BIOTECHNOLOGY AND FOOD

Second edition

Prepared for the American Council on Science and Health
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by Alan McHughen, D.Phil.
(First edition by Suzanne Huttner, Ph.D.)

Project Coordinator
Ruth Kava, Ph.D., R.D.
Director of Nutrition, ACSH

Art Director
Yelena Ponirovskaya

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AMERICAN COUNCIL ON SCIENCE AND HEALTH
1995 Broadway, 2nd Floor, New York, NY 10023-5860
Tel. (212) 362-7044 • Fax (212) 362-4919
URL: http://www.acsh.org • E-mail: acsh@acsh.org

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Gale A. Buchanan, Ph.D.
University of Georgia

Joseph Borzelleca, Ph.D.
Virginia Commonwealth University

Emil W. Chynn, M.D.
St. Vincent's Hospital, New York

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The Wistar Institute

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Ontario, Canada

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American Council on Science and Health

Sarah Short, Ph.D., Ed.D., R.D.
Syracuse University College for Human Development

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Fredric M. Steinberg, M.D.
England

Glenn Swogger, Jr., M.D.
Menninger Clinic

Elizabeth M. Whelan, Sc.D., M.P.H., M.S.
American Council on Science and Health

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EXECUTIVE SUMMARY

Modern biotechnology greatly benefits the quality and quantity of food, human and animal health, and the environment. Unfortunately, misinformation and misunderstandings about biotechnology in the popular media make it difficult for consumers to make informed assessments. This booklet explains the facts behind genetic modification (GM) and explores some of the issues surrounding the increasingly contentious debate over its use in food production.

Traditional biotechnology has given us almost all of our foods, from corn and beef to bread and wine. In the 1970s, modern biotechnology (i.e. genetic modification, genetic engineering, recombinant DNA or rDNA, gene splicing, etc.) started giving us lifesaving drugs such as Humulin((human insulin). In the past several years, the same technology has been applied to enhance agriculture and food production. Gene modification is a natural event. Many of our traditional foods are products of natural mutations or genetic recombinations. Nature is constantly mutating genes and even moving them from one species to another. With biotechnology, humans can direct genetic changes to benefit human endeavors.

Agricultural scientists have already produced GM crops with:

- herbicide resistance, allowing farmers to use fewer chemicals and obtain weed-free crops;
- insect resistance to control insect pests feeding on the crops, while leaving non-pest insects alone;
- disease resistance to limit crop losses from epidemics;
- delayed ripening fruits that maintain their freshness longer;
- healthier vegetable oils, with lower saturated fat content.

New products under development include:

Agricultural

- Crops tolerant of environmental stresses such as drought, flooding, soil salinity, and frost;
- Crops with greater protection from insects, diseases and weeds.

Consumer-oriented

More consumer-oriented GM products will appear on our shelves, including

- Nutritionally enhanced foods;
- Lower calorie sugar (fructans) from GM sugar beets;
- Foods from which naturally occurring allergenic and antinutritional compounds have been eliminated.

Animal Husbandry

- GM medicines and vaccines can be delivered to animals via their feed, saving the expense of sick animals and veterinary bills;
- Quick-growing game fish;
- Important and valuable chemicals might be produced in GM goats' milk, where they can be readily separated and purified.

Other Products

- Biomaterials such as biodegradable plastics made from GM plant starch;
- GM plants to make diesel fuel;
- Cotton and linen modified to increase quality and durability;
- Textiles and fabrics with built in dyes.

Assistance to developing nations. Rice, the major food staple throughout the developing world, has been nutritionally enhanced for increased iron and beta-carotene (provitamin A) content and increased yields. Cassava, another major food staple, can be protected from viral and other diseases through biotechnology. Inexpensive vitamins, minerals, medicines, and vaccines may soon be delivered to the ill and malnourished via GM fruit.

Public concerns over the safety of GM remain an issue of debate. However, most scientists conversant with GM technology are supporters; they know GM products are not inherently hazardous. **Three hundred million North American consumers have been eating several dozen GM foods grown on hundreds of millions of acres since 1994, with no documented adverse effects.**

Some widespread myths and misconceptions, which may cause consumer concern, include:

- GM potatoes being toxic to rats;
- GM soy becoming allergenic;
- GM corn killing butterflies.

All of these are readily refuted by the facts in each case.

FDA regulations already require answers to crucial safety questions:

- Does the food contain genes from known allergenic sources?
- Does it contain genes from toxic sources?
- Are the concentrations of natural toxic substances increased?
- Is the fat, cholesterol or other nutrient content changed?
- Does the food contain a substance that is new to the food supply?

Like all foods, GM foods bear labels if they carry allergens or toxins, or if they are substantially altered in nutritional composition, so consumers will be able to identify such foods.

Conclusion Current regulatory scrutiny, plus the excellent track record of GM food safety, gives us confidence that GM foods are rigorously scrutinized and that the technology is safe. Consumers and farmers can expect a wide variety of beneficial new products in the not-too-distant future to augment those currently on the market.

INTRODUC

Biotechnology and the Consumer

Biotechnology is simply using living systems to give society more or better foods, drugs and other products. In this sense, we've been applying biotechnology since the dawn of civilization.

In recent times, our understanding of science, especially genetics, has advanced to the point where we can optimize specific genes and traits to provide even greater benefits while reducing or eliminating undesirable features. This technology, based on recombinant DNA (rDNA), is often called Gene Splicing, Genetic Engineering (GE), or Genetic Modification (GM), giving rise to a Genetically Modified Organism (GMO).[1]

The precision attained by such molecular plant breeding can provide, for example, greatly increased crop production and nutritional enhancements at little or no additional cost. Fruits and vegetables can be picked and delivered at the height of flavor and ripeness thanks to carefully tailored improvements that reduce softening and bruising. For

[1] While the term "gene splicing" is more technically correct, most consumers are familiar with the term genetic modification or GM to signify changing genomes or organisms by inserting or deleting genes. Thus, in this booklet, we will use the more familiar terminology of genetic modification.

health-conscious consumers, cooking oils from GM corn, soy, or canola[2] will provide lower saturated fat content. Any interest in reduced calorie French fries? GM potatoes with enhanced starch content absorb less fat during frying. Leaner meats will be available from cattle and pigs improved both directly and through improved feeds. Sensitive new testing kits can detect tiny amounts of potentially harmful toxic contaminants in foods. New plant varieties that are biologically protected against insects and diseases are now on the market, just in time to help farmers hard-pressed to maintain efficient production with fewer chemical control agents.

As our knowledge of molecular genetics increases, our ability to improve our foods and farming will increasingly benefit consumers at home and around the world. Among the benefits to consumers are more nutritious food, more diverse foods, less expensive food and, in regions of most crucial need, more abundant food.

Unfortunately, there is much misinformation, misunderstanding, and confusion about this technology. These circumstances give rise to needless anxiety and, at the same time, obscure any real hazards that might exist as well as possible means of controlling them. A basic understanding of the techniques and goals of biotechnology research is important for deciding the merits of concerns and proposed solutions. The purpose of this booklet is to provide an overview of what is now available through modern biotechnology, what's in the pipeline, and what's on the drawing board. The report is not intended to cover all issues and concerns in depth, but rather to briefly discuss various salient points. References to sources for further reading are presented as a guide for those wishing to delve deeper into particular areas.

Real informed choice requires real information. This booklet explains the facts behind GM and explores some of the issues surrounding the increasingly contentious debate over its use. Armed with facts, we can identify and discuss the actual benefits as well as how to manage or avoid any potential risks.

Biotechnology: The Background Facts

Biotechnology has given us almost all of our foods, from corn and beef (via various traditional plant and animal breeding technologies) to bread and wine (from traditional fermentation technologies).

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1 Canola is a genetic variation of rapeseed developed by Canadian plant breeders. Canola oil is low in saturated fatty acids and high in monounsaturated fatty acids. Though less familiar to most Americans than soy or corn oils, canola oil is now widely used in the U.S.

The era of modern biotechnology started in the early 1970s, when American scientists Herb Boyer and Stan Cohen developed recombinant DNA (rDNA) or "gene splicing" methods, in which fragments of DNA are joined together to create a new genetic combination.

DNA (deoxyribonucleic acid) is the hereditary "molecule of life" that carries the recipes for creating an organism. It is the genetic molecule inside the cells of bacteria, plants, and animals, including humans. DNA carries the genes, which hold genetic information. A gene is a unit of genetic information; it tells the cell how to make a specific protein. It is the presence or absence of the specific protein that gives an organism a trait or characteristic. Many common genes are already shared by many different species, and rDNA allows us to transfer genes from one organism to another, even across the usual species barriers faced by conventional breeders.

Over the past quarter century, genetic modification, or rDNA technology, has given us lifesaving drugs such as Humulin((human insulin); Pulmozyme((dornase alpha), a breakthrough treatment for cystic fibrosis; Betaseron((interferon beta-1b), a powerful new drug for certain multiple sclerosis patients; and Activase(, a clot-dissolving tissue plasminogen activator used as a treatment for heart attacks. It has also provided a range of precise genetic diagnostic tools to identify, at an early stage, muscular dystrophy and AIDS, among other conditions.

Genetic technology has also given us safer medical treatments. For example, the standard hepatitis B vaccine was derived from blood pooled from people who had had hepatitis B. The problem was that before AIDS was recognized as a blood-borne disease, some donors might also have had the virus that causes AIDS (HIV) in their bloodstreams. Because hepatitis B vaccines from modern rDNA technology are not derived from human blood, unknown blood infections cannot contaminate the rDNA vaccines.

The application of rDNA to medical problems was rapidly embraced by researchers and by the public. However, the same technology, applied to agriculture, is facing resistance by some people who think it might be inherently hazardous.

The first GM plants were produced in 1983, and food scientists lost no time in applying GM technology to improving crops. Biotechnology provides new tools for scientists working on long-standing agricultural problems in pest and disease management, animal and crop yield, and food quality. These tools complement and extend traditional selective-breeding techniques by providing the means for making selective, single-gene changes in plants and animals. In contrast, offspring created through conventional breeding present a random combination of thousands of genes from each parent. The traditional and modern methods differ primarily in precision, speed and certainty. Moreover, because DNA is biochemically equivalent in all organisms, the modern techniques also enable scientists to take advantage of the full spectrum of genes present in nature—genes derived from microbes, plants and animals—in their efforts to improve agriculture. So, while the goals of traditional breeding and modern genetic engineering are similar, the new techniques greatly expand the realm of possible strategies by eliminating the interspecies barriers presented by sexual reproduction.

Adding one or two specific genes to a crop plant can help it resist disease infection. Add other genes and the plant can produce biological insecticides to ward off pests. Still other genes will make the plant resistant to herbicides commonly used in weed control. Other strategies, with the puzzling names "antisense DNA" and "co-suppression," use GM to shut down production of a plant's own molecules. "Antisense DNA" produced the first GM whole food on the market, the Flavr Savr® tomato, by inverting a natural gene for a ripening enzyme, resulting in tomatoes with extended shelf-life. In this gene inversion process, the relevant gene is cut out of the DNA, turned 180 degrees, and reinserted. We can visualize it like the writing in a book, where a line is placed in reverse orientation, like this: "AND eht fo tuo tuc si eneg tnaveler ehT."

Genetic engineering also provides sensitive diagnostics for veterinary medicine, e.g., for disease detection and gender identification. New animal vaccines are being developed, including vaccines with broader host ranges for diseases such as rabies that pose serious public health threats, and to protect wild animals from diseases such as the devastating rinderpest. Animals are being bred with additional genes for growth hormones—hormones that increase the ratio of protein to fat in the meat of pigs and cattle or the rate of milk production by dairy cows.

Modern biotechnology is well established in food processing—particularly in the genetic improvement of bacteria and yeast strains used in various fermentation systems including improved bread yeast and brewing yeast. Vegetarians might now enjoy cheese made with GM chymosin instead of animal source rennin. Some recent developments in agricultural biotechnology involve using plants and animals to make products not traditionally associated with agriculture—products such as medically important pharmaceuticals and industrial materials to replace petroleum-based oils and plastics. In the future, we will all benefit from enhancements to our quality of life, environmental stewardship, and animal welfare. American farmers may open entirely new markets for their products and provide new products for their current markets.

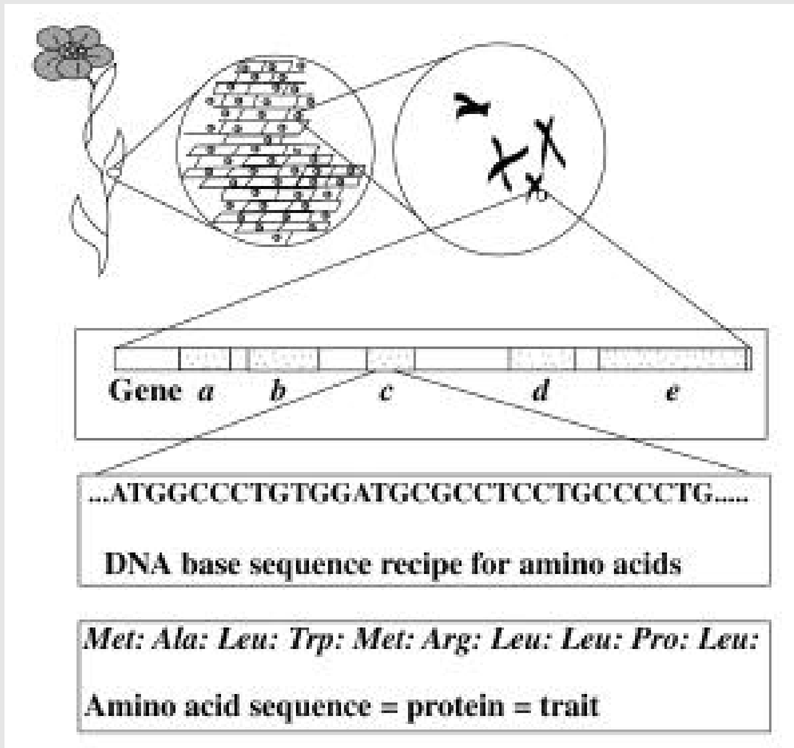
DNA, Genes and Proteins

DNA is a threadlike molecule composed of long chains of four small chemical compounds—usually called bases—Adenine, Thymine, Cytosine, and Guanine (usually abbreviated A, T, C, and G, respectively), arranged in a particular order (see Figure 1). Although the DNA of all organisms uses these same bases, differences in the sequence of bases account for differences between species and even between individuals of the same species. We can think of the bases as being like letters in a language: where English uses 26 letters, DNA uses only four. Like English, DNA makes different words by placing the letters in different order. Differences in base sequence account for all the genetic differences between living things. The DNA base sequence of apparently unrelated humans is remarkably similar. The base sequence of the DNA of identical twins is identical, but the DNA of fraternal twins differs as much as that of other siblings.

Genes are portions of DNA providing the organism with information on how to make a specific protein. It is the presence or absence of a specific protein that gives an organism a particular trait. As DNAis passed from one generation to the next, so are the specific genes, allowing us to "inherit" traits from our parents. Throughout the history of life on earth, genes have carried information from one generation to the next. Genes are the fundamental drivers of evolution. Over millions of years, the evolution of complex organisms—plants, animals, and humans—was achieved through the transfer, deletion, and mutation of genes. Without genetic variability, evolution could not occur, and the world would be devoid of most, if not all, life. In a sense, every organism on earth is the product of genetic engineering by nature. Each of us is in fact the product of a genetic-engineering experiment performed by our ancestors. The same is true for other animals, plants and microbes.

These natural mechanisms for genetic change allow an organism to gain new genes and new traits, and they drive evolution. Biotechnology, both traditional and modern, simply takes advantage of these natural genetic phenomena to produce useful organisms and products from those organisms.

Figure 1.



This diagram shows, using the progressive magnification from a typical organism (upper left), how the genes in every living cell carry instructions for specific traits. A plant leaf (upper left) is magnified to show the cells, each containing a round nucleus (top center). A magnification of the nucleus shows the chromosomes (top right).

All higher organisms are made of cells, and all living cells carry nucleii. Chromosomes, which are composed of DNA and proteins, are carried inside every nucleus. If a portion of the DNA from a chromosome is stretched out, we can visualize how the genes are arranged (top horizontal panel). Here, five genes (*a, b, c, d,* and *e*) are shown; each is a recipe for a different protein, and each is a different segment and length of DNA, with some interspersed DNA not being part of any gene. A further magnification of gene *c* (center horizontal panel) shows a portion of the DNA base sequence. The DNA sequence of each gene will differ, but all use the same four base "letters." The cell machinery reads the recipe three letters at a time to make a protein. The lower horizontal panel shows the amino acid sequence as dictated by the DNA base sequence. ATG calls for the amino acid Methionine followed by Alanine from the next three bases, GCC. Each succeeding triplet of bases calls for a specific amino acid; our example continues with Leucine, Tryptophan, then (not shown on bottom panel) another Methionine, Arginine, Leucine, Leucine, Proline and Leucine. The cell machinery finds the appropriate amino acid in the cell and attaches it to the preceding one, creating a long chain, the basic structure of the protein. An average gene consists of about 1000 bases, translating to over 300 amino acids in the resulting protein. The example here is the start of the actual DNA base sequence and amino acid sequence of human insulin. (Adapted from McHughen, A. Pandora's Picnic Basket. Oxford Univ. Press, New York, 2000 ISBN 0-19-850674-0)

GENETIC MODIFICATION OF FOOD

Yesterday's Biotechnology

Gene modification is a natural event. Almost all of our traditional foods are products of natural mutations or genetic recombinations. Even ordinary wheat for making bread, for example, is a product of the combination of DNA from three different species. This genetic modification, directed by Nature over the course of eons, gave us a more productive, palatable, and nutritious food than was provided by any of the three originating species alone. Modern corn looks almost nothing like teosinte (Figure 2), its primitive genetic forebear. Even the human genome (the complete collection of genetic information) carries on it remnants of viral genes deposited by the passing pathogens in our ancestors thousands of years ago.

Natural gene transfer is not limited to evolutionary time—it is an ongoing process and occurs daily. *Agrobacterium* is a soil-borne microbe with the natural ability to transfer pieces of DNA into plant cells, where the bacterial genes are inserted into the plant genome; it does so every day without any human intervention. Other forms of natural genetic modification result in changes to the genome similar to human-mediated modifications. A transposon is a naturally occurring piece of DNA with the ability to excise itself from one part of the genome and insert itself somewhere else. Spontaneous mutations are also natural phenomena resulting in sometimes dramatic changes in the genetic information of an organism.

Conventional Breeding Practices

Genetic modification directed by humans started about 10,000 years ago, when human agricultural activities began. Traditional methods

Figure 2.

Traditional plant biotechnology has had profound impacts on our food crops. This photograph shows the ancestor of modern corn, teosinte, at the far left. At the far right is an ear of what we would recognize as corn today. The two images in the center of the picture are hybrids—the result of crossing teosinte and modern corn. It took many generations to derive modern corn from the ancestral teosinte. Picture courtesy of Dr. John Doebley, University of Wisconsin.

of modifying food products have been very successful, introducing substantial improvements to generate crops that would not otherwise occur in nature. Humans developed methods of introducing genetic material into crops to provide us with the remarkable diversity of fruits, vegetables, and animals we enjoy today. These techniques have helped to provide the incredible volume of food required to allow the world population to grow to its present six billion. Traditional selective breeding has given us crops and strains with combinations of traits that would not occur without human intervention—pumpkins, potatoes, sugar beets, corn, oats, rice, and blackcurrants are common examples.

Using cross breeding methods, breeders transfer the complete set of genes from the parent plants to the new offspring. This introduces not only the one or two desired useful genes, but thousands of other genes also, some benign and some undesirable. Breeders have developed effective but often expensive and time-consuming methods to eliminate the unwanted genes and to retain the desired improvements. Some conventional breeding programs involve quite dramatic gene shuffling. For example, most of our modern corn varieties are "double-cross hybrids," which means breeders cross variety A with B to produce C; variety D is crossed with E to make F, which is then crossed with C to produce the desired seed. Other "traditional" methods of plant breeding include mutation breeding, using ionizing radiation or other mutagenic agents to create genetic changes.

As useful as conventional genetic techniques have proven to be, they are also limited in their capability. If a desired gene is not available in a particular species, or cannot be mutated from existing genes, the traditional breeder, farmers, and society will usually be out of luck.

Today's Modern (rDNA) Biotechnology

The new biotechnology offers important improvements on traditional methods. Recombinant DNA methods enable breeders to select, transfer, or modify single genes, thereby reducing the time-consuming and labor-intensive need to "select out" the undesirable genes. It also allows the acquisition of useful genes from any species.

Food Crops

The first rDNA whole food on the market was the Flavr Savr® tomato, produced by Calgene and released in 1994. Other companies also developed various GM tomatoes, along with corn, soy, and other crops. Table 1 shows the GM food crops that have been approved by the Food and Drug Administration (FDA) to date.

Some critics argue that current GM crops benefit only the companies producing them, and perhaps the farmers, but offer nothing for consumers. While it's true that most of the first GM crops carry simple, single gene improvements such as pesticide resistance which directly benefit farmers and chemical companies, they also benefit consumers. We consumers benefit from fewer weed and insect contaminants in the food (weeds not only diminish crop yields, they also harbor insects and microbes) and lower prices (from enhanced production). Most con-

Table 1. Genetically Modified Crops Approved by the U.S. Food and Drug Administration

Crop	Primary Improvement*; Major Gene(s) Inserted#	Developer
Canola	Feed digestibility; phytase gene	BASF
Canola	Weed control, increased productivity (hybrid); PAT, Barnase, barstar	AgrEvo
Canola	Weed control; PAT gene	AgrEvo
Canola	Weed control; PAT	AgrEvo
Canola	Increased productivity (hybrid); Barnase	PGS
Canola	High laurate oil; 12:0 thioesterase	Calgene
Canola	Weed control; Nitrilase	Rhone-Poulenc
Canola	Weed control; EPSP synthase	Monsanto
Cantaloupe	Delayed ripening; S-adenosylmethionine hydrolase	Agritope
Chicory	Increased productivity (hybrid); Barnase	Bejo Zaden
Corn	Weed and insect protected; Bt Cry9c, Bar	AgrEvo
Corn	Weed control; Modified EPSP Synthase	Monsanto
Corn	Increased productivity (hybrid); Adenine methylase	Pioneer Hi-Bred
Corn	Insect protected; Bt CryIA(c)	Dekalb Genetics
Corn	Weed control; PAT	Dekalb Genetics
Corn	Insect protected; Bt CryIA(b)	Monsanto
Corn	Insect protected; Bt CryIA(b)	Monsanto
Corn	Weed and insect protected; EPSP Synthase, glyphosate oxidoreductase and Bt CryIA(b)	Monsanto
Corn	Insect protected; Bt CryIA(b)	Northrup King
Corn	Increased productivity (hybrid); Barnase	AgrEvo
Corn	Weed control; PAT	AgrEvo
Corn	Insect protected; Bt CryIA(B)	Ciba-Geigy
Cotton	Weed and insect control; Nitrilase and Bt CryIA(c)	Calgene

Cotton	Weed control; Acetolactate synthase	DuPont
Cotton	Weed control; EPSP synthase	Monsanto
Cotton	Insect protected; Bt CryIA(c)	Monsanto
Cotton	Weed control; Nitrilase	Calgene
Flax	Soil bioremediation; Modified Acetolactate Synthase	University of Saskatchewan
Papaya	Disease protected; Papaya ringspot virus coat protein gene	Univ. Hawaii and Cornell Univ.
Potato	Insect and disease protected; Bt CryIIIA and virus replicase	Monsanto
Potato	Insect and disease protected; Bt CryIIIA, virus coat protein	Monsanto
Potato	Insect protected; Bt CryIIIA	Monsanto
Potato	Insect protected; Bt CryIIIA	Monsanto
Soybean	Weed control; PAT	AgrEvo
Soybean	Improved oil; Gmfad2-1 from soybean	DuPont
Soybean	Weed control; EPSP Synthase	Monsanto
Squash	Disease protected; three virus coat protein genes	Seminis
Squash	Disease protected; virus coat protein gene	Asgrow
Sugar beet	Weed control; PAT	AgrEvo
Sugar beet	Weed control; EPSP Synthase and glyphosate oxidoreductase	Monsanto/ Novartis
Tomato	Insect protected; Bt CryIA(c)	Monsanto
Tomato	Delayed ripening; S-adenosylmethionine hydrolase	Agritope
Tomato	Delayed ripening; Antisense polygalacturonase	Calgene
Tomato	Improved ripening; Aminocyclopropane carboxylic acid synthase	DNA Plant Tech
Tomato	Improved ripening; Aminocyclopropane carboxylic acid deaminase	Monsanto
Tomato	Delayed softening; Polygalacturonase gene fragment	Zeneca

* Most GM crops have more than one inserted gene
# See Glossary/Appendix for more detail.

sumers say they benefit from, and would support, a food product made with fewer chemicals. Farmers growing GM crops use fewer and more environmentally benign pesticides than with non-GM crops. Reduced pesticide use also results in lower production costs, which means lower food costs in the market.

Herbicide resistance. Many of the first GM crops display genetic resistance to an herbicide. Some critics complained that this would lead to an increase in farm chemical use, because the farmer would have to spray the crops with a particular herbicide, and society would prefer farmers to use fewer, not more chemicals. However, recent analyses by the U.S. Department of Agriculture (USDA) and others have shown a drop in herbicide use with GM crops. Why? Current agricultural production often necessitates the use of several different herbicides to control the wide range of weed species present in a field. With herbicide-resistant GM crops, farmers are able to grow weed-free fields by applying a single herbicide instead of spraying several different chemicals. Farmers benefit because they can buy fewer chemicals and spray less often (thus saving time, fuel, and wear and tear on equipment). In addition, the crop is of higher quality, due to decreased competition from weeds. Consumers benefit from lower prices (due to enhanced production and lower input costs) and higher quality product (from fewer weed, insect, and microbial contaminants). The environment benefits from burning less tractor fuel and having fewer farm chemicals sprayed, and those being used are newer, safer chemicals with fewer residue or runoff problems.

Insect resistance. A commonly used gene confers resistance to insect attacks. A gene from the bacterium *Bacillus thuringiensis*, usually called simply “Bt,” produces a crystal protein toxic to certain insects but safe for humans and other animals. The insecticide Bt has been sprayed on crops to control insects for half a century. Now, by inserting the responsible gene directly into the crop plants, farmers need not spray Bt into the environment, potentially affecting non-pest insects. With the Bt crystal protein produced only inside the plant, only those insects feeding on the plant, i.e., the pests, are exposed to, and killed by, the insect-specific toxin. Not only are other, non-pest insects spared, the farmer saves money, fuel, and time by not having to spray.

Much of the crop in developing countries is lost to insects, even after harvest, as insects quickly devour stockpiled grain. If farmers grow Bt-containing GM crops, more grain will be available to feed humans, not insects, and poorer countries will become more self-reliant.

Disease resistance. Using GM technology, American scientists saved the papaya industry in Hawaii. Papaya ring spot virus, which devastates the fruit and for which there is no cure, was making its way across Hawaii, destroying the papaya industry as it went. Dennis Gonsalves and his team produced a type of vaccine against the virus by inserting a portion of the virus genetic material into papaya trees. The "vaccinated" papayas were immune to the virus and kept producing fruit after the virus had destroyed all the other papaya trees in the region. Indigenous farmers and the entire Hawaiian papaya industry owe their continuing livelihood to Dr. Gonsalves's team and GM technology. Similar approved products include virus-resistant squash and potatoes.

Delayed Ripening. Other products include the first GM whole food approved in the US, the delayed ripening Flavr Savr® tomato. The modification here was not the insertion of a foreign gene, but an alteration of a naturally occurring tomato gene. Polygalacturonase (PG) is an enzyme controlling the ripening of tomatoes (and other fruits). By reinserting a normal tomato PG gene into the tomato in reverse orientation, Calgene scientists found they could delay the expression of PG in the tomato, slowing the ripening process. The delayed ripening meant that the GM tomatoes had a prolonged shelf life and also facilitated harvesting and transport to markets.

Enhanced Quality. The first nutritionally enhanced GM foods are on the market, with many more on the way. DuPont has made a soybean with a modified oil composition, increasing the desirable monounsaturated fatty acid oleic acid to over 80% of the oil from about 24%. Several companies are developing soy, canola, and other vegetable oils with reduced saturated fat content and other quality enhancements.

Other uses of molecular genetic technologies do not depend on gene transfer or modification. For example, early detection and treatment of crop disease is an important strategy for reducing chemical inputs in American farming. Biotechnology offers highly sensitive and selective diagnostic tools to detect low levels of infection or infestation. This is essential for speeding the delivery of control measures before the problem grows. Field kits based on antibodies that specifically recognize a disease or pest agent are already in use for soybean root rot and certain bacterial diseases of tomatoes and grapes. DNA fingerprinting—famous for its use in forensics—is also used in identifying plant diseases and infestations.

Food-Processing Advances

Processed foods have gained acceptance among time-conscious American consumers in search of easy-to-prepare, nutritious, and flavorful meals. Three components of the food-processing system are targeted by new biotechnologies: 1) chemical composition (such as proteins, fats, and carbohydrates); 2) bacteria and yeast used in fermentation and other processes; and 3) enzymes used to enhance color, flavor, and texture.

Starter cultures of bacteria and yeast are the mainstay of much of the processed-food industry. Biotechnology has contributed substantially to microbial genetics, improving our understanding of bacterial and yeast genes that are involved in making foods as diverse as bread, yogurt, cheese, wine, and beer.

Using modern genetics, food processors are culturing new genetically modified strains of microorganisms that have combinations of enzymes useful in food processing. Biotechnology is also useful in the isolation and production of enzymes used directly in food processing. For example, the enzyme amylase affects the texture and freshness of bread dough. Chymosin, the active enzyme in rennin extracts (which are isolated from calf stomach), curdles milk to make cheese. Purified chymosin produced through genetic engineering now accounts for the majority of enzyme used in cheese production in the United States. It allows both vegetarians and those who follow kosher rules access to cheeses. Other enzymes, such as proteases and lipases, are used to provide the aged quality of cheese.

There is also an effort to help meet consumer demands for foods that can be kept fresh without synthetic additives or special packaging materials. Modern molecular methods are being used to produce substances that eliminate bacterial contamination, including propionic acid to reduce fungal contamination, trehalose sugars for dried and frozen foods, and antioxidant enzymes to prevent free-radical formation.

Tomorrow's Biotechnology: Anticipated Products and Benefits

Farmer-oriented Products

Drought, flooding, soil salinity, frost, and other environmental stresses take heavy tolls on agricultural production in the United States and around the world. Several naturally occurring genes involved in plant responses to these stressors have been identified and isolated.

Researchers are now transferring them to enable food crops to withstand environmental challenges. Considering the huge impact these environmental stresses have on loss of food products, even modest success will have enormous benefit.

Consumer-oriented Products

More consumer-oriented GM products will soon appear on our shelves. These will include nutritionally enhanced foods, such as fats and oils with reduced amounts of saturated fatty acids (as mentioned above); potatoes that absorb less fat in frying; and lower calorie "sugar" (fructans) from GM sugar beets. Researchers are also developing methods for enhancing the vitamin C and E content of processed foods.

In some future GM food products, naturally occurring allergenic and antinutritional compounds will be reduced or eliminated. Some people, for example, are allergic to peanuts and, considering the preponderance of peanuts in so many snacks, baked goods, and other common foods, have to deal with the anxiety of encountering them on a daily basis. Imagine the relief if peanuts can be made non-allergenic perhaps by removing one or more genes for allergenic proteins. Similarly, many foods naturally produce antinutritional compounds, such as alkaloids or cyanogenic glycosides. While current procedures monitor levels of these undesirable compounds in new crop varieties produced by either traditional or modern techniques, GM may be used to eliminate or reduce the capacity of plants to produce such compounds.

Improved quality foods are also coming to less fortunate peoples. Cassava is a major food for millions of people but is not especially nutritious because of poor protein quality. It also contains toxic cyanogenic glycosides. GM could be used to reduce the antinutritional factors and, at the same time, enhance the protein quality of this food.

Over 180 million children, mostly in developing countries, suffer Vitamin A deficiency; some two million die from it each year. About a billion people suffer anemia from iron deficiency. Genes producing beta-carotene, a precursor of vitamin A, have been inserted into rice, the most important crop species in the developing world, but one deficient in this crucial nutrient. The GM rice produces beta-carotene, giving it a bronze-orange appearance, hence the name "Golden Rice." It also has genes to increase iron content. This nutritionally enhanced GM rice, generated by a team led by Swiss researcher Ingo Potrykus, is being distributed, free of charge, to public rice breeding institutions around the world. Local breeders will incorporate the new rice trait into local rice varieties for growing by local farmers. Millions of people who are at risk of anemia from iron deficiency, as well as blindness or other manifestations of vitamin A deficiency, will soon be able to greatly reduce their risks of these disabling conditions at little or no additional cost.

GM food plants are also being developed to deliver vaccines. Poor people in developing countries suffer unnecessary afflictions because they lack easy access to immunizations. Conventional vaccines are often difficult to deliver because they require expensive production, sterilization, and refrigerated transport mechanisms. Tropical fruits such as bananas or even temperate crops such as potatoes and tomatoes can be genetically enhanced to produce vaccines, and they might be grown locally and more easily transported for local consumption. Current cost for delivery of a conventional vaccine injection into a patient in remote areas is about $125 per dose. Estimated cost for a banana-delivered vaccine, about $ 0.02. Vaccinating against hepatitis, typhoid fever and cholera would dramatically improve the lot of many people.

Closer to home, vaccines delivered via GM fruits might be more efficacious and also easier to deliver, especially for the very young or elderly for whom conventional vaccination systems are less effective.

GM Animals and Animal Husbandry Advances

GM animals are not too far behind GM plants. We've all heard of Dolly the Scottish sheep, a clone derived from a single mature cell from her mother. Cloning is not really genetic modification, because cloning implies a genetically identical copy as opposed to a genetically altered version, but both are products of modern technology. Cloning sheep and other animals can allow us to increase populations of nutritionally enhanced or more productive animals, without going through a lengthy and expensive breeding program.

The first GM (in contrast to cloned) whole animals likely to hit the market will be fish. Several firms around the world are producing fast-growing, meaty GM salmon in controlled fish farms.

On the production side, conventional farm animals often suffer diseases. GM vaccines can be delivered to animals via their feed, preventing disease and saving the expense of unnecessary veterinary treatment bills.

Veterinary Medicine. By identifying and mapping genes, veterinary scientists are able to understand and help correct the pathological processes that underlie animal diseases. The identification of genes involved in serious inherited diseases helps animal breeders select the healthiest animals and improve the characteristics of their herds.

Genetic diagnostic kits are becoming commonplace in animal husbandry. New biotechnology vaccines are also playing important roles in veterinary medicine—both in the United States and in developing countries where more stable animal food production systems are of critical importance. One genetically engineered vaccine successfully controls rinderpest, a viral disease that periodically destroys entire cattle herds in Africa and Asia. Another biotechnology vaccine has proven effective against the rabies virus in trials in the eastern United States. Genetically modified vaccines can control everything from ticks on cattle to *E. coli* infections in piglets and calves.

Animal Growth and Food Production. The genetic engineering of farm animals is still at an early stage of development. Most current research (with a few exceptions, such as bovine and porcine somatotropins) is preliminary, and extensive development will be required before genetically engineered meats reach the marketplace. However, we can foresee genetic engineering eventually being used to improve the metabolic efficiency of animals, thereby enhancing the utilization of feed and improving meat and milk quality and production.

Food-Processing Advances

Strategies derived from our knowledge of the mammalian immune system are being applied to food-production problems. The immune system attacks foreign molecules in the body by producing highly selective antibodies that identify and help destroy invaders. Exploiting that defense system, food scientists have developed antibodies that specifically target food contaminants that are potentially toxic or pathogenic. These new detection systems are being tested and packaged in easy-to-use kits. Food processors and handlers are able to identify and eliminate contaminated foods before they reach supermarket shelves.

Helping the Developing World

We've seen the advent of nutritionally enhanced Golden Rice and the utility of using GM plants to deliver medicines. Other projects will have especially important effects in poorer countries, where most of the world's population growth will occur. Food is almost always in short supply. A recent report announced the GM of rice to make it more efficient at converting sunlight to food through photosynthesis. The GM rice yields about 20% more grain than conventional rice, at no extra cost to the plant, to farmers, or to consumers.

Some crops are productive and nutritious but are deficient in specific nutrients. The varied and balanced diet we enjoy in developed countries often makes up for these deficiencies, but many people don't enjoy the luxury of a diverse diet. Legumes such as beans and peas, for example, are low in the amino acids cysteine and methionine. People forced to eat a diet consisting predominantly of these legumes can suffer deficiencies. GM can be used to insert genes for proteins rich in the lacking nutrients to provide a more balanced diet, even without adding other foodstuffs.

Industrial Products

Beyond food, industrial products are also targets of genetic modification. For example, plant fiber characteristics are often genetically controlled. Textiles such as cotton and linen (from flax) can be modified to increase quality and wearability at lower processing cost. They may also be modified to produce their own pigments, thus saving materials and labor now needed to color them.

Biomaterials such as bioplastics made from GM plant starch can be just as versatile as plastics produced from fossil fuel. The GM plastics are superior in that they will be made from a renewable resource and, being biodegradable, will also be more environmentally friendly.

Certain plants produce oils quite similar to diesel fuel. GM might be used to modify plants to produce fuel more efficiently.

THE PUBLIC DEBATE

Modern biotechnology has sparked both optimism and controversy. Debate about the impact of the research tools and products of biotechnology encompasses health, farm economics, global biodiversity, environmental quality and, not unimportantly, hunger and malnutrition. Unfortunately, the public debate over the benefits and hazards of genetic technology suffers from an astounding array of misinformation, misunderstanding, and manipulation. Unsubstantiated scare stories abound. The following sections of this report will focus on two major concerns about GM foods; 1) their effect on biodiversity, and 2) their safety for human consumers.

Biodiversity: Enhancing Yield, Sparing Primitive Forests

The world population, currently six billion people, is expected to grow by an additional two billion over the next twenty years. Much of the growth is occurring in developing countries, where local capacity for food production is seriously unstable because of poverty, political disruption, climatic stresses, soil erosion, pests, and disease. The pace at which primitive forests and other natural lands are being converted to food production is increasing, but this trend need not continue. When biotechnology is used in combination with other strategies, it can help us address several of the central problems faced by the developing world. The new molecular tools are both enhancing our understanding of the range and importance of biodiversity and supporting strategies that will spare and even return land to natural habitats while helping to feed the world's peoples.

The Green Revolution of the 1950s, '60s and '70s, with its introduction of high-yield wheat and rice varieties, proved that carefully targeted plant breeding can substantially improve local food production. The new genetic tools can extend those improvements by delivering technological enhancements directly, in the seed. Biotechnology research is underway in agricultural centers in South and Central America, the Caribbean, Africa, Asia, and the Pacific Islands. Much of this research focuses on crops that are important for indigenous farmers—rice, beans, maize, squash, melons, cassava, papaya, sorghum, potatoes, and sweet potatoes. Superior varieties will help farmers achieve greater yields of nutritionally enhanced crops with lower inputs on less land.

Biotechnology offers novel products to replace those derived from forestry or agriculture. Biomaterials are under development to reduce our reliance on plant fiber- and petroleum-based products. Plant cells can be grown in large-scale vats, or bioreactors, to make products ranging from oils to flavorings and amino acids without cultivating land. These approaches all help to reduce the need to bring greater acreage under cultivation and reduce the need to harvest the world's forests.

Sustaining Biodiversity

The world today supports a remarkable diversity of plant and animal life. For centuries, plant and animal breeders have sought the best traits from wild species and genetically integrated them into domesticated crops and food animals. Extensive seed banks—literally, gene banks—have been established to collect a broad range of seeds and other germplasm both to document and characterize the world's various species and to support future breeding needs. Thus, an appreciation and utilization of biodiversity has been a hallmark of traditional plant and animal breeding programs around the world.

Biotechnology offers several strategies for sustaining and utilizing the world's biodiversity. First, it offers tools for identifying and characterizing living organisms at the genetic level. Molecular diagnostic techniques enable scientists to distinguish between and compare species with remarkable precision. Used in combination with traditional techniques, genetic engineering techniques are expanding our knowledge of the range and evolution of organisms living in American meadows and tropical rain forests alike. They allow researchers to monitor and track changes in specific populations over time. Knowledge of the genetic composition of wild species also enables breeders to identify and make use of genes that encode traits that are beneficial for food production.

Some critics argue that by promoting monoculture (i.e., intensive growth of one species), GM contributes to the problem of reduced world biodiversity. However, the opposite is true. Adding genetic information does nothing to diminish what is already present. Adding a gene to a genome does not delete any genes from the species, so biodiversity is maintained. Molecular genetic technology is being applied to identify and characterize genes in many species, thus helping to establish seed banks and gene banks to ensure the preservation of biodiversity. For example, the genome of rice was recently analyzed and the information is being made available to breeders around the world. This is an important advance not just for rice breeders but for all crop breeders, because many genes responsible for food production and quality are present in other food crops as well as rice. The genomes of other major crops are being similarly analyzed and this additional knowledge will facilitate even greater contributions to food production and nutrition.

Biodiversity is at risk not from genetic modification, but from natural environments being converted to farmland to provide more food for the growing population. When more productive GM crops are grown, less wild land is destroyed to make farmland. Parks and refuge areas can be left undisturbed for everyone to enjoy and for biodiversity to flourish.

View of Scientists on the Safety of Biotechnology

Most scientists knowledgeable about genetic engineering support this technology. They know that much of the negative information in the public debate is based on false assumptions, and they know that the tremendous potential benefits far outweigh the manageable hazards. But most importantly, they understand that risks are associated with particular products, not with the methods by which those products are made. That is, genetic modification is only a process used to make a certain product, just as cooking is a process used to generate healthy meals. In each case, the process might be used to make hazardous products instead.

The poor state of the public debate on GM foods prompted C.S. Prakash and his colleagues from Tuskegee University to draft and circulate a petition. It began "We, the undersigned members of the scientific community, believe that recombinant DNA techniques constitute powerful and safe means for the modification of organisms and can contribute substantially in enhancing quality of life by improving agriculture, health care, and the environment." The petition, entitled Declaration of Scientists in Support of Agricultural Biotechnology, has been signed by over 2100 scientists worldwide, including US Nobel laureates James Watson, who jointly discovered the structure of DNA in 1953, and Norman Borlaug, the 1970 peace prize winner and father of the "Green Revolution."

At the same time, scientists are aware of the potential for undesirable features in certain GMOs and carefully assess all new GM products for any sign of unexpected or unintended results.

General Food Safety Issues

GM products are not inherently hazardous. Manufacturers have been using GM to make pharmaceuticals for a quarter century, with no documented cases of harm attributable to the genetic modification process. Three hundred million North American consumers have been eating several dozen GM foods grown on over 100 million acres since 1994. Again, there are no documented cases of harm attributable to the process by which the GM crops were bred. In early 2000, the Organization for Economic Cooperation and Development (OECD) invited 400 world experts, including academic researchers and representatives of government and industry as well as environmental activist groups to a conference on safety of GM foods. Groups adamantly opposed to GM foods were given the chance to present evidence to support their assertions. They were unable to cite any cases of harm from GM foods.

In April 2000, the House of Representatives Committee on Science Subcommittee on Basic Research, chaired by Representative Nick Smith (R-MI), released a report ("Seeds of opportunity: an assessment of the benefits, safety and oversight of plant genomics and agricultural biotechnology"), which concluded there is no significant difference between plant varieties created using agricultural biotechnology and similar plants created using traditional cross breeding.

In the same month, the US National Academy of Sciences released a report of its blue-ribbon group (Committee on Genetically Modified Pest-Protected Plants) to study the matter and issued its own statement, which concluded, “The committee is not aware of any evidence that foods on the market are unsafe to eat as a result of genetic modification.”

Since GM foods have now been consumed by very large numbers of humans for several years, any inherent problems with genetic modification as a technology would almost certainly have been revealed by now. But not one problem has been documented.

Overall, many thousands of GMOs have been generated and tested in labs and field trials around the world since the mid-1970s. These include many plant, animal, and microbial species modified with a range of different genes from diverse sources. Only a small proportion of these was intended for ultimate commercial release. Instead, most were developed to test the environmental and health safety of the process and the products. In spite of considerable effort to find evidence of harm from the genetic modification process, none was found. Certainly some products were identified as potentially hazardous, for example the allergenic Brazil nut storage protein gene in GM soybean was clearly a health hazard to those allergic to Brazil nuts (see more on this below). But in each case, the hazard was due to the nature of the specific new trait, not to the process by which it was made.

Similarly hazardous products are occasionally seen using conventional plant breeding methods. For example, some conventional tomatoes produce too much tomatine, a potentially hazardous naturally occurring alkaloid. Current regulatory practice and due diligence on the part of developers identify and eliminate potentially hazardous products long before they get to the market. Regardless of the specific method of breeding, new foods are vigorously tested to minimize risk. Plant breeders spend eight to twelve years or more analyzing and evaluating prospective new varieties. In addition to the usual measures of seed yield, maturity, response to disease infection, and other farmer-oriented traits, they also conduct chemical analyses to ensure that quality characteristics are preserved. In addition, the new lines are scrutinized for the presence of naturally occurring but undesirable compounds, like cyanogenic glycosides. Prospective new foods whether produced by conventional or modern biotechnology are eliminated if they show any sign of unmanageable potential hazard.

Specific Issues in the Popular Press

Rats!

A scientist in Scotland, Arpad Pusztai, was testing a strain of GM potatoes by feeding them to rats. After 10 days of eating nothing but the GM potatoes, the six rats were sacrificed and a number of measurements taken of their internal organs. Astonished at the preliminary results, Dr. Pusztai decided he had to share his findings with the world and went on national TV before seeking peer review and before repeating the experiments. He claimed the rats fed GM potatoes suffered suppression of their immune systems and internal organ damage. Millions of viewers reached the conclusion that the potatoes became toxic as a result of the GM. The resulting furor spurred the prestigious Royal Society to convene an expert panel to assess the results. After considerable deliberations and review of all available data, they reported that the evidence did not support Dr. Pusztai's conclusions.

The Royal Society criticized almost every facet of the experiment, from design to execution and interpretation. An important point missed by much of the media was that the genetic modification introduced a gene to make lectins, a toxin. The public, relying on the media accounts, were not told the rats were being forced to eat a toxic lectin, and that this toxin, not the method used to introduce it, might have been responsible for their illness.

Allergens

Do genes and their associated proteins change character when inserted into a different species? Although many thousands of GMOs have been produced and tested, no unexpected character changes have been reported. One case illustrates how GM doesn't change fundamental characteristics. In an effort to improve the nutritional value of a legume by providing a gene for a protein rich in methionine and cysteine, scientists at Pioneer HiBred identified a gene for such a protein from Brazil nut and transferred it to soybean. When the scientists were checking into potential allergenicity, they found that Brazil nut was highly allergenic to some people and that the protein was responsible. When they conducted lab tests on the GM soybean carrying the Brazil nut gene, they discovered that it, too, was allergenic to those people allergic to Brazil nut. The project was abandoned before any consumer was exposed to the soybean modified with the Brazil nut gene; the product never appeared on the market, and the public was not exposed to any risk. The allergenic result shows, conclusively, that the undesirable properties of the Brazil nut protein were transferred when the gene was moved into a different species. If a gene produces an allergenic protein in one species, it will likely do so in a new species. Similarly, if a gene is non-allergenic in one species, it is not likely to become allergenic when transferred to another.

While GM does not change the fundamental nature of an allergenic protein, GM might be able to remove allergens from food. Any parent with a child allergic to common foods knows the anxiety of trying to discern the contents of fast food, meals at friends' homes, or shared snacks at school. Imagine the relief to allergy sufferers and their parents if we can provide, using GM, non-allergenic peanuts, dairy products, cereals, seafood or other common allergenic foods. So, while GM does not increase allergies, it might be used to alleviate food allergy problems.

Bt Corn and Monarch Butterflies

Among the most popular GM traits is insect resistance. The common bacterium *Bacillus thuringiensis* (Bt) has been used for half a century to combat caterpillars on crops. It's still used widely by farmers, including organic growers, as a safe, natural insecticide. The bacterium produces, from a single gene, a crystal protein lethal to caterpillars and some other insects, but harmless to other animals, including humans. That gene, or enhanced forms of it, has been transferred to several crops, including corn, soy, potato, and cotton. With the plant making its own Bt, the farmer need not purchase Bt and need not spray the crop with it. When insect pests start eating the crop, they ingest the crystal protein and die before causing any measurable damage to the crop. Only insects that eat parts of the Bt-enhanced plants are affected.

In 1999, a preliminary lab study found that Monarch butterfly larvae suffered when forced to eat pollen from genetically modified Bt corn. This raised concern in some quarters because it was widely and incorrectly interpreted to mean that GM crops were threatening non-pest insects, such as the Monarch. Several follow-up studies showed the effect of GM pollen on non-target insects, including the Monarch butterfly, to be negligible under "real-life" field conditions. The scientific community discounted the original report because 1) it was conducted under artificial lab conditions, 2) the larvae were allowed to eat only corn pollen (which they don't often encounter in the open environment), and 3) there was no comparison group of larvae fed on ordinary corn pollen sprayed with regular Bt insecticide.

Plants with Selectable Marker Genes

Researchers often introduce a gene that encodes an easily detected substance that can be used as a signal or "marker" to help determine which plant cells and tissues have successfully taken up new genetic material. These selectable marker genes give a growth or survival benefit to successfully engineered cells. They are very useful because the efficiency of introducing genes into cells is relatively low. Marker genes provide researchers with a simple mechanism to separate cells that contain new genes from those that do not. Marker genes are also routinely used in combination with other genes that encode specific traits of interest. If a plant cell has taken up one gene, it is generally the case that it has taken up both the marker and the gene of commercial interest. The presence of a marker gene provides an easy indicator that the other desired gene is also present. Recently some critics called the safety of these marker genes into question.

Are Marker Genes Safe? Several groups are concerned about the safety of selectable marker genes in foods. The mere presence of a marker gene (or any other "foreign" DNA) is not a food-safety concern, because scientific evidence shows DNA itself is not hazardous. The pertinent issue is whether the gene product, the protein made from the gene recipe, is safe. As consumers, we routinely ingest vast amounts of foreign, uncharacterized, and largely extraneous genetic material (and its encoded proteins). This is a consequence of conventional plant reproduction, both natural and via human intervention, in all the fruits, nuts, vegetables, and grains we eat every day. We have learned from this experience that new combinations of genes or entirely new kinds of genes or proteins in our foods are not, in and of themselves, indicators of risk.

Consider, as a case in point, the kanamycin (an antibiotic) resistance gene (used as a selectable marker in the production of Calgene's Flavr Savr® tomato). That same gene is found in harmless bacteria that are normally found on fresh fruits and vegetables, which we eat every day without undue harm. The kanamycin resistance gene is also found in bacteria that populate the human gastrointestinal tract. In considering safety, it is no more or less relevant to know that the gene is used as a selectable marker in genetically engineered plants than it is to know that it is a normal component of bacteria that live on many of our foods or in our intestines.

Safety is not determined by how or why the gene (and its product) was introduced into food—it is determined solely by the characteristics of the gene product and our experience with it in the food supply. There is no merit to the argument that selectable marker genes, as a class of introduced genes, should be removed before genetically engineered foods enter the consumer marketplace. Most scientists believe safety can be judged effectively by the same procedures and criteria articulated by the FDA policy for other introduced genes.

The Safety of Biotechnology Foods

Are genetic engineering techniques in any way inherently dangerous or unpredictable? The National Research Council of the National Academy of Sciences and numerous international scientific organizations have all emphasized that the new single-gene techniques are both precise and reliable. These organizations recommend that safety determinations focus on the nature of the trait that is introduced into a plant or animal. New biotechnology foods are compared with similar foods produced using more traditional methods.

The genetic engineering of crops and food has been more carefully scrutinized by the federal government and by state and university scientists than any crop-breeding technology in the history of agriculture. Over the past 25 years, millions of laboratory experiments have been conducted with rDNA techniques and with genetically modified organisms. There have been thousands of field experiments with rDNA-modified plants throughout the world. The genetic and phenotypic characteristics of every new genetically engineered plant are evaluated at each stage of development—laboratory, greenhouse and small-scale field trial—under guidelines and regulations of the National Institutes of Health (NIH), the USDA, the Environmental Protection Agency (EPA), and the FDA.

There is no evidence that rDNA techniques or genetically modified organisms pose any unique or unforeseen environmental or health hazards. Common sense combined with empirical evidence and observation dictates that, compared to traditional breeding processes that involve hundreds of thousands of genes, transferring single genes greatly enhances our ability to judge risk and safety. Greater certainty about the genetic modification means greater accuracy in safety assessments.

How Does the FDA Ensure Safety?

The FDA requires that the following questions be addressed before a new food—genetically engineered or produced through traditional methods—is introduced to the marketplace:

- Does the food contain genes from known allergenic sources?

- Does it contain genes from toxigenic sources?
- Are the concentrations of natural toxigenic substances increased?
- Is the nutrient (including fat or cholesterol) content changed?
- Does the food contain a substance that is new to the food supply?

A policy, published in 1992, established that the FDA would treat as equivalent foods derived from plants modified by older breeding techniques and foods derived from plants modified by rDNA. Although the vast majority of foods from genetically modified plants would be considered equivalent to foods with a long history of safe use, certain foods would be subject to the food-additive provisions of the Food, Drug and Cosmetic Act. A new substance might be considered a food additive, for example, if it was not substantially similar to substances with a history of safe use in the food supply.

Thus, under this policy, FDA did not ordinarily require premarket review if the food constituents of the new plant variety were the same or substantially similar to substances currently found in other foods. Premarket approval was required when the characteristics of the new varieties raised safety questions or when substances in the new food were not considered substantially equivalent to those in common foods. Any food that contained a substance new to the food supply and that did not have a history of safe use required premarket approval. Any food that contained increased levels of a natural toxicant required approval and could be banned from the marketplace.

The policy also addressed the potential for introducing an allergen into a food in which a consumer would not expect it. Foods derived from known allergenic sources had to be demonstrated not to be allergenic or were required to be labeled to identify the source. In cases of potentially serious allergenicity risk, such foods would be banned from the food supply.

This approach was supported by the American Medical Association and the American Dietetic Association. As it happened, all GM foods offered for sale in the US during the period when this policy was in effect went through the premarket process voluntarily.

In a recent policy change, largely due to lobbying by anti-technology groups, all new GM food products must face mandatory FDA assessment, even where there is little or no scientific basis for such a formal review.

Why Is Mandatory Premarket Testing for All Genetically Modified Foods a Bad Idea?

There are at least two reasons that mandating premarket testing is a bad idea: cost and diminishing returns. Extensive testing increases cost of the food-production process. Those costs are passed on to consumers in the form of higher prices. Thus, most consumers will probably agree that extensive testing of the sort required under the Food Additive provisions of the Food, Drug and Cosmetic Act should be limited to those new food products where there is a reason to believe a safety problem may exist or where the product is substantially different from any substance commonly used in the food supply. Consumers are used to paying for bulk food by the pound and for pharmaceuticals by the milligram. There is a million-fold difference, much of which is attributable to regulatory compliance and testing costs. Why would we want to substantially increase food costs in the absence of any indication of hazard?

The second reason, diminishing returns, stems from the fact that for potential safety problems the most reliable tests are difficult and extremely expensive. Our food supply has an enviable record of safety and security. Our current regulatory process is scientifically sound and efficient. To increase the level of confidence in our regulations requires a substantial cost with very little prospective gain. Say, for example, we are currently 99.999% confident that a certain food process is “safe.” If we wish to increase our confidence to, say, 99.9999%, we would have to apply extremely costly and sensitive tests (all the simpler and less expensive tests have already been conducted). And all we could hope to achieve is an increase in confidence of a measly 0.0009%. Is it worth it?

Labeling Issues

Many consumers claim they want GM foods to carry a label. But labels are intended to convey meaningful information on the contents—either for nutritional or health-related reasons. Current regulations require GM foods to carry a label if the food is substantially different from similar conventional foods, for example if there is significantly more or less of a vitamin, or if there is an allergen or otherwise toxic substance in the food. But if the food is identical to regular version of the same food, the label is misleading.

Some say we must have labels to allow “consumer choice,” to accommodate those who, for whatever reason, don’t want to buy GM foods. To these people, all foods produced or derived from a GMO must carry a label. The rationale, however, is important for effective labeling, even when it's simply to facilitate choice. Some consumers justify wanting labels on GM foods because they believe insertion of DNA—a chemical—into food is an adulteration or contamination of food with a foreign chemical. However, all living things—including food plants, animals and microbes—contain DNA. Consumers'concern usually dissipates when they are informed that DNA is a normal component of every healthy diet; DNA is an ingredient in virtually all foods.

Many of the same people demanding a label on all GM-derived foods would support a mandatory label on any food containing "chemicals." Since all foods are composed of chemicals, a generic label "this product contains chemicals" would be meaningless, as it does not provide any nutritional or health related information with which to make an "informed choice." Also, as it would necessarily appear on every package, it would also become ignored very quickly, debasing the entire labeling utility.

Well, what about using the criterion of "foreign DNA" to identify those products requiring a label? Then we have complications defining "foreign," as many genes are common across many organisms. Also, a tomato engineered with a gene from a different variety of tomato wouldn't carry any "foreign" DNA, yet advocates of labeling would insist it be labeled because it was produced using GM techniques.

A soybean carrying a bacterial gene would clearly be a GM plant with "foreign DNA" and so subject to the mandatory label. But what about the oil squeezed from the soybean? The oil carries no DNA, foreign or otherwise, so if we used the "foreign DNA" criterion, the oil would not need to be labeled. Yet advocates insist it would.

What if we later discover that the soybean plant naturally carries a gene that is functionally identical to the one inserted from bacteria? Many genes from many species are quite similar to each other, so this is not an outlandish possibility. Although the inserted gene came from a bacterium, it would not be considered "foreign" if the soy already carried a natural version, would it? In this case, if "foreign gene" were the criterion for labeling, the soybean, clearly GM with a gene from bacteria, would need no label.

We should also consider the case of a tomato gene inserted into a bean plant. The bean plant would be GM with tomato DNA present inside it. Advocates of mandatory labels expect such a bean to be labeled. What if we use this bean to make a casserole, complete with ordinary tomatoes? The casserole would consist of beans and bean genes along with tomatoes and tomato genes. Would the casserole have to be labeled? It is indistinguishable in every way from a casserole made with ordinary beans and tomatoes.

Labels are useful when they tell us about meaningful differences, like when a food has “added calcium” or “contains peanuts.” Consumers use this information to make considered choices to purchase a beneficial product, such as one with enhanced vitamin content, or to avoid potentially hazardous products, as consumers with peanut allergies avoid foods containing peanuts. When there is no discernable difference between two foods, labeling one of them only causes confusion and jeopardizes the value of meaningful labels.

All health authorities agree DNA by itself is a non-hazardous nutrient, so a label only becomes meaningful when associated with what federal regulators call “material information,” such as a specific hazard. In those cases, current regulations already assure appropriate labels.

What About the Sources of Genes in Foods?

Some people wonder whether the source of a gene affects the safety of foods. Given the tremendous overlap in genes among humans, animals, plants and even microorganisms, and given the fundamental chemical relatedness of DNA in all organisms, the source of the gene is of limited importance to judgments on safety. Rather, information on the gene product—the function of the protein that the gene encodes, its effect on the food, and the way in which that food is intended to be used—all bear importantly on the safety of the food. For example, a substantial number of people are allergic to peanuts. If a gene from the peanut is transferred into a tomato, one might reasonably worry about the potential allergenicity of the tomato. However, if the protein encoded by that gene is known not to contribute to the allergenicity of peanuts, then the new tomato will not be a problem for people allergic to peanuts. Information about the source of the gene alone is thus of minimal usefulness.

CONCLUSI

Modern biotechnology is being used in agriculture and food production to provide more, better, and safer products. The extent to which it will be fully utilized for the benefit of consumers depends on support for innovation and improvement in farming and food production, on the one hand, and on support for scientifically sound regulatory policies that protect against tangible food safety risks, on the other. This is a delicate balance. Medical and human health biotechnology, using similar genetic techniques, is well accepted by the public and professional communities as a safe and effective means to provide more and better treatments. Because agricultural biotechnology is younger and some critics remain wary, new food products will appear gradually in the marketplace over the next few years. However, with the continuing accumulation of evidence of safety and efficiency, and the complete absence of any evidence of harm to the public or the environment, more and more consumers are becoming as comfortable with agricultural biotechnology as they are with medical biotechnology. With the research pipeline filled, consumers and farmers can expect a wide variety of new products in the not too distant future.

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US GOVERNMENT AGENCY RELEVANT WEB SITES:

US Environmental Protection Agency (microbials)
http://www.epa.gov/opptintr/biotech/
FDA biotechnology information
http://vm.cfsan.fda.gov/~lrd/biotechm.html
FDA biotech final consultations
http://vm.cfsan.fda.gov/~lrd/biocon.html
USDA biotechnology information http://www.aphis.usda.gov/bbep/bp/
USDA— status of petitions
http://www.aphis.usda.gov/biotech/petday.html

OTHER INTERESTING WEB SITES:

Biotechnology Industry sites

Biotechnology Industry Organization (USA) http://www.bio.org/
EuropaBio (EU) http://www.europa-bio.be/
The BioIndustry Association (UK) http://www.bioindustry.org/
AgWest Biotech (Canada) www.agwest.sk.ca
Genentech http://www.genentech.com/Company/timeline.html
Monsanto (USA) http://www.monsanto.com
DuPont http://www.dupont.com/index.html
Zeneca http://www.zenecaag.com/resrch/f_biotec.htm
Novartis http://www.seeds.novartis.com/
Aventis http://www2.aventis.com/cropsc/cro_main.htm

GLOSSARY/API

Acetolactate synthase (ALS) A plant and microbial enzyme responsible for biosynthesis of the essential amino acids leucine, isoleucine, and valine. Several common herbicides attack this enzyme, causing the plant to starve. A modified form, inserted into flax, allows the crop to grow in soil containing excess residue of sulfonylurea chemicals, an agronomic problem in parts of the Great Plains.

Adenine methylase The *dam* gene, derived from *Escherichia coli*, expresses a DNA adenine methylase enzyme. The enzyme, when expressed in anthers or pollen, results in the inability of the transformed plants to produce fertile male plants because it kills the developing pollen grain. The sterile male plants facilitate production of hybrids, as they cannot self-pollinate. See also **Hybrid**.

Aminocyclopropane carboxylic acid synthase/deaminase Enzymes involved in the fruit ripening process that regulate biosynthesis of ethylene. Ethylene is an endogenous plant hormone known to play an important role in fruit ripening, so manipulation of these genes can result in fruit with altered ripening periods. See also **S-Adenosylmethionine hydrolase**.

Antisense DNA A process to inactivate a gene by excising the relevant gene, turning it 180 degrees and reinserting it back into the genome. The Flavr Savr® tomato has extended shelf life because of an antisense polygalacturonase (an enzyme involved in ripening) gene.

Barnase An enzyme which destroys nucleic acids, thus killing the cell. When the gene is inserted into plants and activated only in pollen (as is the typical use), the plant becomes male-sterile, facilitating the development of hybrids. An associated product, Barstar, may be used to restore male fertility to the plant.

Bt Cry9c, Bt CryIIIA, BtCryIA(b), etc. Insecticidal crystal proteins produced by various strains of *Bacillus thuringiensis*, commonly used in insect-protected crops and also, as a spray, by organic and conventional farmers.

DNA The chemical carrying genetic information. It is a double helix composed of a sugar-phosphate backbone with rungs of the bases A, T, C, or G. The genetic information is coded by the specific sequence of the As, Ts, Cs, and Gs along the molecule. The DNA from a single human cell, if extracted and pulled taut, would be about six feet long.

Enzyme A protein responsible for facilitating a chemical reaction; a biological catalyst. Most genes code for proteins with enzyme activities.

EPSP synthase The enzyme 5-enolpyruvylshikimate-3-phosphate synthase (EPSPS), responsible for the biosynthesis of the amino acids tyrosine, phenylalanine, and tryptophan. The herbicide glyphosate inhibits this enzyme, causing the plant's death by starvation for the amino acids.

Gene A unit of genetic information carried on a given portion of a cell's DNA. The specific sequence of DNA base letters (A, T, C, and G) provides a recipe for the cell to make a particular protein. The presence or absence of the protein contributes, either individually or in combination, a specific trait to the organism. Humans carry about 80,000 genes; a typical plant about 25,000 (see Figure 1).

Gene splicing The precise joining of pieces of DNA from different sources to create a novel gene construct. See Recombinant DNA.

Genetic engineering, genetic modification In the general sense, any change, using classical or modern breeding methods, in the genetic structure of an organism to provide an improved strain. In the specific sense, the application of recombinant DNA (rDNA) or gene splicing technology to living organisms, usually to produce a predicted and intended improvement. See Recombinant DNA.

Genome The total complement of genetic information in an organism.

Glyphosate oxidoreductase A modified (goxv247) gene from Ochrobactrum anthropi produces glyphosate oxidoreductase, an enzyme that breaks down glyphosate, conferring resistance to the herbicide.

GmFad2-1 The GmFad2-1 gene codes for a delta-12 desaturase enzyme involved in the synthesis of polyunsaturated fatty acids (e.g., linoleic acid) from monounsaturated fatty acids (e.g., oleic acid) in developing seeds. The soybean GmFad2-1 gene, when inserted into soybean, can cause a silencing (co-suppression) of itself and of the endogenous GmFad2-1 gene, resulting in a soybean whose oil has an oleic acid content that exceeds 80%. Conventional soybeans have an oleic acid content of about 24%.

Hybrid Many plants experience increased productivity from hybrid vigor, the mating of different parents. Corn producers have benefited from hybrid seed for years, but many crops are naturally self-pollinating and so cannot readily provide hybrid seed. Several genetic technologies have been developed to interfere with pollen development, thus ensuring pollination from other plants and giving rise to hybrid seed.

Nitrilase The product of the BXN gene, derived from the soil microbe Klebsiella pneumoniae subsp. Ozaenae. Nitrilase degrades the herbicide bromoxynil, thus conferring protection from this herbicide.

Papaya Ring Spot Virus (PRSV) Devastating disease of these tropical fruit, responsible for destroying the entire industry wherever it hits. PRSV was defeated by GM technology, which saved the industry in Hawaii.

Phosphinothricin acetyltransferase (PAT) An enzyme that breaks down phosphinothricin, a herbicidal molecule in Liberty™, Basta™ and other herbicides. The gene, originally isolated from the soil microbe Streptomyces viridochromogenes, was modified for optimal utility in plants.

Phytase Phosphorus from plant-based feed is not readily available as a nutrient for swine and poultry. Phytase, an enzyme, converts phosphorus from plant feed into a more available form for poultry and swine.

Polygalacturonase A common fruit enzyme responsible for softening /over-ripening. The gene can be used to interfere with normal fruit ripening (giving longer shelf-life) by insertion into a plant either in the normal orientation (co-suppression) or reverse orientation (antisense).

Recombinant DNA (rDNA) Gene splicing; the precise joining of pieces of DNA from different sources ("recombining" genes) to create a novel gene construct. The construct is often inserted into a host organism to produce a protein, providing the host with a new trait. See Genetic engineering.

S-Adenosylmethionine hydrolase The sam-k gene is derived from E. coli bacteriophage T3. When inserted into plants, this gene reduces levels of S-adenosylmethionine (SAM), which is normally converted to 1-aminocyclopropane-1-carboxylic acid (ACC) (see above), which is the first committed step in ethylene biosynthesis. Lack of SAM for conversion to ACC results in fruit with significantly reduced ethylene and so ripening is delayed.

Thioesterase The thioesterase gene isolated from California bay (Umbellularia californica) is the recipe for the 12:0 thioesterase enzyme. This enzyme results in the seed accumulation of the 12-carbon saturated fatty acid, laurate, used in soaps and detergents.

Transposon A piece of DNA with the ability, under certain conditions, to remove itself from one location (locus) in a chromosome and re-insert itself at another. Also called a "jumping gene."

Virus coat protein Crucial protein for viruses; the gene can be used to confer immunity to the pathogen when transferred to a host organism.

Virus replicase An enzyme responsible for virus reproduction. The isolated gene, when inserted into a plant, can confer immunity to an attack by the pathogen.