolerate herbicides and environmental stresses, such as freezing temperatures, drought, and high salinity, will make agriculture more efficient and sustainable by reducing synthetic chemical inputs and promoting no-tillage agricultural practices. Stress-tolerant crops also will reduce pressure on irreplaceable natural resources like rainforests by opening up presently nonarable lands to agriculture. Other plants are being developed that will produce renewable industrial products, such as lubricating oils and biodegradable plastics, and perform bioremediation of contaminated soils.

Biotechnology will be a key element in the fight against malnutrition worldwide. Deficiencies of vitamin A and iron, for example, are very serious health issues in many regions of the developing

world, causing childhood blindness and maternal anemia in millions of people who rely on rice as a dietary staple. Biotechnology has been used to produce a new strain of rice—Golden Rice—that contains both vitamin A (by providing its precursor, beta-carotene) and iron. The Subcommittee heard about other research aimed at improving the nutrition of a wide variety of food staples, such as cassava, corn, rice, and other cereal grains, that can be a significant help in the fight for food security in many developing countries.

The merging of medical and agricultural biotechnology has opened up new ways to develop plant varieties with characteristics to enhance health. Advanced understanding of how natural plant substances, known as phytochemicals, confer protection against cancer and other diseases is being used to enhance the level of these substances in the food supply. Work is underway that will deliver medicines and edible vaccines through common foods that could be used to immunize individuals against a wide variety of enteric and other infectious diseases. These developments will have far-reaching implications for improving human health worldwide, potentially saving millions of lives in the poorest areas of the world by providing a simpler medicine production and distribution system.

Set against these benefits, however, is the idea that transferring a gene from one organism to an unrelated organism using recombinant DNA techniques inherently entails greater risks than traditional cross breeding. The weight of the scientific evidence leads to the conclusion that there is nothing to substantiate scientifically the view that the products of agricultural biotechnology are inherently different or more risky than similar products of conventional breeding.

The overwhelming view of the scientific community—including the National Academy of Sciences, the National Research Council, many professional scientific societies, the Organization for Economic Cooperation and Development, the World Health Organization, and the research scientists who appeared before the Subcommittee—is that risk assessment should focus on the characteristics of the plant and the environment into which it is to be introduced, not on the method of genetic manipulation and the source of the genetic material transferred. These risk factors apply equally to traditionally-bred plants.

Years of research and experience demonstrate that plant varieties produced using biotechnology, and the foods derived from them, are just as safe as similar varieties produced using classical plant breeding, and they may even be safer. Because more is known about the changes being made and because common crop varieties with which we have a broad range of experience are being modified, plants breeders can answer questions about safety that cannot be answered for the products of classical breeding techniques.

FDA has adopted a risk-based regulatory approach consistent with these principles and with the long history of safe use of genetically-modified plants and the foods derived from them. Its policies on voluntary consultation and labeling are consistent with the scientific consensus and provide essential public health protection.

Unlike FDA regulations on food, USDA has instituted plant pest regulations, and EPA proposes to institute new plant pesticide regulations, that target selectively plants produced using

biotechnology and apply substantive regulatory requirements to early stages of plant research and development. These regulations add greatly to the cost of developing new biotech plant varieties, harming both an emerging industry and the largely publicly-funded research base upon which it depends. Regulations and regulatory proposals that selectively capture the products of biotechnology should be modified to reflect the scientific consensus that the source of the gene and the methods used to transfer it are poor indicators of risk.

In the international arena, the United States should work to ensure that access to existing markets for agricultural products are maintained. The United States should not accept any international agreements that endorse the precautionary principle—which asserts that governments may make political decisions to restrict a product even in the absence of scientific evidence that a risk exists—and that depart from the principle of substantial equivalence adopted by a number of international bodies.

Finally, the Administration, industry, and scientific community have a responsibility to educate the public and improve the availability of information on the long record of safe use of agricultural biotechnology products. This is critically important to building consumer confidence and ensuring that sound science is used to make regulatory decisions.

INTRODUCTION

Throughout history, new scientific discoveries have challenged conventional thinking. Observations made by Galileo Galilei confirming the Copernican theory that the Earth revolves around the Sun challenged the authority of the Church in 17th century Italy and ushered in a new era of science. Marcello Malpighi was another 17th century scientist whose work was denounced by the established order, but it provided a foundation for advances in comparative anatomy. The history of science has many other examples of new discoveries that have been initially greeted with little enthusiasm. However, over the years society has learned to accept—indeed, celebrate—these discoveries and the social and intellectual benefits they have conveyed.

The introduction of new biotechnology methods in agriculture also has met with resistance. Traditionally, genetic enhancements of crop plants have come from breeding programs that capitalize on the natural variation between sexually compatible plants. In this process, plants exhibiting desirable traits—such as enhanced hardiness or resistance to pests, better yields, or fruits with improved flavor or shelf life—are identified and then introduced into plant breeding programs.

Selective breeding has been used for centuries to produce new plant varieties. However, hybridization, the most commonly-used technique, is subject to severe shortcomings. The plants must be sexually-compatible, which limits the diversity of the genetic material available for crossing, and the process results in uncontrolled combinations of thousands of uncharacterized genes.

Biotechnology has made it possible to produce precise genetic changes at the level of single, well-characterized genes selected from one organism and introduced into another. The plant's own genome also may be modified selectively to control, increase, or turn off specific functions within the plant.

Applications of biotechnology already have had a profound impact on fields such as biomedical research, medicine, and food processing, and over a thousand biotechnology products have been approved and are in use. In agriculture, biotechnology has been used to develop desirable characteristics in plants with more precision and knowledge than afforded by conventional breeding techniques. Some of these plants have been genetically modified to tolerate specific broad-spectrum herbicides. Others have been altered so that they are biologically protected against insect or viral pests, eliminating the need for some applications of synthetic pesticides.

Future varieties of plants could be enhanced to produce plants and foods with improved nutritional content or added health benefits, greater tolerance to environmental stresses such as drought, frost, or high salinity, and the ability to provide renewable sources of fuel, industrial oils, and plastics. The federally-funded plant genome program will provide much of the basic research that will be used to develop these new, improved plant varieties.

Despite an unblemished record of safe use, critics have mounted well-funded campaigns against this technology and have raised concerns about its potential impact on human health and the environment. In Europe, these campaigns and other unrelated foods scares have seriously

undermined public confidence in the safety of foods produced using this new, genetics-based science. In response, many European countries and the European Union have established new rules and procedures designed specifically to address “genetically-modified organisms.” These actions have created an international trade conflict that has cost farmers hundreds of millions of dollars¹ and now threatens to drive scientists and agricultural researchers away from a field of research that has tremendous potential for solving food security and environmental problems.

Unlike in Europe, similar campaigns in the United States have not resulted in widespread antibiotechnology sentiment among the public. The reaction of U.S. industry, however, has been less sanguine. The first indication that these campaigns were having an effect was the decision announced by Gerber—a subsidiary of the Swiss pharmaceutical and biotechnology company Novartis—that it would no longer use biotech varieties of corn or soybean in its baby foods, even those grown from seeds developed by its parent company. Though little noticed, the company's announcement did not rule out using new bioengineered varieties providing enhanced nutrition and other benefits. Nevertheless, the decision by Gerber created the perception among the public that biotechnology foods were inherently different and less safe, without acknowledging that almost all foods the company sells have been genetically modified using traditional techniques. Many other companies have since followed Gerber's lead and discontinued the use of bioengineered foods in their products.

The ostensible basis for the attacks on biotechnology is the idea that transferring genes between unrelated organisms is unnatural and inherently entails greater risks than traditional cross breeding. At the core of this debate is food safety, particularly the possibility that unexpected genetic effects could introduce allergens or toxins into the food supply. The use of antibiotic resistance markers has been criticized as possibly dangerous to human health. These concerns have led to calls both for increased regulation and for mandatory labeling of biotech food products.

Concerns also have been raised about the impact of pest-resistant and herbicide-tolerant crops on the environment. For example, some biotechnology foes claim that widespread use of bioengineered pest-resistant plants could accelerate the development of pesticide-resistant insects or could have a negative impact on the populations of beneficial, non-target insects, such as the Monarch butterfly. It also has been suggested that the use of herbicide-tolerant plants actually will increase herbicide use and that “superweeds” could be developed through cross-pollination with nearby weedy relatives.

It is understandable that these negative claims could create a climate of unease about this new technology. Therefore, the Subcommittee on Basic Research conducted a series of public hearings during the First Session of the 106th Congress in which leading scientists were given the opportunity to assess these controversies. This Report is based on the testimony and other documents made available to the Subcommittee over the course of those hearings. It provides a brief history of agricultural biotechnology and its oversight, a discussion of findings concerning the benefits, safety, and environmental impact of agricultural plants modified using biotechnology, and a list of recommendations.

¹ According to the U.S. Department of Agriculture's Foreign Agriculture Service, the prolonged approval of U.S. varieties of biotech corn led to a \$200 million loss for U.S. farmers in 1998 alone (Kelch, *et al.*, 1998).

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SUBCOMMITTEE HEARINGS

The Subcommittee on Basic Research of the Committee on Science held a series of three hearings entitled, "Plant Genome Research: From the Lab to the Field to the Market: Parts I-III," to examine plant genomics, its application to commercially-important crops plants, and the benefits, safety, and oversight of plant varieties produced using biotechnology.

On August 3, 1999, the Subcommittee held the first of its hearings and heard testimony concerning current plant genome research projects and their application to industry, as well as the regulatory and market barriers to agricultural biotechnology products. Testifying before Subcommittee were: Dr. Mary Clutter, Assistant Director, Directorate for Biological Sciences, National Science Foundation (NSF); Dr. Eileen Kennedy, Deputy Assistant Secretary, Research, Education, and Economics, U.S. Department of Agriculture (USDA); Dr. Kenneth Keegstra, Director and Professor, Michigan State University Plant Research Laboratory, Michigan State University; Dr. John Ryals, Chief Executive Officer, Paradigm Genetics; and Dr. Susanne Huttner, Director of the Biotechnology Research and Education Program, University of California.

On October 5, 1999, the Subcommittee examined the benefits and risks involved in applying biotechnology to agricultural plants. Witnesses for this hearing included: Dr. Michael Thomashow, Professor of Plant and Soil Science, Michigan State University; Dr. Rebecca Goldberg, Director, Biotechnology Programs, Environmental Defense Fund (EDF); Dr. Abigail A. Salyers, Professor of Microbiology, University of Illinois; Dr. Anthony M. Shelton, Professor of Entomology, Cornell University; Dr. R. James Cook, Professor of Plant Pathology, Washington State University.

In addition, the Subcommittee received written testimony for the record from: Dr. Charles J. Arntzen, President and CEO, Boyce Thompson Institute for Plant Research and Adjunct Professor, College of Agriculture and Life Sciences, Cornell University; Dr. Roger N. Beachy, President, Donald Danforth Plant Science Center; Mr. Leonard P. Gianessi, Senior Research Associate, and Ms. Janet E. Carpenter, Research Associate, National Center for Food and Agriculture Policy; Dr. Brian A. Larkins, Porterfield Professor of Plant Sciences, Department of Plant Sciences, University of Arizona; and Dr. Channapatna S. Prakash, Professor and Director, Center for Plant Biotechnology Research, Tuskegee University.

On October 19, 1999, the Subcommittee held the final hearing in this series to review and assess current and proposed regulations for agricultural biotechnology. Witnesses at this hearing included: Dr. Sally L. McCammon, Science Advisor, Animal and Plant Health Inspection Service (APHIS), USDA; Dr. Janet Anderson, Director, Bio-Pesticide and Pollution Prevention Division, Environmental Protection Agency (EPA); Dr. James Maryanski, Biotechnology Coordinator, Center for Food Safety and Applied Nutrition, Food and Drug Administration (FDA); Mr. Mark Silbergeld, Co-Director, Washington Office of Consumers Union; and Dr. Stephen Taylor, Professor of Food Technology, University of Nebraska. The Subcommittee also received written testimony for the record from Dr. Stephen C. Joseph, President and CEO, National Center for Genome Resources.

The record of these hearings is available in Committee on Science print Serial No. 106-60. All references to witness testimony include written testimony, oral testimony, and responses to follow-up questions submitted by the Subcommittee. Where practicable, other material referred to in this document has been included in the record of the hearings. An electronic version of the Report is available on the Committee on Science World Wide Web site at "<http://www.house.gov/science>." Site visits to universities conducting plant genomic and breeding research and meetings held with interested parties also were important in gathering information for this Report.

BACKGROUND

A BRIEF HISTORY OF PLANT GENETICS AND AGRICULTURAL BIOTECHNOLOGY

Almost without exception, the fruit, vegetable, and other crop plants grown commercially today have been genetically modified.² The adoption of new plant varieties developed through selective breeding has been improving the food supply for thousands of years. Since prehistoric times, farmers have selected seeds from the strongest, most desirable plants, and used them to produce the next generation of crops. This process of selection, combined with genetic modification through crossbreeding, has resulted in a wide range of crop plants suited for different purposes and adapted to particular regions.

The impact of plant selection and cross breeding on crop species has been tremendous. Although the wild ancestors of few plants, such as carrots, lettuce, and sunflowers, are readily identifiable, most important food crops have been altered to such an extent that their wild ancestors are unrecognizable, and in some cases they are unknown altogether. The closest wild relative of maize (*Zea mays*), for example, is teosinte (*Euchlaena mexicana*), which may alternatively be an ancestor, descendant, or sibling. Finding the precise connection between domesticated maize and its tropical-American ancestor has proved elusive despite extensive study.

Not all genetic modification, of course, relies on human intervention. By the 18th century, naturalists were able to identify many kinds of hybrid plants that clearly were the result of the natural combination of two varieties of plants. However, these observations, while useful, were not systematized in any way. For most of man's history, plant breeding understandably focused exclusively on results, with little regard for the hereditary mechanisms involved. That began to change in the 19th century.

The Science of Genetics Comes of Age

The basic principles of heredity were discovered by Gregor Johann Mendel, an Augustinian monk at Brunn, Austria (now Brno, Czech Republic). His now-classic studies on inheritance of traits in garden peas (*Pisum sativum*), begun in 1856 in a small monastery garden, laid the foundation for the modern science of genetics. Unlike previous investigators, who attempted to explain all variations, whether heritable or not, Mendel concentrated his efforts on a few traits observed in a controlled breeding program.

Mendel found that certain traits of the parent plants—such as tallness or dwarfishness, blossom color, seed shape and color, *etc.*—were distributed among offspring in ratios that never varied significantly, and thus were predictable. From these results, he posited a set of rules to explain how characteristics are passed from one generation to the next and theorized that the variability among the parent plants and their descendants was due to paired units of heredity.³ The causal

² Though not really “crop” plants, wild berries provide examples of plant-derived foods that are widely consumed but have not been genetically modified through human intervention.

³ Mendel owed much of his success to his selection of a plant species, the garden pea, that normally is self-pollinating—allowing him to use genetically pure varieties in his experiments—and is easily cross-pollinated. Subsequent studies by Mendel using hawkweed (*Hieracium*)—an apomitic plant able to produce seeds without

“factors” of heredity suggested by Mendel eventually were given the name “genes” by Wilhelm Johannsen in 1905.

Mendel's discoveries were first reported in an obscure Austrian journal in 1866, where they attracted little attention until 1900, when Hugo deVries in The Netherlands, Carl Erich Correns in Germany, and Erich Tschermak von Seysenegg in Austria independently rediscovered them while conducting their own studies on inheritance. In 1903, Walter Sutton concluded that hereditary information was located on chromosomes, and in 1911 it was postulated that genes were arranged linearly.

By the mid 1930s, it was widely speculated that deoxyribonucleic acid—DNA—was the critical constituent of genes. The existence of nucleic acid was discovered earlier, in 1869, by the Swiss biochemist Frederick Miescher, but little attention was paid to this finding until after the turn of the century, when research on nucleic acids increased. By the late 1920s, the basic chemistry of DNA had been determined. Although DNA was found to be concentrated largely in the chromosomes, many scientists nonetheless believed that the complex nucleoproteins associated with DNA were more likely to be the primary constituent of genes. By 1952, several investigations with bacteria and viruses, which have little or no nucleoproteins in their DNA, confirmed that DNA was responsible for transmitting genetic information.

Another crucial piece to the genetic puzzle fell into place during the 1940s, when two American biologists, George Beadle and Edward Tatum, investigated the transmission of hereditary traits in the fungus *Neurospora*. They showed that particular genes were responsible for particular enzymes and that genes regulated all biochemical functions. Since their pioneering work—for which they (along with Joshua Lederberg) received the 1958 Nobel Prize in physiology or medicine—the concept that each gene governs the formation of a single enzyme was refined. It is now recognized that genes control the formation of polypeptide strands,⁴ or proteins, which comprise the “workhorses” of cellular metabolism in all living organisms.

A critical breakthrough occurred in 1953, when James Watson, an American biochemist, and Francis Crick, a British biophysicist, described the double helix structure of DNA. Using stereochemical techniques and evidence developed by Rosalind Franklin and Maurice Wilkins, whose x-ray diffraction studies of DNA suggested a double-spiral structure, Watson and Crick were able to construct a three-dimensional molecular model of DNA. For their work, Watson, Crick, and Wilkins shared the 1962 Nobel Prize in physiology or medicine.⁵ This groundbreaking research set the stage for further studies aimed at deciphering the genetic code and led to rapid advances in the practical applications of genetics.

We now know that DNA is, as Watson and Crick demonstrated, a double helical structure made up of two long strands composed of only four simple base chemicals: adenine, thymine, guanine, and cytosine. The order in which these bases are linked forms the basis of the DNA code and

fertilization—yielded results at odds with his previous results using peas. He died in 1884 little knowing the true significance of his work.

⁴ A polypeptide strand is comprised of a string of amino acid polymers.

⁵ Rosalind Franklin died of cancer at age 37, five years before the Nobel Prize was awarded to her colleagues Watson, Crick, and Wilkins. Nobel Prize rules do not allow the prize to be awarded posthumously.

provides the chemical mechanism for storing genetic information. Genes are segments of DNA that contain enough information to produce a polypeptide strand or protein that, in turn, determines the traits expressed in the organism. DNA governs every biochemical process within the cell and the organism and commonly is referred to as the “Blueprint of Life.”

The field of molecular biology gained one of its most powerful tools—recombinant DNA (rDNA⁶) technology—in the early 1970s. In 1972, researchers at Stanford University created the first recombinant molecule. The scientists, led by Paul Berg, who received a Nobel Prize for the work, used enzymes found in bacteria—called “restriction enzymes”—to cut DNA from two different sources (a bacterium and a virus) and used a different enzymatic reaction to splice these two foreign pieces of DNA together into a functional, hybrid DNA molecule. In 1973, Stanley Cohen, another Stanford researcher, and Herbert Boyer of the University of California at San Francisco took this work one step further by transferring a recombinant molecule into a bacterium where it functioned alongside the bacterium's own genes. In doing so, they created the first rDNA, or “genetically engineered,” organism.

While none of these researchers set out to create the technology we now call gene splicing, they and others were quick to recognize the potential usefulness of this new tool. In fact, shortly after these discoveries, one of the scientists (Boyer) became a co-founder of the world's first biotechnology company, Genentech, which used genetically-engineered bacteria to produce useful human therapeutics and diagnostics, thereby launching an entirely new industry.

Genetics and Classical Plant Breeding

The development of the science of genetics in the 20th century was tremendously important in improving plant breeding. Since the 1920s, refinements of traditional breeding techniques have produced new varieties of old crops with higher yields, greater resistance to pests and diseases, and other desirable qualities. Genetic modification through these methods has given a immense boost to agricultural productivity.

Before the principles of genetics were determined, plant breeders depended on practical knowledge and experience to develop improved crops. One of the most successful plant breeders in America, Luther Burbank, produced new varieties of potatoes and other vegetables and fruits using hybridization and selection without any formal botanical training or understanding of genetics. His first and most famous variety, the Burbank potato—still popular even today—was introduced in 1876 and planted extensively.

In 1908, the American botanist George Shull found that inbreeding tended to purify strains of corn while weakening the plant. By cross-breeding inbred strains, he developed hybrids of maize that produced higher yields than the original varieties from which the crosses were made, and suggested that these hybrids could be used on farms in place of the varieties normally used. However, the drawback with the single-cross method Shull developed was that subsequent generations of the plant lost vigor. This problem was addressed in 1918 with the development of

⁶ There are other techniques used in biotechnology, such as recombinant RNA and cell fusion. For the purposes of this report, the acronym rDNA shall refer to all recombinant technologies.

the double-cross by Donald Jones of the Connecticut Agricultural Experiment Station.⁷ For many years, most of the corn grown in the United States was from double-cross hybrid seed. Today, seed producers are able to use single-cross hybrids because modern inbred corn lines are much more robust than those developed in the early 20th century.

Techniques informed by a better understanding of the genetic basis of heredity have been used extensively in crop improvement worldwide. For many years, the development of hybrids for use in developing countries, particularly those in the tropics, lagged behind developments in industrialized countries. After World War II, the developing world began applying hybrids with great effect. The introduction of a dwarfing gene into wheat by Orville Vogel in the 1940s, led to a tremendous improvement in grain yields and began this trend. Subsequent work in the 1950s and 1960s led to further increases in yields of wheat, rice, and other important staple crops grown by subsistence farmers in the developing world. Norman Borlaug, an American plant breeder, won the Nobel Prize in 1970 for his work in developing improved, high-yield wheat varieties for Mexico. The dramatic improvement in crop diversity and yields experienced over this period was aided by improved management and increased inputs of fertilizer, pesticides, and irrigated water. These improvements helped feed a growing world population and became known as the “Green Revolution.”

In recent years, plant breeders have used advanced genetic techniques to perform wide-hybrid crossing of sexually-incompatible plants that could not occur without human intervention. Oats, for example, have been crossed with a number of very distantly-related wild species to increase pest resistance and protein content. Interspecies and intergeneric protoplast fusion, *in vitro* gene transfer techniques, and somaclonal selection, haploid doubling, induction of polyploidy, and embryo rescue on artificial growth media are all routinely employed by plant breeders to produce viable wide genetic crosses. In addition, plant breeders have used chemical and physical mutagenesis—a highly uncontrolled process—to produce a wide variety of genetic mutants from which they select plants with superior traits. These genetic modification methods have permitted hybridization between plants of the same species, different species, and even different genera to create improved varieties of many plants, including corn, oats, potato, rice, tomato, and wheat, among others.⁸

The development of, and the increasing reliance on, new plant varieties has led to the virtual disappearance of older varieties that could serve usefully as sources of germplasm for future crop improvement and environmental restoration. Therefore, USDA maintains the National Plant Germplasm System, which contains over 400,000 lines and varieties of plants no longer in use or never grown commercially, to provide gene pools for future breeding programs. These plant lines and older varieties may contain genes that could be beneficial in improving the genetic variation of existing or future varieties. They are preserved by USDA as an irreplaceable genetic resource.

The Advent of Agricultural Biotechnology

⁷ The double-cross involves producing two single-cross hybrids from four inbred lines, which are then crossed to produce one “double-crossed” hybrid.

⁸ For a detailed discussion of the techniques used by breeders to improve crop plants, see: Goodman *et al.*, 1987.

Despite advances in our understanding of plant heredity, traditional cross-breeding relies largely on sexual hybridization and remains a time consuming process that can take 15 years or more before a crop is ready for the market. Traditional breeding is hit-or-miss due to the uncontrolled recombination of tens of thousands of genes producing both desirable and undesirable traits. Also, the constraints imposed by sexual compatibility deny plant breeders access to a diverse range of genetic material, severely limiting the ability to improve crops through traditional means.

In 1905, Sir Roland Biffen's experiments with two varieties of wheat demonstrated that resistance to stem rust fungus was inherited. This led to further attempts by plant breeders to develop pest-resistant strains of other crop plants. However, breeders soon were confronted with the fact that the gene for a desired trait may not always be available in a sexually-compatible plant, so no amount of cross-breeding will yield an improved strain. And even where a desirable gene is available, it may be linked unalterably to another trait that is undesirable (*e.g.*, a fruit with bitter taste). Thus, plant breeders have long sought new technologies to increase the diversity of genes for pest resistance and other traits that could be used to improve plants.

With the development of biotechnology and rDNA techniques, plant breeders now possess the tools to introduce select, useful genes from a wide variety of sources into plants to express specific, desirable traits. Current methods of gene insertion include using a “disarmed” (or benign) plasmid from the plant pathogen *Agrobacterium tumefaciens* as a vector,⁹ DNA-coated metal microprojectiles, and direct uptake of DNA by protoplasts of plant cells.¹⁰ Many other promising techniques are under development.

The main advantage of using rDNA technology is that, unlike hybridization, it permits the transfer of specific, well-characterized genes from the source organism to a target plant. The precision of rDNA technology is a vast improvement over traditional cross-breeding, which involves the transfer of all the genes from each parent, requiring repeated rounds of crossing and back-crossing over several generations to produce the desired combination of traits. Using biotechnology, usually only one or two progeny generations are needed to complete the gene transfer.

Gene transfer techniques also are being used increasingly to move genes among plants that could be hybridized using traditional methods and to control, increase, or turn off specific functions within a plant. The greater precision of these techniques will cut significantly the time and cost necessary to bring an improved variety to market.

Once the desired combination of genes has been produced, the process of variety development and scale-up is very much the same regardless of the method used to combine the genes. Thus,

⁹ The bacteria *A. tumefaciens* is the cause of crown gall disease, which produces tumor-like growths on the stems of susceptible plants. Work in the 1970s showed that tumor-inducing genes of *A. tumefaciens* were transferred to the plant via the bacteria's plasmid. Techniques were later developed to locate and then remove the tumor-inducing genes, transforming the plasmid into a useful tool for recombining DNA. For a detailed discussion of the research that led to the development of bioengineered seeds, see: NRC, 1998.

¹⁰ Using these techniques, very few genes actually are transferred. Therefore, “markers” are used to identify and recover those cells or tissues in which the gene transfer has been successful. Antibiotic resistance genes commonly are used for this purpose.

the plant lines under consideration for release as new varieties must still be tested under field conditions at multiple sites over several years to assure that performance will be up to expectations and to reveal any unexpected weaknesses. Most new varieties are subjected to 50 or more site-years (sites _ years) of performance testing before being selected for seed production and farm use.

Applications of rDNA technology already have had a profound impact in biomedical research and human medicine. For example, in 1978, Genentech began using this technology to create bioengineered bacteria to produce human insulin, a product that has replaced bovine and porcine insulin for many diabetics. Other biotechnology products include tissue plasminogen activator for treatment of heart-attack patients, powerful growth factors used in bone marrow transplants, a hepatitis B vaccine, interferon used to attack viruses and stimulate immune response, and diagnostic tests that are keeping America's blood supply safe.

Biotechnology has been used widely in food processing. Chymosin (also called rennin) is an enzyme used to clot milk and produce cheese. In the past, processors obtained chymosin from rennet, a preparation scraped from the fourth stomach of milk-fed calves. Today, the enzyme is purified from a bacterium that has been genetically-altered to produce it. The chymosin obtained in this process is structurally identical to the naturally-occurring form. About 60 percent of the hard cheese produced in the United States is made with chymosin from genetically-modified bacteria.

The first effort at marketing a crop food modified through biotechnology occurred in the 1989, when Calgene Corporation initiated discussions with FDA regarding its Flavr Savr tomato, engineered to provide extended shelf-life. In this case, the plant's own gene for production of an enzyme that naturally softens the fruit was disabled by inserting it "backwards" (antisense) within the tomato genome. Approved by FDA in 1994 and well received by curious consumers, the Flavr Savr tomato was not a commercial success for reasons unrelated to the product. The British company Zeneca, however, achieved greater success marketing a genetically-modified tomato used in making tomato paste for sale in the United Kingdom.

Crops designed to resist pests and viruses or to tolerate certain broad-spectrum herbicides make up the bulk of the first generation of commercially-viable biotechnology crops. "Bt" corn, potato, and cotton each incorporates select genes from the widely-used biological control agent *Bacillus thuringiensis* to resist targeted insect pests. *B. thuringiensis* is a soil microbe that produces proteins—delta-endotoxins—that are selectively toxic to certain kinds of insects but harmless to other insects, humans, and animals.¹¹ Bt corn, for example, produces the endotoxin in the corn, enabling the plant to ward off the European corn borer, a pest that costs U.S. corn growers over \$1 billion each year. Bt potatoes and Bt cotton have been engineered to resist the Colorado potato beetle and the pink boll worm, respectively. These crops are widely planted by American farmers and have resulted in substantial savings.

Many commercially-important plants, such as potato, squash, cucumber, watermelon, and papaya, have been modified to protect themselves against viral infection simply by introducing virus genes that produce viral coat proteins. Viral coat proteins are components of the outer wall

¹¹ Spray insecticides derived from *B. thuringiensis* are used widely in organic farming.

that enclose the genetic material of a virus. Plants modified to produce viral coat proteins resist viruses through a mechanism known as cross-protection, which is somewhat analogous to immunization. Farmers and consumers have gained from substantial savings by reducing chemical inputs normally required to control virus-carrying insects.

Soybeans and other plants have been modified to tolerate broad-spectrum herbicides used by farmers to control weeds. The most common is the “Roundup® Ready” soybean, a plant that has been designed to tolerate Roundup Herbicide (glyphosate), developed and produced by Monsanto. Unlike many other herbicides, glyphosate has low toxicity, is safe for humans and animals, and degrades quickly in the soil. Other plants have been developed to withstand glufosinate, produced by AgrEvo, and bromoxynil, produced by Rhône-Poulenc Rorer. In the United States, the use of herbicide-tolerant crops has reduced herbicide use and allowed farmers to adopt no-till farming methods that minimize soil erosion and moisture loss.

In addition to pest resistance and herbicide tolerance, other traits are being added to crop plants that will allow them to withstand drought, freezing temperatures, and salt toxicity. Future advances offer the promise of an impressive array of new and useful products that will improve crop yield and quality, provide better nutrition, deliver needed vaccines and medicines, produce more desirable fats and oil, extend the shelf life of fruits and vegetables, lower food costs, and create renewable non-food products that can reduce reliance on nonrenewable resources. Development of these and other new varieties of plants is underway and will open up entirely new markets to farmers and provide enhanced food products to consumers.

Agricultural biotechnology is a thriving industry, and many U.S. farmers have readily adopted this new technology. It is estimated that in 1998, 26 percent of the corn, 43 percent of the cotton, 4 percent of the potato, and 26 percent of the soybean crop in the United States was planted with varieties modified using agricultural biotechnology (Gianessi and Carpenter, 1999).

PLANT GENOME RESEARCH

The plant genome program provides much of the basic research into plant genetics that will be used to produce future products. The United States Government became directly involved in plant genome research in 1989, with the initiation of the Multinational Coordinated *Arabidopsis thaliana* Genome Research Program, supported jointly by NSF, the Department of Energy (DOE), USDA, and the National Institutes of Health (NIH). The project started out with two ambitious goals: (1) to determine the complete sequence of *Arabidopsis thaliana*, a member of the mustard family; and (2) to use this information to understand the physiology, biochemistry, growth, and developmental processes of flowering plants at the molecular level.

The value of *Arabidopsis* in genetics research was first recognized by the German Friedrich Laibach, who published a paper on its chromosomes in 1907 and later promoted its usefulness as a research tool in 1943. Though not a crop plant, *Arabidopsis*—a simple, flowering mustard plant usually described as a weed—nonetheless makes an excellent subject for plant genome research. It has a simple genome (about a fifth the size of the sorghum genome and a hundredth the size of the wheat genome), a short generation time (six weeks), and several plants can be grown in a square centimeter. Moreover, mutations can be induced easily, providing valuable

insights into the plant's genome. In short, *Arabidopsis* is both relatively simple and representative, making it suitable as a model for a whole classification of flowering plants.¹²

The goals of the plant genome program were considered quite risky in 1990 when they were developed "because the biological and computing technology was not yet available to accomplish this feat" (Clutter, 1999). By 1996, technology had matured to the point that it was possible to begin the total sequencing of the *Arabidopsis* genome. Rapid progress was made, and in December 1999, researchers in the United States and England announced the sequencing of two complete chromosomes, or about 30 percent of the estimated 26,000 genes in *Arabidopsis*.¹³ Sequencing the entire genome should be completed by the end of 2000.

In 1997, an Interagency Working Group (IWG) on plant genomics was established under the auspices of the Office of Science and Technology Policy (OSTP). Participants in this working group include representatives from NSF, USDA, DOE, NIH, the Office of Management and Budget, and the Office of Science and Technology Policy (OSTP). IWG developed a five-year strategic plan for the National Plant Genome Initiative (NPGI) with the ultimate goal of understanding the structure and function of every gene. Using DNA microarray analysis and other advanced techniques, scientists will be able to determine the expression of all the genes in an organism.

As part of its five-year plan, the IWG set the following goals for NPGI:

- Complete the sequencing of the model plant species, *Arabidopsis*;
- Participate in an international effort to sequence rice;
- Develop the biological tools to study complex plant genomes, such as corn, wheat, soybean, and cotton;
- Increase our knowledge of gene structure and function of important plant processes;
- Develop appropriate data handling and analysis capabilities; and
- Ensure that this new information will be accessible to the broader community of plant biologists and maximize the training opportunities that will arise from the initiative.

The Plant Genome Research Program at NSF was established in 1998 as part of the NPGI. Since its inception, NSF support has focused on two areas: (1) structural and functional genomics and (2) strengthening the research infrastructure. In addition to the work on *Arabidopsis*, U.S. participation in the international rice genome sequencing project began with support provided by USDA, DOE, and NSF in Fiscal Year 1999. For Fiscal Year 2000, NSF plans to spend \$79.5 million on plant genome research and for Fiscal Year 2001 requested an additional \$22.5 million (to \$102 million).

OVERSIGHT OF AGRICULTURAL BIOTECHNOLOGY

Oversight of agricultural biotechnology includes both regulatory and nonregulatory mechanisms that have been developed over many years for crop plants. The following discussion of

¹² For more on *Arabidopsis*, see: Meinke *et al.*, 1998.

¹³ *Arabidopsis* contains an estimated 130 million base pairs of DNA. In contrast, the human genome is estimated to contain more than 100,000 genes with three billion base pairs of DNA.

regulatory oversight that follows concentrates on the federal agencies, but it should be pointed out that state regulatory agencies also have an important, if subordinate, oversight function.

The Responsibilities of the Plant Breeder

Today, plant breeding programs are conducted by State Agricultural Experiment Stations (SAES), Land Grant colleges and universities, USDA Agricultural Research Service stations (usually in cooperation with SAES), and private companies. Based on agronomic need, crop development teams decide on a trait to be introduced to a variety of plant. If such a trait is available among the many genetic resources available, a decision is made on how to impart it to the crop. This can be done through sexual hybridization, various wide-cross techniques, or rDNA technology.

Regardless of the method, once the genetic transformation has been made, offspring of the plant are grown and observed. This process ensures genetic stability by establishing that the added trait is permanent and predictable and is expressed under varying conditions (OECD, 1993a). After producing and observing subsequent generations and eliminating plants with undesirable traits, the breeder selects a few plant lines for large-scale testing.

By the time a new variety of plant is ready for release or commercialization, it has undergone significant review and testing. The plant breeder is responsible for considering agronomic and ecological factors during the development phase, including yielding potential, reproductive stability, uniformity of traits, weediness, vulnerability to attack by pests, sensitivity to environmental stresses, and other factors. When developing varieties with unusual risks, the breeder will adopt evaluation methods designed to assess and manage the risk. If the plant is to be used as a food, the breeder also is responsible for evaluating the food product for toxins and allergens.

After extensive performance tests and reviews, a new variety may be released. The Association of Official Seed Certifying Agencies has set up variety review boards for many important crop plants. Breeders are not required to submit their new varieties to these boards, but for seed crops eligible for protection under the Plant Variety Protection Act, such protection is exercised only through the seed certification process. In applying for certification, the breeder must submit a detailed description and broad array of other information about the new plant variety.

Peer-reviewed journals also are used to register the release of plants either as a new variety, germplasm, or genetic stock. The scientific societies that publish these journals establish their own specific criteria and protocols, but in all cases the published information, which is in the public domain, provides valuable data on the new variety.

Both certification and peer review have been effective in providing non-regulatory oversight. It is important to note that these procedures are not required by law but rather have been developed voluntarily by breeders and growers over decades based on our increasing knowledge and experience. As the techniques to develop new plant varieties become more advanced, the procedures used by plant breeders are expected to keep pace through the evolution of standard best practices informed by increased knowledge. "It is a natural progression of science," noted

11 professional scientific societies, “to adopt ever-better techniques and establish ever-higher standards of performance in research and development” (IFT *et al.*, 1996).

Coordinated Framework and Statement on Scope

The development of rDNA techniques in the 1970s led to concerns about the potential hazards associated with the technology. In 1974, the NIH Recombinant DNA Advisory Committee published guidelines for laboratory research using biotechnology.¹⁴ NIH remained the primary federal body that reviewed and monitored rDNA research until 1986, when OSTP published the “Coordinated Framework for Regulation of Biotechnology” (Coordinated Framework) for the White House Domestic Policy Council Working Group on Biotechnology (OSTP, 1986).¹⁵

The Coordinated Framework provided a regulatory roadmap relevant to biotechnology research and products, and it identified possible gaps in oversight. Under the Coordinated Framework, new products developed through biotechnology would be regulated “in essentially the same manner for safety and efficacy as products obtained by other techniques” and would be regulated under authority granted under existing federal statutes and regulations. The framework also identified lead agencies to coordinate activities where jurisdiction overlapped, and it explained the proper allocation and coordination of regulatory oversight under various statutes and among relevant agencies.

The regulation of plants and foods created through agricultural biotechnology is handled by three federal agencies: USDA, which is responsible for ensuring that new varieties are safe to grow; EPA, which is responsible for ensuring that new pest-resistant varieties are safe to grow and consume; and FDA, which is responsible for ensuring that new varieties are safe to consume.¹⁶

While the Coordinated Framework took into account the different statutory bases for regulation among the agencies, it also emphasized that common principles should govern decisions concerning the exercise of discretionary regulatory authority. Under the auspices of a White House Working Group, the involved Federal agencies—including USDA, EPA, and FDA—agreed to a common statement on federal oversight within the scope of statutory authority. This “Statement on Scope” was published by OSTP in 1992 and addressed how oversight authority should be exercised in situations “in which a statute leaves the implementing agency latitude for discretion” (OSTP, 1992).¹⁷

The Statement on Scope lays out a scientific, risk-based approach as the proper basis for regulatory oversight. It establishes two main criteria for regulation of biotechnology products: (1) oversight authority should be exercised only where there is evidence that the “risk posed by the introduction is unreasonable”; and (2) regulatory oversight “should focus on the characteristics and risks of the biotechnology product—not the process by which it was created.”

¹⁴ It is worth noting that within a few years, NIH deemed that there was sufficient scientific knowledge regarding the safety of rDNA techniques to relax these guidelines substantially.

¹⁵ OSTP published a proposed “Coordinated Framework” in the *Federal Register* on December 31, 1984.

¹⁶ In addition, the Department of Labor’s Occupational Safety and Health Administration was given responsibility for the safety and health of biotechnology workers and NIH was given responsibility for the safety of rDNA research.

¹⁷ OSTP published a proposed “Statement on Scope” in the *Federal Register* on July 31, 1990.

In setting these guidelines, it was expected that the agencies would implement them “in a manner appropriate to each statutory framework” and “consistent with the risk-based principles” set out in the document (OSTP, 1992).

U.S. Department of Agriculture

Under authority found in the Federal Plant Pest Act and the Plant Quarantine Act, USDA's APHIS issues field-test permits for new plants that have the potential to create pest problems in domestic agriculture. APHIS regulations provide procedures for obtaining a permit or for providing notification prior to importing, moving interstate, or releasing a “regulated article” in the United States.

Regulated articles are defined by APHIS as plants or microorganisms that are, or are believed to be, plant pests or are produced using plant pests. Under the Coordinated Framework, APHIS is responsible for regulating bioengineered agricultural plants produced using a pathogenic source organism. Genes commonly are introduced into plants using the disarmed plasmid of *A. tumefaciens* (which in nature causes plant gall) as the vector, and their expression is promoted by a DNA regulatory sequence from the cauliflower mosaic virus (another plant pest). Consequently, regulated-article status has been applied to most of the genetically-modified plants that have been developed to date.

APHIS regulations provide procedures for obtaining a permit for field testing. To receive a permit, the plant breeder must provide information pertaining to how the plant was developed and the control measures that will be taken during the trials, including field design, monitoring, and reporting requirements. If, after a review of the disclosure information submitted by the plant developer, the agency reaches a “finding of no significant impact,” a field test permit is issued.

The growing familiarity with rDNA-altered crops led APHIS to introduce in 1993, and later expand in 1997, an expedited procedure for approving field testing of plants developed using rDNA techniques. Instead of submitting a formal application for a permit, plant breeders wanting to field test plants that meet certain eligibility requirements and performance standards need only submit a “notification” letter to the Agency. The notification must include a description of the gene, the characteristics of the plant, and the location of the proposed tests. As part of this procedure, APHIS then notifies the department of agriculture in the state where the proposed trials will be conducted.

After several years of field trials, the plant breeder may petition APHIS to release its new plant variety from regulatory requirements through a determination of “nonregulated status.” Before a determination to deregulate is made, USDA requires data on the rationale for development of the plant, the system used to transform the genome, the donor genes and regulatory sequences used, genetic analysis and agronomic performance, the environmental consequences of introduction, and the adverse consequences of introduction.¹⁸ If the petitioner has demonstrated that its new plant variety is free from risk under applicable regulations, APHIS will issue a determination of

¹⁸ APHIS maintains an extensive database, accessible to the public, describing the characteristics and the results of the field tests for each regulated plant that goes through the approval process.

nonregulated status. As part of its review, APHIS performs an environmental assessment under National Environmental Policy Act requirements.

Once APHIS confers nonregulated status, unregulated interstate movement and release of the new plant is allowed. If, however, APHIS determines that the new variety poses an environmental risk—for example, if the plant demonstrates a significant potential to outcross with wild relatives and create problems—it has the authority to suspend the field trials and halt further development of the plant.

Since 1987, APHIS has processed more than 5,000 permits and notifications for field testing at over 22,000 sites and nearly 50 petitions for deregulation. Of the 44 different types of plants modified using rDNA techniques, field testing has occurred for varieties altered for herbicide tolerance (28%), insect resistance (24%), product quality (19%), virus resistance (10%), agronomic properties (6%), fungal resistance (5%), and other properties, including bacterial resistance (8%). In no instance has a biotech plant approved for field testing by USDA created an environmental hazard or exhibited any unpredictable or unusual behavior compared to similar crops modified using conventional breeding methods (McCammon, 1999).

Organic Rule. The debate over agricultural biotechnology also has spilled over in the discussion of what should or should not be labeled as an organic food. The Organic Foods Production Act of 1990, part of the 1990 Farm Bill, requires USDA to develop national standards for organically-grown foods and to ensure that foods labeled “organic” are grown consistent with these requirements. On March 7, 2000, USDA announced a new proposal for organic standards. Under the proposed rules, foods derived from crop plants developed using biotechnology would not qualify for the organic label, even if grown in conformity with organic standards.

Environmental Protection Agency

EPA's Office of Pesticides Programs, Biopesticides and Pollution Prevention Division, regulates and registers “plant pesticides” under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and the Federal Food, Drug, and Cosmetic Act (FFDCA).¹⁹ Bt corn is perhaps the most well known example of a plant modified to produce its own pesticide.

In November 1994, EPA issued a new proposal detailing how it would regulate plant pesticides to meet the requirements of FIFRA and FFDCA. This proposal is now in the final stages of the rule-making process and is expected to be concluded sometime in 2000.

While the proposed plant pesticide rule has been moving through the review and public comment process, EPA has been using approval and registration guidelines that have been established for testing chemical, microbial, and biochemical pesticides. The Agency also is required under FFDCA to establish a safe level of pesticide residue in foods, known as a “tolerance.”

Before submitting an application for field-test approval and registration, the plant breeder consults with EPA scientific staff to decide upon the data requirements that will support the

¹⁹ EPA also regulates bioengineered microorganisms under the Toxic Substances Control Act.

Experimental Use Permit (EUP). The studies done under the EUP are used to support the application for registration.

EPA's registration requirements include data on product characterization, toxicology, effects on non-target organisms, exposure, and environmental fate. Data on product characterization includes the source of the gene, how the gene is expressed, the nature of the pesticidal substance produced, modifications to the introduced trait as compared to that trait in nature, and the biology of the recipient plant. For toxicology, acute oral toxicity of the pesticidal substances administered to mice has been required. EPA also requires a digestibility test to determine the amount of time it takes for the protein to break down in gastric and intestinal fluids. Allergenicity of the substance also must be considered. For ecological effects, EPA examines the exposure and toxicity of the plant-pesticide to non-target organisms, such as wildlife and beneficial insects. EPA also has evaluated the degradation rates of the proteins in soil and plant residues (Anderson, 1999).

EPA registered its first plant pesticide in March 1995. Since then, EPA has registered and granted tolerance exemptions to 12 plant pesticides. Six of these products are for Bt toxins produced in corn, potato, and cotton, and four are for viral coat proteins that have been transferred to potato, cucumber, watermelon, and papaya. EPA also approved and exempted from tolerance requirements a protein from the potato leaf roll virus and the potato virus Y. Dr. Anderson testified that "EPA . . . has found no documented case of environmental harm caused by a plant-pesticide produced through biotechnology."

Insect Resistance Management. Consumer groups and organic farmers have expressed concern that widespread use of plants engineered for specific types of pest resistance—particularly those manipulated to express Bt toxins, which have been used widely in a spray formulation by organic farmers—could accelerate the development of pesticide-resistant insects. To address this issue, EPA now makes insect resistance management plans a central part of its regulatory decisions on plant pesticides, and seed companies require purchasers of their seeds to implement such plans. These agreements require farmers to establish "refugia" of non-modified plants that can nurture populations of wild type pests. The view is that refugia will help maintain the genetic basis of susceptibility of the target pest species and delay the onset of genetic resistance.²⁰

On April 19, 1999, a biotechnology industry group²¹ submitted an insect resistance management plan to EPA, and on January 14, 2000, EPA announced new measures for resistance management in Bt corn for the 2000 growing season that mirrored the industry plan. It directs registrants to ensure that growers maintain refugia of at least 20 percent non-Bt corn—50 percent in areas where cotton is grown. The agency also requires increased monitoring and restrictions on planting Bt corn in certain areas.

Proposed Plant Pesticide Rule. In November 1994, EPA published in the *Federal Register* its proposed regulations outlining how it would determine that new varieties of pest-resistant plants

²⁰ Refugia of non-Bt crops work by ensuring that pests susceptible to Bt toxins are available to mate with any resistant strains that may emerge within an insect population exposed to crops modified to produce Bt toxins.

²¹ This group was composed of Novartis, Pioneer Hi-Bred International, Mycogen Seeds/Dow AgroSciences, and Monsanto in conjunction with the National Corn Growers Association.

would meet the requirements of FIFRA and FFDCA. A plant pesticide is defined by EPA as a “pesticidal substance that is produced in a living plant and the genetic material necessary for the production of the substance, where the substance is intended for use in the living plant” (EPA, 1994).

The Agency states that the purpose of the new proposal is to focus regulatory oversight on plant-pesticides that create novel exposures or operate with a more toxic mode of action. It would: (1) clarify the regulatory status of plants and plant-pesticides under FIFRA and FFDCA; (2) specify that EPA regulates the plant-pesticide rather than the plant itself; and (3) describe the categories of products subject to, and exempt from, regulation (Anderson, 1999). Exemptions would be made for plant pesticides derived from plants related to the recipient plant,²² those that act by affecting the plant,²³ and those based on a coat protein from a plant virus (EPA, 1994).²⁴

According to Dr. Anderson, “The primary focus of the new regulations is to separate out and exempt from regulation those compounds the Agency believes have a low probability of risk and instead concentrate on plant-pesticides that present new dietary and/or environmental exposures. For example, plant-pesticides introduced from unrelated species of plants, bacterium or virus, insects, etc.” The focus of EPA's proposed rules clearly would be on new pest-resistant varieties produced using biotechnology. It has been argued that by targeting the *process* by which the a new plant is produced, EPA is departing from the risk-based scientific principle that regulations should focus on a plant's characteristics, not its method of production (IFT *et al.*, 1996; Huttner, 1999).

Food and Drug Administration

Often overlooked in the debate over food safety is that it is the legal responsibility of the food producer to ensure the safety of foods they offer consumers. In addition, food producers are subject to Federal, State, and local regulations. At the Federal level, FFDCA gives FDA a broad range of legal authority and regulatory tools to ensure the safety of whole foods. It has the authority to require premarket review and approval in cases where protection of public health is required, such as when a substance is added intentionally to a food and there are questions about its safety. FDA also has postmarket authority to remove a food product from commerce and sanction those marketing the food if it poses a risk to public health. The complex array of criminal and civil sanctions, including tort and contractual remedies, available to governments and private parties provides producers with every incentive to bring safe, wholesome foods to market.

Foods produced through biotechnology must adhere to the same safety standards that apply to traditionally-produced foods under FFDCA. In 1992, FDA published in the *Federal Register* a Statement of Policy on its approach to regulation of foods derived from genetically-modified

²² Among the options for exemption are plant pesticides derived from plants that are sexual compatible, within the same genus (though not necessarily sexually compatible), or both sexually compatible or within the same genus (EPA, 1994).

²³ An example includes plants altered to grow larger leaf “hairs” (trichomes) to prevent insects such as aphids from feeding on them.

²⁴ EPA's preferred option is to exempt all viral coat proteins; a second option is to exempt only those coat proteins in plants with a low probability of outcrossing to wild relatives (EPA, 1994).

plants (FDA, 1992).²⁵ It is important to note that these rules apply equally to plant-derived foods produced using traditional breeding techniques as well as biotechnology.²⁶ FDA's guidelines provide a risk-based "decision tree" to guide plant breeders and food manufacturers through issues critical to ensuring the safety, nutritional value, and wholesomeness of new genetically-altered foods. This approach is based on many decades of FDA experience dealing with a complex array of new fruits, vegetables, and grains that have been modified using conventional methods and safely introduced into the food supply without the agency's intervention.

Guided by the decision tree, plant developers and food manufacturers conduct a safety assessment of the new food, paying particular attention to changes in naturally-occurring or introduced toxicants and allergens, nutrient levels, and fat, oil, or modified carbohydrate content, as well as the introduction of new substances that do not have a history of safe use. Where significant alterations are found, formal FDA review and approval are required. FDA requires approval and labeling only where unexpected effects are produced (such as allergens or toxins are introduced), the nutrients in or composition of the product is substantially different from traditional edible varieties, or pharmaceuticals are present.

Food producers are not required to seek FDA pre-market approval or to apply a special label, for a new variety of food if it is substantially equivalent to existing varieties already on the market. They are, however, encouraged to consult with the agency in considering safety issues. If a new food contains a "food additive," FDA would not require pre-market approval or special labeling if it could be shown that the additive is "generally recognized as safe" (GRAS). An ingredient with a long history of safe use, for example, would be considered GRAS. Other new ingredients, however, would require a submission of a GRAS petition to FDA that would be reviewed in a way similar to a FDA review of a new food additive.

Without exception biotech companies have participated in a "voluntary consultation" with FDA before bringing a new biotech food to market. During these consultations, companies are expected to provide FDA with data on the agronomic and quality attributes of the plant, genetic analysis of the modification and stability of expected genomic traits, evaluation of the safety of newly introduced proteins (*e.g.*, for allergenicity), and chemical analyses of important toxicants and nutrients. When all safety and regulatory issues have been resolved, FDA provides written notification to the company.

When asked if FDA was aware of any examples of a biotech food causing a human health problem, Dr. Maryanski responded: "No, FDA is not aware of any such case" (Maryanski, 1999). To date, the vast majority of foods developed using rDNA techniques have not required pre-market approval, and none has required labeling.

²⁵ For a good summary of this document, see: Kessler *et al.* 1992.

²⁶ FDA's Statement of Policy defines genetic modification as the "alteration of the genotype of a plant using any technique, new or traditional."

FINDINGS

The testimony and other materials and documents made available to the Subcommittee lead to the following findings.

PLANT GENOME RESEARCH

Finding: The plant genome program represents a sound use of federal research funding.

Understanding *Arabidopsis*, the relatively simple mustard plant that is the focus of NSF's Plant Genome Research Program, promises to unlock a wealth of understanding about how other plants work. As Dr. Ryals noted in his testimony, the main rate-limiting step in agricultural biotechnology is gene discovery (Ryals, 1999). Future breakthroughs in plant genomics may very well rest upon the successes of the *Arabidopsis* project and other federally-funded research initiatives that involve corn, rice, tomato, and other plants.

The federal government has supported plant genome research directly since the initiation of the Multinational Coordinated *Arabidopsis thaliana* Genome Research Program in 1989. The Project began with the ambitious goals of determining the complete sequence of the *Arabidopsis* genome and developing an understanding of the physiology, biochemistry, growth, and developmental processes of flowering plants at the molecular level.

In her testimony, Dr. Clutter highlighted a number of practical applications that have resulted from *Arabidopsis* research, including:

- Demonstrating that plants can be used to manufacture renewable biodegradable plastics in quantities suitable for industrial production.
- Elucidating complex genetic pathways by which a plant produces various oils. These genes have been used to modify canola and soybeans to produce oils of improved nutritional value; the same genes can be used to produce industrial lubricants and fuels.
- Identifying a gene that confers tolerance to sulfonylurea, a commonly used herbicide. This discovery is being used to develop crops suitable for no-till agriculture.
- Showing that plants can be modified to clean up heavy metals in the environment, such as mercury and cadmium.
- Discovering how plants take up iron and other micronutrients in the soil. This information is immediately applicable in producing crops that contain high iron and other essential mineral nutrients.
- Developing plants naturally fortified with vitamins, opening up a new area of study, "nutritional genomics."

The *Arabidopsis* project also has provided insight into the nature of complex genetic traits. In his testimony, Dr. Larkins commented that, in addition to aiding plant breeders in creating new varieties using biotechnology, "the knowledge gained from understanding the molecular basis of such traits can be applied to crop improvement through conventional breeding programs" (Larkins, 1999).

With the rapidly growing amounts of genetic information being discovered comes a serious need for new information technologies to catalogue and mine the data. The data requirements of the *Arabidopsis* program has led to a considerable investment in the field of bioinformatics—a merging of information technology, biotechnology, and agricultural sciences. The *Arabidopsis* Information Resource (TAIR) project, for example, accessible to researchers worldwide over the Internet, will include all information about the *Arabidopsis* genome project.²⁷ The USDA Agricultural Research Service also funds a Plant Genome Database.²⁸ In addition to these Federal databases, the National Center for Genome Resources, a non-profit research organization in Santa Fe, New Mexico, also supplies bioinformatics resources to assist researchers both in identifying problems that could be solved by genetic strategies and in developing new plant varieties (Joseph, 1999).

As a result of these efforts, researchers are well on their way towards fulfilling the first goal of sequencing the entire *Arabidopsis* genome. Dr. Clutter testified that work on the second goal—determining the function of the plant's estimated 25,000 genes—begins with the initiation of NSF's proposed “2010 Project.” “At present,” said Dr. Keegstra, “scientists are able to determine experimentally, or predict by comparison with other known genes, the function of just over half of the identified genes. . . This large gap in our knowledge represents a major challenge for biologists, and addressing this problem for *Arabidopsis* is the goal” (Keegstra, 1999). Improving our understanding of the function of all the genes in the *Arabidopsis* genome will help plant breeders and researchers create ever-larger numbers of new and beneficial cultivars.

Publicly-funded research data are mined actively by agricultural companies. U.S. Patent Office records reveal that prior to 1990, just one patent for *Arabidopsis*-based discoveries was issued. The current total of 622 patents represents an exponential increase in patent grants in for *Arabidopsis*-related innovations over the last 10 years (Clutter, 1999). Dr. Kennedy also described USDA efforts at technology transfer through Cooperative Research and Development Agreements. The Cooperative Extension Service is another route used for technology transfer (Kennedy, 1999).

Ensuring that the results of genome research finds its way to market still remains a challenge. Dr. Huttner commented that “there is a substantial gap between the basic research bench and...end users,” a gap similar to that faced by the biomedical sector in its infancy and one ultimately filled by small business. “Small companies tap into the tremendous creativity found in university faculty and students, whereas big companies have extensive in-house research operations, tend to be more risk averse, and often discount advances achieved in publicly-funded institutions.” She argued that basic research results are transferred more easily to small start-ups willing to take risks big agribusiness may not. This transfer could be furthered by the creation of NSF- and USDA-funded research centers—public-private partnerships that could combine basic research in genomics with plant development for small, specialty markets.

²⁷ TAIR replaces the *Arabidopsis thaliana* Database (AtDB).

²⁸ This database is comprised of a Stock Center Database, which provides researchers with information on genetic variations through the Germplasm Research Information Network; the Genome Mapping Database, which includes physical and genetic map types of many agricultural plant species and some model systems from non-agricultural species; and DNA Sequences, which are placed into the widely used GenBank/GenInfo/European Molecular Biology Laboratories and DNA Databand of Japan.

CHEMICAL INPUTS

Finding: The current generation of pest-resistant and herbicide-tolerant agricultural plants produced using biotechnology has reduced chemical inputs and improved yields for American farmers. Future adoption of new varieties will continue this trend and will solve intractable pest problems, help protect the environment, and lower costs to consumers.

Agricultural producers must defend their crops from a variety of plant pests and diseases. Insects such as the European corn borer and the Colorado potato beetle can inflict terrible damage on crops, affecting yields significantly. Pressures from weeds, disease, and weather can further hinder crop production.

Traditionally, producers have relied upon a variety of different "inputs," such as applications of herbicides, insecticides, fertilizers, and irrigated water to protect crops and boost production. Each of these inputs adds—sometimes greatly—to the cost of the product, but they are necessary investments to prevent crop losses caused by infestation, drought, or other circumstances. In addition to the financial costs of inputs, environmental costs may be exacted as well. Thus, reducing the use of chemicals without reducing crop yield or quality is a goal that will deliver both economic and environmental benefits.²⁹

The recent experience with biotech crops indicates that they significantly reduce input use and costs. Pest-resistant corn and herbicide-tolerant soybeans already are used widely in the United States, reducing pesticide and herbicide usage and, correspondingly, decreasing costs to producers and increasing farm income (USDA 1999). In testimony submitted to the Subcommittee, Dr. Prakash estimated that biotech crops saved United States and Canadian producers nearly \$500 million in 1998, and are projected to save \$6 billion by 2005 (Prakash, 1999).

Pest-Resistant Plants. Pest-resistant Bt cotton varieties have been notably effective in reducing chemical insecticide inputs and lowering costs to producers, particularly cotton growers. By introducing Bt genes into varieties of cotton, they have become biologically protected from three common and costly pests: tobacco budworm, cotton bollworm, and pink bollworm. In 1995, resistant budworms in Alabama caused yield losses of nearly 30 percent. In the absence of Bt crops, producers rely upon pyrethroid insecticides to control these pests. However, the tobacco budworm has developed a resistance to pyrethroid insecticides, severely limiting their effectiveness (Gianessi and Carpenter 1999).

Mr. Gianessi and Ms. Carpenter reported that producers who adopted Bt varieties controlled all three target pests: "USDA pesticide use data show a reduction of 2 million pounds of the insecticides that are recommended for the control of these insects since the introduction of Bt cotton varieties." As a result, they expect growers will experience increased yields using Bt varieties compared to conventional varieties, resulting in increased returns of approximately \$40 per acre. Some of these gains are being realized today. USDA's Economic Research Service

²⁹ Biotechnology also has the potential to reduce chemical inputs on lawns and golf courses, which account for a significant portion of pesticide use.

(ERS), for example, found that “adopting Bt cotton had significantly increased yields and variable profits in 1997” (ERS, 1999b).

The situation with respect to the use Bt corn is somewhat different, and it is often cited by critics of biotechnology as an example of a bioengineered crop that has not met expectations. For example, Dr. Goldberg, citing recent USDA data, argued that “Bt corn largely supplements rather than substitutes for insecticide use on field corn—the type of corn planted on the vast majority of U.S. corn acreage. Across the midwestern corn belt, only about 5% of corn acreage is treated with insecticides for the European corn borer, the primary target pest of Bt corn. Thus, for the most part, farmers planting Bt corn are not substituting Bt genes for conventional chemical insecticides. . . [I]nsecticide use against European corn borers in 1997 in the ‘Heartland’ region of the United States...was only slightly higher on non-Bt corn than on Bt corn” (Goldberg, 1999).³⁰

However, Bt varieties are aimed at controlling pests that were previously difficult or impossible to control, not replacing chemical pesticides. Defending corn requires expensive management practices, such as plowing and rotation, as well as chemical pesticides, that may not always work. As Mr. Gianessi and Ms. Carpenter explained, “[D]ue to the difficulty in scouting for this pest and the importance of timing insecticide application before the caterpillar bores into the corn stalk and is protected from insecticides, it is estimated that less than 5 percent of corn field acreage in the U.S. Corn Belt was being treated with insecticides for the European Corn Borer prior to the introduction of Bt corn varieties.” As a result, the introduction and adoption of Bt corn varieties may not have a large impact on pesticide usage, but it does have the potential to stem corn losses ranging from 33 million bushels to over 300 million bushels per year.³¹

Herbicide-Tolerant Plants. Herbicide-tolerant crops show promise in reducing herbicide input levels and costs and shifting herbicide use to more environmentally-benign formulations. Farmers growing traditional varieties of soybeans, for example, typically use high levels of more residual herbicides that persist throughout the growing season, with greater environmental risk. Glyphosate—marketed under the brand name Roundup®—is an effective broad-spectrum herbicide that degrades quickly in the soil and has low toxicity. However, because the chemical affects a wide range of plants, including crop plants, it could not be used after planting because it would kill both weeds and crops. Biotechnology has helped farmers solve this problem. “Through the power of genetic engineering,” said Dr. Thomashow, “genes have been isolated, modified and transformed back into crop species to make them resistant to the herbicide. This, then, has made it possible for farmers to use the herbicide to kill weeds, but grow healthy crops” (Thomashow, 1999).

³⁰ It should be noted that more recent research has shown even greater reduction in insecticide use. An Iowa State University study found that 26 percent of the Midwestern farmers who planted Bt corn in 1998 decreased their insecticide use. The study also noted that 82 percent of farmers said their primary reason for planting Bt corn was to prevent losses from the corn borer, while 27 percent wanted to eliminate the need for insecticide to control the pest (AP, 1999).

³¹ Dr. Huttner reported similar results in her testimony, observing that growers using Bt corn varieties in 1998 produced an additional 4.2 bushels per acre and saved 60 million bushels of corn from European corn borer losses—the equivalent of 450,000 acres that would otherwise have been destroyed.

The impact of herbicide-tolerant soybeans has been dramatic. An analysis by USDA's ERS found that in 1997, herbicide treatments for soybeans were significantly lower. "As GMO [genetically-modified organism] adoption increased, use of glyphosate herbicide (such as Roundup®) also increased but use of other synthetic herbicides decreased by a larger amount. The net result was a decrease in the overall pounds of herbicide applied" (ERS, 1999c).

This reduction in herbicide use has brought material benefits to the farmer. Dr. Prakash noted an independent study that estimates the use of Roundup Ready soybeans "saved farmers nearly \$30 a hectare because of a 40 percent reduction in herbicide usage, and also increased crop yield due to less competition from weeds" (Prakash, 1999).

Just as significantly, herbicide-tolerant crops enable no-tillage farming, a technique that greatly minimizes moisture loss and soil erosion, a severe problem in many areas of the country. Dr. Cook testified that in his 20 years of research into growing crops without tillage, "I can say unequivocally that the development of Roundup as a tool has been the single greatest tool for moving forward to growing crops with less tillage" (Cook, 1999).

Plant Pathogens. Agricultural biotechnology also is aiding farmers in the fight against other crop infestations. Plant pathologists have spent decades using traditional cross-breeding techniques in an attempt to develop new varieties of commodity crops that are resistant to viruses, fungi, and bacteria, with varied success. Despite decades of focused efforts using traditional breeding methods by USDA, Land Grant colleges, and seed companies, there are many pests for which scientists have not been able to develop pest resistance because the gene for resistance is not found in any sexually-compatible plant. Dr. Cook estimates that resistant varieties have been developed for no more than twenty-five percent of fungal diseases, an even smaller percentage of virus and bacterial diseases, and very few specific insects.

For many stubborn problems, such as soil-borne pathogens, biotechnology may offer the only option. Dr. Cook told the Subcommittee of his work in the root diseases of wheat and barley. He said, "We have been waiting 35 years to have access to genes that we can now put into wheat or barley to have resistance. There have been no genes in the whole pool of germplasm of wheat and barley that I could use for this . . . but we now have the means to bring genes in from natural enemies of some of these pathogens in the same way that Bt has been put into corn."

The Subcommittee also heard testimony about the economic devastation pest epidemics can cause in rural communities. The outbreak of wheat scab in western Minnesota and eastern North Dakota, for example, caused hundreds of millions of dollars in crop losses. Biotechnology will provide researchers with new tools to solve some of the most persistent pest problems in agriculture and help prevent severe economic losses in vulnerable farm communities.

CONSUMER BENEFITS AND GLOBAL FOOD PRODUCTION

Finding: The promise of agricultural biotechnology is immense. Advances in this technology will result in crops with a wide range of desirable traits that will directly benefit farmers, consumers, and the environment and increase global food production and quality.

Thomas Jefferson once said, “The greatest service which can be rendered any country is to add a useful plant to its culture.” If the testimony presented before the Subcommittee is representative, then in the coming decade the Nation and the world can look forward to the addition of many new plants producing higher yields and possessing desirable traits because of plant genomics and agricultural biotechnology.

Current applications of agricultural biotechnology have been criticized because they have conferred direct benefits to producers, not consumers. That, in turn, has slowed public acceptance of this technology, especially in Europe.

Biotechnology offers the promise of an impressive array of new and useful products that will improve crop yield and quality, provide better nutrition, deliver needed vaccines and medicines, and create new markets for renewable non-food products while using fewer resources, lowering costs, and reducing the environmental footprint of farming. And at a time when many are worried about the fate of the family farm, biotechnology can provide an array specialty products—such as “designer” foods, “pharmafoods,” biodegradable plastics, *etc.*—ideal for small-scale agriculture.

But the potential impact of agricultural biotechnology goes far beyond designer crops and products. In meeting the challenge of feeding a rapidly-growing world population, this technology will be seen increasingly as a necessity, not a luxury.

The scope of this challenge is vast. Today, almost 1 billion people live in abject poverty and suffer chronic hunger, about 70 percent of which are farmers (Persley and Doyle, 1999). Future population growth promises to place further demands on food production. It is projected that between 1995 and 2020, approximately 73 million people will be added to the earth's population each year, increasing the world's population by 32 percent to 7.5 billion; 97.5 percent of this growth will take place in the developing world (Pinstrup-Anderson *et al.* 1999).

Over this period, the developing countries will provide the largest increase in demand for food, accounting for about 85 percent of increased global demand for cereals and meat. However, because of environmental concerns and the availability of arable land, it is estimated that the amount of land used for farming can only increase by approximately 7 percent. As a result, the increased demand for foodstuffs will have to be met through greater production. As the rapid growth in yields experienced during the Green Revolution begins to slow, new ways to increase yields will have to be developed (Pinstrup-Anderson *et al.* 1999). Agricultural biotechnology can play a major role in helping developing countries become self-sufficient in food production.

Improving Environmental Stress Tolerance

Combined with a greater understanding of plant genomics, biotechnology can expand the environmental range in which plants can be grown and increase agricultural production in regions of the world with low agricultural output and high rates of malnutrition. Crops that can withstand drought conditions, high salinity, or toxic metals, for example, could enable populations living in currently nonarable regions to farm their land, reducing the pressure on other regions of the world, such as rainforests, that are currently being converted to farmland.

Approximately one-third of the world's irrigated land, including large areas of the Indian-subcontinent, is unsuitable for growing crops due to salt contamination. Researchers have already genetically engineered salt-tolerant *Arabidopsis* and theorize that it should be possible to engineer a whole spectrum of salt-tolerant plants. This would allow farmers to irrigate crops with salt water or water of marginal quality (Frommer *et al.*, 1999).

Other forms of environmental stresses, such as extremes in temperature and drought, have a major impact on crop production. It has been estimated that in the U.S., the average annual yield of the major row crops is only 20 percent of their genetic potential, with most of the “missing” 80 percent being lost due to environmental stresses (Boyer, 1982). In addition, environmental stresses greatly limit the locations where crops can be grown. For instance, due to freezing temperatures, winter canola cannot be grown throughout the northern U.S. or most of Canada. Sudden or unexpected changes in weather conditions can have dramatic effects as well; in California, for example, the citrus industry experienced some \$600 million in losses during a spell of freezing temperatures in the winter of 1999 (Thomashow, 1999).

Many traditional plant breeding programs have included efforts to increase environmental stress tolerance. However, these efforts have met with little success because of the physiological and genetic complexities involved in enhancing stress tolerance. The most freeze-tolerant wheat varieties available today, for instance, are only marginally better than those developed in the early part of the 20th century.

In one example of the gains that can be realized by agricultural biotechnology, recent research on environmental stress tolerance has led to the identification of “master switch” genes that control freezing tolerance. As these genes also affect tolerance to drought and high-salinity stress, plants incorporating these master switch genes are currently being developed and tested in a wide range of crop and horticultural species (Thomashow, 1999).

Contamination of soil by toxic metals is another serious problem with which farmers have to cope. Aluminum, for example, is a problem in acid soils in many parts of the Southeastern United States, Central and South America, North Africa, and parts of India and China. Recent research has identified metal-resistance genes in *Arabidopsis*, wheat, and yeast that could be inserted into plants to enable them to grow in soil containing these metals in otherwise-toxic amounts. Taking this technology one step further, researchers are attempting to develop plants that can be used as a cost-effective way to perform environmental cleanup of soils contaminated with metals such as mercury, copper, or cadmium (Moffat, 1999a).

The ability to grow crops in regions of the globe that are presently nonarable, or only marginally so, will greatly reduce the strain on available land, enable those who currently struggle to gain subsistence from the land to feed themselves, and reduce the costs of environmental remediation.

Improving Nutrition

One of the most promising payoffs of agricultural biotechnology is the production of foods with enhanced nutrition. From mitigating the horrific human costs of starvation and malnutrition in

the developing world to reducing disease through dietary improvement, biotech foods have the potential to benefit virtually everyone, no matter where on the planet they reside. These foods will take many forms—plants with higher levels of certain essential amino acids or vitamins, reduced fat levels, increased fiber content, better quality oils, and even anti-cancer properties. The following is a short list of biotech food products that are already on the market or in development:

- Potatoes that contain less starch and therefore absorb less fat during frying;
- Corn and sweet potatoes that contain higher levels of important amino acids, such as lysine;
- Soybeans that contain higher levels of amino acids, such as lysine and methionine, for improved animal nutrition;
- High-sucrose soybeans that taste better and have greater digestibility; and
- New varieties of canola bred for superior oil qualities (ERS, 1999a).

Foods that contain higher levels of beta-carotene or other anti-cancer components are possible and could greatly improve nutritional intake. Advanced understanding of how natural plant substances, known as phytochemicals, confer protection against cancer and other diseases is being used to enhance the level of these substances in the food supply. As Dr. Ryals said, "[W]e can envision a future where...you go to a restaurant and you eat a spaghetti dinner, the spaghetti will be enhanced, possibly [with] a compound that will lower your risk of colon cancer if you eat it once a week. And the sauce that you eat will have antioxidants at a high enough level that it will have some potential benefit...the possibility of this technology is only limited by one's imagination."

Biotechnology will be an critical element in the fight against malnutrition in the developing world. The United Nations Children's Fund estimates that over 200 million children around the world suffer from severe malnutrition, and each year, malnutrition causes the death of nearly 12 million children under the age of five (UNICEF, 1998).

Deficiencies of vitamin A and iron are very serious health issues in many regions of the developing world where rice is a dietary staple. According to the World Health Organization, vitamin A deficiency, which makes individuals vulnerable to infections and blindness, affects approximately a quarter of a billion children. In some regions of the globe, one out of four child deaths is related to vitamin A deficiency. Iron deficiency affects an estimated 3.7 billion people, especially women and children, leaving them weakened by anemia (Gura, 1999).

Recent research conducted jointly by the Swiss Federal Institute of Technology and the University of Frieberg has the potential to address this particular problem. Researchers at these two institutions have used biotechnology to incorporate a total of seven genes from other plants, bacteria, and fungi into rice to produce a new rice strain—Golden Rice—that contains both beta-carotene (the precursor to vitamin A) and iron.

With the assistance of the International Rice Research Institute, this newly-produced rice variety will be cross-bred with commercial strains, field tested, and eventually made available to farmers in all parts of the developing world. Commenting on these developments in the context of the

concerns about agricultural biotechnology raised by activists in the developed world, the journal *Nature* recently editorialized that “such gains could become casualties of the battle being waged over GM crops. If they do, it would be the loss of a golden opportunity to actually help the several billion people in the world whose food doesn't arrive in packaging requiring labeling, if it arrives at all” (*Nature Biotechnology*, 1999).

The Subcommittee also heard about research aimed at improving the protein content of food staples. In many cases, foods such as corn, rice, and other cereal grains are not nutritionally complete because they do not contain all of the essential amino acids needed to build muscle. Diets dependent on these nutritionally-incomplete foods can lead to malnutrition, causing developmental disorders and even death. Because cereal grains comprise as much as 70 percent of the dietary protein for humans in the developing world, 195 million children worldwide are undernourished for protein and suffer stunted growth, weakened resistance to infection, and impaired intellectual development (Larkins, 1999).

Efforts to improve protein content through traditional breeding have been only modestly successful. “Plant breeders throughout the world have worked for more than 30 years to improve the protein quality of maize and other cereals,” Dr. Larkins testified. In contrast, he added, “[U]sing molecular genetic and genomic approaches, we were able to unravel the complex problem of the inheritance of lysine-rich proteins in corn. Furthermore, it appears our findings are applicable to other types of cereal grains, including sorghum and wheat, and thus it may be possible to generally improve the protein quality [of] cereals through this strategy” (Larkins, 1999).

Preventing and Curing Disease

Plants have been used for medicinal purposes for thousands of years, if not always to great effect. Medieval “herbals,” for example, were medicobotanical compendiums of flora that featured often fanciful accounts of the medicinal value of selected plants. More recently, taxol, a leading anti-cancer drug, was developed from the bark of the Pacific yew tree.

The merging of medical and agricultural biotechnology has opened up new ways to develop plant varieties with medicinal characteristics, including foods that contain pharmaceuticals—“pharmafoods.” Dr. Ryals' s testimony pointed to the tremendous possibilities for pharmafoods. “[C]onsider that over 50% of all marketed drugs are derived from fungi, bacteria and plants,” he said, “With genetic engineering and the rapid discovery pace of genomics, there is no reason why we could not provide these benefits through enhanced diet.”

The development of these new varieties will be especially important for populations where access to health care is limited. Vaccination programs remain a problem in many parts of the world, particularly in developing nations, where they are needed most. This is due in large part to a lack of equipment needed to make, store, and deliver vaccines and cultural differences that impede acceptance of injection-based immunization. Given these hurdles, researchers have begun to examine the idea of developing foods enhanced with vaccines that could immunize against disease. Benefits include fewer problems with vaccine storage, more economical production, and avoidance of technical and cultural problems (Thomashow, 1999).

Such considerations have led a number of investigators to pursue the development of edible plant vaccines that could provide more convenient, less costly immunizations. Dr. Arntzen reported that at least 40 new vaccines developed using biotechnology are under evaluation. His research focuses on developing plants capable of delivering vaccines that would protect individuals from the enteric diseases cholera and diarrhea, leading causes of infant deaths in the developing world. While preliminary, these encouraging results suggest that plant-based vaccines may one day provide new strategies for vaccinating humans, farm animals, and pets from these deadly diseases (Arntzen, 1999).

Some plants also may be converted into "factories" designed to produce medicines quickly and cheaply. Scientists are looking at alfalfa, for example, to see if it can be modified to produce interferon-beta, a potentially effective treatment for a form of pneumonia. Other efforts at "molecular farming" also are underway using a variety of plants to produce an array of useful medical products.

Agricultural biotechnology has the potential to provide medicines and edible vaccines to immunize individuals against a wide variety of infectious diseases. These developments will have far-reaching implications for improving human health worldwide, potentially saving millions of lives in the poorest areas of the world.

Providing Renewable Resources

Genetic engineering makes it possible to increase dramatically the use of plants to produce "industrial feedstocks," such as specialty oils for lubricants, precursors of plastics, and valuable health-related biomolecules. New types of fibers and trees enhanced to provide better, faster wood and paper production also are under consideration or development. In all of these examples, biotech plants can provide a renewable alternative to nonrenewable resources.

One example of a crop that could have significant ramifications for long-term environmental protection is genetically engineered cotton with special colors. Such cotton is already available on a niche market basis and may eventually reduce the need for harsh chemical dyes (Dunahay, 1999).

From grain, high-performance industrial lubricants can be generated using biotechnology. An example is found in the work of Anthony Sinskey and his colleges at the Massachusetts Institute of Technology. In June 1999, these researchers launched a multimillion-dollar project to engineer the oil palm to produce everything from improved oils to, conceivably, biodegradable plastics (Moffat, 1999b).

These developments will not only directly benefit the consumer, they also will open up new markets for American farm products and afford farmers greater opportunities in choosing what crops to grow.

ASSESSING RISKS

Finding: There is no evidence that transferring genes from unrelated organisms to plants poses unique risks. The risks associated with plant varieties developed using agricultural biotechnology are the same as those for similar varieties developed using classical breeding methods. As the new methods are more precise and allow for better characterization of the changes being made, plant developers and food producers are in better position assess safety than when using classical breeding methods.

Central to the debate over agricultural biotechnology is the proposition that new rDNA techniques are inherently different than traditional breeding methods—that the products of these techniques are not “natural,” and thus entail greater and often unpredictable risk. In its essentials, this is the message the pejorative “Frankenfoods” is supposed to convey about biotech food products.

Almost all commercially-important crop plants being grown today, including those used in organic farming, have been developed through human intervention and are, in the strictest sense, unnatural. The primary purpose of plant breeding is to create domesticated plants with desirable qualities suited to a managed agricultural environment. As a result, most food crops now in use have been genetically manipulated to such an extent that they bear little resemblance to their wild ancestors.

The ability to move beyond the limits of traditional breeding accounts for much of the appeal of biotechnology to plant breeders. However, it is this ability that is the main concern of many who argue that the new biotech plant varieties, especially those developed using genes from unrelated organisms, entail greater risk than their traditionally-bred counterparts.

The testimony of Mr. Silbergeld is representative of these concerns: “It may be true,” he said, “that many applications of this technology are no different than what Luther Burbank did in his time. But Mr. Chairman, you can't cross a fish with a tomato. Fish and tomatoes don't mate. And when, as has already happened, a fish gene is put into a tomato, there should be far different requirements for testing than there is when you are crossing a squash with a tomato or a tomato with a tomato. And so our concern is that things can in fact be done and have been done that can't be done with traditional cross-hybridization” (Silbergeld, 1999).

This argument, however, neglects the salient fact that fish, squash, and tomato genes are not unique to themselves, but are likely to be found in a wide variety of plants and animals. As Dr. Cook explained to the Subcommittee, “One of the great marvels of life discovered mainly during the current era of genomics research is that different life forms already share a remarkably high percentage of the same genes. Even plants and humans have many genes in common naturally. Every biology student learns early that a given gene produces the same protein no matter where in the hierarchy of life forms it may reside. Different life forms are due not only to their gene makeup, but also how all the genes are arranged and coordinately played out. For this and many other reasons, science names genes according to their function or protein they produce and not according to whether they were found in a fish, chicken, or wheat plant.”

There are many examples. The genetic material that encodes for the production of the enzyme lysozyme, for instance, is present in both the human and rice genomes.³² In a recent study published in *Science*, researchers reported that the genome for the fruit fly (*Drosophila melanogaster*) shares 177 of 289 human genes known to cause disease (Rubin, *et al.*, 2000). A more dramatic illustration is the pathogenic bacterium *Escherichia coli*, which shares part of its nucleic acid sequence with plants, amphibians, birds, mammals, and humans (Miller, 1999).

An appreciation of the conservation of genetic material across the plant, animal, and microbial kingdoms is critically important to an understanding of biotechnology and helps explain why the source of the transferred gene—whether from a rat or a pig or a jellyfish—is largely irrelevant in assessing the risk of the new plant variety produced using rDNA techniques.³³ Rather, scientists focus on the function of the gene, the properties of the plant into which it is introduced, and the environment in which the plant will be grown.

Safety questions related to agricultural biotechnology have been examined in great detail by a number of scientific organizations since the mid-1970s, and they have concluded uniformly that bioengineered crops pose no special hazards. In 1987, the National Academy of Sciences determined that “There is no evidence that unique hazards exist either in the use of r-DNA techniques or in the transfer of genes between unrelated organisms,” and that “The risks associated with the introduction of r-DNA organisms are the same in kind as those associated with the introduction in the environment of unmodified organisms and organisms modified by other genetic techniques” (NAS, 1987).

These basic principles have been reaffirmed in reports by many other organizations, including the National Research Council (NRC, 1989),³⁴ OSTP (OSTP, 1992), the Organization for Economic Cooperation and Development (OECD, 1993b), 11 professional scientific societies (IFT *et al.*, 1996), and the Council on Agricultural Science and Technology (CAST, 1998).³⁵ Dr. Cook informed the Subcommittee that all the field trials conducted and scientific evidence produced since the 1987 NAS report have supported these findings.³⁶

³² It is estimated that one fourth of the genes in plants are in humans (Cook, 1999).

³³ A good example of this is Golden Rice, which was developed using genetic material from the daffodil, considered a poisonous garden plant.

³⁴ “[N]o conceptual distinction exists between genetic modification of plants and microorganisms by classical methods or by molecular methods that modify DNA and transfer genes. . . Crops modified by molecular and cellular methods pose risks no different from those modified by classical genetic methods for similar traits” (NRC, 1989).

³⁵ This consortium—comprising the Institute of Food Technologists, American Institute of Biological Science, American Phytopathological Society, American Society for Horticulture Science, American Society for Microbiology, American Society of Agronomy, American Society of Plant Physiologists, Crop Science Society of America, Entomological Society of America, Institute of Foods Technologists, Society of Nematologists, and Weed Society of America—wrote: “The level of risk of a plant variety is not determined by novelty or lack of familiarity, the source of the gene or genes that produce a pest-defense substance or initiate a pest-defense reaction, nor the method by which a gene for pest defense is transferred into the variety” (IFT *et al.*, 1996).

³⁶ A report by the United Kingdom's House of Lords Select Committee on the European Communities (SCEC) also found agreement in the scientific community on this issue. “In much of the evidence we received,” it observes, “witnesses did not distinguish between risks inherent in or particular to the new technology and risks present in standard agricultural practice. . .” (SCEC, 1998).

The testimony also showed that there is broad scientific agreement that rDNA techniques allow greater precision in the introduction of genetic material into a plant compared to hybridization and other conventional breeding methods. Traditional breeding—which Dr. Salyers described as “a genetic crap shoot”—involves the crossing of thousands of genes whose functions are largely unknown. Nevertheless, according to Dr. Huttner, “Each year, thousands of new varieties of fruits, vegetables, and grains are introduced into the food supply. The vast majority include genetic and phenotypic changes that are completely uncharacterized at the chemical or physiological level.”

It is worthwhile noting that no product of conventional plant breeding—particularly those involving wide-hybrid crossing, used extensively in crop improvement for many years—could meet the data requirements imposed on biotechnology products by U.S. regulatory agencies. Yet, these foods are widely and properly regarded as safe and beneficial by plant developers, regulators, and consumers.³⁷

It is against this background that agricultural biotechnology should be judged. Biotechnology provides plant breeders with ways to insert individual genes into a plant to confer a desired trait without inadvertently introducing an undesirable one. It also enables the complete characterization of the genetics, biochemistry, and mode of action of the genes and the traits they encode. This makes the traits added using rDNA methods much more predictable. “As the molecular methods are more specific,” NRC said in its 1989 report, “users of these methods will be more certain about the traits they introduce into the plants.”³⁸ Further, it should be kept in mind that the traits introduced by biotechnology are conferred to commonly-used varieties about which we have a wealth of knowledge.

Since much more is known about the traits introduced using these methods, scientists are able to answer questions about safety that could not be answered for products of conventional breeding. These advantages were explained by Dr. Cook, who said, “Because we know both the genes and their proteins when making transfers by gene-splicing techniques, it also becomes possible to know which proteins are actual or potential toxins before they become part of our food supply. Having this kind of information is much more difficult if not impossible with traditionally bred crops where the genes may be known but the protein products of the genes are only rarely known.”

This is not to imply that crops developed using traditional methods are unsafe—centuries of experience with them demonstrates otherwise. Rather, it is to suggest that, as Dr. Cook remarked, “Since traditionally bred crops are accepted as the standard of safety, then crops developed by genetic engineering are at least as safe and are probably safer because of the

³⁷ There have been exceptions. For example, the Lenape potato was withdrawn from the U.S. market in the 1960s when it was found to contain dangerously high levels of solanidine glycoside toxins, and a new variety of celery was discontinued in the 1980s because it contained high levels of psoralens, which caused farm workers to develop skin rashes. Both varieties were produced through conventional breeding, but such cases are rare. Given the rigorous scientific and testing protocols in place for biotech crops today, there is no chance that similar products developed using recombinant DNA techniques would pass muster with plant developers or regulatory agencies.

³⁸ Eleven professional scientific societies reached a similar conclusion: “The more information available about parents and genes transferred to produce a new variety, the more predictable the end-use quality characteristics of that variety” (IFT *et al.*, 1996).

greater precision of the genetic modifications and knowledge of the protein products and their function.”³⁹

Much of the criticism of agricultural biotechnology focuses on perceived risks. In his testimony before the Subcommittee, for example, Mr. Silbergeld said, “*Consumer Reports* stated quite clearly: there is no evidence that the genetically engineered foods now on the market present safety problems. At the same time, neither can it be said that they have been proven ‘safe’. . . [M]any growers and food producer industries characterize these foods as ‘safe’ because there is no evidence of harm to consumers. However, the ‘safe-unsafe’ dichotomy may be false. Between these two categories lies a chasm of uncertainty due to lack of knowledge and experience.” This concern has been formalized in the “precautionary principle,” which calls for regulatory intervention by governments even in the absence of scientific evidence of risk.

The specific areas of concern identified by Mr. Silbergeld, Dr. Goldberg, and others—such as outcrossing, the development of pesticide-resistant insects, allergenicity, toxicity, and antibiotic resistance—will be addressed in detail later in the report. But as a general matter, hypothetical concerns are virtually impossible to dispel. Dr. Beachy put it this way in testimony he submitted to the Subcommittee: “Some of the concerns that are raised lie in the category of perceived vs. actual risk, and we find it difficult, if not impossible, to formulate experiments that address the extremely improbable” (Beachy, 1999).

It is highly questionable, therefore, that raising the regulatory bar and requiring lengthy examinations of improbable risks would advance either public health or environmental protection. A more scientifically-defensible approach is that suggested in a report by 11 professional scientific societies: “Reasonable and continued assurance of safety of each new variety to people and the environment does not require addressing every question that might be asked or every hypothetical concern that might be raised about that variety. The focus must be on high-probability risk rather than hypothetical or unrecognizable risk” (IFT *et al.*, 1996).⁴⁰ Adopting a risk-based regulatory approach will ensure that real risks are identified and assessed before a crop or food is released into the environment or the market.

The research scientists who appeared before the Subcommittee made a compelling case that the new varieties developed using agricultural biotechnology are safe. The weight of their testimony over three hearings leads to the conclusion that there is nothing to substantiate scientifically the view that the products of agricultural biotechnology are inherently different or more risky than similar products of conventional breeding because of the method by which they are produced. Dr. Huttner's testimony provides a fitting summary: “The new biotech is actually part of a continuum of breeding technologies that have steadily improved plant and animal breeding and

³⁹ The same conclusion was reached in a report on agricultural biotechnology published by 11 scientific societies. They said, “[T]he new tools of recombinant DNA technology as an aid to plant variety development are more likely to increase the *safety* rather than the *risk* of new varieties of crop plants to people and the environment” [emphasis in original] (IFT *et al.*, 1996).

⁴⁰ This view also was endorsed by the independent research scientists appearing before the Subcommittee.

that provide a centuries-long context for assessing the safety and risk of genetically enhanced plants, animals, and microorganisms.”⁴¹

OUTCROSSING

Finding: The risks that new plant varieties developed using agricultural biotechnology will become weedy or outcross are the same as those for similar varieties developed using classical breeding methods and for introduced species.

Concerns have been expressed that bioengineered crops could develop into weeds or that the genetic innovations produced through agricultural biotechnology could spread to the gene pool of other plants, creating “superweeds” or “genetic pollution.” Often, the concern is expressed in a way that links the environmental release of biotech crops with nonindigenous pest species, such as the kudzu vine (*Pueraria lobata*), a nonindigenous plant pest that has been difficult to control since it was introduced in the southeastern United States in the late 19th century.⁴²

Extensive field trials overseen by USDA and scientific assessments by major scientific organizations demonstrate that the environmental risk of biotech crops is no different from the environmental risk associated with similar crops bred using conventional means. Because the genetic manipulations being performed today are on crop varieties that already are being grown commercially, we have a broad base of knowledge from which to assess these risks. Standard practices in crop development, field testing, and management will ensure the environmental safety of these crops.

Since the time of Luther Burbank, U.S. plant breeders and agronomists have accumulated a vast storehouse of knowledge and experience on the introduction of genetically-modified plants into the environment and their management. Of the approximately 250 crops plants currently grown in the United States, the large majority are not native species. The early colonists were the first to import plants into North America, and more recently plant breeders and other scientists have imported plants through plant introduction centers maintained by USDA. Nearly all of the plants introduced into the U.S. have undergone extensive selection and breeding to improve their characteristics, adapt them to prevailing environmental conditions, confer resistance to domestic pests, and make them acceptable to consumers (IFT *et al.*, 1996; NRC, 1989).

The risk of a domesticated crop plant accidentally reverting to a weedy condition was described by NAS as “negligible” (NAS, 1987). This is particularly true for crops that have undergone long-term breeding, during which the weedy characters of the wild plant have been removed deliberately from the hybrid.⁴³ The traits normally associated with domestication make crop plants reliant on a managed agricultural environment, and thus less capable of competing and surviving in the wild and becoming an invasive weed.⁴⁴ The addition of herbicide tolerance, pest

⁴¹ Goodman *et al.* (1987) made a similar point: “[I]n plants, and particularly in crop improvement over the last century, interspecific and even intergeneric gene transfer is not new. Gene transfer by recombinant DNA is just the latest in a long history of increasingly more powerful methods available for crop improvement.”

⁴² For an example, see: Yoon, 1999.

⁴³ Weedy characteristics can include seed shattering, efficient seed dispersal, long-term seed viability, and thorns, among others.

⁴⁴ Examples of crops plants that are minor weeds include sunflower, oilseed rape, and cereal rye.

resistance, and other traits important to improve cultivation have not been shown to confer weediness to domesticated crop plants (NRC, 1989; IFT *et al.*, 1996).⁴⁵

Dr. Cook made this point in his testimony. “I am not aware of a crop plant having become an invasive weed because of plant breeding,” he said. “In fact, just the opposite occurs: through plant breeding and selection, wild plants with their tendency to be weeds are made into high-yielding crop plants increasingly more dependent for their survival on human nurturing. There is no evidence after some 20 years of experience with gene splicing to suggest that these trends will somehow reverse towards more wild as we move toward greater use of this new technology.”

Moreover, the notional thread between nonindigenous plant pests, such as kudzu, and transgenic crop plants is slender at best. “[Kudzu] illustrates the public's worst perceptions of errant organisms and simultaneously exemplifies an exotic organism that is not analogous to any hypothetical genetically modified organism” (NRC, 1989). Kudzu is a pest not because of any genetic changes made to it through breeding; it is a pest because it was introduced into a wild environment for which it is particularly well-adapted and in which no natural enemies existed. Crops plants modified by means of recombinant DNA techniques, however, are reintroduced “into the same or a similar environment from which they were taken, so they are not analogous to the introduction of nonnative species” (NAS, 1987).

In fact, under today's rigorous regulatory system, there is no way that kudzu would be approved for import or release into the United States. If anything, our experience with kudzu and other nonindigenous pests demonstrates that the introduction—accidental or otherwise—of wild non-indigenous species is a more recognizable and sizeable risk than that posed by the improvement of highly-domesticated crops using biotechnology.⁴⁶

Another concern that has been raised is that herbicide-tolerant or pest-resistant plants could transfer their genetic advantage to nearby weeds, creating superweeds. Gene transfer through outcrossing is a natural process between related plants, but is extremely rare when species are not related. As most crop species in the United States originated elsewhere, there are few wild relatives available for outcrossing, and thus gene flow is a not a significant environmental risk.⁴⁷

In the relatively few cases in which a cross-hybridizing wild relative is present—such as squash and canola—many conditions must be met for gene transfer to occur: the wild relative must be in the range of the crop pollen; the wild relative must flower at the time the crop pollen is available; fertilization must occur in the wild relative and viable seeds must be produced; the seeds must survive and germinate; and the progeny of the hybrid seeds must be fertile or survive vegetatively. If any one of these conditions is not met, the transfer will not be successful (OECD, 1993b).

⁴⁵ In fact, it would be extremely difficult to alter intentionally a domesticated crop plant so that it became a weed because of the complex gene interactions required for such a transformation.

⁴⁶ For example, in a recent review of the Nation's biological resources, the United States Geological Survey (USGS) stated, “Nonindigenous species are a major threat to endangered and threaten biota” (USGS, 1998).

⁴⁷ Concerning herbicide-tolerant weeds, Dr. Cook observed that they are “a common problem for agriculture, not because of gene transfer, but because of selection for natural resistance.”

Even when these conditions are met, the chance that the resistance trait will become incorporated in the wild population absent strong selection pressure is very small. IFT *et al.* (1996), for example, noted that, “Progeny that result from outcrossing may be sterile, but, if fertile, will be hybrids with genomes containing not only the new gene but also millions of other genes transferred with the gamete [*i.e.*, pollen] from the crop plant. Whether such hybrids could then survive and establish or create new hybrids within the wild population is possible but highly unlikely.”

In the improbable event that a resistance gene from a crop plant became established in a weed population, the fact that a number of other genes from the crop plant also would be part of the weed's genome means that it will behave more like the crop plant, and its impact will be confined primarily to agricultural fields where it can be controlled through standard management practices (NRC, 1989; IFT *et al.*, 1996).⁴⁸ Of course, where the potential for environmental damage is significant, both USDA and EPA have the authority to discontinue field trials and suspend further development of the plant.

Dr. Cook attached as part of his testimony an OECD report, cited previously, that addressed these issues in detail. He said, “This report lists the safety issues for crop plants with genes introduced by the new tools of biotechnology and concludes that they are the same issues raised for crop plants introduced into cultivation directly from the wild without genetic modification or modified by gene transfer within the limits of natural hybridization.”

In the years in which have been developing plants using of biotechnology, there is no instance of a new plant variety having created an environmental hazard. The protocols for assessing environmental risks of traditionally-bred plants, developed over many years, are sufficient to provide environmental protection for new rDNA varieties. Regulatory determinations should be based on risk factors, such as the characteristics of the plant and the ecology of the environment into which it is to be introduced, not on the method used to produce it.

PEST-RESISTANT CROPS AND THE POTENTIAL FOR PESTICIDE-RESISTANT INSECTS

Finding: Widespread use of pest-resistant crop varieties developed using agricultural biotechnology is unlikely to accelerate the emergence of pesticide-resistant insect strains and may actually be more effective in preventing their emergence when compared to spray applications of similar pesticides.

Another concern regarding potential harm to the environment through the use of biotech crops involves plants designed to express various forms of toxins from the naturally-occurring soil bacterium *B. thuringiensis* (“Bt” crops). In her testimony, Dr. Goldberg argued that “Unlike traditional Bt sprays, which degrade quickly in the environment, most transgenic Bt crops produce Bt toxins in all their tissue all the time—whether or not the toxins are needed to control economically damaging pest infestations. The upshot is that Bt crops appear to exert strong selection pressure for the evolution of pests resistant to Bt toxins.” If pest resistance to Bt were

⁴⁸ For a brief discussion Bt corn and its probable negligible impact on native teosinte in Mexico, see: Martínez-Soriano and Leal-Klevezas, 2000.

to become widespread, then the sprayed form of Bt, which is used widely by organic farmers and backyard gardeners to control pests, would be rendered ineffective.

Insects have proven to be remarkably adaptable and capable of becoming resistant to pesticides. “[T]he emergence of biotypes of pests with ability to defeat genes deployed in crops for resistance to them is nature’s way of assuring survival of the species,” noted Dr. Cook, “This issue is not new to agriculture. Resistance breeding is an ongoing effort for crops just to stay ahead of the ever-evolving populations of pest species.”

The goal of farmers and pesticide manufacturers, therefore, is to stay one step ahead of the insects, not to try to find a pesticide that is “resistance-proof.” Such a goal may not be attainable. The possibility exists that Bt-resistant insects will arise regardless of whether Bt crops are planted by farmers. Thus, it is impossible to determine if—or even when—Bt resistance will develop in pest populations.

Concerns about the acquisition of resistance are shared by organic and traditional farmers alike, by the companies that manufacture and market Bt sprays and Bt plants, and by regulators. As a result, industry and EPA, working with farmers, have developed insect resistance management (IRM) programs, such as the requirement of farmers to plant refugia of non-Bt crops. Dr. Goldberg argued that “elements of the [IRM] plans are highly controversial among entomologists and others who believe they are inadequate to forestall the evolution of resistant pests.”

The rationale for these refugia is that they will allow Bt-susceptible populations of insects to proliferate, which will then be available to mate with insects that might be carriers of a resistance gene. The existence of the susceptible population will make it less likely that two insects, both of which carry a resistance gene, will mate and thereby create offspring that are resistant to Bt by virtue of having received a resistance gene from each parent—*e.g.* is homozygous for the resistance gene.

The success of the refuge-based IRM plan is based on the assumption that resistance to Bt will likely be a recessive trait, not a dominant one. Thus a recent study (Huang *et al.*, 1999) suggesting that a dominant form of resistance to Bt had been found led some to speculate that the refuge strategy was destined to failure. However, as Dr. Shelton and Dr. Richard Roush, another expert in the field, explained in an article in the journal *Nature Biotechnology*, “Several scientists (including us) have expressed concern about the methodology used in the Huang *et al.* Paper, particularly as the authors did not demonstrate that resistance was actually to the same Bt toxin as in the plant, and did not demonstrate that their ‘resistant’ population could survive on Bt-corn engineered to express the toxin (a footnote implies that the larvae don’t)” (Shelton and Roush, 1999). Without this proof, the study shows only that Bt resistance can arise naturally, in a manner that is totally unrelated to the presence of Bt in the plant.

Another study also published recently in *Nature* led some to question the refuge strategy on different grounds (Liu *et al.*, 1999). The authors of this study reported that insects that eat Bt crops develop slower than non-Bt feeders. They suggested that resistance management programs might therefore fail because the insects eating Bt plants would develop more slowly than their

non-Bt eating counterparts, and thus there might not be any non-Bt eaters around with which to mate (a key element of the refuge strategy) by the time they finally develop. But as Dr. Shelton and Dr. Roush point out, insect generations overlap. Thus, even in insect populations never exposed to Bt cotton, many insects will end up mating with insects from a different generation.

Concerns about insect resistance to Bt predate the existence of biotech Bt crops. Insects resistant to the sprayed form of Bt have been found in the past, and there is some evidence that the sprayed form of Bt may be *more* likely to induce resistance than Bt plants (Roush, 1994). “[T]he only problems with resistance to date for Bt,” Dr. Shelton observed, “are as a result of the heavy use of Bt sprays against diamondback moth.”

In fact, there is ample evidence to suggest that Bt plants may be a potent weapon in the fight against development of Bt resistance among pest populations. The sprayed form of Bt contains a “cocktail” of different compounds made by the *B. thuringiensis* bacteria, many of which are toxic to insects; each different compound is encoded by a different gene. Today's Bt crops express only one of these genes, thereby producing only one of these compounds. If insects were to gain resistance because of exposure to a particular Bt toxin produced in a plant, it is likely that they would be resistant to that particular toxin only and would still be susceptible to other Bt toxins.

This point was summarized by Dr. Milton Gordon, a pioneer in the field of agricultural biotechnology, in a letter to the Subcommittee: "Talking about *Bacillus thuringiensis* toxin as a single compound is very similar to talking about all of the antibiotics that have been discovered and are now being used in humans as a single compound. If the pathogenic bacteria become resistant to one type of antibiotic, it is possible to switch to another type and still get good results. The same is true of Bt" (Gordon, 1999).

While current versions of Bt plants probably are more effective in reducing resistance than sprayed versions of Bt, future varieties of biotech plants may be more effective still. The technology of “gene stacking,” which involves putting multiple genes into a single plant variety, could help achieve this. Although current versions of Bt crops produce only a single form of Bt toxin, future plants can be generated that produce two or more forms. To survive, insects would have to be resistant to each form of the toxin. Multiple genes for resistance have been used for decades to control wheat stem rust in North America, with no evidence of super races emerging that cannot be controlled (Roelfs, 1988). The probability that insects with multiple resistance would arise in an insect population is extremely small.

Another advantage offered by Bt crops is that the dosage is both more predictable and constant. To make the refuge strategy viable, the dose must be high enough to ensure that the vast majority of insects that come in contact with the insecticide die. If the dose is too low, resistance is more likely to develop. Transgenic crops may more effective in preventing the onset of resistance because, as Dr. Shelton explained, "one can regulate the dose of Bt more effectively when it is engineered into a plant than when it is sprayed onto the plant...Sprays will create more variable deposits of Bt on the plant and thus insects will be exposed to a wider series of doses of Bt, including low doses.”

MONARCH BUTTERFLY

Finding: The threat posed by pest-resistant crop varieties developed using agricultural biotechnology to the Monarch butterfly and other non-target species has been vastly overblown and is probably insignificant.

In a recent research letter to the scientific journal *Nature*, scientists reported evidence that Bt corn pollen could be deadly to Monarch butterfly larvae (Losey *et al.*, 1999).⁴⁹ The study created an immediate stir in the media and was touted by many antibiotechnology activists as evidence that the worst fears about the potential environmental impact of agricultural biotechnology had come true. In her testimony before the Subcommittee, Dr. Goldberg of EDF stated, "widespread planting of Bt corn could harm significant numbers of Monarchs."

Since publication of the Losey *et al.* letter in *Nature*, serious questions have been raised about its findings. A number of prominent entomologists and other experts have dismissed the report as preliminary in nature, restricted to a laboratory environment and thus unrepresentative of real-life conditions, and of limited scientific value. It is also worth pointing out that, as Dr. Shelton testified, the Losey *et al.* study was rejected as a research article by peer reviewers at both *Nature* and *Science*, another highly-respected scientific journal, before being published in the letters section of *Nature*.

Among the reasons for the paper's rejection was that its main finding was not at all unexpected: "[T]he Bt/Monarch study has been heavily criticized in the scientific community because every entomologist knows that...if you feed Monarch butterfly larvae Bt toxin, whether it be in corn or whether it be on a spray, that insect will die" (Shelton, 1999).⁵⁰ This opinion was echoed by many respected entomologists, such as University of Nebraska professor John Foster, who wrote in a recent article, "there probably was not an entomologist in the world who was not aware that corn pollen containing the Bt gene could harm butterflies—if butterflies ate corn pollen, which they don't" (Foster, 1999).

Nonetheless, Dr. Goldberg maintained in her testimony that "I think the study was a surprise, unfortunately, to the Environmental Protection Agency....EPA had not even considered this risk," a statement repeated in EDF press releases. However, this claim was directly refuted by the EPA's Dr. Anderson, who said in her testimony, "Our scientists knew the Bt protein is toxic to many insect pests, and in this particular order, the *Lepidoptera*."⁵¹

Clearly, scientists were well aware of the potential toxicity of Bt corn pollen to species such as the Monarch butterfly, and were not surprised by the results reported in the *Nature* correspondence. Many have been highly critical of activists and the media, who have portrayed

⁴⁹ In this laboratory-based study, scientists fed Monarch butterfly larvae milkweed leaves (the Monarch's normal food) that had been coated with Bt corn pollen. These larvae were compared to larvae that were fed milkweed coated with non-Bt corn pollen. The comparison revealed higher rates of death or growth defects in the group that was forced to eat Bt corn pollen.

⁵⁰ That the various proteins produced by the *B. thuringiensis* are species-specific has been known for some time. The proteins encoded by the *cryI* and *cryII* genes are toxic to insects in the order *Lepidoptera*, of which the Monarch is a member.

⁵¹ This order includes moths and butterflies.

the study as evidence of a real threat to the Monarch butterfly. But in the scientific community, the Losey *et al.* letter was taken for what it was; a preliminary laboratory study that offered little new information and was likely to have little relevance to wild Monarch populations in the field. Even the letter's lead author cautioned that "it would be inappropriate to draw any conclusions about the risk to Monarch populations in the field" (Fumento, 1999).

Since this letter was published, its results have been criticized by many in the scientific community (*e.g.*, Shelton and Roush, 1999; Hodgson, 1999). Preliminary data from other researchers performing field studies show that the concentration of pollen on the milkweed leaves in the Losey *et al.* laboratory study was greater than could be expected in the field (Hansen and Obrycki, 1999). The Monarch's migratory pattern does not bring it in contact with corn during the short time it sheds pollen. Monarchs also prefer to lay their eggs on milkweed plants in open meadows, prairies, and roadsides, not in or around cornfields, as even the *Nature* letter's authors recognized.⁵² And as EDF's own literature states, it is widely recognized that "most corn pollen settles out within a few dozen feet of the corn plant" (EDF, 1999), a finding supported by the Hansen and Obrycki field study. Results similar to those recounted above were reported in a conference of scientists held to discuss the issue last November in Chicago (Kendall, 1999).

Taken together, the evidence cited above suggests that the threat of Bt corn to wild populations of Monarch butterflies is vastly overblown. And as for the current state of the Monarch, recent reports indicate that it is flourishing despite widespread use of Bt corn in the Nation's Corn Belt. Jeffery Glassberg, President of the North American Butterfly Association, has added some needed perspective to this controversy. "I think there are a lot more dire threats than that [Bt corn] to Monarchs," he said. "In the Midwest, mowing roadsides and using herbicides is probably much more devastating, actually" (Branom, 1999).

Finally, it should be recognized that any potential effects on non-target species must be compared to other techniques used to mitigate the effects of pests. In the past, pest control has been effected primarily through the use of sprayed insecticides, which often kill both the targeted pest as well as beneficial insects, such as ladybeetles or green lacewings. In contrast, Bt crops preserve beneficial insects that prey on harmful insect pests, thus reducing the need for additional insecticide sprays. Another benefit from using Bt plants is that growers can dramatically reduce the handling and exposure of insecticides on the farm.

ALLERGENS AND TOXINS

Finding: The risks of introducing an allergen or toxin into the food supply are the same for plant varieties developed using agricultural biotechnology as those for similar varieties developed using classical breeding methods.

⁵² Earlier research shows that Monarchs identify milkweed plants by sight and typically lay their eggs on small plants that are only three to 18 inches tall (Urquhart, 1998). It is likely, therefore, that Monarchs could identify small milkweed plants scattered among tall corn stalks only with great difficulty.

Americans have come to enjoy a food supply that is not only plentiful, but is widely recognized as among the safest in the world. The suggestion that agricultural biotechnology could threaten the safety of the food supply is a potent argument in the debate over modern agriculture.

Allergens

One of the major food safety concerns raised in connection with agricultural biotechnology is the risk of introducing an allergen into an otherwise-safe food. “The dominant food safety risk associated with genetically engineered crops,” Dr. Goldberg testified, “is that foods derived from these crops will cause allergic reactions in susceptible individuals. Genes code for proteins, and when genetic engineers add a new gene to a crop plant they are in most cases adding a new protein to foods derived from the crop. Some of these proteins may be allergens, since all known food allergens are proteins.”

Allergies are a reaction of the immune system to a particular protein. Proteins consist of long chains of amino acids, the order of which is unique to every different protein. Allergies are triggered when a person's immune system recognizes a particular protein, or even just a piece of that protein. There are many sources of allergenic proteins. These include nuts, milk, eggs, grains, and fruits, among others.

A first and important line of defense in protecting susceptible persons from exposure to food-borne allergens involves proper testing when known allergenic foods are used in the creation of a new food type. Thus, when a food crop that is known to be allergenic is used as the donor of genetic material in the creation of a new plant-based food, a high standard of proof of non-allergenicity in the resulting food is used.

This is a key component of the approach taken by the FDA in determining the safety of new plant-based foods. As outlined in FDA's Statement of Policy, if a company developing a new plant-based food uses genes from a known allergenic source of genetic material for transfer, the company should assume that this genetic material encodes an allergen unless they can conclusively prove otherwise.

An example of just such a transfer occurred in the mid-1990s, when the Pioneer Hi-Bred International undertook a project to increase the protein content of a soybean variety by introducing a gene from a Brazil nut. Testing discovered that the gene taken from the Brazil nut encoded for an allergen (Nordlee, 1996), and the product was never commercialized. “This [was] a perfect example of how the system works,” Dr. Cook testified, “It is always cited as how things can go wrong, but it is exactly how good testing in the laboratory can provide for safety.”

It also has been suggested that when a gene is transferred from a non-food organism to a food plant, “it may not be known in advance whether humans will develop food allergies to proteins produced by the non-food gene” (Silbergeld, 1999). While it is highly unlikely that a gene transferred from a non-food organism to a food plant might cause allergic reactions, that possibility cannot be ruled out. However, valuable clues exist that can point to potential trouble, and these clues are used by scientists to avoid this situation. For example, there is a correlation between a protein's stability in the human gut and allergenicity, as food allergens tend to be

more stable than non-allergenic proteins (Astwood *et al.*, 1996).⁵³ In addition, the protein's amino acid sequence can be compared to other known allergens, and if there are similarities, it can be tested to see if it, too, elicits an allergic response in susceptible individuals.

Although it cannot be determined absolutely that a gene that sits benignly in one organism will not cause an allergic response when put in another organism, it is important to remember that the introduction of new allergens to the food supply can come from any new food—not just those created through biotechnology. For example, when the kiwi fruit was introduced to this country, a small number of individuals experienced allergic reactions to it. As even Dr. Goldberg, who made clear in her testimony that she is critical of FDA's policies regarding testing for allergenicity, had to admit, “there is no clear-cut mechanism” for determining the allergenicity of any new food product, whether imported or produced using classical breeding or biotechnology methods. Clearly, this is an area where more research is needed. Finally, if a company were to insist upon going ahead with bringing the new food containing a known allergenic compound to market, current FDA policy would *require* labeling of the product.

In summary, the risks surrounding the potential allergenicity of foods created using agricultural biotechnology, while not zero, are quite likely *lower* than for other new foods, because there is at least a target of concern—that being the newly introduced protein and any enzymatic byproducts of it. Once again, the evidence suggests that since more is known about the traits being introduced into a food crop when biotechnology is used, scientists can address safety issues with greater confidence.⁵⁴

Toxins

Another area of debate has been over the question of whether genetic transfers using rDNA technology could result in foods with increased toxicity. Dr. Silbergeld, for example, voiced his concern that “Traditional plants may contain constituent chemicals that are toxic at higher levels but not present in the food at sufficient levels to cause harm. For instance, edible potatoes contain alkaloids that, at higher levels, would be toxic. It is of concern that genetic engineering of a potato, or of another plant that presents this problem, could result in a dangerous increase in toxicity.”

Many of the issues surrounding the potential of introducing food toxins to newly created plant-based foods are similar to those involving allergenicity. As with allergens, there is an existing body of knowledge regarding potentially toxic compounds in plants, and so introduction of a gene from a plant known to contain such toxins to another plant is approached carefully and with thorough testing.

Many plant species contain naturally occurring toxins. Potatoes can have high levels of solanine, for example, which can make people ill. Many legumes, such as kidney beans, contain high levels of lectins, which if not destroyed by cooking or removed by soaking, can cause severe

⁵³ The human stomach is replete with proteases, enzymes that break down proteins into short pieces and even individual amino acids.

⁵⁴ Biotechnology also is being used to remove or neutralize food allergens, which will expand the choice of foods available for those who suffer from food-related allergies.

gastro-intestinal distress. Another component of legumes, cyanogenic glycosides, can produce cyanide if the food is not prepared properly. The levels of these cyanogenic glycosides are so high in some foods, such as cassava, that death can result from improper preparation. Cruciferous vegetables (*e.g.*, broccoli and cauliflower), squash, cucumbers, chickpeas, spinach, celery, and many other fruits and vegetables also contain chemicals that are toxic to humans. Yet, each of these foods is consumed widely.

As with allergens, FDA's Statement of Policy outlines a prudent scientific approach to minimize the risk of transfer of a toxicant. A company using a food with a known capacity to harbor toxins as either the donor or the recipient of genetic material is required to verify that any resulting plants do not have unacceptable levels of the toxins.

It is also important to place the potential for creating a new plant-based food with unacceptable levels of toxicity in the context of plants created through cross-breeding. Again, examples exist of foods created through conventional methods that contained unacceptable levels of toxins: the Lenape potato variety in the 1960s and a celery variety in the 1980s. As Dr. Salyers said in her testimony, "making targeted, defined changes in the genomes of plants [using biotechnology] should be safer than the process that created the Lenape potato. Cross breeding, especially between distantly related plants, can bring along all sorts of bad traits with the desired ones" (Salyers, 1999).

Biotech plants also are subject to a greater level of scrutiny than traditionally-bred plants, making it virtually impossible for a biotech version of the Lenape potato to make it to market. These differences were noted by FDA's Dr. Maryanski, who explained that "in the case of most conventional varieties of crops, there are relatively few analytical studies that are conducted during development. This is in contrast to what is done with engineered varieties, where there are far more tests being done for nutrients, toxins, vitamins and minerals and so forth." Again, current FDA labeling policies would require that if a company decided to bring to market a food containing potentially dangerous levels of a toxicant (one that could be mitigated or eliminated by proper food preparation techniques, for example) it would have to be labeled to that effect.

Another concern that has been raised suggests that the development process itself could result in toxicity for unexpected reasons. This claim is not based on fact or example; rather, it is in the realm of hypothetical risk. Mr. Silbergeld, for example, stated that, "*Consumer Reports*...knows of no genetically modified food now on the marketplace that presents any known risk to consumers." But because this unlikely situation is *theoretically* possible, developers of new foods who choose to use rDNA techniques must contend with critics who set the impossible task of proving a negative.

These critics claim that the key to assessing the safety of plants created through biotechnology for human consumption is through extensive toxicological studies, where the entire food item is fed to test animals. There has been one attempt to test a genetically-modified food in this way, and the results were of questionable value.

In what has become one of the most controversial evaluations of a biotech food product, Dr. Pusztai and his colleague in Scotland tested potatoes modified using rDNA techniques by

feeding them to rats (Ewen and Pusztai, 1999). The potatoes had been modified to produce a lectin, a type of chemical compound known to be toxic. The experimental protocol, which has been highly criticized as improperly controlled and executed,⁵⁵ involved the feeding of either the lectin-modified potatoes, unmodified potatoes, and unmodified potatoes “spiked” with lectin⁵⁶ to small groups of rats.

The researchers claimed that the rats fed the genetically-modified potatoes showed evidence of physiological damage not seen in the rats in the other two groups. However, in the experiment, the rats were forced essentially onto a starvation diet, as rats neither like potatoes nor can get enough of certain essential nutrients from them. Thus, many of the results the researchers saw were quite possibly artifacts of the dietary conditions imposed on the rats.

Many scientific observers see this paper as seriously flawed, as even the editor of the journal in which the article was published—the *Lancet*—recognized. He wrote in an editorial accompanying the research paper that it had been rejected by half of its peer reviewers and that a sizable number of the author's initial claims were left out of the published version because they were unsupported by the evidence. Deflecting criticism of the decision to publish the article, he said, “This is absolutely not a vindication of Dr. Pusztai's claims.”

Besides the obvious scientific shortcomings noted in the experimental design of the study, it provides an example of the inherent problems in toxicological analyses of whole foods. These types of toxicological studies are intrinsically difficult. As reported in one article on the subject (MacKensie, 1999), a Dutch researcher attempted to test a genetically modified tomato on rats by freeze-drying the tomatoes so that each rat could be fed the equivalent of 13 fresh tomatoes a day. The scientist is quoted as saying “toxicologists still said we hadn't fed them enough to get a meaningful result.” However, the article also pointed out, if they had been fed any more, they would have been poisoned by normally benign nutrients found in tomatoes, such as potassium.

Unable to point to a single documented instance in which a biotech food presented a health risk, critics have focused their concerns on hypothetical risks. However, there was no scientific evidence presented to the Subcommittee that would suggest that the risks of toxicity that attend foods produced using biotechnology are different either in type or degree from those produced using more traditional methods.

ANTIBIOTIC RESISTANCE

Finding: The risk that a health hazard will be created through the use of antibiotic resistance markers in the development of new plant varieties using agricultural biotechnology is insignificant.

In transferring genes to an organism, antibiotic resistance genes often are used to help researchers trace introduced DNA and determine if the transfer was successful. The antibiotic

⁵⁵ Among other things, the sample size (6 mice in each group) has been criticized as being too small to draw scientifically meaningful conclusions.

⁵⁶ In this case, the lectin was added *to* the unmodified potatoes, as opposed to being produced *by* the potato, as in the genetically-modified version.

resistance gene's only purpose is to serve as a "marker" for the presence or absence of the gene of interest.⁵⁷ For this reason, these genes are often referred to as "marker genes," and their use has raised fears that new antibiotic resistant strains of bacteria will emerge. These issues are raised against a backdrop of increasing medical and public concern about serious public health threats arising from antibiotic resistance in disease-causing bacteria.

Some types of bacteria are normal residents of the human body. They are referred to as "normal fauna," and they exist in the human intestinal tract without causing any health risk or discomfort to their host. Many are already resistant to common antibiotics. "Virtually all the scientists I have talked with," Dr. Salyers informed the Subcommittee, "agree that since these [antibiotic resistance] genes are already widespread in intestinal and environmental bacteria, an occasional introduction of these genes into bacteria would have no medical significance."

The possibility that normal intestinal bacteria could acquire antibiotic resistance is of little concern to scientists and medical practitioners. Rather, it is the transfer of antibiotic resistance to pathogenic bacteria—bacteria that by definition do not normally inhabit the human body—that is potentially a serious health concern. The British Medical Association has argued that there should be a ban on the use of antibiotic-resistant marker genes because the risk to human health from antibiotic resistance is one of the major health threats facing the public (BMA, 1999).

Molecular biology techniques often involve the transfer of antibiotic resistance genes from one organism to another. The application of biotechnology to agricultural products has been no different, and has resulted in plants that carry within their chromosomes DNA that encodes resistance to an antibiotic. Fruits, vegetables, grains, and other foods derived from these plant products will contain this DNA unless treatment of the plant product results in the destruction or removal of genetic material, as is the case in the processing of grains to become cereal or oil. Humans eat DNA from other organisms every day, and all unprocessed plant or animal food products—fruits, grains, vegetables, meat, poultry, eggs, *etc.*—contain the DNA of that organism.

Theoretically, the possibility that an antibiotic resistance gene could be transferred from the DNA of an ingested plant or plant product to pathogenic bacteria exists, but it is exceedingly unlikely because it demands numerous steps, each of which also is highly unlikely: the antibiotic-resistance DNA would first have to be liberated from the plant cell and remain intact long enough to be absorbed by a bacterium; it would have to be taken up by a bacterium after evading its defenses; it would have to become part of the bacterium's own chromosome through a rarely-occurring "illegitimate recombination" event; it would have to become integrated into the bacterial chromosome in just the right way and in the correct position; and finally, it would have to be transferred from the harmless bacterium into which it has been incorporated to a pathogenic one.

⁵⁷ For example, if a plant breeder wants to transfer a gene for Bt toxin into plant cells, the researcher first creates a piece of DNA that contains both the Bt gene as well as a gene that confers resistance to an antibiotic, such as kanamycin. To test that the gene transfer was completed, the plant cells are grown in the presence of kanamycin. Resistance to the antibiotic is an indication that the genes were incorporated successfully into the plant cell.

No one actually has been able to demonstrate that such a transfer of resistance genes has occurred in the human gut (Latta, 1999), but it is this scenario that scientists, including Dr. Salyers, agree could create a very a serious health problem.⁵⁸ However, a pool of antibiotic resistant non-pathogenic bacteria exists already, and so the impact that biotech foods could have on antibiotic resistance is likely to be insignificant. "There is some disagreement about what the medical consequences of this would be, but most people feel that since the genes are already so widespread in nature, that there would be no medical consequences at all" (Salyers, 1999).

The focus on unfounded concerns over antibiotic resistance transfer from biotech foods has led public health officials in Europe to make poor decisions with potentially grave consequences. As Dr. Salyers explained, "The EU [European Union], distracted by the debate over marker genes in transgenic corn, approved with virtually no debate the use of avoparcin as a growth promoter in animals. As a result, a very serious form of bacteria resistant to vancomycin (an analog of avoparcin) has been introduced into their food supply. Since colonization of the intestines of humans by these bacteria could possibly lead to their death due to subsequent untreatable post-surgical infection, this is a serious health concern." Thus we are provided with another instance in which a more immediate risk has been ignored while the insignificant risks posed by agricultural biotechnology have been blown out of proportion.

In any event, as scientists find ways to use marker genes that do not involve antibiotic resistance, the point will become moot. As recently reported in *Nature Biotechnology*, researchers already have begun to develop such alternative marker genes (Kunkel *et al.*, 1999). Although this should quell the debate over antibiotic resistance transfer from biotech foods, Dr. Salyers suggested that the ongoing controversy over antibiotic resistance markers "sets yet another precedent for allowing public policy decisions to be driven by bad science."

SUBSTANTIAL EQUIVALENCE

Finding: The concept of "substantial equivalence" in the regulation of foods developed using agricultural biotechnology is scientifically sound and provides a useful historical baseline for judging safety.

The principle of "substantial equivalence" has been adopted by many national and international governmental and scientific organizations as a way to assess the risk of biotech food products. This principle holds that the risks of a new food variety produced using biotechnology are the same as those for an existing variety with essentially the same characteristics. It therefore establishes existing varieties, the vast majority of which have a history of safe use, as the standard for safety.

This concept—though widely accepted by the scientific community as a sound basis for risk-based regulation—is not without its detractors. As Millstone and colleagues have argued, "Showing that a genetically modified food is chemically similar to its natural counterpart is not adequate evidence that it is safe for human consumption" (Millstone, *et al.*, 1999).

⁵⁸ Attempts by researchers at the University of Leeds to get various bacteria to take up and activate the *bla* gene, which confers resistance to ampicillin, from maize developed using rDNA technology have been unsuccessful so far (Coghlan, 2000).

Genetic manipulation by any method raises the possibility of inducing one or more unexpected and unrelated changes in a plant. These changes, referred to as pleiotropic events, are not a unique risk factor in biotechnological approaches. These unexpected events could include (1) activation of a normally latent gene or set of genes and (2) disruption and subsequent deactivation of a normally active gene or set of genes, and they could occur with any genetic modification process.

Determining conclusively that genetic modification—whether done through traditional breeding techniques or biotechnology—has not resulted in any unexpected events in the plant is extremely difficult. Even if such tests were practicable, it is questionable whether the differences that emerged would be meaningful or indicative of potential danger, as they could easily lie within the normal—and perfectly safe—ranges of variability brought on by different agronomic conditions.

FDA's policy approach is consistent with the concept of substantial equivalence. In evaluating substantial equivalence, factors such as the concentration and bioavailability of important nutrients for which the plant-based food is consumed are measured. These typically involve biochemical measurements of the levels of protein, carbohydrates, fats, oils, and certain vitamins or other important nutrients.

These standards, and the concept of substantial equivalence itself, are applied only to biotech plants, even though the same potential risks exist for plants created through more traditional means. In comparing these standards for crops created through agricultural biotechnology versus those that are not, Dr. Maryanski said during testimony before the Subcommittee, “in the case of conventional varieties of crops, there are relatively few analytical studies that are conducted during development. This is in contrast to what is done with engineered varieties, where there are far more tests being done for nutrients, toxins, vitamins and minerals and so forth, as a way of providing that additional assurance that the important components of the plant are at the levels that are expected.”

Critics of substantial equivalence contend that toxicological tests on the whole food, not just the novel components of the food, must be done on products of agricultural biotechnology to draw conclusions about their safety. Toxicological studies involve clinical analyses, where a whole food is consumed by a test animal to determine if unexpected events show up. In short, critics of substantial equivalence contend that “the total food is greater than the sum of its parts,” and that whole-food testing is superior to detailed biochemical and immunological analyses or toxicological studies of individual components (Millstone, *et al.*, 1999).

However, the testimony suggests that toxicological tests on whole foods do not provide a sound basis upon which to draw informed conclusions about food safety. “Such testing,” said Dr. Taylor, “would be tremendously unfocused, wasteful of laboratory animal resources, and unlikely to detect any harmful substances, even if they were present. The novel proteins and their products in GMO foods are often present at very low levels and their effects, if any, would not be detected by feeding the whole GMO food to lab animals” (Taylor, 1999). To date, there is only one published example of whole-food toxicological testing of a biotech food (Ewen and

Pusztai, 1999), and that, as we have seen, was not regarded highly even by the editors of the journal that published it.

What critics of the concept of substantial equivalence tend to lose sight of—or gloss over entirely—is the fact the same risk factors that they contend are present in foods developed using agricultural biotechnology are every bit as possible for plants created using more conventional means, such as cross breeding. Genetic events that result in the reshuffling of genes, for example, or that could cause a normally inactive gene product or biochemical pathway to become active (or vice versa), also can occur in the course of conventional plant breeding. Thus, even if toxicological testing were feasible and provided useful and meaningful data, proponents of this type of analysis should be demanding with equal fervor that such testing be done for all new varieties of plant-based foods.

The concept of substantial equivalence is widely regarded in the international scientific community as more than adequate to safeguard food quality and wholesomeness. OECD, for example, concluded: “For food and food components from organisms developed by the application of modern biotechnology, the most practical approach to the determination of safety is to consider whether they are *substantially equivalent* to analogous conventional food product(s), if such exist” (OECD, 1993c). It also has been validated by the World Health Organization (WHO), the United Nations Food and Agricultural Organization (FAO), and the International Life Sciences Institute. Further, many governments have adopted this concept as part of their review of food crops created using biotechnology, and it provides the conceptual basis of FDA's 1992 Statement of Policy. “With the global endorsement of the concept of substantial equivalence,” Dr. Taylor said, “I think that I am on rather solid ground to advise that this concept should be retained.”

Based on the testimony and other material reviewed by the Subcommittee, there is no reason to question the validity of substantial equivalence. Although the focus of this discussion has been food safety, the evidence suggests that this regulatory approach applies equally well when considering environmental safety.

LABELING

Finding: There is no scientific justification for labeling foods based on the method by which they are produced. Labeling of agricultural biotechnology products would confuse, not inform, consumers and send a misleading message on safety.

Whether FDA should mandate labeling of foods produced using agricultural biotechnology is another area of growing controversy. Consumers Union, which was represented at hearings held by the Subcommittee, is one such group calling for labeling of biotech foods, and it has accused FDA of being “a cheerleader for a technology” for not agreeing to implement such a requirement (Silbergeld, 1999). On November 30, 1999, legislation was introduced in the House of Representatives that would require that foods containing genetically engineered material, or produced with a genetically engineered material, be labeled accordingly.

The criticisms of FDA's policy on labeling are unfounded. The FDA now has more than 15 years of experience in evaluating the food-based products of biotechnology and more than 20 years of experience with medical products of biotechnology. The agency's decision not to require labeling is consistent both with the law and with its Statement of Policy. More to the point, consumers have a lifetime of direct personal experience with foods genetically modified through hybridization that are indistinguishable from those produced using biotechnology.

FDA bases labeling decisions on whether there are material differences between the new plant-based food and its traditional counterpart. These material differences include changes in the new plant that are significant enough that the common or usual name of the plant no longer applies, or if a safety or usage issue exists that warrants consumer notification (FDA, 1992).

One such safety issue involves the introduction of allergens from one food source to another. As discussed earlier, FDA has stated that a gene that is introduced into a plant from a source that is a known allergen will be presumed to be allergenic—and thus be labeled as such—unless the company that wishes to bring the new food to market is able to demonstrate otherwise. This is a rigorous standard that places the burden of proof squarely on the company developing a new plant-based food.

Despite this sensible policy, biotechnology's critics continue to argue that foods created using rDNA techniques should bear a label revealing that fact. This view is based in large part on the faulty supposition that the potential for unintended and undetected differences between these foods and those produced through conventional means is cause for a label based solely on the method of production of the plant.

The risks for potentially unintended effects of agricultural biotechnology on the safety of new plant-based foods are conceptually no different than the risks for those plants derived from conventional breeding. As described in FDA's Statement of Policy, "The agency is not aware of any information showing that foods derived by these new methods differ from other food in any meaningful or uniform way, or that, as a class, foods developed by the new techniques present any different or greater safety concern than foods developed by traditional plant breeding" (FDA, 1992). This view was echoed by the research scientists who testified before the Subcommittee on the subject.

Some activists and consumer groups, however, have suggested that foods created through biotechnology should be labeled in the interests of providing consumers with information. But when given the option, consumers favor all sorts of information that could not possibly fit on a label—everything from information on where and under what environmental and labor regulations it was grown to the pesticides, herbicides, and fertilizers used to protect it and promote its growth. None of this information is required by FFDCA, which focuses on the nutritional and health aspects of food. When asked if he supported labeling of foods produced using biotechnology, Dr. Cook responded by saying, "labeling of foods...just because of the method used to genetically modify the crop...would not provide useful information on safety or nutritional value of the food."

Whether a label provides relevant information to a consumer also depends on how the consumer perceives the label. Dr Salyers, for example, made the following point: "Whether genetically engineered foods should be labeled or not depends on what the label means to the public...In the current atmosphere, where the public has been given erroneous and misleading information about genetically engineered foods, labels would have exactly the opposite effect from the intended effect."

There is a genuine fear that labeling biotech foods based on their method of production would be the equivalent of a "skull and crossbones"—that the very presence of a label would indicate to the average consumer that safety risks exist, when the evidence shows that they do not. Labeling advocates who argue otherwise are being disingenuous. The United Kingdom's new mandatory labeling law, for example, was put forward to enhance consumer choice. Instead, it has prompted British food producers and retailers to remove all rDNA constituents from the products they sell to avoid labeling.

Polls showing public support for labeling of biotech foods also need to be put into perspective. A poll of New Jersey residents, for example, found that only 59 percent of the citizens surveyed approved of the production of plants through traditional hybridization techniques,⁵⁹ and 20 percent believe that it is morally wrong to produce plants this way (Hallman and Metcalfe, 1999). Given the apparent lack of knowledge of traditional plant production methods—methods that have been used safely for hundreds of years—labels indicating the method of genetic manipulation clearly would be extremely confusing, and of little relevance, to consumers.

OVERSIGHT

Finding: Federal regulations should focus on the characteristics of the plant, its intended use, and the environment into which it will be introduced, not the method used to produce it. Regulations that capture selectively the products of agricultural biotechnology do not reflect the scientific consensus on risk, are overly burdensome, and stifle scientific research.

The conceptual basis for risk-based oversight policies established in the Statement on Scope is that the risks of organisms produced by biotechnology are the same as those produced by traditional methods, such as hybridization, and that regulations should focus on the characteristics of the plant, not how it was produced. There is a broad scientific consensus in support of this premise.

For example, a 1987 NAS report concluded that, "There is no evidence that a gene will convert a benign organism onto a hazardous one simply because the gene came from an unrelated species," and that environmental risk assessment of genetically-engineered organisms "should be based on the nature of the organism and the environment into which it will be introduced, not by the method by which it was modified" (NAS, 1987). These findings were reaffirmed in subsequent reports by NRC (NRC, 1989), OECD (OECD, 1993b), 11 professional scientific societies (IFT *et al.*, 1996), CAST (1998), and the testimony of the research scientists who appeared before the Subcommittee.

⁵⁹ Interestingly, the same poll found that 61 percent of respondents approved using biotechnology to produce new varieties of plants.

However, application of these principles across regulatory agencies has been uneven. While FDA has done a reasonably good job of resisting regulations designed to capture products developed using biotechnology, regulations at USDA and proposed regulations at EPA deviate from the risk-based, scientifically-sound regulatory principles set out in the Statement on Scope and in reports by various scientific bodies.

U.S. Department of Agriculture

In 1986, as part of the Coordinated Framework, USDA's APHIS proposed new regulations under the Plant Pest Act and the Plant Quarantine Act restricting the introduction of plants engineered through rDNA techniques that are "plant pests or which there is reason to believe are plant pests" (OSTP, 1996). As the plasmid of *A. tumefaciens* and the regulatory sequence from the cauliflower mosaic virus often are used to introduce and drive the expression of genes, respectively, in bioengineered plants, these regulations ensure that the majority of plants developed using rDNA technology are regulated by the Department.

The DNA molecules used in these transfers are efficient and reliable mechanisms for introducing new traits in plants. They do not cause domesticated crop plants to become plant pests. Nevertheless, USDA regulatory requirements are triggered by the use of these rDNA methods, and thus depart from scientifically-based measures of plant pest risk.

Dr. Huttner argued that USDA's interpretation of the Plant Pest Act "essentially equated a genetically engineered plant as a potential plant pest and created new permit requirements for plant breeding research involving even small scale field trials. The regulation turns on a new definition, 'regulated article,' which determined that the presence of any part of a known plant pest could provide reason to believe a genetically engineered plant could present risk as a plant pest."⁶⁰ She added that USDA's policy also could create the odd situation in which "two identical plants that differ only in their method of genetic modification would be treated very differently by the agency: one would be subject to stringent regulation and the other would be completely free of regulation."

It is understandable that USDA initially took a cautious approach when dealing with a new technology. However, as Dr. Huttner noted, many years of successful field tests and other information on biotech plants have demonstrated that these methods of recombining DNA do not turn harmless crop plants into plant pests. An editorial by Dr. Arntzen appearing in *Science* magazine in 1992 drew the same conclusions and called for USDA to change its regulatory policy. "The scientific community acquiesced to these regulations," he wrote, "largely based on uncertainty of public acceptance of biotechnology products and the specter of interference from activists in field-testing research. The successes of field tests conducted to date . . . removes the earlier uncertainty. . . There is an urgent need to revise the USDA/APHIS regulations to focus on the behavior of rDNA-modified plants and not on experimental protocols" (Arntzen, 1992).

⁶⁰ Dr. Arntzen made a similar comment in a 1992 *Science* editorial: "The premise [of USDA/APHIS regulations] is that when plants are developed using genetic material from pathogenic sources or when a pathogenic organism is involved in causing the plant transformation, the resultant plant must be subjected to regulatory analysis to assure that it does not pose a risk to other plants" (Arntzen, 1992).

USDA's notification policy has streamlined the process somewhat, but as regulated articles, these plants are still subject to monitoring and reporting requirements, adding substantially to the cost of developing new varieties using existing rDNA techniques. Dr. Huttner estimates that USDA's regulatory policy makes current approaches to rDNA modification 10 to 1,000 times more expensive for plant breeders than conventional approaches.

Proposed Organic Standards. USDA's recently-announced proposal on national standards for organic foods also differentiates between plants developed using rDNA technology and traditional breeding methods. The proposed rules, which reflect intensive lobbying from the organic farming industry, prohibit foods derived from biotech plants from carrying the organic label. This is especially ironic in that genetic manipulation to develop plants with pest resistance has made organic farming possible. There is no scientific justification for excluding plants modified using rDNA techniques from the organic standards if they are grown and processed in accordance with those standards.

Environmental Protection Agency

The scientific community also has voiced its misgivings about EPA's proposed rule on plant pesticides. EPA's proposal would exempt or regulate plant pesticides based on the sexual or taxonomic relationship between the organism from which the gene came and the plant into which it is inserted or the novelty of the trait conferred.

Application of this standard would lead to peculiar effects. If a gene encoding for a substance that enables a plant to resist pests was moved from one tomato variety to another via rDNA techniques, for example, it would be exempt from EPA regulations. But if that same gene came from a species of bacteria, it would be subject to regulation. "These new crop varieties," said Dr. Anderson, "have no long-term established record of safe human consumption. It is incumbent upon the Agency to protect the public from any potential risks stemming from their use by evaluating potential risks, establishing tolerance levels, and registering safe products." Further, she added that EPA's approach would focus only on those plant products "that present novel exposures and more toxic modes of action . . . EPA does believe that pesticidal substances with new exposure to humans or the environment need to be carefully reviewed before being released into commercial agriculture."

By relying on sexual incompatibility or novelty as a regulatory trigger, EPA's proposed rule would place the focus squarely on pest-resistant plants produced using biotechnology. So concerned was the scientific community with this proposal that in 1996, 11 professional scientific societies—representing 80,000 plant, food, and microbiological scientists—took the unusual step of issuing a report on it. They observed that EPA assumes "that traits transferred from outside the normal range of sexual compatibility of the recipient plant will increase the likelihood of novel exposures or hazards to human health or the environment," even if the gene is present in other crop plants (IFT *et al.*, 1996).

In examining EPA's proposed rule, they found that: (1) it is scientifically indefensible to regulate pesticides produced by plants under statutes developed specifically for chemical pesticides

applied externally to plants; (2) all plants are able to prevent, destroy, repel or mitigate most potential pests; (3) while pest resistance can be conferred by specific genes, the ability to resist pests is a characteristic that cannot be separated from the plant itself for regulatory purposes; and (4) the evaluation of the safety of substances in plants should be based on the toxicological and exposure characteristics of the substance and not on whether the substance confers protection against a plant pest.

From this, IFT *et al.* concluded that EPA's proposal is at odds with the principle, put forth by many scientific panels, that the risks of introducing a new variety into the environment are related to the characteristics of the organism and its growing environment, not the source of the genetic material and the process used to transfer it. A panel convened by CAST—whose membership includes over 40 different scientific organizations from the United States and Canada—reviewed the IFT *et al.* report and reached the same conclusion: “[R]egulating the inherited traits of plants for pest resistance because the traits were introduced by genetic engineering and not through conventional breeding is scientifically invalid” (CAST, 1998).

EPA's proposal would erode unnecessarily consumer confidence in agricultural biotechnology by implying that biotech plants contain pesticides, as that term is commonly understood. As both IFT *et al.* and CAST point out, resistance to pests is the rule, not the exception, in plants, and plant breeders have been improving natural defenses using conventional breeding techniques. These pest-resistant varieties have been grown and consumed safely for many years, yet we have very little knowledge of how the resistance is expressed either chemically or physically. This led both groups to conclude that it is scientifically indefensible to regulate pest-resistant biotech plants under rules designed to regulate chemical pesticides applied externally to plants.

Further, there is no scientific reason for EPA to exempt plants developed using rDNA technology if the transferred gene came from a sexually compatible plant. New genetic techniques now allow plant breeders to increase production of naturally-produced pesticidal substances within plants that at low levels are harmless but that at higher levels may pose risks. It bears repeating that the scientific community is in agreement that oversight should focus on the characteristics of the plant, regardless of the source of the transferred genetic material.

Unnecessary Regulation Creates Disincentives

In the nearly two decades in which the United States has dealt with agricultural biotechnology, there has never been a single case in which a crop plant or food developed using rDNA techniques has resulted in damage to the environment or human health.⁶¹ Despite this uninterrupted record of safety, U.S. oversight has been criticized as being too lax.⁶² Dr. Cook's

⁶¹ There is a temptation to credit the stringent U.S. regulatory system for this impressive record of safety. The main reason for this success is much simpler—the products of agricultural biotechnology are inherently as safe as the products of classical breeding.

⁶² The suspicion with which European critics view U.S. regulatory institutions stems in part from the number of food- and health-related scares that have occurred in Western Europe recently—*e.g.* “mad cow” disease (bovine spongiform encephalopathy) in the United Kingdom, contaminated soft drinks in Belgium, and HIV-tainted blood in France. Surveys show that while American consumers display a high degree of confidence their regulatory agencies

testimony provides an apt response: “[B]etween the extensive performance trials and institutional reviews conducted by the developers of genetically modified crops, typically involving years of field testing, and the regulatory framework in place at the federal and state levels to assure safety of new crops or old crops with new traits, it is hard to imagine what more can be done to assure the safety of genetically modified crops to people and the environment.”

Indeed, there needs to be greater recognition that regulations that discriminate against the products of biotechnology, based on their method of production, create disincentives for researchers and plant developers. Dr. Huttner, in particular, voiced her concern that existing regulations at USDA and the proposed regulations at EPA could increase significantly the cost of developing new plant varieties using rDNA technologies. She said, “Because the regulations selectively apply to the use of new biotechnologies, the resulting added costs put biotech businesses at a disadvantage relative to competitors that use conventional, older techniques. The effect on entrepreneurial start-up firms can be particularly serious, affecting even the structure of an emerging industry.” IFT *et al.* and CAST also commented on the harmful impact increased regulations can have on small companies and public plant breeding programs developing biotechnology products for niche markets.

Unwarranted regulations also will have an impact on the academic community engaged in biotechnology research. It is already happening in Europe, where researchers reportedly either are leaving the field or are seeking opportunities elsewhere. If the United States is to keep its lead in this area, it is important to maintain a top-notch research capacity. Tangling up researchers in red tape will waste research dollars and stall progress.

POLITICALLY-MOTIVATED OPPOSITION

Finding: Much of the opposition to agricultural biotechnology is politically motivated, not scientifically based.

Notwithstanding the scientific consensus that new crop varieties and foods developed using agricultural biotechnology are at least as safe as those developed using conventional breeding, well-funded anti-biotechnology activists have been effective in using a patina of science to spread unfounded fears about these products. In the words of Dr. Cook, “What needs to be more widely recognized is that raising doubts about safety is only a route to carrying out a more fundamental social, economic, or political agenda. What better way to generate a ground-swell for labeling or even outright elimination of GMOs from commercial agriculture than to raise doubts in the minds of people about safety, when safety is not really the issue?” (quoted in Huttner, 1999). When Norman Borlaug, the Nobel Prize-winning agronomist, was asked recently to explain the opposition to agricultural biotechnology, he said simply: “It's political. It's not scientific.”

For many biotechnology opponents, the political agenda to which Dr. Cook referred seems to be to stymie the biotechnology industry and to replace large-scale agriculture with primarily organic farming to meet the world's food needs. Modern agricultural practices often have been criticized as being unsustainable because of their reliance on inputs of chemicals and water. But as many

can ensure food safety, European consumers display a high degree of distrust in their regulatory agencies (Gaskell *et al.*, 1999).

witnesses expressed to the Subcommittee, the driving motivation of much of the research in plant genetics is to reduce the environmental impact of farming, ostensibly a goal of many of biotechnology's sternest critics. There is substantial evidence that agricultural biotechnology will provide environmental benefits well beyond decreases in pesticide and herbicide use. For example, new varieties of low-phytate corn for animal feed produce less phosphorous in the waste passed by the animal, thus reducing pollution from animal farms. In addition, higher yields resulting from genetic improvements can reduce the pressure to convert valuable ecosystems, such as rainforests, to agricultural production. These and other significant environmental benefits are neglected deliberately in the international campaigns of activist groups.

The biotechnology industry also has been criticized for being concentrated in the hands of a few large multinational companies based in economically-advanced countries. This concern also is misplaced. Both Dr. Ryals and Dr. Cook pointed out that agricultural biotechnology represents a technological revolution comparable to those that gave birth to the power, transportation, and computer industries, each of which has conferred tremendous benefits to consumers. It is expected that as agricultural biotechnology becomes more industrialized, increasing competition will lead to consolidation within the industry and adoption of the technology by consumers worldwide, similar to what has happened in these other industries. But consolidation will not lead to monopoly, as entrepreneurs will develop niche markets for specialty products, similar to those that have developed in other mature industries.

In an industry changing as rapidly as biotechnology, it is hard to foresee a company or small group of companies gaining domination over global food production. Ironically, increasing the regulatory burdens on agricultural biotechnology, which many biotechnology critics advocate, would succeed only in giving a distinct competitive advantage to large companies able to pay the added costs of regulation. This is hardly the way to promote competition or to foster the spread of this technology to developing countries.

The most potentially damaging claims of activist groups, as Dr. Cook observed, raise doubts about the safety of foods from bioengineered plants, despite overwhelming scientific evidence that these doubts are unfounded. It is interesting to note, therefore, that among agricultural biotechnology's most ardent critics is the organic farming industry. The irony of this was noted by Dr. Salyers, who told the Subcommittee, "There is no question that organic produce is potentially more dangerous than genetically engineered plants. In particular, insect damage creates tissue that is easily invaded and colonized by fungi that produce a variety of mycotoxins, of which ergot and aflatoxin are two examples."⁶³ In addition to higher levels of certain mycotoxins, data suggest that organic foods also are more likely to contain harmful bacteria, such as *E. coli* (Avery, 1998).⁶⁴

⁶³ Other witnesses appearing before the Subcommittee made similar comments. For example, Dr. Ryals said, "Organically-grown' is not synonymous with safe and it is a mystery to me why anyone thinks that it is."

⁶⁴ In an analysis of data from the Centers for Disease Control, Dennis Avery, Director of the Center for Global Food Issues, found that people who eat organic foods are eight times more likely to contract a new strain of *E. coli* bacteria (0157: H7) from food. "Organic and 'natural' food producers supply only about 1 percent of the nation's food," he wrote, "but the Centers for Disease Control have traced approximately 8 percent of the confirmed *E. coli* cases to such foods" (Avery, 1998).

Biotechnology can improve food safety by lowering exposure to harmful substances in foods. Dr. Cook told the Subcommittee of research showing that grain from Bt corn has significantly lower concentrations of fumonisin, a mycotoxin produced by the fungus *Fusarium moniliforme* that has been linked with esophageal cancer. *F. moniliforme* is known to thrive in ears of corn damaged by the corn ear worm. “It would be more difficult to control the corn ear worm with BT sprayed as a biopesticide on the corn, as approved by the organic standards,” he said, “since this kind of application would be less likely to control worms that burrow inside the ears and kernels of corn.”

Capitalizing on the near-hysteria in Europe about food safety, Europe's political leaders have invoked the “precautionary principle”—which asserts that governments may make political decisions to restrict a product even in the absence of scientific evidence that a risk exists—as cover for protectionist regulatory policies that have shut out American farm products from European markets. Biotech crops also are seen as an economic threat in Europe, where governments encourage low-yield farming techniques. In a free-trade environment, trade decisions should be science-based, as World Trade Organization (WTO) rules stipulate. American researchers and farmers need to know that they will have a market for their products.

What is perhaps of greater concern is the impact European attitudes could have in other agricultural and food markets around the world, particularly in the developing world, where biotechnology can address so many health and environmental problems. A well-reasoned view of needs of the developing world has been provided by Dr. Florence Wambugu, a prominent agricultural researcher in Kenya. She recently wrote, “The needs of Africa and Europe are different. Europe has surplus food and has never experienced hunger, mass starvation and death on the regular scale we sadly witness in Africa. The priority of Africa is to feed her people with safe foods and to sustain agricultural production and the environment...The criticism of agribiotech products in Europe is based on socioeconomic issues and not food safety issues, and no evidence so far justifies the opinion of some in Europe that Africa should be excluded from transgenic crops. Africans can speak for themselves...The African continent, more than any other, urgently needs agricultural biotechnology” (Wambugu, 1999).⁶⁵

In the politically-charged atmosphere created by antibiotechnology activists, scientists like those who appeared before the Subcommittee operate at a distinct disadvantage because of the demands placed on them by the scientific culture, which prizes dispassionate discussion of the evidence and the arguments, not hyperbole and sound bites. Dr. Henry Miller, founding Director of FDA's Office of Biotechnology, recently summed up the situation this way: “We cannot change [the antibiotechnology extremists'] minds by making scientifically reasonable arguments, asserting the primacy of empirical evidence and the scientific method, or invoking the benefits to the public of new products and new choices. They are not engaged in a good-faith effort to advance the public interest” (Miller, 2000).

As if to confirm Dr. Miller's assessment, some extreme antibiotechnology groups have resorted to vandalism and worse. Since Greenpeace activists first destroyed a farm field in Iowa in 1996,

⁶⁵ Biotechnology already is having an impact on farming in Africa, where a new variety of sweet potato developed by Monsanto and the Kenya Agricultural Research Institute to resist the feathery mottle virus has been introduced. See: Qaim, 1999.

there have been over 100 reports of property destruction, arson, assaults, and other acts of intimidation against people involved in biotechnology.⁶⁶ Recently, Michigan State University's Agriculture Hall, a 91-year old landmark building housing the university's Agricultural Biotechnology Support Project, was severely damaged in a fire for which a radical environmental group, the Earth Liberation Front, claimed "credit." Weeks later, the same group broke into a University of Minnesota lab and uprooted 800 oat plants that were part of a study aimed at improving disease resistance. These criminal acts have put people's lives at risk, disrupted careers and important research, threatened scientists, and violated the accepted norms of debate and decency in a free and democratic society.

The scare stories now being spread about agricultural biotechnology bear no relation to the testimony received by the Subcommittee. The research scientists have exciting stories to tell, but they must be told more forcefully if they are to rise above the strident voices of those whose political agenda, if adopted, would significantly set back scientific progress and limit consumer choice.

⁶⁶ In the United Kingdom, Friends of the Earth, an antibiotechnology activist group, mailed letters threatening legal action to scientists working for research centers involved in agricultural biotechnology. The letters said that researchers would be held "personally legally liable" for damage caused by the growing or consumption of genetically modified crops. Representatives of the John Innes Centre, which received such a letter, stated that the campaign was a "crude attempt to harass and intimidate individuals" (Radford, 1999).

RECOMMENDATIONS

An analysis of all the testimony and other material made available to the Subcommittee leads to the following recommendations.

PLANT GENOME RESEARCH

Recommendation: Congress should ensure adequate levels of funding for the National Plant Genome Initiative. Efforts to link basic research in plant genomics with local plant breeding programs at Agricultural Experiment Stations and with Cooperative Extension should be increased.

The United States is the world leader in agricultural biotechnology. However, maintaining preeminence in this field will require a sound research base from which new technologies and products can be developed.

The National Plant Genome Initiative is a well-managed public asset that represents a wise use of taxpayer dollars. Current sequencing efforts on *A. thaliana* have improved immeasurably our understanding of the genomics of a typical flowering plant. The shift in emphasis from gene sequencing to functional genomics is the logical next step that should provide the intellectual basis for new varieties of commercially-important crops and other plants. Further understanding of plant genomics also should provide insights that could be used to inform and streamline the regulatory process.

The testimony is clear that plant genome research already has paid off in significant ways, and further advances have the potential to reap new knowledge and spawn entire new industries. Dr. Ryals, in particular, noted that the foremost rate-limiting step in agricultural biotechnology is gene discovery. Therefore, in making appropriations, Congress should provide sufficient funding to continue this important work.

It also is important that we use productively the research results generated through this program. NSF, USDA, and the other participants in the plant genome program have done a credible job of making the results of the research it funds available to other researchers and the private sector. Partnerships among universities participating in the program, agricultural experiment stations, and private-sector companies also have developed. These should be encouraged further, and more formal structures concentrating research efforts in plant genomics, plant breeding, and agricultural extension should be considered to attract increased private sector participation and get new varieties to the field sooner.

The American taxpayer is making a considerable investment in basic plant genome research. The payoffs from this investment will depend in large part on our ability to capture and apply the social benefits from it. As with other new technologies, such as information technology, small, entrepreneurial firms will be the source of much of the innovation and commercialization in agricultural biotechnology. Venture capital will materialize, but only in the right business climate. It is imperative, therefore, that we do not throw up unwarranted regulatory roadblocks that would reduce the value of this research and dry up private-sector investment. Important

intellectual property issues also will have to be addressed if we are to reap the full potential of this research.

REGULATION

Recommendation: Federal regulatory oversight of agricultural biotechnology should be risk-based and guided by the characteristics of the plant, its intended use, and the environment into which it is to be introduced, not by the method used to produce it. Existing regulations at USDA and proposed regulations at EPA targeting the products of biotechnology do not conform with the scientific consensus and should be revised to stay current with advances in scientific knowledge.

Oversight should be commensurate with risk. The overwhelming view of the scientific community—including in reports by NAS, NRC, OECD, 11 professional scientific societies, and CAST—is that plants and plant-derived foods developed using biotechnology do not pose risks different from those for similar plants developed using traditional methods of genetic manipulation. The conclusion of these scientific bodies is that regulatory oversight should focus on characteristics of the product, not process by which it was produced. This principle also was accepted by OSTP and the regulatory agencies in their Statement on Scope—which provided regulatory agencies guidance on the application of discretionary authority under existing statutes—and it forms a scientifically-sound basis for regulation to ensure the safety of new plant and food varieties both to human health and the environment.

The present situation facing USDA, EPA, and FDA in dealing with agricultural biotechnology is analogous in many respects to the situation faced by the Federal Communications Commission (FCC) when it dealt with the issue of data transmission over telephone lines in the mid 1960s. A recent analysis of the FCC's role in creating an environment in which the Internet could flourish said, "Predicting that the future would bring the convergence and interdependence of computers and communications, the Commission recognized the difficulty of separating the two into discrete categories" (Oxman, 1999). In 1971, the FCC adopted a policy that data transmission would be treated no differently than voice transmission. The decision not to throw up new regulatory roadblocks for data transmission was extremely important in spurring subsequent development of the Internet.⁶⁷

For regulatory purposes, the distinctions among traditional plant breeding, wide-hybrid crossing, mutagenesis, and rDNA methods in crop improvement are as conceptually artificial as those once suggested for voice and data transmission. The history of crop improvement over the 20th century suggests that biotechnology is just the latest in a continuum of technological innovations that have enhanced agricultural productivity enormously.

The Coordinated Framework foresaw that federal regulations would need to be modified to reflect increased understanding of the risks of rDNA technologies. "The regulatory framework anticipates that that future scientific developments will lead to further refinements," it said, adding that "evolution is anticipated in the regulation of commercial products as scientists and

⁶⁷ In Europe, regulators have treated voice and data transmissions differently. This has slowed the growth and development of data networks, and many European networks now are outmoded.

regulators learn to predict more precisely particular product use that require greater or lesser controls or even exemption from any federal review" (OSTP, 1986).

A wealth of information has been amassed by the scientific community and the regulatory agencies on agricultural biotechnology. We now have 25 years of experience worldwide, an extensive record of field trials overseen by USDA and EPA (over 5,000 at USDA alone), and over a decade's worth of analyses by FDA on a broad range of biotechnology products. This vast body of knowledge and experience has demonstrated the substantial equivalence of plants produced using traditional breeding and rDNA methods.

Today, it often costs hundreds of millions of dollars to develop a new plant variety using biotechnology, much of which is related to meeting regulatory requirements. These costs largely outweigh the advantages of using recombinant techniques. There is a genuine concern that persisting with current, and imposing new, regulatory restrictions may harm an emerging industry and the publicly-funded university research base on which it depends.

Further, there are indications that EPA and USDA policies that result in selective regulation of rDNA-modified plants have been used against the United States by EU countries in international negotiations. It is difficult for the Administration to argue in international venues that international agreements should adhere to accepted scientific norms if those same norms are not applied consistently in the domestic sphere.

For these reasons, the Administration should begin work to eliminate artificial regulatory distinctions based on the method by which a new plant or food variety is produced or the source of the gene that has been transferred. In addition, agencies should make better use of the effective nonregulatory oversight mechanisms, including scientific peer review, that have been developed over many years. More specifically, USDA's interpretation of the Plant Pest Act and EPA's proposed plant pesticide rule, each of which effectively singles out some plants based on their method of production, should be modified to reflect the risk-based principles accepted by the scientific community.

USDA Plant Pest Regulations

USDA should revise regulations that target biotech plants based on the source of the genetic material, the vector used to transfer it, or the regulatory sequences used to express it. After thousands of successful field trials and years of scientific research, there is no reason to continue under the assumption that transferring a gene from a plant pest to a crop plant poses an environmental hazard.

The scientific evidence is clear that the method used to introduce or express a transferred gene is a poor indicator of risk. USDA's notification procedure for field-test permits for certain regulated articles is a step in the right direction, but plant breeders are still subject to rigorous testing, monitoring, and reporting requirements that add unnecessarily to the costs of developing a new plant variety using biotechnology. USDA should consider developing risk-based guidelines similar to those employed by FDA, which have been effective in getting new products to market quickly and safely.

EPA Proposed Plant Pesticide Rule

EPA's proposed plant pesticide rule would use sexual compatibility or novelty—*i.e.*, the source of the gene—as justification for initiating regulatory oversight. The testimony and other material made available to the Subcommittee, particularly the reports of 11 professional scientific societies and CAST, make a strong case that novelty is not synonymous with risk and that EPA's approach is not scientifically valid.

In its present form, the proposed regulatory requirements would apply when a gene encoding for a pesticidal substance from one plant is transferred to another, sexually-incompatible plant—even when the donor plant has a history of safe use. As our knowledge of plant genomics advances, it is not hard to imagine a situation in which a plant is regulated because the gene encoding for plant pesticide was transferred from a sexual incompatibility organism only to discover subsequently that the same or similar gene is found in a wild relative of the regulated plant. Moreover, EPA is on scientifically shaky ground in exempting a rDNA plant where the pest-resistant trait is transferred from a sexual compatible plant.

The basis of EPA's proposed rule—that sexual incompatibility or novelty indicate increased risk and sexual compatibility indicates decreased risk—is not a scientifically-sound one for regulation. As NAS said in 1987, “There is no evidence that a gene will convert a benign organism into a hazardous one simply because the gene came from an unrelated species,” and there has been no information developed in the intervening years to cast doubt on that conclusion. Therefore, EPA should reconsider its current proposal and develop new rules consistent with the scientific consensus on risk, the Statement on Scope, and a single approach to plant breeding involving biological pest resistance, regardless of the genetic method used. Risk-based guidelines on pest-protected plant analogous to those employed by FDA in its Statement of Policy should be developed.

VOLUNTARY CONSULTATION AT FDA

Recommendation: FDA should maintain its current science-based policy of equating foods developed using biotechnology and classical plant breeding methods, and it should maintain its policy of voluntary consultation with companies developing foods using genetic modification, regardless of the method employed.

Critics of agricultural biotechnology, particularly those in Europe, have derided FDA's oversight policy as “voluntary.” This criticism rests on the mistaken presumption that foods derived from biotech plants pose greater risks than traditional foods and that current oversight practices are not adequate to protect public safety. There is no scientific evidence to support either of these contentions. Mandatory consultation would not enhance public safety, but would saddle taxpayers and consumers with additional costs.

Current FDA policy regarding food additives—for foods created through either traditional or rDNA methods—states that food additives already require pre-market approval unless they are recognized as safe on the basis of a history of safe use in the food supply or scientific analysis.

Under FDA policy, plant-food developers (using either traditional or biotech methods) are allowed to make this determination.

To date, all companies that have brought a food derived from bioengineered plants to market have participated in the voluntary consultation process. But even in the absence of such consultation, there is no reason to believe that the safety analyses performed by the food producer are not rigorous. Critics of this technology often overlook or dismiss as insufficient the legal duty of food producers, rather than FDA, to ensure the safety of the foods they bring to market. FDA has broad post-market enforcement powers, including criminal prosecution. These facts, as well as the ever-present threat of civil action by consumers who claim to have suffered harm as the result of eating an unsafe food product, is strong inducement for companies to produce safe, wholesome foods.

FDA needs to be more forceful in standing by and explaining its regulatory decisions. That America's food supply is among the safest in the world demonstrates that current regulatory oversight, applied to a remarkable and expanding array of plant-derived food products, is more than adequate to protect human health. Therefore, Congress should reject legislative proposals that would make the voluntary consultative process at FDA mandatory.

LABELING

Recommendation: FDA should maintain its current science-based policy on labeling of foods created using biotechnology as described in its 1992 Statement of Policy. There is no scientific justification for special labeling of food products developed using agricultural biotechnology, as a class.

Current FDA policy, based on its 1992 Statement of Policy, states that foods should be labeled according to their characteristics, and not their method of production. This policy is consistent with the Statement on Scope and the scientific consensus on the risk of plant-derived foods developed using biotechnology. Testimony before the Subcommittee from both FDA and independent research scientists confirms that this policy is scientifically sound and protects consumer interests.

FDA's policy mandates that substances that are added to biotech foods must be regulated—and labeled—as additives unless it is determined that these substances are "generally recognized as safe." The same standard applies to all food additives, regardless of their origin. The FDA has indicated clearly that biotech foods containing allergens or toxins, or those that are substantially different nutritionally from current varieties, must carry a label to this effect. This is appropriate from a scientific perspective and has been effective in protecting human health.

It should be noted that producers are free to label the foods they produce as free of genetic modification through rDNA techniques. In contrast, it would be misleading to label the products of conventional plant breeding as being free of genetically-modified substances. Moreover, there is no scientific justification to impose the costs of segregation and identity preservation on all farmers, food processors, and distributors simply because new genetic methods were used in food production. Market forces will signal the degree to which producers and suppliers select

labeling or identity preservation. As more foods are developed with enhanced nutrient, taste, or other characteristics that consumers want, food producers likely will both label their products accordingly and actively advertise them and their enhancements.

FDA's current policy on labeling is scientifically and legally sound and should be maintained. Legislation mandating the labeling of food products derived from agricultural biotechnology would raise costs to consumers and discourage the development and marketing of new, beneficial biotech products. Congress should oppose mandatory labeling legislation.

INTERNATIONAL AGREEMENTS

Recommendation: The Administration should work to ensure that markets for products of agricultural biotechnology products are not restricted by scientifically unsound measures. The United States should not accept any international agreements that violate scientific principles and limit trade in, or mandate labeling of, a plant or food product based on the method used to develop it.

Unfounded fears about biotechnology and, in some cases, simple economic protectionism have led some nations to impose restrictions on biotechnology products, costing American farmers hundreds of millions of dollars and disrupting fair U.S. access to export markets. Congress and the Administration should work to ensure that international markets for agricultural biotechnology products are not harmed. The Administration, in particular, needs to take the lead role in explaining and defending the extraordinary record of safe use of biotechnology products that has been built up over many years.

The United Nations Convention on Biodiversity, which stemmed from the 1992 Earth Summit in Rio de Janeiro, recently met in Montreal and announced on January 29, 2000 a new protocol (Biosafety Protocol) covering the “transboundary movement, transit, handling and use of all living modified organisms that may have adverse effects on the conservation and sustainable use of biological diversity” (UNEP, 2000).⁶⁸ The Biosafety Protocol—which strictly speaking is an environmental agreement, not a trade agreement—allows a country to require prior notification from countries exporting biotech seeds and living organisms that are intended to be introduced into the environment. In addition, it requires that shipments of products that may contain living modified organisms (such as bulk commodities for food, feed, or processing) be identified as such.

Many delegates to the Montreal negotiations also wanted the agreement to supercede WTO's Sanitary Phytosanitary Standards, which require health and sanitary restrictions to have a scientific basis. Both the State Department and the U.S. Trade Representative have made assurances that the superiority of the WTO standards is maintained in the agreement.

The Biosafety Protocol has been interpreted by some observers as implicitly endorsing the precautionary principle, although it is not mentioned specifically in the document. This principle maintains that, at the political level, governments may implement measures to restrict a product if there is any perceived uncertainty about risk. As the testimony shows, science can never

⁶⁸ The agreement does not cover processed foods or pharmaceuticals.

demonstrate zero risk. Therefore, risk assertions may be considered by a government to justify trade restrictions, even where there is no credible scientific evidence that a risk exists. The European Union maintains that invoking the precautionary principle is an “eminently political decision” that “may be based on a less objective appraisal” (EU, 2000).

Set against the political nature of the precautionary principle is the scientific consensus that risk assessment should focus on probable, not hypothetical, risks. Historically, the United States has not endorsed the precautionary principle as a basis for regulatory decisions. Doing so would completely undermine the science-based regulatory structure that has relied on a cautious approach in the scientifically-objective assessment of risk, which has served the Nation well for decades.

The United States has not ratified the Convention on Biological Diversity and was not an official participant in the Montreal talks. Nevertheless, the Administration has said it will abide by the agreement. Some analysts have suggested that, by pledging to accede to the Biosafety Protocol, the Administration appears to have given tacit approval to the idea that the products of agricultural biotechnology are intrinsically different from traditionally-produced foods—a view the scientific community roundly rejects.

While interpretations of the agreement differ, there is near unanimity that it does not impinge on U.S. trade rights. However, questions remain on how it will be implemented. Of perhaps even greater concern is that the Biosafety Protocol could be used by opponents of biotechnology to create mischief in other international venues, particularly WTO and the FAO and WHO standards commission, which oversees the Codex Alimentarius, the international food code.

The concept of substantial equivalence as a basis for regulation of agricultural biotechnology has been accepted by a number of international bodies, including OECD, WHO, FAO, and the International Life Sciences Institute. Moreover, WTO rules require a scientific basis for restrictions on agricultural products related to health and safety.

Adoption of the precautionary principle by FAO and WHO could have a devastating effect in U.S. trade and scientific interests. Annually, U.S. farmers—the most efficient in the world—sell about \$50 billion of goods in international markets. Treaties or other international obligations that undermine the concept of substantial equivalence and WTO rules will hurt U.S. farmers, academic researchers, the biotechnology industry, and consumers.

The United States, as the world leader in biotechnology, has an obligation to demonstrate leadership and resist false scientific premises both at home and abroad. In addition to revising U.S. regulations, the Administration should actively oppose international agreements that do not meet scientific principles and that penalize the products of agricultural biotechnology. To accept less will only encourage the injection of even more protectionist politics into international agreements and harm U.S. interests.

PUBLIC EDUCATION

Recommendation: The Administration, industry, and scientific community have a responsibility to educate the public and improve the availability of information on the long record of safe use of agricultural biotechnology products and research activities.

Testimony before the Subcommittee indicated concern about the spread of misinformation and the lack of public access to accurate information about technical advances in biotechnology. Both reinforce irrational fears about biotechnology.

The evidence that the risks associated with traditional and rDNA techniques for plant breeding are equivalent is overwhelming. However, policymakers and the public are largely unaware of the vast information and findings gathered by the regulatory agencies and eminent scientific bodies over the 25 years that rDNA technologies have been developed and widely used. In her testimony before the Subcommittee, Dr. Salyers said, “I think what we really need is some sort of a public education initiative . . . We really need to inform consumers about this, because otherwise I think there are going to be some very bad decisions made for the wrong reasons.”

The regulatory agencies have not been as active in the public debate as they could, given the substantive knowledge they have to share on the subject of risk. The Administration has an obligation to ensure that information about the application of agricultural biotechnology is disseminated widely. Some information already is available—for example, USDA, EPA, and FDA have developed a coordinated Website for information on regulations. But there is no comparable site for the considerable biosafety information and scientific analyses they have compiled over the many years in which they have been regulating the products this technology. Individual agency Web pages do provide some of this information, but much of it is highly technical and geared towards specialists, and thus is difficult for the general public to interpret.

The Administration should instruct USDA, EPA, FDA, NIH, and NSF to develop, in consultation with OSTP, a coordinated Web-based system to provide public access to pertinent, factual information on plant genomics and agricultural biotechnology. Each of these agencies should convey—in terms understandable to the general public—its experience in researching and regulating this technology: USDA and EPA for field trials; FDA on the principles and structure of its risk-based policies; NIH on rDNA research; and NSF and USDA on plant genomics. Information also should be provided explaining the historical mechanisms, including nonstatutory oversight by professional and scientific bodies, used to ensure the safety of the U.S. food supply over the past five decades.

The biotechnology industry also needs to be more forceful in its defense of biotechnology. For years the industry has played by the rules to bring new, safe products to market. U.S. companies have spent hundreds of millions of dollars of research and development capital and have conducted years of rigorous testing and evaluation required by USDA, EPA, and FDA regulations. Biotechnology companies have been held to a high level of accountability and possess an outstanding record of safety. Consumers need to know this.

In fulfilling their responsibilities to shareholders, farmers, and consumers, biotechnology companies need to add their voices to the debate. Specifically, they need to address the purpose and benefits of their products on the market and in development. They should use familiar

products produced using traditional methods to provide consumers a familiar context for making comparisons.

Lastly, independent scientists—like those who appeared before the Subcommittee—need to take a more active role in explaining their work to the public, especially the research that will lead to improvements in human health and help feed a growing world population. Scientists working in plant genomics and agricultural extension at Land Grant colleges are particularly well-suited to provide this sort of information. Scientific organizations also have a role to play. The reports of NAS, NRC, 11 scientific societies, and CAST, cited throughout this report, are particularly good examples of how professional organizations can aid policymakers. Expanded efforts should be directed to educating the general public.

For many scientists, this can be a burden that takes time away from research. However, the issues are so important that they need to make a special effort to become more involved. They should make themselves available to the press and legislators and speak at civic organizations. Participation on government panels that review biotechnology issues also is encouraged.

It has been said that “Error is a hardy plant: it flourisheth in every soil.”⁶⁹ In the debate over agricultural biotechnology, the stakes are too great to allow the error and misinformation that have flourished in Europe to take root here. By engaging the critics and making information available to the public, regulators, plant developers, and researchers can address Dr. Salyers's concern and help consumers and policymakers make good decisions for the right reasons.

⁶⁹ Martin Tupper, *Proverbial Philosophy (1838-1842), Of Truth in Things False*.

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APPENDIX 1: LIST OF FINDINGS AND RECOMMENDATIONS

Findings

The Report makes the following findings:

Plant Genome Research. The plant genome program represents a sound use of federal research funding

Chemical Inputs. The current generation of pest-resistant and herbicide-tolerant agricultural plants produced using biotechnology has reduced chemical inputs and improved yields for American farmers. Future adoption of new varieties will continue this trend and will solve intractable pest problems, help protect the environment, and lower costs to consumers.

Consumer Benefits and Global Food Production. The promise of agricultural biotechnology is immense. Advances in this technology will result in crops with a wide range of desirable traits that will directly benefit farmers, consumers, and the environment and increase global food production and quality.

Assessing Risks. There is no evidence that transferring genes from unrelated organisms to plants poses unique risks. The risks associated with plant varieties developed using agricultural biotechnology are the same as those for similar varieties developed using classical breeding methods. As the new methods are more precise and allow for better characterization of the changes being made, plant developers and food producers are in better position assess safety than when using classical breeding methods.

Outcrossing. The risks that new plant varieties developed using agricultural biotechnology will become weedy or outcross are the same as those for similar varieties developed using classical breeding methods and for introduced species.

Pest-Resistant Crops and the Potential for Pesticide-Resistant Insects. Widespread use of pest-resistant crop varieties developed using agricultural biotechnology is unlikely to accelerate the emergence of pesticide-resistant insect strains and may actually be more effective in preventing their emergence when compared to spray applications of similar pesticides.

Monarch Butterfly. The threat posed by pest-resistant crop varieties developed using agricultural biotechnology to the Monarch butterfly and other non-target species has been vastly overblown and is probably insignificant.

Allergens and Toxins. The risks of introducing an allergen or toxin into the food supply are the same for plant varieties developed using agricultural biotechnology as those for similar varieties developed using classical breeding methods.

Antibiotic Resistance. The risk that a health hazard will be created through the use of antibiotic resistance markers in the development of new plant varieties using agricultural biotechnology is insignificant.

Substantial Equivalence. The concept of “substantial equivalence” in the regulation of foods developed using agricultural biotechnology is scientifically sound and provides a useful historical baseline for judging safety.

Labeling. There is no scientific justification for labeling foods based on the method by which they are produced. Labeling of agricultural biotechnology products would confuse, not inform, consumers and send a misleading message on safety.

Oversight. Federal regulations should focus on the characteristics of the plant, its intended use, and the environment into which it will be introduced, not the method used to produce it. Regulations that capture selectively the products of agricultural biotechnology do not reflect the scientific consensus on risk, are overly burdensome, and stifle scientific research.

Politically-Motivated Opposition. Much of the opposition to agricultural biotechnology is not scientifically based.

Recommendations

The Report makes the following recommendations:

Plant Genome Research. Congress should ensure adequate levels of funding for the National Plant Genome Initiative. Efforts to link basic research in plant genomics with local plant breeding programs at Agricultural Experiment Stations and with Cooperative Extension should be increased.

Regulation. Federal regulatory oversight of agricultural biotechnology should be risk-based and guided by the characteristics of the plant, its intended use, and the environment into which it is to be introduced, not by the method used to produce it. Existing regulations at USDA and proposed regulations at EPA targeting the products of biotechnology do not conform with the scientific consensus and should be revised to stay current with advances in scientific knowledge.

Voluntary Consultation at FDA. FDA should maintain its current science-based policy of equating foods developed using biotechnology and classical plant breeding methods, and it should maintain its policy of voluntary consultation with companies developing foods using genetic modification, regardless of the method employed.

Labeling. FDA should maintain its current science-based policy on labeling of foods created using biotechnology as described in its 1992 Statement of Policy. There is no scientific justification for special labeling of food products developed using agricultural biotechnology, as a class.

International Agreements. The Administration should work to ensure that markets for products of agricultural biotechnology products are not restricted by scientifically unsound measures. The United States should not accept any international agreements that violate

scientific principles and limit trade in, or mandate labeling of, a plant or food product based on the method used to develop it.

Public Education. The Administration, industry, and scientific community have a responsibility to educate the public and improve the availability of information on the long record of safe use of agricultural biotechnology products and research activities.

APPENDIX 2: ACRONYMS

APHIS	Animal and Plant Health Inspection Service
BMA	British Medical Association
Bt	<i>Bacillus thuringiensis</i>
CAST	Council on Agricultural Science and Technology
DNA	deoxyribonucleic acid
DOE	Department of Energy
EDF	Environmental Defense Fund
EPA	Environmental Protection Agency
ERS	Economic Research Service
EU	European Union
EUP	Experimental Use Permit
FAO	United Nations Food and Agricultural Organization
FCC	Federal Communications Commission
FDA	Food and Drug Administration
FFDCA	Federal Food, Drug, and Cosmetic Act
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
GM	genetically modified
GMO	genetically modified organism
GRAS	generally recognized as safe
HIV	Human Immunodeficiency Virus
IFT	Institute of Food Technologists
IWG	Interagency Working Group on plant genomics

NAS	National Academy of Sciences
NIH	National Institutes of Health
NPGI	National Plant Genome Initiative
NRC	National Research Council
OECD	Organisation of Economic Co-operation and Development
OSTP	Office of Science and Technology Policy
rDNA	recombinant DNA
SAES	State Agricultural Experiment Stations
SCEC	Select Committee on the European Communities
UNICEF	United Nations Children's Fund
USDA	United States Department of Agriculture
USGS	United States Geological Survey
WHO	World Health Organization