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Food Biotechnology in the United States: Science, Regulation, and Issues

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Summary

The use of biotechnology to produce genetically engineered foods can potentially provide greater yields of nutritionally enhanced foods from less land with reduced use of pesticides and herbicides. This technology has both critics and supporters. Concerns presented to Congress include potential detrimental effects to human and animal health and the environment, and violation of religious customs. Supporters, including individual companies, trade organizations, scientific professional societies, and academic groups, promote benefits such as enhanced crop yields, better nutritional content in food, less pesticide use, and greater agricultural efficiency. They want Congress to defend the U.S. competitive position in export trade of food biotechnology products. Calls for "right-to-know" labeling or other federal regulatory requirements, on the other hand, spark concerns about possibly impeding innovation and adding costs.

In the United States, the regulation of biotechnology food products does not differ fundamentally from regulation of conventional food products. Three federal agencies are primarily responsible for the regulation of genetically engineered foods — the Food and Drug Administration (FDA), the Environmental Protection Agency (EPA), and the U.S. Department of Agriculture (USDA). Each federal agency is assigned certain regulatory responsibilities. FDA provides voluntary pre-market consultations with food companies, seed companies, and plant developers (which they propose to make mandatory) to ensure that biotechnology derived foods meet regulatory standards for safety. USDA's Animal and Plant Health Inspection Service (APHIS) licenses field testing of crops prior to commercial release of newly developed plant strains. EPA registers pesticides in U.S. commerce (including plants engineered to produce pesticides) and establishes levels at which pesticides in foods are permitted. The White House outlined this multi-agency approach to regulating the products of biotechnology in a 1986 document entitled Coordinated Framework for Regulation of Biotechnology.

Some critics are concerned about genes from genetically modified plants escaping into the environment through cross fertilization. Others fear the potential overuse of Bt, a natural insecticide, will cause insects to develop resistance to its toxic effects. They want more testing on the long-term environmental and health impact of crops that are altered to produce it. Plus they want the government and academic institutions to conduct independent testing to verify industry data. Industry groups, however, contend that current regulations more than adequately ensure human health and safety. The United States is leading the world in privately funded biotechnological research, genetically modified products, and sales of the technology. During the last days of the Clinton Administration, FDA published a proposed rule changing the way the agency currently regulates bioengineered foods, and published a draft of a guidance document that will advise the biotechnology industry on how to label its food products. In addition, EPA published final rules on how the agency will regulate bioengineered crops, called pest-incorporated protectants.

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Introduction

Genetic modification of agricultural crops promises the availability of food products with more desirable traits, such as higher quantities of vitamins or lowered amounts of saturated fats for consumers, reduced use of pesticides and other chemicals for environmentalists, and increased yields for growers. Traditional plant breeding, the conventional method to modify plants' genes, has produced similar benefits. But recent biotechnological innovations allow scientists to select specific genes from one plant or animal and introduce them into another to confer desirable traits. This produces the new plant or animal more quickly than conventional methods, and creates plants and animals with traits not found previously in nature. Proponents argue that advances in genetics and new technologies can produce foods with greater yields to feed the growing world population in the 21st century. Critics are concerned that this technology produces uncertainties about potential long-term impacts on public health and the environment, and increases problems related to trade.

The federal government under statute and through regulation attempts to ensure that food manufacturers produce safe products. However, some Members of Congress have asked whether federal regulations adequately manage genetic engineering risks to public health and safety, and the environment. Nine bills introduced into the 106th Congress asked that the Administration pay more attention to these risks. Similar bills are likely to be introduced into the 107th Congress which will call for the same additional scrutiny and research.

This report discusses the science of food biotechnology, and the federal structure by which it is regulated. Because U.S. farmers are adopting this technology at a rapid rate, some observers advocate a more active role for the federal government to ensure that farmers have equal access to this technology. Others believe that federal officials should play a more active role in protecting the environment, funding more research, and participating in international trade negotiations to ensure that trade continues to expand for genetically engineered crops. Trading partners often label food products that have been genetically modified as genetically modified organisms (GMOs). Many of those partners have labeling requirements for GMOs to allow consumers the "right to know" their food content.

Several congressional committees oversee federal governance of genetically engineered foods and biotechnology. In the Senate, food biotechnology issues are considered by the Committees on Agriculture, Nutrition, and Forestry; Health, Education, Labor and Pensions; Environment and Public Works; and Governmental

Affairs. In the House, food biotechnology issues are considered by the Committees on Agriculture; Energy and Commerce; Government Reform; and Science. The Appropriations Committees of both the House and Senate have oversight responsibility on how the major federal agencies set and enforce policies affecting the safety of genetically engineered foods.

The Science of Genetic Engineering

Biotechnology is defined as the use of biological processes for the development of products such as foods, enzymes, drugs, and vaccines. Biotechnology is the new label for a process that humans have used for thousands of years to ferment foods such as beer, wine, bread, and cheese. In these cases, biological processes are used to alter raw food products to produce more stable foods. Presently, the term biotechnology is used to describe genetically engineered foods that contain genes modified by modern technologies.

When plants breed in the wild, genetic changes occur spontaneously and result in a haphazard transfer of a large number of genes within closely related species. Traditional plant breeding is more selective and creates plants with improved yields or some other desirable trait among closely related species. Often, unwanted genes conferring undesired characteristics may be transferred along with the desired characteristics. Breeding itself takes time due to the need to backcross each plant to eliminate undesirable traits.

Modern genetic engineering gives greater control of the process and transfers specific genetic material into the cells of a plant. This method can reduce the likelihood of unexpected results. Also, plant breeders can use the newer genetic techniques to move genes among unrelated species to yield plants with novel traits that could not be produced by traditional breeding.

Several techniques are employed by genetic engineers. All involve DNA transfers from one plant or animal to another. DNA, deoxyribonucleic acid, is the chemical from which genes are constructed. Specialized laboratory techniques, generally referred to as recombinant DNA (rDNA) techniques are used to manipulate DNA isolated from animal, plant, or microbial cells and to introduce the engineered DNA sequences into another organism. The laboratory techniques of genetic engineering may involve direct cellular uptake of DNA, forced introduction of DNA into a cell, or the use of a non-pathogenic carrier to transmit genetic material into a cell. Additionally, some microbial cells in immediate contact can transfer DNA directly from one cell to another. Plants may also be genetically modified by fusion of whole cells.[1]

After plant cells are genetically modified, tissue culture techniques are used to encourage growth of the modified cells into whole plant systems with leaves, stems,

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[1]Grosser, J., and F. Gmitter. "Protoplast Fusion And Citrus Improvement." *Plant Breeding Reviews*, (Ed., J. Janick), v. 8, Chap.10. Timer Press, Portland, OR.,1990.

and roots. New food plant characteristics depend on which genes are transferred, whether these genes are switched on (expressed), and the interaction between genes and the cellular environment in which they reside.

Use of Biotechnology to Produce Food

The first wave of agricultural biotechnology food products is not substantially different from those foods already familiar and available to consumers. These modified agricultural commodities have, for the most part, directly benefitted agricultural producers with increased yields and reduced production costs. According to an industry trade association, genetically engineered food crops planted and marketed by U.S. farmers include corn, canola, rice, tomatoes, potatoes, and soybeans. Peppers, sunflowers and peanuts are in the pipeline for approval. Other genetically engineered food crops, such as sugar beets, wheat, squash, papayas, berries, bananas, and pineapples, have been developed in laboratories, and will go through the approval process for marketing within the next few years. Non-food plants that are being genetically modified include trees, for pulp wood, and cotton, although cotton seed oil may be used in food products.

Genetically Modified Whole Food Products. Some of the products referred to above have been genetically modified to be either resistant to pesticides,[2] or to make their own pesticides. Those modified to resist pesticides allow farmers to use a herbicide for weed control without killing the food crop. This use reduces competition from weeds for nutrients and increases yields. Other products of bioengineering produce insecticides within their cells. Crops such as corn, cotton, and potatoes, have been genetically engineered to make their own pesticide.

Farmers rapidly accepted these genetically engineered field crops with increasing acreage of herbicide resistant crops. The use of these plants reduces the need to plow, decreases the amount of chemical herbicide needed, produces higher yields, and can deliver a cleaner and higher grade of grain and product.[3] Of the total 1998 crop, approximately 25% of planted corn was genetically modified, 38% of planted soybeans, 45% of cotton, and 42% of canola.[4] In 1999 the percentage of acres

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[2]The term "pesticide" is the general category of substances that are toxic to pests; herbicides, insecticides, and rodenticides are all pesticides.

[3]James, Clive. "Global Review of Commercialized Transgenic Crops." *International Service for the Acquisition of Agri-biotech Applications Briefs*, no. 8, 1998, ISAAA: Ithaca, NY.

[4]Statistics come from the following sources: Terri Dunahay. Economic Research Service, January 20, 1999; A.S. Moffat. "Toting Up the Early Harvest of Transgenic Plants." *Science*, v. 282. p. 2176-2178; M. Pollan. "Playing God in the Garden." *New York Times Magazine*, October 25, 1998. p. 44-51, 62-63, 92-93; R. Ortiz. "Critical Role of Plant Biotechnology for the Genetic Improvement of Food Crops: Perspectives for the New Millennium." *Electronic Journal of Biotechnology*, v. 1, no. 3, December 15, 1998. [http://www.ejb.com]; J. Bernice. "Medicine Man." *Farm Journal*, mid-January 1998. p. 22; *Genetic Engineering News*, February 1, 1999: "Cancer Vaccine Made in a Plant-based System", p. 1 were collected from: *Science* (1998), v. 282, p. 2176; Michael Pollan, *N.Y. Times Magazine*, October 1998; R. Ortiz, *Electronic J. Biotechnology*, v. 1, no. 3, December

(continued...)

planted with corn grew to 37% but declined to 25% in 2000. In 1998 in the United States, herbicide tolerant soybeans became the dominant bioengineered crop, with 4.1 million acres planted (about 36% of the total U.S. acreage planted in soybeans). In 1999, bioengineered soybean plantings increased to 47% and continued to increase to 54% in 2000. Cotton has followed a similar trend. Herbicide resistant crops of soybeans, corn, and cotton accounted for most of the acreage planted in biotech crops.

Various companies have targeted different genetic modifications to produce tomatoes that remain firm for a longer time and are reputedly more flavorful than traditional tomatoes. Calgene's Flavr Savr tomato was one of the first genetically engineered consumer-ready foods to receive federal approval for production and marketing in the United States (see text box on page 9). Another tomato engineered by Zeneca, used for production of a reduced-price tomato paste for sale in the United Kingdom, was withdrawn due to consumer protests.

Biotechnology is also used to produce experimental "transgenic" animals, in which the genetic material has been deliberately modified and to produce "clones" in which animals are reproduced artificially but the DNA is not modified. In agriculture, transgenic animals may be altered to produce higher yields of specific products (meat, milk, etc.) or to bring about commodities with enhanced characteristics, such as less cholesterol or reduced fat content. Although cloning has been used to reproduce animals for scientific purposes since the 1950s, its usefulness for the reproduction of identical livestock animals was only recently investigated. In 1995, sheep were cloned from embryonic cells in Scotland. In 1996, a substantial breakthrough followed when a sheep, Dolly, was cloned from an adult, nonembryonic cell.[5] Japanese scientists are creating high-value beef cattle through cloning. They have successfully cloned at least 19 calves from adult bovine cells. Because the cost of some premium beef roasts can be between $100 and $200 per pound in Japan, the Japanese cattle industry can support the expense of cloning prize beef cattle.[6] But even with those prices, the cost of genetically engineering cattle on a large scale could be prohibitive.

At this time, most of the research on transgenic animals in agriculture is experimental. The Biotechnology Industry Organization (BIO), an industry trade organization, estimates that the only transgenic animals that will be marketed within the next 6 years are transgenic fish that can grow to market size more rapidly than traditional farm-raised fish. Experiments are also being conducted to produce transgenic animals that yield human pharmaceuticals such as vaccines, growth hormones, blood-clotting factors, monoclonal antibodies and other drugs.

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[4](...continued)
15, 1998. [http://www.ejb.com]; S.D. Moore. "Agro-chemical Rivalry Heats Up: AHP-Monsanto Pact Raises Pressure." *The Wall Street Journal Europe*, June 5-6, 1998, p. 10.

[5]Wilmut, I., A. E. Schnieke, J. McWhir, A.J. Kind, and K.H.S. Campbell. "Viable Offspring Derived from Fetal and Adult Mammalian Cells." *Nature*, v. 385, February 1997. p. 810-813.

[6]Normile, Dennis. "Bid for Better Beef Gives Japan a Leg Up on Cattle." *Science*, December 11, 1998. p. 1975-1976.

Enhancement of milk from cows, goats and sheep to contain these drugs is the target of much of this research.[7]

Animal products also have been changed by biotechnology. A food processing agent, chymosin (also called rennin) is an enzyme required to manufacture cheese. It was the first genetically engineered food additive to be used commercially. Traditionally, processors obtained chymosin from rennet, a preparation derived from the fourth stomach of milk-fed calves. Scientists engineered a non-pathogenic strain (K-12) of *E. coli* bacteria for large-scale laboratory production of the enzyme. This microbiologically produced recombinant enzyme, identical structurally to the calf derived enzyme, costs less and is produced in abundant quantities. Today about 60% of U.S. hard cheese is made with genetically engineered chymosin.[8] In 1990, FDA granted chymosin "generally-recognized-as-safe" (GRAS) status based on data showing that the enzyme was safe.[9] The final enzyme product is purified by removing potentially harmful substances, including the gene for antibiotic resistance used to engineer the microorganism that produces chymosin.

Bovine somatotropin (BST), also known as bovine growth hormone (BGH), occurs naturally in cows. When recombinant bovine somatotropin (rBST), is injected supplementally into dairy cattle, milk production may increase 10% to 15% (see text box). Genetically engineered microorganisms produce a consistent and affordable supply of this hormone as opposed to isolating the compound from limited bovine sources. According to an industry trade association, it is possible that up to 30% of U.S. dairy cows are injected with recombinant BST to increase milk yield.[10]

Future Products. Experts indicate that the "second wave" of genetically modified food products will target consumer and animal health issues and improve the nutrition content of certain foods. For example, vitamin A shortages that are a significant health concern in developing countries could be addressed by increasing the vitamin A content in canola oil. Genetically engineered soybeans, peanuts, and sunflowers may contain reduced levels of saturated fats or have altered fatty acid compositions for enhanced health benefits and to improve vegetable oil stability without the need for chemical hydrogenation. (Hydrogenation is used to create fats that are solid at room temperature — margarine, solid Crisco, etc.) Fruits may also

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[7]Charles, Craig. "Near-term Benefits of Cloning Likely To Be Medical." *Washington Post*, March 29, 1997.

[8]BIO: Website of the Biotechnology Industry Organization, Washington, D.C. [http://www.bio.org/library/foodrep8.html].

[9]FDA classifies food additives into four categories: GRAS additives (generally- recognized-as-safe) are exempt from regulation because their extensive use has produced no known harmful effects; direct additives are intentionally added to foods; prior-sanctioned substances are substances which were approved by FDA or USDA before the passage of the 1958 food additives amendment to the FFDCA (Section 409, 21 U.S.C. 348); and indirect additives, sometimes called food contact substances, are often trace substances that leach from packaging materials and migrate to food during processing or storage.

[10]BIO: Website of the Biotechnology Industry Organization, Washington, D.C. [http://www.bio.org/whatis/ foodwelcome.html].

be genetically engineered to contain vaccines. These fruits could be delivered without special care to developing countries which often don't have refrigeration necessary for current vaccines.[11] Genetically engineered salmon, trout, and flounder achieve market size in half the time of non-genetically engineered fish. Commercialization of such fish may help curtail over-fishing of native fish, as well as reduce consumer prices. In addition, scientists are using genetic engineering to make high-value products, such as special oils and chemicals. Rapeseed plants have been genetically modified to produce 35% more of a fatty acid, laurate, for use in soaps, detergents and other household items. Other plants and animals are being engineered to produce pharmaceuticals, specialty chemicals, and biologic agents.

Federal Responsibilities for Regulating Genetically Modified Foods

During the 1970s, the development of new techniques for transferring genes raised concerns about potential hazards. At the Asilomar Conference in February 1975, scientists working with this technology tried to reach a consensus to self-regulate research involving rDNA technology until its safety could be assured. The National Institutes of Health (NIH) became involved in 1976 when it published research guidelines using rDNA techniques. Until 1984, the NIH Recombinant DNA Advisory Committee was the primary federal entity that reviewed and monitored DNA research. However, a legal challenge forced the Reagan Administration to consider and propose policies to guide activities of federal agencies responsible for reviewing biotechnology research and its products.[12] In 1984, the White House Office of Science and Technology Policy (OSTP) published the "Coordinated Framework for Regulation of Biotechnology," a framework proposing that genetically engineered products would continue to be regulated according to their characteristics and novel features and not by their method of production. It also proposed that new biotechnology products be regulated under the existing web of federal statutory authority and regulation.[13]

In 1986, OSTP finalized this framework. The framework identified lead agencies to coordinate activities when and if jurisdictions overlapped. For example, the Food and Drug Administration (FDA) is responsible for regulating food and feeds in the market that have been modified through genetic engineering. The U.S. Department of Agriculture (USDA), Animal and Plant Health Inspection Service (APHIS), regulates importation, interstate movement, and environmental release of transgenic plants that contain plant pest components. It licenses, through permits, the field

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[11]Tacket, Carol O. "Vaccines from Edible Plants," paper presented at the 1998 FDA Science Forum, *Biotechnology: Advances, Applications and Regulatory Challenges.* Washington, December 8, 1998.

[12]*Foundation on Economic Trends* v. *Heckler*, 587 F. Supp 753 (D.C. 1984) 756 F.2d 143 (D.C. 1985).

[13]U.S. Congress. OTA. New Developments in Biotechnology — Field Testing Engineered Organisms, Genetic and Ecological Issues, no. 3, OTA-BA-350, May 1988. Washington, GPO, 1988. p. 60.

testing of food crops prior to commercial release. But agencies' responsibilities overlap as some plants have been modified to contain plant-pesticides. The Environmental Protection Agency (EPA) registers certain pesticides produced in transgenic plants prior to their distribution and sale and establishes pesticide tolerances for residues in foods.[14] APHIS and EPA together established that APHIS would regulate the plant itself, particularly those plants engineered to resist herbicides, and EPA would regulate the pesticide used on the herbicide resistant plant. They also together established procedures to review and approve field tests of modified plants and microorganisms. FDA has post-market authority to remove a food from the market. **Table 1** shows an overview of federal agencies' responsibilities.

Table 1. Overview of Agency Responsibilities

Agency	Products Regulated	Reviews for Safety
FDA	Food, feed, food additives, veterinary drugs	Safe to eat
USDA	Plant pests, plants, veterinary biologic	Safe to grow
EPA	Microbial/plant pesticides, new uses of existing pesticides, novel microorganisms	Safe for the environment. Safety of a new use of a companion herbicide

Source: This data was compiled from tables found at the APHIS website: [http://www.aphis.usda.gov/biotech/OECD/usregs.htm]

Food and Drug Administration

The Federal Food, Drug, and Cosmetic Act (FFDCA) gives FDA broad authority to regulate foods by prohibiting the entry into interstate commerce of adulterated or misbranded foods. It is the legal responsibility of food manufacturers to produce foods that are not adulterated, unsafe, filthy, or produced under unsanitary conditions. FDA has authority to inspect foods and food facilities, both domestic and imported, to ensure that they are manufactured and held under acceptable conditions and are properly labeled. FDA can seize products or request that they be removed from the market if they do not meet federal requirements.

The Act also requires that "food additives" not be marketed unless they have received approval from FDA. But substances added to foods that are considered generally-recognized-as-safe or GRAS substances do not need agency approval. First articulated in the OSTP framework document in 1986, FDA determined in 1992 that bioengineered foods pose the kinds of scientific and regulatory issues that are not substantively different from those raised by non-bioengineered foods. Thus, FDA

[14]EPA defines "plant-pesticides" as a "pesticidal substance that is intended to be produced and used in a living plant, or in the product thereof, and the genetic material necessary for the production of such a pesticidal substance." The DNA is not itself a pesticide. The plant uses the DNA to produce a pesticidal substance which is toxic to pests.

regulates foods that have been genetically modified or engineered no differently than foods created by conventional means.

In a May 1992 policy statement FDA described how its regulatory authority applies to new plant varieties and derived food products, including those developed through genetic engineering. The agency decided that companies developing genetically engineered foods would have to go through a special review in FDA only if :

- the gene transfer produces unexpected genetic effects;
- the levels of toxicants in the food are significantly higher than present in other edible varieties of the same species;
- nutrients in the bioengineered food differ from those in traditional varieties;
- the sources of the newly introduced genetic material come from a food plant associated with allergies;
- the food from the new variety differs significantly in composition from food of comparable varieties;
- the food contains marker genes that theoretically may reduce the therapeutic effects of clinically useful antibiotics;
- the plants are developed to make substances like pharmaceuticals or polymers, and will also be used for food; or
- the food to be used for animal feed has changes in nutrients or toxicants.

So far, most genetically modified foods have not required pre-market approval, although a few have had their composition changed significantly such that they were labeled differently. Most proteins from genes transferred into foods to give them new traits are either GRAS or otherwise exempt from regulation. A GRAS substance is excluded from the definition of a food additive.[15]

FDA has, however, instituted a voluntary consultation process whereby the developer can resolve any safety or regulatory issues prior to marketing. The agency has proposed keeping this process voluntary when it published a proposed rule in January 2001. The proposed rule would require that a food company notify the agency 120 days prior to marketing a bioengineered food and supply the agency with safety test data. FDA strongly urges companies to consult the agency prior to the mandated notification deadline in order to ensure agreement on the types of safety testing that will be needed. By the end of 2000, developers had consulted with FDA officials on 44 products: 12 times for corn; 5 for tomatoes; 8 for canola; 5 for cotton seed; 4 for potatoes; 3 for soybeans; 2 each for sugar beets and squash; and once for flax, radicchio, and papaya.

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[15] Affirmation petitions for "generally-recognized-as-safe" (GRAS) status must be filed to gain FDA's formal agreement with a sponsor's independent determination that a substance is GRAS. FDA considers that bioengineered substances intentionally added to food are food additives. FDA must review and approve any food additives that do not have GRAS status before foods containing new additives can be introduced onto the market.

Case Study of a Commercial Genetically Modified Food: Flavr Savr Tomato

Although a few corporations have made substantial, long-term investments in the application of biotechnology to foods, not all genetically modified foods are commercially successful. Calgene's Flavr Savr tomato, for example, had limited technical success and did not meet commercial expectations. Calgene genetically modified a strain of tomato to reduce activity of a particular enzyme (polygalacturonase) that affects softening of outer tissue during ripening. Because the genetically modified tomato had less of this enzyme, it could remain longer on the vine prior to harvest thereby enhancing its tomato flavor. However, Calgene chose to manipulate genetically a tomato strain that had qualities more useful for processing than for the fresh market. The Flavr Savr never achieved commercial success because it cost more and did not taste better than competing cheaper tomatoes.

After its founding in 1980, Calgene conducted basic molecular biology research to investigate optimum techniques for the genetic manipulation of foods. In the mid 1980s, Campbell Soup co. decided to support Calgene's research efforts to produce a genetically modified tomato, presumably for use in Campbell's products. In 1989, officials at Calgene initiated discussions with FDA regarding the regulatory status of the tomato. FDA responded in 1992 by publishing its policy on foods derived from transgenic plants. Essentially, FDA decided to regulate genetically modified foods as any other food derived from traditional practices. The genetic technology needed to alter the tomato used an antibiotic marker that produced very small amounts of a non-tomato protein in Flavr Savr. According to FDA, the protein was viewed as a food additive since it changed the tomato's composition. Calgene officially petitioned FDA in January 1993 to allow the presence of this protein as a food additive. In May 1994, FDA approved Calgene's petition.

This approval opened the way for commercial marketing of the Flavr Savr tomato. However, in 1993 with significant public opposition to the genetically engineered tomato Campbell Soup Co. decided not to use genetically modified tomatoes in its products. Calgene then began efforts to market Flavr Savr as a freshmarket tomato rather than for use in processing. However, the tomato bruised easily and was less firm than expected. This characteristic caused production, transportation, and distribution problems. Competition from new tomato strains bred by traditional methods was an additional obstacle.

As reports of problems with commercialization of Flavr Savr grew, Calgene's financial condition weakened. In June 1995, Monsanto acquired a 49.9% equity stake in Calgene through the purchase of Calgene stock. In August 1996, Monsanto acquired controlling interest in Calgene. Monsanto emphasized other research programs at Calgene and subsequently moved control of Flavr Savr to another of its subsidiaries, Gargiulo Inc. in Naples, FL. According to industry sources, Gargiulo discontinued the effort to commercialize Flavr Savr.

In contrast, a British company, Zeneca, succeeded in marketing a genetically modified tomato in England. Now grown in California and processed into tomato paste for sale in the United Kingdom (U.K.), the Zeneca tomato has a label declaring that the paste is produced from genetically modified tomatoes. This product has since been withdrawn from the market because of consumer protests.

Development of this tomato used genetic technology virtually identical to that used by Calgene. Zeneca chose to genetically modify similar ripening-related enzymes in a tomato strain that had desirable processing characteristics. The Zeneca tomato yields a paste that is perceived as thicker and more flavorful than other tomato pastes. When combined with a comparatively low price plus marketing efforts through established market chains in England, this product has become the best selling tomato paste in the U.K.

Source: J.H. Maryanski. "FDA's Policy For Foods Developed By Biotechnology." *Genetically Modified Foods: Safety Issues* (Ed.s, Engel, Takeoka and Teranishi). American Chemical Society, Symposium Series 605, Ch. 2, 1995. p. 12-22; "Biotechnology of food." *FDA Backgrounder*. May 1994. [http://www.fda.gov/opacom/backgrounders/ biotech.html.]; M. Schechtman, Animal and Plant Health Inspection Service, USDA. "Assurance of Environmental Biosafety for Agricultural Products Derived through Modern Biotechnology: The Case Study of a Delayed Ripening Tomato. " *The Organization for Economic Co-Operation and Development Environment Monograph No. 107*, Report of the OECD Workshop on The Commercialization of Agricultural Products Derived Through Modern Biotechnology. [www.oecd.org/ehs/mn107sc.htm.]; M. Groves. "The Cutting Edge." *Los Angeles Times*, August 18, 1997; S. Lehrman. "Biotech Tomato Bruised." *San Francisco Examiner*, January 10, 1993.

On a food product's label, the FFDCA requires producers of foods to describe the product by its common name and reveal important facts associated with claims made or suggested. The agency interprets the FFDCA as not giving it authority to mandate labeling based solely on a consumer's "right to know" the method of production if the final product is considered "safe." Therefore, the agency does not mandate labeling to indicate the method by which a new variety was developed (e.g., that it was genetically engineered). However, the FFDCA does require that all information on labels be truthful and not misleading. Special labeling may be required if the developed food significantly differs from its conventional counterpart such that the common name would no longer apply. For example, FDA required the renaming of a soybean oil whose fatty acid composition had been altered by engineering. The new name, "high oleic acid soybeans," describes what is different about the oil but not its production method.

FDA requires special labeling for foods if they pose special safety or usage issues. For example, if a food had a new protein introduced into it to which people were allergic, FDA would require the label to reveal that information. In its 1992 policy statement, the agency noted that labeling would be required if genes were introduced from foods that were commonly allergenic, unless the developer could scientifically demonstrate that the protein was not responsible for the allergenicity of the original food. Examples of commonly allergenic food include milk, eggs, wheat, shellfish, tree nuts, and legumes. In one case, a developer demonstrated that DNA transferred to soybeans from a Brazil nut caused the production of a protein responsible for an allergic reaction. Consequently, the private developer discontinued research on that particular modified soybean. FDA has asked that developers of genetically modified food demonstrate that the introduced proteins do not share structural similarity to known allergens and are not resistant to digestive enzymes and acid.

On January 18, 2001, FDA published in the *Federal Register* a "Draft Guidance for Industry: Voluntary Labeling Indicating Whether Foods Have or Have Not Been Developed Using Bioengineering" and is seeking comments. In this document, FDA reaffirmed that it believes most genetically engineered foods are substantially equivalent to their conventional counterparts, and it decided it would not require special labeling of all bioengineered foods because it believes that the use of bioengineering, or its absence, does not itself cause a material difference in the food. However, the agency did suggest that because of the strongly divergent views on labeling, manufacturers may consider providing more information about bioengineered food. The information given, however, must be shown to be truthful and not misleading. To avoid false or misleading statements[16] about the absence of bioengineered ingredients (because there are no established threshold levels of bioengineered constituents or ingredients in foods), or to avoid implying that one food is superior to others, FDA suggests not using statements such as "GM free" or "biotech free." The agency does suggest the word "biotechnology" is preferred by

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[16]U.S. Dept. of Health and Human Services. Food and Drug Administration. "Draft Guidance for Industry: Voluntary Labeling Indicating Whether Foods Have or Have Not Been Developed Using Bioengineering." *Federal Register*, v. 66, no. 12, January 18, 2001. p. 4739-4742.

some consumers over "genetic engineering" or "genetic modification." It also claims that if validated testing is available, it can be used to verify whether the label is truthful. Or manufacturers could keep records to document the reasons why a food's label is truthful. Comments on the draft guidance are requested.

That same day, January 18, 2001, FDA proposed to make mandatory a notification system whereby a food company would notify the agency 120 days prior to releasing a genetically engineered food onto the market.[17] Along with the notification must be data that show that the is safe. FDA is not proposing to require that genetically engineered foods undergo a "food additive" review — the extensive pre-market approval process. The agency is encouraging industry to consult FDA about the types of tests that could be needed to prove safety. FDA would then have time to review the company supplied data and would make it available to the public for comment. Proprietary information would not however be released to the public. Critics of this proposed rule think that independent testing of the safety data is necessary to restore consumer confidence in this food. They assert that the testing should be done either by the agency or independent contractors but not by the company that has a vested interest in showing only the product's safety.

U.S. Department of Agriculture (USDA), Animal and Plant Health Inspection Service (APHIS)

APHIS issues permits for the importation and domestic interstate shipment of certain plants, animals, and microbes that have the potential for creating pest problems in domestic agriculture. The agency has historically regulated pests that attack plants — any living stage of any insect, mite, nematode, slug, snail, protozoa, and/or other invertebrate animal, bacteria, fungi, or parasitic plant or reproductive part. It is also interested in viruses — infectious substances that would directly or indirectly injure or cause disease or damage plants or plant parts or any processed, manufactured, or other plant products.[18]

For new plants that could become pests, APHIS issues site specific permits for field tests or for release into the environment. The agency reviews permit applications and prepares an environmental assessment in which it evaluates the probable environmental impact of the release. The permit application process requires that the developer disclose information about the development of the plant and that appropriate facilities and control measures are in place during transport and field tests. If the agency reaches a "Finding of No Significant Impact" (FONSI), a permit is issued.[19] Before decisions are made, APHIS seeks concurrence with states on regulatory actions.

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[17]U.S. Dept. of Health and Human Services. Food and Drug Administration. " Premarket Notice Concerning Bioengineered Foods"(Proposed Rule). *Federal Register*, v. 66, no. 12, January 18, 2001. p. 4706-4738, to amend 21 CFR Parts 192 and 592.

[18]7 CFR 340, et seq.

[19]U.S. Congress. OTA. New Developments in Biotechnology — Field Testing Engineered Organisms. *Genetic and Ecological Issues*, no. 3, OTA-BA-350, May 1988. Washington, GPO, 1988. Chapter 3.

In 1993, APHIS introduced an expedited procedure for approving limited permits so that field testing of six crops could begin without a completed formal application that included an environmental assessment. For genetically engineered plants that meet certain eligibility requirements and performance standards, the sponsoring company need only submit a "notification" letter to the agency, a modified and abbreviated application which describes the gene, where the tests will take place, and the characteristics of the plant. The agency has 30 days to process the application before the sponsor can proceed with the field test. In 1997, APHIS expanded the expedited procedure to cover many more crops; by 1998, 99% of all applicants used the expedited process.

After tests are completed and an application is submitted, APHIS has 120 days to decide whether the product poses a risk of being a plant pest and whether a product is ready for full "release" onto the market. APHIS then completes an environmental assessment before making its decision.

Case Study of a Genetically Modified Hormone: rBST

Bovine somatotropin (BST), also referred to as bovine growth hormone (BGH), is produced within the pituitary gland of all cows. It helps in the lactation process and is a normal trace constituent of milk. Farmers inject doses of the genetically modified hormone (called commercially Posilac) into cows to enhance milk yields and lengthen the lactation cycle. The result is an increase in milk yields of up to 15%. Prior to the 1980s, BST treatments were experimental and costly, since extractions of bovine tissues were the only source of the compound. With recombinant DNA technology, the supply of recombinant BST (rBST or rBGH) is more abundant and less expensive.

Critics are concerned that excessive amounts of rBST could compromise human and animal safety. They state that FDA did not provide adequate review of data to establish safety of the product prior to its approval. Six scientists within Health Canada, the Canadian federal agency involved in approving drugs, contend that the drug may not be safe for human consumption. However, the expert panel charged by Health Canada to review the drug found no risks to human safety. On January 14, 1999, Health Canada rejected approval of rBST based on concerns for animal health.

In June 1992, a joint expert committee of FAO/WHO concluded that rBST is safe for use and that Maximum Residue Limits (MRLs) are unnecessary. After a second review in February 1998, the committee arrived at the same conclusion. On March 10, 1999, the EU Scientific Committee on *Animal Health and Animal Welfare* recommended that the current EU ban on the use of rBST should continue in effect.

In 1989, Monsanto petitioned FDA's Center for Veterinary Medicine to approve an rBST product as a new animal drug. The review process took 4 years and was more extensive than most approval processes due to the controversial nature of the product. In August 1990, FDA published a review of data on rBST and concluded that it "presents no increased health risk." An August 1992 GAO report suggested that there may be an increase in mastitis in cows treated with rBST. The report also suggested there could possibly be indirect human health effects from residues of antibiotics used to treat cows for mastitis (udder infections). On March 31, 1993, an advisory committee of FDA's Center for Veterinary Medicine concluded that adequate safeguards are in place to prevent unsafe levels of antibiotic residues from entering the milk supply due to increased mastitis in rBST treated cows.

FDA approved the rBST product, Posilac, on November 5, 1993, with the stipulation that its developer, Monsanto, conduct a post approval monitoring program (PAMP) to provide further information related to possible effects on animal health experienced by rBST treated cows. FDA publishes occasional PAMP updates to summarize clinical manifestations associated with rBST treated cows. Since 1994, there have been 1,235 reports of adverse reactions in cows treated with Posilac although FDA states "the reported clinical manifestations are known to occur in dairy cattle not supplemented with Posilac." It also indicates that the number and types of reported effects raise no new animal health concerns.

On February 7, 1994, FDA offered interim guidance on labeling of milk from untreated cows, since some companies wanted to label their milk products as "BST-free." Products may be labeled as coming from animals not treated with rBST, but since BST is a normal constituent of milk, FDA determined that it is misleading to label milk as "BST-free." In May 1994, FDA's Food Advisory Committee and Veterinary Medicine Advisory Committee discussed whether foods derived from cows given supplemental rBST should be labeled as such. The committee report states "deliberations indicate that any method for instituting labeling for food from BST-supplemented cows would have to resolve many difficult scientific and policy questions." In 1999, FDA requires no labeling of milk products produced from cows supplemented with rBST.

On December 15, 1998, the non-profit Washington, D.C.-based Center for Food Safety petitioned FDA to withdraw approval of rBST citing possible health effects not addressed by FDA. As of January 2001 this issue is pending within the agency.

U.S. Department of Agriculture, Food Safety and Inspection Service (FSIS)

Developers of transgenic animals must submit data to FSIS to prove that the livestock and poultry involved in biotechnology experiments are not adulterated and can be slaughtered and sold as food with other beef and poultry. Prior to approving slaughter and sale, FSIS inspectors look at the number, age, sex, and other factors. The ultimate disposition of transgenic animal carcasses, whether by rendering, slaughter for food, or other disposal is of concern to regulators.[20]

Environmental Protection Agency

The EPA regulates pesticides. Pesticides are broadly defined as any substance or mixture of substances intended for "preventing, destroying, repelling, or mitigating" pests. EPA currently refers to "plant-pesticides," now called "plant-incorporated protectants," as plants that produce pesticides within their tissues.[21] Scientists have also genetically engineered plants that are resistant to specific herbicides. Although herbicide resistant plants are not "plant-incorporated protectants," they are subject to EPA regulation since they can affect the use of herbicides.

EPA regulates plant-incorporated protectants, under the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) and FFDCA. Under FIFRA, EPA determines the risk the pesticide substance in the plant poses to humans and the environment and approves registration of those substances for particular uses that will not generally cause unreasonable adverse effects. This determination involves balancing risks from the pesticide with benefits associated with its use.[22] A pesticide (including a plant-incorporated protectant) cannot be sold or distributed in the United States unless it is registered with EPA.

If the plant producing the plant-incorporated protectant is a food crop, EPA must establish a "safe level" of pesticide residue allowed, a tolerance level, under the authority of Section 408 of the FFDCA. A "safe level" of the pesticide residue is defined as that level at which there is "a reasonable certainty that no harm will result from aggregate exposure to the pesticide chemical residue, including all anticipated

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[20]At the FDA Science Forum on December 9, 1998, Dr. Steve Sundlof of the Food and Drug Administration stated that appropriate disposition of transgenic animals is becoming a concern as their numbers increase. He recommended that companies needing to dispose of carcasses consult with Center for Veterinary Medicine.

[21]EPA has proposed new nomenclature in the *Federal Register,"*Plant-Pesticides, Proposed Rule, Supplemental Notice of Availability of Information,"April 23, 1999 (v. 64, no.78) to amend 40 CFR parts 152, 174 and 180.

[22]International Life Sciences Institute, Health and Environmental Sciences Institute. *An Evaluation of Insect Resistance Management in Bt Field Corn: A Science-Based Framework for Risk Assessment and Risk Management.* Washington, D.C. 1998.

dietary exposures and all other exposures for which there is reliable information."[23] Because no tests of the registered (approved) plant-incorporated protectant have shown toxicity to humans so far, EPA has given them an exemption from the requirement for a tolerance level.[24]

Table 2. EPA Registered Plant-Incorporated Protectant

Pesticide substance	Crop	Registrant	Year Registered
Bt Cry3A	Potato	Monsanto	1995
Bt Cry1Ab	Corn	Mycogen/Novartis	1995/8
Bt Cry1Ac	Cotton	Monsanto	1995
Bt Cry1Ab	Corn	Monsanto	1996
Bt Cry1Ab	Corn	Novartis	1996/8
Bt Cry 1Ac	Corn	Dekalb	1997
Bt Cry 9C	Corn	AgrEvo	1998
Potato Leaf Roll Virus	Potato	Monsanto	1998

Source: Environmental Protection Agency, Biopesticides and Pollution Prevention Division.

EPA has registered few plant-incorporated protectants. **Table 2** shows that EPA has registered three genetically modified crops containing plant-incorporated protectant: potatoes, cotton, and corn (including field corn, sweet corn, and popcorn). **Table 3** shows that EPA has exempted from the requirement for a tolerance several genetically engineered viral coat proteins that can be used in food commodities. So far, all but one EPA-approved products contain a "Bt" delta-endotoxin. The delta-endotoxins are proteins, one of the many toxins that may be naturally produced by the bacterium, *Bacillus thuringiensis*, and are species-specific, affecting only certain insects. They are also virtually harmless to humans and animals. When a susceptible insect consumes the protein, its digestion is severely disrupted, further feeding stops, and the pest eventually dies, usually within 2 days.

[23]Section 408 of the FFDCA as amended by the Food Quality Protection Act of 1996.

[24]40 CFR 180.1155. The plant-incorporated protectant registered so far contain *Bacillus thuringiensis*, listed in **Table 2**, and have exemptions from the tolerance requirements.

Table 3. Exemptions of Viral Coat-Proteins[a] from Requirements of a Tolerance

Viral Coat Proteins
Watermelon Mosaic Virus-2 and Zucchini Yellow Mosaic Virus — in or on Asgrow line ZW20 of *Cucurbita pepo* L.
Potato Virus Y — in or on all food commodities
Potato Leaf Roll Virus — in or on all food commodities
Zucchini Yellow Mosaic Virus — in or on all food commodities
Watermelon Mosaic Virus-2 — in or on all food commodities
Papaya Ringspot Virus — in or on all food commodities
Cucumber Mosaic Virus — in or on all food commodities

Source: Environmental Protection Agency, Biopesticides and Pollution Prevention Division.

[a] Viral coat proteins are components of the outer cell wall that encloses a virus' genetic material. Expression of the coat protein in the plant confers resistance to the virus by a mechanism known as cross-protection.

In 1994, EPA proposed a rule to refine its regulatory oversight of plant-incorporated protectant. As a part of the rule, EPA included in its definition both the plant-incorporated protectant and the genetic material transferred into the plant. Under this rule, EPA proposed to exempt several categories of plant-incorporated protectant from FIFRA and FFDCA section 408 requirements.[25] Under this rule, EPA proposed to exempt: (1) plant-incorporated protectants derived from plants sexually compatible with the recipient plant; (2) plant-incorporated protectants that act by primarily affecting the plant;[26] and (3) plant-incorporated protectants based on a coat protein from a plant virus. These rules were designed to exempt certain categories of substances that EPA believes are low risk based on familiarity and presence in the food supply, e.g., plant hormones and coat proteins from plant viruses. The agency believed that these proposed exemptions would result in little or no effects on plants produced by conventional plant breeding. They could, however, affect research into innovative plants, according to critics, because of the additional regulatory burden that the rule would represent. The rule was finalized on January 18, 2001.

EPA's Final Plant-Incorporated Protectant Regulation. In the January 18, 2001 final rule, EPA clarified three regulations governing plant-incorporated protectants. With this regulation, EPA intends to ensure that plant-incorporated protectants derived from genetically engineering will meet federal safety standards under both the FFDCA and FIFRA. EPA will also set food tolerances for residues of

[25] 40 CFR 152.20

[26] An example of a plant-pesticide acting to affect the plant would be the modification of hairs on tomato plants to inhibit aphids from feeding on the plant.

plant-incorporated protectants (or give exemptions) found in foods. The agency also exempted from registration plant-incorporated protectants derived from conventional breeding of sexually compatible plants and genetic material necessary for the production of plant-incorporated protectants. The final rule did not exempt plant-incorporated protectants derived through genetic engineering from sexually compatible plants; plant-incorporated protectants that act primarily by affecting the plant; and plant-incorporated protectants based on viral coat proteins. Both these exemptions were questioned in the National Academy of Sciences report, published in April 2000, entitled "Genetically Modified Pest-Protected Plants: Science and Regulation." EPA has asked for comments on the report's recommendations.

In September 2000, StarLink corn containing a Cry9C protein, a protein approved only for use in animal feed, turned up in taco shells. Without approval for human use, or exemption from approval, the Cry9C protein is considered an adulterant. The current regulatory system would still not necessarily have caught this adulterant in human food, even if there had been a mandatory notification and labeling program. The incident and subsequent problems with StarLink corn being found in shipments that would have been used in food, however, has led EPA to state publically that it will probably never again allow the entry of bioengineered products onto the market that cannot be used in human food. The incident also led FDA to develop sampling and testing guidance for the industry so that testing results could be used to verify the labeling of corn with or without the Cry9C protein.

Issues

Congress' attention will likely be drawn to a number of biotechnology issues due to public concern. Issues include concerns about public health, religious issues, labeling, the environment, the economic impact of this technology, and international trade competitiveness.

Labeling for Public Health and Religious Practices

Public Health Concerns. Many consumers express wariness of new "supercrops" and novelty foods, fearing that introduced genes could prove allergenic or harmful to human health. For example, if new genes inadvertently caused a plant to produce toxins at higher levels than are present naturally, there could be long-term health consequences for humans.[27] Some consumers are worried that a gene

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[27]In August 1998, Dr. Arpad Pusztai, a scientist from the United Kingdom, told a television team that a potato that he had genetically engineered to contain a lectin (a naturally occurring insect resistant protein) had led to harmful health effects in rats. (The 10-day feeding trials showed rats with weakened kidney, thymus, spleen, stomach wall, and immune system damage. The rats' brain size decreased.) His research was disowned by the institute for which he worked and he was forced to resign. On February 16, 1999, *The Guardian* reported that 21 scientists who reviewed the data from the experiments found it credible and protested this treatment. Michael Sean Gillard, Laurie Flynn, and Andy Rowell. "Food Scandal Exposed." *The Guardian*, February 12, 1999. p.1. Other scientists think that the quality of (continued...)

introduced into plants to protect against pests could also cause the plant to alter its pollen, thereby affecting the health of humans prone to some sensitivities.

Some critics are dismayed that FDA is placing all the responsibility on manufacturers to generate safety data, as it does normally under its pre-market approval system, and is reviewing only the conclusions of industry-sponsored studies, rather than conducting its own tests.[28] Critics have asked that more tests be conducted for chronic effects prior to products being placed on the market to ensure that all uncertainties regarding human health be explored.[29] Proponents argue that additional testing of genetically engineered foods is unnecessary because all foods must meet the same federal safety standards regardless of whether they are genetically engineered.

There is a growing movement among consumer groups that advocate the labeling of all genetically modified foods (GMO foods) that were produced through the process of genetic engineering. This position reflects a policy of "consumer sovereignty" or the "right to know," which supports the disclosure of all relevant information on a label so consumers may make food choices based on their own values.[30]

Religious Practices. Others, particularly religious groups, are concerned that foods might contain genes from animals, such as swine prohibited by some religions, and they maintain that they have a right to know if foods contain those genes.[31] Both the kosher (Jewish) and halal (Muslim) communities have mechanisms in place to determine which products are acceptable to their adherents, and thus have not concerned themselves with secular labeling issues.[32] However, both Orthodox Rabbis and Muslim leaders have ruled that simple gene additions that lead to one or

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[27](...continued)
the potatoes fed to the rats may not have been consistently monitored and may itself have caused these problems ("Seeds of Discontent," *The Economist*, February 20, 1999, p. 75-77.)

[28]FDA typically uses data generated by individual companies to make regulatory decisions for food additives, drugs, medical devices, and biologics.

[29]Lehman, H. and J.F. Hurnik, "Concerns about the Ethics of Genetic Modification." Paper presented at the Fifth World Congress on Genetics Applied to Livestock Production, August 7-12, 1994. Proceedings, v. 20, as found at:
[http://www.oac.uoguelph.ca/www/CRSC/faculty/eac/lehman.htm]

[30]Thompson, Paul B. "Food Biotechnology's Challenge to Cultural Integrity and Individual Consent." *Hastings Center Report,* v. 27, no. 4, July-August 1997. p. 34-38.

[31]Flamm, Eric. Office of Policy, Food and Drug Administration, conversation with authors, January 28 , 1999. Mr. Flamm also said that the arguments about religious freedom issues are theoretical so far because there are no products on the market that insert genes from animals into plant species.

[32]Regenstein, Joe, Professor of Food Science, Cornell University, conversation with the authors, February 12, 1999.

a few new components in a species are acceptable for kosher and halal law.[33] The Muslim community has not yet resolved whether a gene derived from swine is an exception to the above acceptance. For example, both groups have raised no objection to the use of bioengineered chymosin (rennin) in the production of cheese. The status of more significant changes in the genetic makeup of species remains to be decided. However, cloning, in particular, raises serious ethical/moral issues for religious leaders of all faiths. That discussion has involved a much broader range of clergy within the respective communities as well as other communities without dietary laws.

Labeling. Currently, no federal agency requires foods to be labeled as genetically modified. One reason is because the agency sees these products as substantiallly equivalent to traditional food products. This assumption has been supported by the courts. Under Vermont's 1995 mandatory rBST labeling rule retailers rather than producers paid the expense of enforcement to ensure that all milk produced using rBST was so labeled. A federal appeals court overturned this requirement, and since the spring of 1997, Vermont has authorized voluntary labels for rBST-free dairy products.[34]

On January 18, 2001, FDA published a draft guidance for the industry giving examples of how the food industry could label foods that have or have not been developed using bioengineering. The guidance suggests that consumers prefer labels that explain why it was used in the food or how it is different from traditional food. The guidance suggests that all labels be "value-neutral." It also suggests that using the terms "GMO-free" or "not genetically modified" labeling could be misleading because such a label implies there is a zero level of bioengineered material which is almost always impossible to verify. The phrase "derived from biotechnology " would explain that the claim is being made and would allow consumers a choice about whether to purchase products produced by the new technology, to make better judgements about the compliance of the food product with ethical and religious beliefs, and lessen objections to its use.[35] Critics of this draft say that all labeling should be mandatory, not voluntary. They also claim that if the food companies are not forced to label genetically engineered foods, if there are health or safety problems, it would be more difficult to trace illnesses stemming from a particular bioengineered food.

The food industry generally opposes all biotech labeling because consumers may interpret these to be "warning labels," implying that the foods produced through

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[33]Chaudry, M.M. and J.M. Regenstein. "Implications of Biotechnology and Genetic Engineering for Kosher and Halal Foods." *Trends in Food Science Technology*, v.5, 1994. p. 165-168.

[34]Kolodinsky, Jane, Qingbin Wang, and David Conner. "rBST Labeling and Notification: Lessons from Vermont." *Choices*, third quarter 1998. p. 38-40. U.S. Court of Appeals for the Second Circuit. No. 876, August Term, 1995. (Argued: November 2, 1995 Decided: August 8, 1996) Docket No. 95-7819.

[35]Some have suggested that the industry use USDA's organic food labeling regulations, currently under development, as one way of telling consumers that foods are free of biotechnology products. Comment by Alan Goldhammer, scientific director of BIO, February 8, 1999.

biotechnology are less safe or nutritious than conventional foods. Food production interests believe that consumers, thinking that a product is different from conventional foods, may not gain the benefits from foods that have been modified genetically because they are uneasy with the technology and may not try the products. The industry supports FDA's reasoning in the draft guidance.[36]

Defenders of the agencies' policies suggest that to date genetically modified foods are similar to non-GMO foods and are easily regulated under the current policy structure. If they are substantially different, these foods must be regulated as if they were food additives and receive FDA approval before being marketed. They state that current GMOs are not a risk as no scientific evidence shows an effect on human or animal health. For instance, most plant toxins are acute toxins and are well known, and tests have been developed to detect them quickly.[37] So defenders argue that there are no proven long-term health consequences for humans. However, few long-term studies have been completed.

On May 27, 1998, FDA was sued by a group of concerned citizens over the agency's "traditional" policy on the sale of genetically modified foods (*Alliance for Bio-Integrity v. Shalala*, D.D.C., No. 1:98CV01300, May 27, 1998). The group claimed that FDA's refusal to require labeling and safety testing raises health and environmental concerns and makes it difficult to comply with religious dietary laws. The suit identified 36 genetically modified foods being consumed daily without the knowledge of U.S. consumers. The suit cited both the First Amendment's protection of religious freedom and the Religious Freedom Restoration Act of 1993, which requires that federal laws or regulations not impede the free exercise of religion. The plaintiffs said that FDA's policy failed to abide by the public notice and comment procedures of the Administrative Procedures Act, and allowed genetically modified foods into the marketplace without being identified as such. The suit also claimed that FDA's policy is a burden to consumers' abilities to follow religious dietary laws. The lawsuit challenged FDA's policy that genetically modified foods are considered safe unless they contain substances identified in the 1992 policy which are allergens or would change the character of the food. The plaintiffs want the agency to carry out the same testing and safety evaluations conducted for food additive petition approval because, they argue, changes that might occur as a result of genetic engineering might include unwanted, unpredictable new toxins and/or carcinogens, elevated levels of inherent toxins and/or carcinogens, and/or degradation of nutritional quality. In

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[36]The agencies have authority under existing laws to regulate these new products in the same manner as those developed through traditional agricultural and food processing. Food companies have not been required to disclose their method of development on the label. For example, sweet corn does not need to be labeled "hybrid sweet corn" because it was developed through cross-hybridization. Nor did FDA require special labeling for the Flavr Savr tomato, because the new tomato is not significantly different from conventional tomatoes. If a new food contains a protein derived from a food that commonly causes allergic reactions, and the developer cannot demonstrate that the protein is not an allergen, labeling is mandatory to alert sensitive consumers, because they would not expect to be allergic to the food.

[37]International Food Biotechnology Council, "Biotechnologies and Food: Assuring the Safety of Foods Produced by Genetic Modification," *Regulatory Toxicology and Pharmacology*, v. 12, 1990. p. S1- S196.

particular, they wanted FDA to require the labeling of these foods because the foods have been changed "materially" and allegedly violate the FFDCA. The suit stated that "FDA is permitting unpredictable changes to the characteristics of certain foods which may be difficult for consumers to detect."[38] On August 7, 1998, FDA, through the Department of Justice, asked the U.S. District Court for the District of Columbia to dismiss this case because it felt that such charges are not unique to genetic engineering and the same changes occur in foods that have not been modified. On September 29, 2000, the Court accepted FDA's view that genetically engineered foods did not need special labeling because of consumer demand or because of the process used to develop these foods. Nor did the court require premarket approval of the food.[39]

Environmental Issues

Proponents of bioengineered crops claim that genetic modification can be less harsh on the environment than other technologies. They suggest that fewer agricultural chemicals might be needed to grow pesticide tolerant or insect resistant crops and that land would need less repeated tilling, which could lead to less erosion and soil infertility.[40] Supporters of genetic modification think that new developments contribute to environmentally sustainable development and greater food production. While they believe government regulatory efforts adequately ensure consumer and environmental health, they are aware of growing consumer concerns and some want to increase transparency of the regulatory and development process.

Critics have expressed strong concerns about the long-term risks and consequences of cross-pollination and of the disruption to the "cellular ecology" of plants. They state that the U.S. policy is based on the assumption of safety but there is little research on ecological or food safety risks. Scientists have shown that genetically modified rapeseed (canola) pollen was spread to wild radish weed relatives in nearby fields. The experiment demonstrated that it was possible to create new strains of weeds resistant to herbicides.[41] If such weeds emerged widely, farmers would need new, different, or stronger herbicides to counter their spread. Such super weeds could severely decrease crop productivity. Furthermore, some scientists have expressed concern that the widespread use of genetically engineered plants could alter

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[38]Dern, Adrienne. "Justice Department Asks Court to Dismiss Lawsuit Challenging FDA's Policy on Genetically Engineered Foods," *Food Chemical News*, August 31, 1998. p. 10-13.

[39]FDA Talk Paper: "U.S. District Court Dismisses Genetically Engineered Food Law Suit Against FDA." October 6, 2000.

[40]Doyle, John J. and Gabrielle J. Persley, eds. *Enabling the Safe Use of Biotechnology: Principles and Practice*, Environmentally Sustainable Development Studies and Monograph Series No. 10 (Washington, D.C.: The World Bank, 1996). p. 7. Also several biotechnology companies modified corn to contain Bt, to kill the corn borer and other pests. The corn borer causes huge losses. Corn with Bt had a 7% increase in yield per acre, bringing the farmer, on average, an increased net return per acre of $16.88. Moffat, Anne Simon. "Toting Up the Early Harvest of Transgenic Plants," *Science, v.* 282, December 18, 1998. p. 2176-2178.

[41]Brookes, Martin. "Running Wild," *New Scientist*, v. 160, no. 2158, October 31, 1998. p. 38-41.

the ecology of natural plant communities and of wildlife food chains. Certain seed and herbicide companies agree with these critics, their point of view shaped by the possibility of development of "super weeds," rendering their products useless.[42]

Bt Resistance and Intervention Strategies. Concerns revolve around plants engineered to produce within their cells an insecticide called Bt that is produced naturally by strains of the bacterium *Bacillus thuringiensis.* The release of a study that showed in a laboratory that Bt corn pollen when eaten by Monarch butterfly larvae kill or stunt their growth engendered public concern.[43] Another concern is that large scale planting of crops containing Bt might lead to faster resistance development by insects. Critics of this technology state that large-scale production of engineered corn, soybeans and other foods will cause pests to develop resistance to Bt, thereby limiting its usefulness. It is not unusual for insects to develop resistance to pesticides that have been used for long periods of time. Organic farmers, in particular, are concerned because they do not have as many crop protection tools available as conventional farmers, and the loss of effectiveness of Bt could be a serious blow to their production. Due to these concerns, on February 18, 1999, Greenpeace, the Center for Food Safety, and some organic farmers sued EPA over its registrations of plant-incorporated protectant.[44] The suit calls on EPA to cancel all existing registrations for Bt crops, to cease the approval process for any new registrations, and to perform an environmental impact assessment analyzing the cumulative impacts from the current registrations.

Prior to these complaints, EPA determined that resistance to Bt can be slowed by requiring farmers to plant significant numbers of non-Bt seeds near the genetically modified resistant plants in designated separate areas called "refuges." The non-Bt plants allow pests to grow that will not develop Bt resistance. Since these pests will interbreed with their counterparts that eat Bt plants, there is less likelihood that a resistant super-pest could develop. If the "refuge" system is used by farmers, EPA

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[42]Critics also worry about altered organisms causing unpredictable and costly environmental damage over extended eco-ranges for sustained periods, and point to the cases of Dutch Elm disease, myxomatosis, and gypsy moths to illustrate their point of organisms spreading uncontrollably . Supporters claim that these invaders were not disease-causing GMOs, but were unpredicted consequences of unplanned introductions into new environments. Given multiple ecological problems related to farming practices such as nutrient runoff, for which there are no liability claims, it seems inappropriate to supporters that GMOs are lumped into these arguments. Critics suggest, however, that because genetically modified plant-incorporated protectant may be unsafe, their release into the environment is irreversible and unpredicted consequences may be hard to mediate. U.S. Congress, Office of Technology Assessment, *New Developments in Biotechnology — Field Testing Engineered Organisms, Genetic and Ecological Issues*, no. 3, OTA-BA-350 (Washington, DC, May 1988) chapter 5.

[43]Kaesuk Yoon, Carol. "Altered Corn May Imperil Butterfly, Researchers Say," *New York Times*, May 20, 1999. p. A1 and A20.

[44]See website: [http://www.icta.org/legal/bt2.htm]

estimates that the eventual development of resistance to Bt by insect pests could be extended 10 or more years.[45]

EPA now requires the use of insect resistance management (IRM) plans for some crops. EPA originally granted all the plant-incorporated protectants conditional registrations. With the registrations for corn and cotton to expire in 2001, as a condition of re-registration, companies will be required to develop effective IRM plans for these crops. Most re-registration applications have been submitted, and EPA is evaluating the information and could impose new conditions. Critics of the technology want mandatory IRM plans, for they claim that if the plans are voluntary, farmers will either not plant the nonresistant refuges or plant refuges that are too small to be effective.[46]

There is a voluntary IRM plan in place for potatoes, as recommended by a 1995 scientific advisory panel, and Monsanto is requiring compliance by growers who contract with it for the seeds.[47] Ongoing evaluation of IRM may result in additional mandatory requirements.

There is agreement, however, that toxic anti-pest substances produced by plants used for food must be proven safe. EPA points to an example of potato leaves that naturally contain a pesticidal substance that could cause birth defects. Since humans do not eat potato leaves, there is no need to regulate the substance; however, if spinach were genetically modified to contain the potato-leaf toxin, regulation would be needed.

Liability. There is also concern about liability. Who would pay if other crops or fields were ruined because of cross-pollination with these new seeds? An opponent

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[45]Environmental Protection Agency. Scientific Advisory Panel on *Bacillus thuringiensis* (Bt) Plant-incorporated protectant. Transmittal of the final report of the FIFRA Scientific Advisory Panel on *Bacillus thuringiensis* (Bt) Plant-incorporated protectant and Resistance Management. Meeting held on February 9-10, 1998. (Docket Number: OPPTS-00231).

[46]As part of the ongoing discussions with EPA and USDA, major see developers (accounting for more than 90% of the U.S. Bt seed corn market) have proposed that by the year 2000, they will require growers in contracts to plant 20% to 50% of their acreage in non-genetically engineered varieties. The agreement among the seed companies calls for a 20% refuge requirement in primary cotton-growing areas, with the minimum rising to 50% where Bt corn is grown in proximity to Bt cotton. "Industry Plan for Bt Resistance Management Gets Mixed Reaction," *Food Regulation Weekly*, v, 18, January 1999. p. 3-5.
EPA is considering this proposal among its other options for implementation of IRM requirements. In the spring of 1999, EPA and USDA are planning a joint workshop to examine existing Bt crop IRM, including methods, implementation, grower's incentives, remedial actions if insect resistance is discovered, and compliance and enforcement issues. They are also interested in supporting the development and implementation of six to ten USDA Regional Pest Management Centers.

[47]Website: [http://www.monsanto.com/ag/asp/Monsanto.asp?MKTID=9999&PDTID=0] contains a statement, "We require every grower who decides to plant YieldGard corn to sign an agreement to establish a refuge adjacent to his or her YieldGard acreage to ensure a population of susceptible corn borers to mate with any naturally resistant borers that survive exposure to the Bt."

of biotechnology, Jeremy Rifkin, says, "The insurance industry has quietly let it be known that it would not insure the release of genetically engineered organisms into the environment against the possibility of widespread environmental damage, because the industry lacks a risk-assessment science — a predictive ecology — with which to judge the risk of any given introduction."[48] According to Dr. L. Val Giddings, Vice President for Food and Agriculture, Biotechnology Industry Organization, the industry representatives directly dispute this claim, and say there is insurance available.

Economic Concerns

Critics are concerned about the growing presence of large agricultural conglomerate companies controlling the supply of seeds containing bioengineered traits. Growers' profits from bioengineered crops more than tripled from 1996 to 1997.[49] In 1996, U.S. farmers had planted mostly Bt cotton, Bt corn, and herbicide tolerant soybeans. In 1997, they expanded acreage for those crops and added herbicide tolerant cotton and potatoes.[50] Planted acreage has continue to increase for all crops except corn. Adoption rates vary by year, crop product, and location. They depend on the level of infestation of a targeted pest. They also depend on world commodity prices and the kind of corn that importers are willing to accept. Supporters of this technology cite convenience and lower costs as the main reasons for high farmer adoption rates.[51] But critics complain about the consolidation of patent ownership of this new technology which they believe constitutes monopolistic power in the marketplace. Their distrust is based in part on concern about the dependency such concentration brings to the agricultural sector and the possible abuse from such control.

The reasons for this concern vary. The concentration of control of patents in agricultural biotechnology raises concerns for some farmers and consumers that multinational corporations want to simplify the regulatory processes of governments to gain easier approval for their products without adequate review. Because so much of the technology is held by private companies, some regulators and researchers are concerned about how difficult it can be to obtain necessary information for appropriate regulation.

Others are concerned that large companies can conduct field experiments, sell seeds to farmers, and market genetically engineered products without appropriate

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[48]Rifkin, Jeremy. "Genesis II; Commercial Prospects of Genetic Engineering and Biotechnology," *Across the Board*, v. 35, no.6, June, 1998. p. 29.

[49]Beachy, Roger N. Statement Presented to the House Committee on Agriculture, Subcommittee on Risk Management, Research and Specialty Crops, on behalf of the Council for Agricultural Science and Technology, March 3, 1999.

[50]James, Clive. "Global Review of Commercialized Transgenic Crops: 1998," *International Service for the Acquisition of Agri-Biotech Applications Briefs*, no. 8, ISAAA: Ithaca, NY; in 1997, profits totaled $315 million, up from $92 million in 1996.

[51]Riley, Peter A. and Linwood Hoffman. "U.S. Farmers Are Rapidly Adopting Biotech Crops," *Agriculture Outlook*, August 1998. p. 21-24.

attention to tests for the safety of consumers and the environment. Critics want more testing before farmers expand their planted acreage. There is uncertainty about how much testing is required, whether it should focus on the new genes themselves or on the substances they produce in the plant. Federal agencies can ensure adequate safety testing of biotechnology products by requiring companies to review impacts or by conducting tests for themselves. The FDA proposed rule, discussed earlier, could mandate that industry submit this data. However, others feel that independent testing is necessary to validate the safety of the food product.

There also appears to be concern about how much control companies wield over research in food and agricultural biotechnology. Companies hold patents and own specific germplasm[52] and research techniques needed for plant research. Some companies claim partial ownership of a food product created using their patented technologies. Biotechnology researchers have raised concerns that some private company scientists are not permitted to share innovations in research.

Most food biotechnology research is financed with private, not public, money, and the total amount spent is confidential. One newspaper reported that Monsanto estimates that research and development time and costs to create a commercial product are about 10 years and about $300 million. For every genetically engineered seed that goes to field trials, 10,000 have failed along the way.[53] Corporations charge steep prices for this technology, claiming the need to recoup their investment to be able to research the third and fourth wave of products.

Most identifiable public funding for food biotechnology research for plant genome research is being sponsored by the U.S. Department of Agriculture (USDA). The Clinton Administration did not track federal food and agricultural biotechnology funding of research as a line item in federal budget analyses. Consequently, the total amount of public funding for this research is unclear.[54]

Public research funding under the authority of the Bayh-Dole Act of 1985[55] allows universities receiving grants for plant genomics research to hold the intellectual property rights for any useful discoveries. The Act has accelerated the linkages between university research and the creation of consumer products and contributed to the international competitiveness of U.S. industries. It has also encouraged research on minor-use crops.

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[52]Germplasm refers to the basic genetic material of a species. There are germplasm "banks," for a variety of different life forms, where representative species are stored so that they can be reproduced for future studies that require their genetic material.

[53]Weiss, Rick. "Seeds of Discord," *Washington Post*, February 3, 1999. p. A1 and A6.

[54]Gabriel, Cliff, Deputy to the Associate Director of the Science Division, Office of Science and Technology Policy. *The White House, conversations with the authors*. February 23, 1999.

[55]Bayh-Dole Act, P.L. 96-517, §6(a), December 12, 1980, 94 Stat. 3019 (35 §§200 to 212); P.L. 98-620, Title V,§501, November 8, 1984, 98 Stat. 3364 (35§§201 to 203, 206 to 208, 210, 212); P.L. 99-502, §9(c), October 20, 1986, 100 Stat. 1796 (35 § 210).

International Trade Issues

At the present time, the United States is leading the world in biotechnological research, development of genetically modified organisms (GMO's as they are called internationally), and sales of the technology worldwide. The United States has no immediate challengers to this trading position. Some trade experts suggest that trading partners whose policies strongly reflect consumer concerns about the new technology are merely attempting to allow their own domestic industry time to develop a competitive position in this trade. For example, the European Union (EU) has now required that all GMOs be labeled as such, and has severely limited imports of food containing genetically engineered crops and foods. The United States, however, claims that there is not scientific basis to presuppose that genetically modified food products are more risky or substantially different from other products. U.S. officials believe that decisions on trade should be science-based and U.S. regulatory policy reflects this thinking. Such competition for leadership in biotechnology has influenced trade relationships among U.S. trading partners. Japan has diminished its import of U.S. corn after finding StarLink in their imports.

Concluding Remarks

Recombinant DNA technology is producing revolutionary changes in agriculture. Supporters of this technology emphasize the potential benefits from these changes including the promise of higher yields and nutritionally enhanced foods from genetically modified commodities with reduced environmental impact. Opponents of the use of rDNA technology in agriculture are concerned about possible hazards to human, animal, and environmental health. They advocate more safety testing and labeling of products. Many are concerned about the possible consolidation and control of agricultural biotechnology by a handful of multinational corporations.

Since the technology potentially can provide greater yields, farmers are rapidly planting genetically modified seeds. As the U.S. experience with this new technology grows, it may become necessary to amend regulatory policies to protect public safety and the environment while allowing genetically modified crop development to progress. The agencies involved in regulating genetically modified foods (FDA, APHIS, and EPA) are implementing policies based upon a 1986 framework document that coordinates their regulatory activities for biotechnology products. This framework applies the same set of regulations to all food products and does not differentiate between foods that are produced with rDNA technologies and those that are produced by traditional methods. However, with the January 18, 2001 proposed rule, making mandatory the current voluntary consultation process whereby the industry now must formally notify the agency 120 days before releasing a food product onto the market. The proposed rule also lists the safety test data that must accompany the notification.

Although the United States is leading the world in the production and sales of genetically engineered products, a few foreign countries have resisted or diminished their U.S. commodity imports because of concerns over the safety of these bioengineered crops. Some suggest that foreign countries' resistance to genetically engineered crops can be traced to their desire to allow their domestic industry time

to develop a competitive position in this trade and the growing unease in international trade relationships over the fast adoption by U.S. farmers of bioengineered crops. Others argue that Congress could exercise more oversight over the regulation of these food crops, fund more public research, and encourage the Administration to negotiate the easing of trade barriers and harmonizing standards. Congress will be closely monitoring these events.