U.S. REGULATION OF PRODUCTS DERIVED FROM BIOTECHNOLOGY

U.S. authorities regulate bioengineered products based on a determination of their safety to humans and the environment. In the United States, four federal agencies are responsible for ensuring the safety of bioengineered plants, animals, seafood, microorganisms, and the products obtained from them:

- USDA / Animal Plant Health Inspection Service (APHIS)
- Environmental Protection Agency (EPA)
- Food and Drug Administration (FDA)
- USDA / Food Safety and Inspection Service (FSIS)

Depending on the properties and intended use of a bioengineered plant, animal, seafood, microorganism, or product, one or more of these agencies is responsible for regulation or approval:

- APHIS issues a "determination of non-regulated status" for the commercialization of bioengineered plants and pathogenic plant microorganisms that meet its safety criteria, with a particular focus on their environmental release (planting). In addition, APHIS issues permits and acknowledges notifications for field testing, importation, and inter-state movement of genetically engineered organisms. USDA has authority to prevent the introduction and dissemination of plant pests under the Federal Plant Pest Act and the Plant Quarantine Act.

- EPA approves bioengineered pesticides, bioengineered plants with pesticidal characteristics, and reviews "intergeneric microorganisms" (formed by combining genetic material from microorganisms in different taxonomic genera) prior to activities related to commercialization. EPA focuses on food safety (tolerance levels) and the environment (target and non-target organisms). EPA regulates *pesticides* under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and the Federal Food, Drug, and Cosmetic Act (FFDCA). Generally, before a pesticide may be sold, distributed or used in the United States, it must be registered under FIFRA. Under FFDCA, EPA is responsible for setting tolerances or exemptions from the requirement of a tolerance for pesticide residues in foods. EPA regulates *intergeneric microorganisms* under Section 5 of the Toxic Substances Control Act (TSCA). Before a new microorganism can be manufactured, processed or imported for a commercial purpose, a notice must be submitted to EPA.

- FDA regulates foods (except meat, poultry, and egg products: see FSIS below), including fruits, vegetables, grains, fish, and shellfish, milk, and substances added to food such as vegetable oils, flavors, sweeteners, spices, and enzymes. Food additives, color additives, and new animal drugs require pre-market approval by FDA. FDA consultation is recommended for bioengineered foods. Additionally, FDA can take regulatory action

against foods that are adulterated or improperly labeled. A food is considered adulterated, and unlawful, if it bears or contains an added poisonous or deleterious substance that may render the food injurious to health or a naturally occurring substance at a level that is ordinarily injurious.

- FSIS is the public health agency in USDA responsible for ensuring that the nation's commercial supply of meat, poultry, and egg products is safe, wholesome, and correctly labeled and packaged. FSIS approves the slaughter of research animals for food for human consumption. The researcher is required to obtain approval prior to slaughter by submitting appropriate material outlined in guidelines published by FSIS (*Decision Criteria for the Evaluation of Nontransgenic Animals from Transgenic Animal Research and the Points to Consider in the Food Safety Evaluation of Transgenic Animals from Transgenic Animal Research).* The researcher must present the approved animal(s) for slaughter, at the specific date and place noted on the approval, to the FSIS Veterinary Medical Officer (VMO). The animal(s) are passed for human consumption based on the on-site inspection by the VMO.

The timeframe for approval of a bioengineered product depends on which agencies are regulating or being consulted. This normally ranges between 2 and 12 months, with an average product approval time of 6-8 months. APHIS expedites a determination of non-regulated status for organisms which are largely similar to organisms already granted such status. EPA decisions are normally made within 12 months from receipt of the application, but take 60 to 90 days in the case of applications for R&D and commercial use of intergeneric microorganisms. However, product approval can be delayed if the application is incomplete or if more data is required to conclude the safety assessment.

BACKGROUND

Since 1990, more than 25 agricultural biotechnology products have successfully progressed through the U.S. regulatory system to commercialization into the marketplace. Some of these products are very familiar. For example, in 1990, FDA approved the commercial use of chymosin (rennet) produced from bacteria for use in making cheese and other dairy products. In 1994, the "flavr savr" tomato was first commercialized. In 1996, EPA approved the use of a genetically engineered *Bacillus thuringiensis*, a commonly used microbial pesticide. Other products approved in the United States represent technological advances in producing crops with new insect and disease resistances, other improved agronomic characteristics, and improved processing characteristics. In the last three years, the United States approved for commercial use insect resistant corn, cotton and potato; herbicide tolerant canola, cotton, soybeans and corn; delayed ripening tomatoes; and canola with a different oil composition.

In the 1970s, the United States regulatory framework for agricultural biotechnology products initially focused on contained testing in laboratories and greenhouses with the publication of the "National Institutes of Health Guidelines for Research Involving Recombinant DNA Molecules"

(NIH guidelines). As products moved from basic research and development to field testing and eventual commercial release, the United States government published the "Coordinated Framework for Regulation of Biotechnology" in 1986 to explain how the federal agencies would regulate research as well as commercialization.

The Coordinated Framework takes a "vertical" or sectoral approach to the regulation of biotechnology products, including agricultural biotechnology products. Under this approach, biotechnology products are regulated, using existing statutes, as are other similar products. For example, biotechnology products that are food would be regulated by the Food and Drug Administration (FDA) under the Food, Drug and Cosmetic Act (FFDCA), biotechnology products that are pesticides would be regulated by the Environmental Protection Agency (EPA) under the Federal Insecticide Fungicide and Rodenticide Act (FIFRA) and FFDCA, and plant pests would be regulated by the United States Department of Agriculture (USDA) under the Plant Pest Act and the Plant Quarantine Act, while research food animals are regulated by USDA/FSIS under the Federal Meat Inspection Act and the Poultry Products Inspection Act. In the Coordinated Framework, USDA, EPA, and FDA are identified as the primary regulatory agencies responsible for products of agricultural biotechnology. Under this framework, some products may be regulated by all three agencies and some may be regulated by one or two agencies.

The basis of the Coordinated Framework was the belief that use of existing health and safety laws provided more immediate regulatory protection and certainty than was possible with new legislation specific to biotechnology. Moreover, there did not appear to be an alternative, unitary statutory approach because the broad spectrum of products obtained through genetic engineering cuts across many different types of products regulated by different agencies. The U.S. Government believes that the new techniques of genetic engineering are an extension of biotechnology in general and, thus, new products developed through these techniques are extensions of existing product classes.

FOR MORE INFORMATION

Detailed descriptions of procedures and contact information related to biotechnology can be obtained from the following U.S. government websites:

APHIS:	http://www.aphis.usda.gov/oa/new/ab.html
EPA:	http://www.epa.gov/opptintr/biotech/index.html (for TSCA)
	http://www.epa.gov/pesticides/activity.htm#bio (for biopesticides)
FDA:	http://vm.cfsan.fda.gov/~lrd/biopolcy.html
FSIS:	*Website on biotechnology still under construction*. For general information, go to http://www.fsis.usda.gov/index.htm, or contact Pat Basu at pat.basu@usda.gov

Authorities and principles for approval of genetically modified organisms (GMOs) in the United States

	Genetically modified organism / product		
Agency / applicable statute(s)	*Plants/Pathogenic plant microorganisms*	*Pesticides and genetic material necessary for their production*	*Animals, seafood, plants, and their products containing GM "food additives" (includes growth hormones, bio-engineered genetics)*
APHIS (USDA) **Plant Pest Act; Plant Quarantine Act; National Environmental Policy Act** ***FSIS (USDA)*** **Federal Meat Inspection Act; Poultry Products Inspection Act**	APHIS considers the plant pest risk potential of the plant or pathogenic plant microorganism and conducts an environmental assessment that considers potential impacts to human health and the environment. APHIS regulates but does not register these products.	N/A	*Meat of animals:* FSIS must issue a permit for the slaughter of genetically modified research animals for human consumption.
EPA **Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) / Federal Food Drug and Cosmetic Act (FFDCA)** **Toxic Substances Control Act (TSCA)**	EPA assesses genetically modified plant-pesticides and microbial pesticides for adverse effects to humans, nontarget organisms, and the environment. Safe residue tolerance levels are established before the pesticide is registered for sale and distribution. EPA also requires resistance management for Bt toxins as plant-pesticides. --*Under FIFRA/FFDCA*, EPA has responsibility for GM plants and microorganisms with *pesticidal characteristics*. Companies must register these with EPA. --*Under TSCA*, EPA regulates intergeneric microorganisms for commercial purposes, including R&D for commercial purposes. TSCA jurisdiction does not cover substances that fall under the jurisdiction of FIFRA and FFDCA.		N/A
FDA **Federal Food Drug and Cosmetic Act (FFDCA)**	FDA consultation is not required--but is recommended--by FDA to market GM food or food ingredients, unless they are determined to contain "food additives" (see box to right). However, FDA has "post-market" regulatory powers: the adulteration provisions of FFDCA give FDA broad authority to ensure the safety and wholesomeness of foods and food ingredients. For this reason, companies normally choose to consult with FDA before marketing their product. The FDA consultation process is guided by its 1992 "Policy on foods derived from new plant varieties" (for the FDA voluntary consultation process, see table 2).		1. *"Food additives,"* i.e. substances intentionally introduced into food. Such substances must receive FDA approval ("pre-market" authority) unless they are generally recognized as safe (GRAS). 2. Substances introduced into animals are considered to be *"new animal drugs"* (e.g. rBST) if they affect the structure or function of the animal. Review is required by FDA for research ("investigations") and for commercial use. FDA authorizes research animals slaughtered under USDA authority and food use for species not inspected by USDA (e.g. fish, shellfish, bees, gamebirds, wildlife).

GMO product approval procedure for field testing, interstate movement, and importation in the United States

	Genetically modified organism / product		
Agency	*Plants/Pathogenic plant microorganisms, pesticides, and genetic material necessary for their production*	*Animals, seafood, plants, and their products containing GM "food additives"*	**Review period / public comment**
APHIS/FSIS	*APHIS--Plants and pathogenic plant microorganisms:* 1. "Permit" or "notification" is required to initiate field testing. 2. Company submits "petition" showing the plant is safe and does not pose a plant pest risk, based on field trial and any scientific literature. 3. After reviewing the petition, APHIS issues a "Determination of Non-regulated Status." Note: new organisms that are similar to previously deregulated organisms and which pose no new plant pest risks undergo an expedited process.	*FSIS--GM research animals for slaughter:* FSIS issues permits under Title 9 CFR part 309.17 and 381.75.	*Determination of Non-regulated Status*: 180 days (60-day public comment period). *Field Testing permits*: 120 days ("Notification" turn-around of 10-30 days). *Permissions to slaughter*: no fixed FSIS review period has been established. This is mainly due to the very small number of cases to date.
EPA	*Plant-pesticides and microbial pesticides only (FIFRA/FFDCA):* 1. EPA issues an "experimental use permit" to test the plant-pesticide or microorganism, based on criteria for test containment and potential hazards to humans and nontarget organisms. 2. Based on the experiment's results and other data submitted, EPA issues a "registration" for sale and distribution after assessing risks to humans and the environment. *Microorganisms (TSCA):* Under TSCA, a Microbial Commercial Activity Notice (MCAN) is required at least 90 days prior to commercial activities (manufacture, import or processing). A TSCA Experimental Release Application (TERA) is required at least 60 days prior to field testing of microorganisms in R&D for commercial purposes. Some exemptions from reporting apply for microorganisms meeting specific criteria. TSCA does not yet regulate transgenic plants.		*Under FIFRA/FFDCA*, there is no statutory time frame for EPA approval of new products, but a decision is usually made within 12 months if the application is complete. *Under TSCA*, the review period is 60 days for TERAs and 90 days for MCANs.
FDA	*Food and feed products from new plant varieties not containing "food additives":* -Voluntary consultation process: no pre-market approval necessary. -FDA "decision tree" describes the standard industry must meet in ensuring safety of these foods. -FDA consultation can occur any time before use of product, independent of APHIS (or EPA) review.	Pre-market approval necessary: - If food additive, approval process under Title 21 CFR, part 171. - If new animal drug, approval process under Title 21 CFR, part 500.	*Food additives and new animal drugs requiring pre-market approval*: 180 day review period.

U.S. government contact list for regulatory issues related to biotechnology

Animal Plant Health Inspection Service (USDA)

Sivramiah Shantharam, Branch Chief, Biotechnology Evaluations Branch, Scientific Services, PPQ, tel: (301) 734-4882 / fax: (301) 734-8669
Other contacts: Rebecca Bech, Arnold Foudin, James White

Environmental Protection Agency

--*FIFRA/FFDCA implementation*:
Janet Anderson, Director, Biopesticides and Pollution Prevention Division, Office of Pesticide Programs, tel: (703) 308-8712 / fax: (703) 308-7026
Phil Hutton, Chief, Microbial Pesticides Branch, Biopesticides and Pollution Prevention Division, tel: (703) 308-8712 / fax: (703) 308-7026 hutton.phil@epamail.epa.gov

--*TSCA implementation*:
Flora Chow, Chief, New Chemical Notice Management Branch, Chemical Control Division, Office of Pollution Prevention and Toxics, tel: (202) 260-3406 / fax: (202) 260-0118

Foreign Agriculture Service (USDA)
Bernice Slutsky, Biotechnology and Biosafety Coordinator, Food Safety and Technical Services Division, International Trade Policy, tel: (202) 720-4261 / fax: (202) 690-0677
Kate DeRemer, Agricultural Economist, Food Safety and Technical Services Division, International Trade Policy, tel: (202) 690-4898 / fax: (202) 690-0677

Food and Drug Administration
James Maryanski, tel: (202) 205-4359 / fax: (202) 401-2893

Food Safety Inspection Service (USDA)
Pat Basu, Director, Chemistry and Toxicology Division, tel: (202) 501-7319 / fax: (202) 501-7639
Bharat Patel, Inspection System Development Division, tel: (202) 720-0334 / fax: (202) 205-0281

Office of the United States Trade Representative
James Murphy, Assistant USTR for Agricultural Affairs, tel: (202) 395-6127 / fax: (202) 395-4579

State Department
Marilyn Bruno, Trade Officer, Office of Agricultural Trade Policy and Programs, Bureau of Economic and Business Affairs, tel: (202) 647-2062 / fax: (202) 647-1894

Mary McLeod, Director, Office of Ecology and Terrestrial Conservation, Bureau of Oceans, Environment and Science, tel: (202) 647-2418 / fax: (202) 736-7351 mmcleod@state.gov

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