The Coordinated Framework for the Regulation of Biotechnology

Plain language information on the biotechnology regulatory system

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The U.S. Department of Agriculture
The U.S. Environmental Protection Agency
The U.S. Food and Drug Administration

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The goal of this document is to provide plain language information that will be easily accessible to new entrants to the regulatory system and members of the public.

THE COORDINATED FRAMEWORK FOR REGULATION OF BIOTECHNOLOGY

The Coordinated Framework for the Regulation of Biotechnology outlines a comprehensive U.S. regulatory policy for ensuring the safety of biotechnology products. It was adopted in 1986 and most recently updated in 2017. This policy supports innovation, protects health and the environment, and promotes trust in the regulatory system. To help developers and the public better understand U.S. regulatory processes for biotechnology products, this document provides a high-level overview of the roles and responsibilities of U.S. regulatory agencies under the Coordinated Framework.

U.S. biotechnology regulatory policy is that regulation should be based on science, proportionate to the risks posed, and based on the product (not the process used to develop the product). It also states that existing laws provide necessary authorities for agencies to regulate biotechnology and agencies have separate responsibilities. Agencies coordinate as needed, and the regulatory status of a product with one agency does not affect the regulatory status of that product with other agencies. Meeting with regulatory agencies early in product development can help developers determine the process or processes that are most relevant for a product.

The United States uses existing laws to regulate products of biotechnology rather than a special biotechnology law. As a result, different agencies may regulate different aspects and uses of a product. The primary agencies involved in U.S. biotechnology regulation are the Animal and Plant Health Inspection Service (APHIS) in the U.S. Department of Agriculture (USDA); the Food and Drug Administration (FDA) in the Department of Health and Human Services (HHS); and the Environmental Protection Agency (EPA). Multiple offices, programs, and centers within the agencies are involved in biotechnology regulation (Table 1). New entrants to the regulatory system and members of the public can use Table 2 to determine which agency or agencies may regulate particular product types. Individuals with questions about the regulation of a particular product can submit their questions to one or more agencies via the Contact Us page on the Unified Website for Biotechnology Regulation. Examples of case studies describing how specific product types would be regulated by each agency are included for plants, plant cells, plant products of biotechnology in Table 3; for animals, animal cells, and animal products produced with biotechnology in Table 4; and for microorganisms produced with biotechnology, microbial cells, and microbial products produced with biotechnology in Table 5. These case study examples are not intended to be inclusive of all products of biotechnology.

TABLE 1. U.S. GOVERNMENT AGENCIES, OFFICES, AND PROGRAMS THAT OVERSEE PRODUCTS OF BIOTECHNOLOGY

DEPARTMENT	AGENCY	OFFICE OR PROGRAM
DEPARTMENT OF AGRICULTURE (USDA)	Agricultural Marketing Service (AMS)	Food Labeling and Disclosure Division (FDLD)
	Animal and Plant Health Inspection Service (APHIS)	Biotechnology Regulatory Service (BRS)
		Veterinary Services (VS)
	Food Safety and Inspection Service (FSIS)	Office of Field Operations (OFO)
		Office of Policy and Program Development (OPPD)
		Office of Public Health Science (OPHS)
DEPARTMENT OF HEALTH AND HUMAN SERVICES (HHS)	Food and Drug Administration (FDA)	Center for Biologics Evaluation and Research (CBER)
		Center for Drug Evaluation and Research (CDER)
		Center for Devices and Radiological Health (CDRH)
		Center for Food Safety and Applied Nutrition (CFSAN)
		Center for Veterinary Medicine (CVM)
ENVIRONMENTAL PROTECTION AGENCY (EPA)	Office of Chemical Safety and Pollution Prevention (OCSPP)	Office of Pesticide Programs (OPP)
		Office of Pollution Prevention and Toxics (OPPT)

TABLE 2. SUMMARY OF U.S. REGULATORY AGENCY ROLES IN REGULATING DIFFERENT CATEGORIES OF PRODUCTS PRODUCED WITH BIOTECHNOLOGY

Ensure you review the categories below to identify all the agencies that may be involved in regulating your product.

PRODUCT	AGENCY	PLANTS, PLANT CELLS, PLANT PRODUCTS	ANIMALS, ANIMAL CELLS, ANIMAL PRODUCTS	MICROORGANISMS AND OTHER PRODUCTS
FOOD FOR HUMANS	USDA-AMS	FDLD is responsible for enforcing compliance with bioengineered labeling requirements of human foods that contain recombinant DNA, including certain foods that are or contain plants, animal products, or microorganisms. Information can be found at National Bioengineered Food Disclosure Standard.		
	USDA-APHIS	BRS regulates importation, interstate movement, and environmental release of modified plants that may pose a plant pest risk. Information about this process can be found at Regulatory Exemptions and Confirmations, Regulatory Status Review, and Biotechnology Permits.	BRS regulates importation, interstate movement, and environmental release of modified animals that may pose a plant pest risk. Information about this process can be found at Biotechnology Permits. VS regulates importation of livestock (including poultry and aquatic animals) that may pose a health risk to	BRS regulates importation, interstate movement, and environmental release of modified microorganisms that may pose a plant pest risk. Information about this process can be found at Biotechnology Permits and draft Guide for Submitting Applications for Microorganisms.

			livestock, as well as importation of their cell lines and germplasm, and materials derived from them. (VS also regulates, or supports regulation of, interstate movement of livestock, including poultry, and germplasm in conjunction with each State's regulations. Information including VS guidance and permitting for importing animal products, live animals (includes semen and embryos), and veterinary biologics, as well as VS guidance and permitting for import and interstate movement for organisms and vectors, can be found at Imports: Animal and Animal Products. Additional information about APHIS VS regulatory authority is codified in 9CFR Subchapter I.	
	USDA-FSIS	OPPD and OFO verify the labeling of meat, poultry, Siluriformes fish and egg products, including those containing ingredients developed with modified plants if FDLD requires disclosure. Information about this process can be found at labeling and label approval.	FSIS ensures domestic and imported meat (including Siluriformes fish), poultry, and egg products are safe, wholesome, and properly labeled, including products made from modified animals and products made from animal cells. FSIS has a collaborative role with FDA following FDA's safety assessment, where FDA determines whether meat, poultry, and egg products derived from the intentional genomic alterations are safe for food. FSIS reviews and approves products of new technologies, including products	FSIS is responsible for determining the suitability of ingredients, including those developed with microorganisms and that they are properly labeled, including use of processing aids for use in meat (including Siluriformes fish), poultry, or egg products. OPPD and OFO verify the labeling of meat (including Siluriformes fish), poultry, and egg products, including those containing ingredients developed with modified microorganisms. Information about this process can be found at labeling and label approval.

			developed with biotechnology, and ensures the suitability of all ingredients used in meat and poultry products. Suitability relates to the effectiveness of the ingredient in performing the intended purpose of use and the assurance that the conditions of use will not result in a product that is adulterated or misbranded (labeled in a manner that misleads the consumer). Substances recognized as safe and suitable under the approved conditions of its intended use are those listed in 9 CFR 424.21(c) and those that are listed in FSIS Directive 7120.1, "*Safe and Suitable Ingredients in Meat, Poultry, and Egg Products*." Further information can be found at FSIS Compliance Guideline Procedures for New Technology Notifications and Protocols | Food Safety and Inspection Service (usda.gov), and FSIS Directive 7800.1- FSIS Responsibilities in Establishments Producing Cell-Cultured Meat and Poultry Food Products | Food Safety and Inspection Service (usda.gov).	
	HHS-FDA	CFSAN oversees the safety of all plant food products for humans. Information can be found at Food Ingredients & Packaging | FDA. Food from New Plant Varieties | FDA.	CFSAN oversees the safety of dairy products, eggs (but not egg products), and fish other than Siluriformes (e.g., catfish). Information can be found at Food Ingredients & Packaging | FDA. CFSAN oversees food safety of human food products made from cultured	CFSAN oversees the safety of all microbial food products for humans. Information can be found at Food Ingredients & Packaging | FDA.

			animal cells during cell collection, selection, and growth, when the cells are from animals whose food safety is regulated by FSIS (livestock, poultry, Siluriformes). CFSAN also oversees the subsequent processing, packaging, and labeling when the cells are derived from animals not regulated by FSIS. Information about this program can be found at Human Food Made with Cultured Animal Cells | FDA. CVM reviews human food safety of IGAs in food products derived from modified animals and of drug residues in human food products from animals treated with biotech (and non-biotech) animal drugs. Information about the IGA program can be found at Intentional Genomic Alterations (IGAs) in Animals | FDA. Information about evaluating the food safety of animal drug residues in human food can be found at Evaluating the Human Food Safety of New Animal Drugs | FDA.	
	EPA-OCSPP	OPP regulates PIPs produced by plants for safety of dietary exposure to pesticide residues in human and animal food. Information on regulation of PIPs under FIFRA and FFDCA can be	OPP regulates genetic modifications in pest animals intended for use as a pesticide for safety of dietary exposure in human and animal food. Information on regulation of emerging biotechnology pesticides can be found	OPP regulates microbial pesticides for safety of dietary exposure to residues in human and animal food. Information on regulation of emerging biotechnology pesticides can be found at Regulation of Biotechnology under TSCA and FIFRA.

		found at Overview of Plant Incorporated Protectants	at Regulation of Biotechnology under TSCA and FIFRA.	
FOOD FOR ANIMALS	HHS-FDA	CVM oversees the safety of all plant food products for animals. Information about its programs can be found at Food from New Plant Varieties | FDA. Animal Food & Feeds | FDA.	CVM oversees the safety of all animal-derived food products for animals. CVM also oversees food safety of animal food products made from cultured animal cells during cell collection, selection, and growth, as well as subsequent processing, packaging, and labeling. Information about CVM's procedures for animal food products generally is available at Animal Food & Feeds | FDA. CVM reviews animal food safety of IGAs in food products derived from modified animals. Information about this program can be found at: Intentional Genomic Alterations (IGAs) in Animals | FDA.	CVM oversees the safety of all microbial food products for animals. Information about CVM's procedures for animal food products generally is available at Animal Food & Feeds | FDA.

	USDA-APHIS	BRS regulates importation, interstate movement, and environmental release of modified plants that may pose a plant pest risk. Information about this process can be found at Regulatory Exemptions and Confirmations, Regulatory Status Review, and Biotechnology Permits.	BRS regulates importation, interstate movement, and environmental release of modified animals that may pose a plant pest risk. Information about this process can be found at Biotechnology Permits. VS regulates importation of livestock (including poultry and aquatic animals) that may pose a health risk to livestock, as well as importation of their cell lines and germplasm, and materials derived from them. VS also regulates, or supports regulation of, interstate movement of livestock (including poultry) and germplasm in conjunction with each State's regulations. Information including VS guidance and permitting for importing animal products, live animals (includes semen and embryos), and veterinary biologics, as well as VS guidance and permitting for import and interstate movement for organisms and vectors, can be found at Imports: Animal and Animal Products. Additional information about APHIS VS regulatory authority is codified in 9CFR Subchapter I.	BRS regulates importation, interstate movement, and environmental release of modified microorganisms that may pose a plant pest risk, Information about this process can be found at Biotechnology Permits and draft Guide for Submitting Applications for Microorganisms.

	EPA-OCSPP	OPP regulates PIPs produced by plants for safety of dietary exposure to pesticide residues in human and animal food. Information on regulation of PIPs under FIFRA and FFDCA can be found at Overview of Plant Incorporated Protectants.	OPP regulates genetic modifications in pest animals intended for use as a pesticide for safety of dietary exposure in human and animal food. Information on regulation of emerging biotechnology pesticides can be found at Regulation of Biotechnology under TSCA and FIFRA.	OPP regulates microbial pesticides for safety of dietary exposure to residues in human and animal food. Information on regulation of emerging biotechnology pesticides can be found at Regulation of Biotechnology under TSCA and FIFRA.
PESTICIDES	EPA-OCSPP	OPP regulates PIPs produced by plants for human and environmental risks, including dietary exposure to pesticide residues in human and animal food. Information on regulation of PIPs under FIFRA and FFDCA can be found at Overview of Plant-Incorporated Protectants.	OPP regulates genetic modifications in pest animals intended for use as a pesticide for human and environmental risks, including dietary exposure to pesticide residues in human and animal food. Information on regulation of emerging biotechnology pesticides can be found at Regulation of Biotechnology under TSCA and FIFRA.	OPP regulates pesticides that are made from or include microorganisms for human and environmental risks, including dietary exposure to pesticide residues in human and animal food. OPP also regulates pesticides that consist of nucleic acids or peptides for human and environmental risks. OPPT regulates chemicals (including intergeneric microorganisms) used as pesticide intermediates. Information on regulation of chemicals under TSCA can be found at Reviewing New Chemicals under the Toxic Substances Control Act (TSCA). Additional information on TSCA regulation of microorganisms can be found at Overview of Biotechnology under TSCA. Information on regulation of emerging biotechnology pesticides can be found at Regulation of Biotechnology under TSCA and FIFRA.

	HHS-FDA	Any tolerances for pesticide chemical residues or exemptions from the requirement of a tolerance in or on human or animal food are enforced by FDA. Information about FDA's oversight of pesticide residues in foods is available at Pesticides | FDA.	Any tolerances for pesticide chemical residues or exemptions from the requirement of a tolerance in or on human or animal food are enforced by FDA. Information about FDA's oversight of pesticide residues in foods is available at Pesticides | FDA.	Any tolerances for pesticide chemical residues or exemptions from the requirement of a tolerance in or on human or animal food are enforced by FDA. Information about FDA's oversight of pesticide residues in foods is available at Pesticides | FDA. Any product with pesticide claims that is also intended for use in the "diagnosis, cure, mitigation, treatment, or prevention of disease" and/or intended to affect the structure or any function of the human body, would also be regulated as a human medical product by FDA. Information about FDA oversight of drugs and biologics can be found at Development & Approval Process | Drugs; Therapeutic Biologics Applications (BLA) | FDA; About CBER | FDA; Biologics Regulated Products | FDA and Jurisdictional Information | FDA.

	USDA-APHIS	BRS regulates importation, interstate movement, and environmental release of modified plants that may pose a plant pest risk. Information about this process can be found at Regulatory Exemptions and Confirmations, Regulatory Status Review, and Biotechnology Permits.	BRS regulates importation, interstate movement, and environmental release of modified animals that may pose a plant pest risk. Information about this process can be found at Biotechnology Permits.	BRS regulates importation, interstate movement, and environmental release of modified microorganisms that may pose a plant pest risk. Information about this process can be found at Biotechnology Permits and draft Guide for Submitting Applications for Microorganisms.
	USDA-APHIS	BRS regulates importation, interstate movement, and environmental release of plants modified to express pharmaceutical substances. Information about this process can be found at Biotechnology Permits.		BRS regulates importation, interstate movement, and environmental release of modified microorganisms that may pose a plant pest risk. Information about this process can be found at Biotechnology Permits and draft Guide for Submitting Applications for Microorganisms.
HUMAN MEDICAL PRODUCTS	HHS-FDA	CDER regulates drugs for humans, including products made from modified plants or plant cells. Information about FDA oversight of drugs can be found at Development & Approval Process | Drugs. CDRH regulates medical devices (including diagnostics) for humans and radiation-emitting electronic products. Information about oversight of medical devices can be found at Overview of Device Regulation,	CDER regulates drugs for humans, including some products made from modified animals or animal cells. Information about FDA oversight of drugs can be found at Development & Approval Process | Drugs. CDRH regulates medical devices (including diagnostics) for humans, including some made from modified animal cells or tissues, and radiation-emitting electronic products. Information about oversight of medical devices can be found at: Overview of Device Regulation, and at How to	CDER and/or CBER regulate drugs for humans, including products made from, composed of, or containing microorganisms (modified or unmodified). Information about these programs is available at Therapeutic Biologics Applications (BLA) | FDA and Biologics Regulated Products | FDA. CDRH regulates human medical devices (including diagnostics) for humans. Information about oversight of medical devices can be found at Overview of

		and at How to Determine if Your Product is a Medical Device. CBER and CDER each have regulatory responsibility for certain human biological products. Information about these programs is available at Therapeutic Biologics Applications (BLA) | FDA and Biologics Regulated Products | FDA. FDA has post-market authority that could be applied if plants modified to express pharmaceutical substances, or materials from these plants, entered the food supply and resulted in the adulteration of food. Information can be found at section 402 of the FD&C Act (21 USC 342: Adulterated food).	Determine if Your Product is a Medical Device. CBER and CDER each have regulatory responsibility for certain human biological products including those made from, containing, or composed of modified animal cells or tissues. Information about these programs is available at Therapeutic Biologics Applications (BLA) | FDA, About CBER | FDA, and Biologics Regulated Products | FDA.	Device Regulation, and at How to Determine if Your Product is a Medical Device.
VETERINARY	USDA-APHIS	VS regulates veterinary biologics, including those made from modified plants or plant cells. Information including veterinary biologics can be found at Imports: Animal and Animal Products. Additional information about APHIS VS regulatory authority is codified in 9CFR Subchapter I.	VS regulates veterinary biologics, including those made from modified animals or animal cells. Information including veterinary biologics can be found at Imports: Animal and Animal Products. Additional information about APHIS VS regulatory authority is codified in 9CFR Subchapter I.	VS regulates veterinary biologics, including those made from modified microorganisms. Information about veterinary biologics can be found at Imports: Animal and Animal Products. Additional information about APHIS VS regulatory authority is codified in 9CFR Subchapter I.

		BRS regulates importation, interstate movement, and environmental release of modified plants that may pose a plant pest risk. Information about this process can be found at the following links: Regulatory Exemptions and Confirmations, Regulatory Status Review, and Biotechnology Permits.		
	HHS-FDA	CVM regulates animal drugs and medical devices for animals, including any made from modified plants, and biological products for animals if the product is not regulated by VS as a veterinary biologic. Information about these programs is available at Animal & Veterinary | FDA.	CVM regulates animal drugs and medical devices for animals, including any made from modified animals, and biological products for animals if the product is not regulated by VS as a veterinary biologic. Information about these programs is available at Animal & Veterinary | FDA.	CVM regulates animal drugs and medical devices for animals, including any made from modified microorganisms, and biological products for animals if the product is not regulated by VS as a veterinary biologic. Information about these programs is available at Animal & Veterinary | FDA.
INDUSTRIAL OR CONSUMER CHEMICALS AND OTHER COMMERCIAL USES	USDA-APHIS	BRS regulates environmental release of plants expressing pharmaceuticals, industrials, or plants for phytoremediation. Information about this process can be found at Biotechnology Permits.		BRS regulates importation, interstate movement, and environmental release of modified microorganisms that may pose a plant pest risk. Information about this process can be found at Biotechnology Permits and draft Guide for Submitting Applications for Microorganisms.
	HHS-FDA	FDA has post-market authority that could be applied if, for example, plants expressing	CVM reviews animal and human safety, and effectiveness (e.g., that the industrial product is made) of IGAs in	

		pharmaceuticals or industrials, or materials from these plants, entered the food supply and resulted in the adulteration of food. Information can be found at section 402 of the FD&C Act (21 USC 342: Adulterated food).	animals, including those for producing substances for industrial and other uses. Information about FDA's oversight of IGAs can be found at Intentional Genomic Alterations (IGAs) in Animals | FDA.	
	EPA-OCSPP	OPPT regulates chemicals derived from plants if they are intended for uses other than food, food additives, drugs, cosmetics, medical devices, tobacco, nuclear material, firearms, or pesticides (but not pesticide intermediates). TSCA requires submission of a notice to EPA before commercial manufacture of a new chemical, including chemicals derived from plants, and EPA takes steps to address risk before the new chemical can enter commerce. Information on regulation of chemicals under TSCA can be found at Reviewing New Chemicals under the Toxic Substances Control Act (TSCA).	OPPT regulates chemicals derived from animals if they are intended for uses other than food, food additives, drugs, cosmetics, medical devices, tobacco, nuclear material, firearms, or pesticides (but not pesticide intermediates). TSCA requires submission of a notice to EPA before commercial manufacture of a new chemical, including chemicals derived from animals, and EPA takes steps to address risk before the new chemical can enter commerce. Information on regulation of chemicals under TSCA can be found at Reviewing New Chemicals under the Toxic Substances Control Act (TSCA).	OPPT regulates chemicals, including those derived from microorganisms, intended for uses other than food, food additives, drugs, cosmetics, medical devices, tobacco, nuclear material, firearms, or pesticides (but not pesticide intermediates). OPPT also regulates microorganisms intended for uses that are not excluded from TSCA coverage (e.g., food, food additives, drugs, cosmetics, medical devices, tobacco, nuclear material, firearms, or pesticides). TSCA requires submission of a notice to EPA before commercial manufacture of a new microorganism or of a new chemical derived from a microorganism, and EPA takes steps to address risk before the new microorganism can enter commerce. Information on regulation of chemicals under TSCA can be found at Reviewing New Chemicals under the Toxic Substances Control Act (TSCA). Information on TSCA regulation of microorganisms can be found at Overview of Biotechnology under TSCA.

ORGANISMS INTENDED FOR AGRICULTURAL USE OR OTHER ENVIRONMENTAL RELEASE THAT DO NOT FALL INTO A CATEGORY LISTED ABOVE	USDA-APHIS	BRS regulates importation, interstate movement, and environmental release of modified plants that may pose a plant pest risk, regardless of intended use. Information about this process can be found at Regulatory Exemptions and Confirmations, Regulatory Status Review, and Biotechnology Permits.	VS regulates importation of livestock (including poultry and aquatic animals) that may pose a health risk to livestock, as well as importation of their cell lines and germplasm, and materials derived from them. (VS also regulates, or supports regulation of, interstate movement of livestock (including poultry) and germplasm in conjunction with each State's regulations. Information including VS guidance and permitting for importing animal products, live animals (includes semen and embryos), and veterinary biologics, as well as VS guidance and permitting for import and interstate movement for organisms and vectors, can be found at Imports: Animal and Animal Products. Additional information about APHIS VS regulatory authority is codified in 9CFR Subchapter I.	BRS regulates importation, interstate movement, and environmental release of modified microorganisms that may pose a plant pest risk, regardless of intended use. Information about this process can be found at Biotechnology Permits and draft Guide for Submitting Applications for Microorganisms.
	HHS-FDA	FDA has post-market authority that could be applied if these plants, or materials from these plants, entered the food supply and microorganisms resulted in the adulteration of food. Information can be found at section 402 of the FD&C Act (21 USC 342: Adulterated food).	CVM reviews animal and human safety, and effectiveness of intentional genomic alterations (IGAs) in animals. Information about FDA's oversight of IGAs can be found at Intentional Genomic Alterations (IGAs) in Animals | FDA.	FDA has post-market authority that could be applied if these microorganisms resulted in the adulteration of food. Information can be found at section 402 of the FD&C Act (21 USC 342: Adulterated food).

THE REGULATORY SYSTEM FOR BIOTECHNOLOGY PRODUCTS

Each regulatory agency has developed regulations and guidances for the regulation of products of biotechnology under existing laws.

U.S. DEPARTMENT OF AGRICULTURE

Agencies within the U.S. Department of Agriculture (USDA) regulate aspects of food and agriculture, including products developed with biotechnology.

USDA Animal and Plant Health Inspection Service

USDA's Animal and Plant Health Inspection Service (APHIS) safeguards plant and animal health, including protecting agriculture and agriculturally important resources. To ensure biotechnology products are safe for plant health and agriculture, APHIS Biotechnology Regulatory Service (BRS) regulates the importation, interstate movement, and environmental release of:

- Modified plants and plant parts capable of propagation that may pose a plant pest risk, regardless of the intended use.
  BRS regulations for modified plants have three key elements: First, individuals can determine whether their modified plant meets the criteria for an exemption from regulation or can request APHIS' confirmation of the plant's exempt status. Additional information about this process and expected timelines can be found at Regulatory Exemptions and Confirmations. Second, applicants can request a regulatory status (RSR) review to determine if their modified plant is subject to the regulations. Additional information about this process and expected timelines can be found at Regulatory Status Review. Third, applicants must apply for a permit to move or release a modified organism that is not exempt or found through the RSR process to be not subject to APHIS's biotechnology regulations. Additional information about this process and expected timelines can be found at Biotechnology Permits.
- Modified invertebrates and microorganisms that are plant pests or that may pose a plant pest risk, regardless of intended use.
  Applicants must apply for a permit to move or release modified invertebrates or microorganisms that are not exempt. Additional information about this process and expected timelines can be found at Biotechnology Permits and Draft Guide for Submitting Applications for Microorganisms.
- Certain plants and plant parts capable of propagation that are modified to express pharmaceuticals or industrial compounds.
  Applicants must apply for a permit to move or release plants modified to express pharmaceuticals or industrial compounds. Additional information about this process and expected timelines can be found at Biotechnology Permits.

APHIS Veterinary Services (VS) regulates the importation of all livestock, birds (including poultry) and their hatching eggs, and certain fish; cell lines and germplasm (e.g., embryos, oocytes, semen, and cloning tissue) from such animals; materials derived from such animals; livestock and poultry pathogens or disease vectors and any cell line containing a livestock or poultry pathogen or gene from a livestock or poultry pathogen. VS also regulates, or supports regulation of, interstate movement of livestock and poultry, including germplasm, in conjunction with each individual State's regulations; livestock and poultry pathogens or disease vectors; and cell lines that contain a livestock or poultry pathogen. VS also regulates veterinary biologics (e.g., vaccines and diagnostic products), some of which are developed with biotechnology, including veterinary biologics that are, or are derived from, modified plants or plant cells, modified animals or animal cells, and modified microorganisms.

Information including VS guidance and permitting for importing animal products, live animals (includes semen and embryos), and veterinary biologics, as well as VS guidance and permitting for import and interstate movement for organisms and vectors, can be found at Imports: Animal and Animal Products. Additional information about APHIS VS regulatory authority is codified in 9CFR Subchapter I.

USDA Agricultural Marketing Service
The USDA Agricultural Marketing Service (AMS) Food Disclosure and Labeling Division (FDLD) is responsible for ensuring that certain foods produced with biotechnology are labeled according to the National Bioengineered Food Disclosure Standard. The Standard requires labeling of bioengineered foods, which are defined as those foods that contain detectable genetic material that has been modified through certain lab techniques and cannot be created through conventional breeding or found in nature. AMS maintains a List of Bioengineered Foods to identify the food or crops that are available in a bioengineered form throughout the world and for which regulated entities must maintain records. Foods are considered for addition to the List when AMS identifies that they are in legal commercial production somewhere in the world. Regulated entities include food manufacturers, importers, and certain retailers who label human food for retail sale.

USDA Food Safety and Inspection Service
The USDA Food Safety and Inspection Service (FSIS) ensures domestic and imported meat (including Siluriformes fish), poultry, and egg products are safe, wholesome, and properly labeled. To achieve its mission, FSIS:

- FSIS has a collaborative role with the Food and Drug Administration (FDA) following FDA's safety assessment, where FDA determines whether the safety of meat, poultry, and egg products derived from the intentional genomic alterations are safe for food. FSIS reviews and approves products of new technologies, including products developed with biotechnology, and ensures the suitability of all ingredients used in meat and poultry products. Suitability relates to the effectiveness of the ingredient in performing the intended purpose of use and the assurance that the conditions of use will not result in a product that is adulterated or misbranded (labeled in a manner that misleads the consumer).
- Verifies an establishment's compliance with the Hazard Analysis and Critical Control Point regulations, Sanitation Standard Operating Procedures (Sanitation SOPs), or other prerequisite program.
- Conducts sampling of meat and poultry products comprised of or containing cultured cells to assess potential hazards and verify food safety.
- Verifies the labeling of meat, poultry, Siluriformes fish, and egg products, including those containing ingredients developed with modified plants or microorganisms.

FOOD AND DRUG ADMINISTRATION
Centers and an Office within the Food and Drug Administration (FDA) within the Department of Health and Human Services (HHS) evaluate safety of human and animal foods, human and animal drugs, veterinary biologics not regulated by USDA Veterinary Services, human biologics and medical devices, and other products, including those developed with biotechnology. Meeting with FDA early in the product development process can help developers determine the program most relevant to a product.

HHS FDA Center for Food Safety and Human Nutrition
Within FDA, the Center for Food Safety and Applied Nutrition (CFSAN) focuses on the safety of human food, other than meat, poultry, catfish, and egg products (which are regulated by USDA-FSIS).

CFSAN offers several programs that help developers ensure their biotechnology-derived foods meet the relevant safety and legal requirements.
Substances added to food require premarket review and approval unless their intended use is generally recognized as safe (GRAS). CFSAN operates petition programs that provide for the premarket review and approval of food additives and color additives. For substances whose intended use is GRAS, CFSAN offers a voluntary GRAS notice program where developers can provide CFSAN with their basis for a GRAS conclusion for the intended use of an ingredient. CFSAN evaluates the submission and responds with a letter indicating whether CFSAN has questions about the firm's GRAS conclusion. CFSAN has information on these programs on its website at Food Ingredients & Packaging | FDA.

CFSAN operates a voluntary consultation program for foods from biotechnology-derived new plant varieties In this program, FDA works with developers to help ensure that foods from new plant varieties meet all relevant pre- and post-market legal requirements (such as whether the new food contains an unapproved food additive or color

additive). FDA has more information about the new plant variety consultation program for both human and animal food on its website at Food from New Plant Varieties | FDA.

CFSAN oversees human food safety of products made from cultured animal cells during cell collection, selection, and growth. CFSAN also oversees subsequent processing, packaging, and labeling for cells derived from animals that are not regulated by USDA. CFSAN has more information about this program on its website at Human Food Made with Cultured Animal Cells | FDA.

HHS FDA Center for Veterinary Medicine
The FDA Center for Veterinary Medicine (CVM) focuses on the safety of products for animals, including animal foods and drugs.

Substances added to animal food require premarket approval if the added substances are unapproved food additives or unapproved color additives. CVM partners with CFSAN in the voluntary food safety consultation process for foods from new plant varieties. CVM also has several other regulatory programs through which firms can submit information regarding the safety and regulatory status of a product in animal food. FDA has more information about the new plant variety consultation process for both human and animal food on its website at Food from New Plant Varieties | FDA. FDA has more information about premarket approval and other regulatory programs for products in animal food on its website at Animal Food & Feeds | FDA. CVM regulates animal drugs, including any made from modified plants, animals, or microorganisms. CVM regulates intentional genomic alterations (IGAs) in animals, including those used to produce a drug product derived from an animal, as well as animal cells, tissues, and cell- and tissue-based products (ACTPs), unless they are used to produce a DNA vaccine or a live vaccine that stimulates a protective immune response (such products are regulated by VS). CVM reviews IGAs in animals for animal safety, human safety (e.g., could proximity to the animals pose a risk to handlers or others), food safety, environmental impacts, and efficacy of the IGA. CVM has more information on its oversight of IGAs in animals on its website at Intentional Genomic Alterations (IGAs) in Animals | FDA.

HHS-FDA Centers that Regulate Human Medical Products
The Center for Biologics Evaluation and Research (CBER), the Center for Drug Evaluation and Research (CDER), and the Center for Devices and Radiological Health (CDRH) each regulate articles (drugs, biological products (biologics) and devices) used in human medicine, including those that are produced with biotechnology. Some human medical products are combination products (e.g., a combination of a drug and a device). The Office of Combination Products issues classification (which type of product is it) and jurisdiction (which FDA Center regulates the product or is the Lead Center regulating it) assignments for human medical products. More information on this process can be found at Jurisdictional Information | FDA.

- CDER regulates drugs and some biological products for humans, including, but not limited to, products made from plants, animals, or microorganisms, or from plant or animal cells. More information can be found at Development & Approval Process | Drugs and Therapeutic Biologics Applications (BLA) | FDA.
- CBER regulates many biologics for humans, including products that are cell-based or tissue-based products, blood and blood products, vaccines, allergenics, human tissues, xenotransplantation products, and gene therapies. CBER also regulates some devices used for blood and blood products, and for human tissues and cellular products. More information can be found at About CBER | FDA and Biologics Regulated Products | FDA.
- CDRH regulates human medical devices (which include diagnostics), including products derived from animal and human tissues. More information can be found at Overview of Device Regulation and How to Determine if Your Product is a Medical Device.

ENVIRONMENTAL PROTECTION AGENCY
The Environmental Protection Agency (EPA) regulates pesticides and chemicals, including those developed with biotechnology.

EPA Office of Pesticide Programs
EPA's Office of Pesticide Programs (OPP) evaluates the risks to the environment and humans from exposure to pesticides, including dietary exposure to pesticide residues in human and animal food. For products developed with biotechnology, OPP regulates plant-incorporated protectants (PIPs) (such as Bt corn), genetically engineered microbial pesticides, genetic modifications in pest animals intended for use as a pesticide (such as for mosquito and rodent population control), pesticides that consist of nucleic acids (such as exogenous/sprayable dsRNA) and peptides. More information is available at Regulation of Biotechnology under TSCA and FIFRA

EPA Office of Pollution Prevention and Toxics
EPA's Office of Pollution Prevention and Toxics (OPPT) evaluates potential risks from new and existing chemicals (including microorganisms) and acts to address any unreasonable risks they may have on human health and the environment. Food, food additives, drugs, cosmetics, medical devices, tobacco, nuclear material, firearms, and pesticides (but not pesticide intermediates) are excluded from regulation under TSCA. For purposes of regulation any chemical or microorganism that is not listed on the Toxic Substances Control Act (TSCA) Chemical Substance Inventory is considered a "new chemical" or "new microorganism."

Developers are required to submit a notice to EPA prior to commercial manufacture of a new chemical or a new microorganism, and EPA makes a risk determination and takes steps to address risk before the new chemical or new microorganism can enter commerce. Some commercial uses of new microorganisms are fully or partially exempt from notification to EPA, such as research and development activities conducted inside a building, manufacture for test marketing, and commercial manufacture of certain exempt taxa under predetermined conditions of use. Some commercial uses of new chemicals are fully or partially exempt from notification to EPA, such as research and development activities, manufacture for test marketing, and commercial uses with low annual production volumes or low releases and exposures. Products developed with biotechnology that are reviewed by OPPT include new microorganisms, new chemicals produced from microbial fermentation, and new chemicals produced from genetically engineered plant and animal cells. Common examples include intergeneric microorganisms used in biofuel or ethanol production, bioremediation, biosensor and biofertilizer applications, production of bioplastics, and the manufacture of enzymes for various commercial and industrial uses. More information is available at Reviewing New Chemicals under the Toxic Substances Control Act (TSCA); Overview of Biotechnology under TSCA.

CASE STUDIES
The tables below provide case study examples of how products would be regulated by each agency. They are not intended to be inclusive of all products of biotechnology. Other examples of product types not specifically listed in a category may require review by different regulatory agencies. This is an area of developing technology and regulation. Additional case studies may be added to this list of examples in the future.

Case study examples for plants, plant cells, plant products of biotechnology (Table 3)

In Table 3 below,

- **EPA-OPP** regulates the sale, distribution, and use of all pesticides including those produced through genetic engineering and evaluates risks to humans and the environment from exposure to pesticides, including dietary exposure to pesticide residues in human and animal food. EPA-OPP requires developers to register pesticides in order to sell or distribute a pesticide product with particular conditions of use. EPA-OPP requires the establishment of a pesticide tolerance (maximum residue levels) or tolerance exemption for residues of a pesticide in or on both domestic and imported foods (for humans and animals). EPA-OPP requires Experimental Use Permits (EUPs) for field testing. Experimental tests are typically presumed not to need an EUP when conducted on a cumulative total of no more than 10 acres of land or less or one surface acre of water or less per pest tested. However, when field testing PIPs at 10

acres or less, developers should consider that PIPs, unlike other types of pesticides, can spread in the environment and enter the food supply, e.g., through gene flow from the test field to crops in surrounding fields, and consult EPA guidance regarding the use of additional containment measures to limit the potential for PIPs to move from the trial plot.

- **EPA-OPPT** determines the likelihood that chemicals produced from the plant for a commercial purpose pose unreasonable risk to human health or the environment if they are intended for uses other than food, food additives, drugs, cosmetics, medical devices, tobacco, nuclear material, firearms, or pesticides (but not pesticide intermediates). EPA requires submission of a notice to EPA before commercial manufacture of a new chemical, including chemicals derived from plants, or before engaging in a significant new use of an existing chemical, and EPA takes steps to address risk before the new chemical can enter commerce or before the significant new use can occur.
- **FDA-CFSAN** offers a voluntary food safety consultation process to help ensure the food is safe for human consumption. Food manufacturers have an obligation to ensure that the foods they market are safe and lawful. FDA has more information about the consultation process for both human and animal food on its website at Food from New Plant Varieties | FDA.
- **FDA-CVM** partners with FDA-CFSAN in the voluntary food safety consultation process to help ensure the food is safe for animals to consume. Food manufacturers have an obligation to ensure that the foods they market are safe and lawful. FDA has more information about the consultation process for both human and animal food on its website at Food from New Plant Varieties | FDA.
- **USDA-BRS** will determine if the plant poses a plant health risk compared to conventional plants. To import a modified plant (or modified germ plasm), move it interstate, or conduct a field trial, you will need permit from USDA-BRS, unless your modified plant is exempt or has successfully completed a Regulatory Status Review process. In the event you no longer wish to operate under permit, you may request a Regulatory Status Review. More information on these processes is available at Biotechnology Permits, Regulatory Exemptions and Confirmations, Regulatory Status Review.
- **USDA-FDLD** will oversee bioengineered labeling if resulting food for human consumption contains detectable modified genetic material produced with recombinant DNA technologies and cannot be created through conventional breeding or found in nature. Consult with USDA-FDLD to see whether your food product may require a BE disclosure. Information can be found at National Bioengineered Food Disclosure Standard.

For a complete list of an agency's roles and responsibilities, see Table 2.

TABLE 3: CASE STUDY EXAMPLES FOR PLANTS, PLANT CELLS, PLANT PRODUCTS OF BIOTECHNOLOGY

	INSECT RESISTANT FOOD PLANT	HERBICIDE TOLERANT FOOD PLANT	ALTERED NUTRITIONAL CONTENT IN FOOD PLANT	FUNGAL RESISTANT PLANT NOT FOR HUMAN FOOD	ALTERED APPEARANCE OF ORNAMENTAL NON-FOOD PLANT
Examples of each product type	*Rootworm-resistant corn*	*Glyphosate-tolerant soybean*	*Soybeans producing increased levels of oleic acid*	*Fusarium-resistant bentgrass*	*Blue petunia*
EPA					
OPP	X	X[1]		X	
FDA					
CFSAN	X	X	X		
CVM	X	X	X	X[2]	
USDA					
BRS[3]	X	X	X	X	X
FDLD	X	X	X		

[1] To determine the safety of herbicide to be used on the plant.

[2] If product goes into animal food.

[3] For products where the modification does not qualify for an exemption. See Regulatory Exemptions and Confirmations.

Case study examples of animals, animal cells, and animal products produced with biotechnology (Table 4)

In Table 4 below,

- **EPA-OPP** regulates the sale, distribution, and use of all pesticides including those produced through genetic engineering and evaluates risks to humans and the environment from exposure to pesticides, including dietary exposure to pesticide residues in human and animal food. EPA-OPP requires developers to register pesticides in order to sell or distribute a pesticide product with particular conditions of use. EPA-OPP requires the establishment of a pesticide tolerance (maximum residue levels) or tolerance exemption for residues of a pesticide in or on both domestic and imported foods (for humans and animals). EPA-OPP requires Experimental Use Permits (EUPs) for field testing. Experimental tests are typically presumed not to need an EUP when conducted on a cumulative total of no more than 10 acres or less of land or one surface acre or less of water per pest tested. However, for genetic modifications in pest animals intended for use as a pesticide, the applicant should notify EPA-OPP when testing is at 10 acres or less of land or one surface acre or less of water in order to confirm an EUP is not required.
- **EPA-OPPT** determines the likelihood that chemicals produced from the animal cells/products for a commercial purpose pose unreasonable risk to human health or the environment if they are intended for uses other than food, food additives, drugs, cosmetics, medical devices, tobacco, nuclear material, firearms, or pesticides (but not pesticide intermediates). EPA requires submission of a notice to EPA before commercial manufacture of a

new chemical, including chemicals derived from animals, or before engaging in a significant new use of an existing chemical, and EPA takes steps to address risk before the new chemical can enter commerce or before the significant new use can occur.

- **FDA-CFSAN** offers a voluntary food safety consultation process for developers of foods from cultured animal cells (columns 4 and 5) to help ensure the food is safe for human consumption. For cells of animals of amenable species (livestock, poultry and Siluriformes fish), the consultation covers cell collection, selection, growth and removal from cell culture. For cells of all other animals, the consultation covers cell collection, selection, growth, removal from cell culture, processing, packaging, and labeling of the final product. Food manufacturers have an obligation to ensure that the foods they market are safe and lawful. CFSAN has information about the consultation process at Human Food Made with Cultured Animal Cells | FDA.
- **FDA-CVM** oversees safety (including food safety for humans and animals, animal safety and human safety), effectiveness (e.g., it achieves its growth claim), and environmental impacts of products such as fast-growing salmon in column 2. CVM has information on its procedures and requirements for such products on its website at Intentional Genomic Alterations (IGAs) in Animals | FDA. CVM recommends that developers contact CVM early in their development of such products to discuss regulatory requirements and data expectations to support review of the intentional genomic alteration in the animal. FDA-CVM uses its existing regulatory programs to oversee cultured animal cell products for use in animal food (column 6). Its oversight covers cells from all animal species and all aspects of the cell culture process: cell collection, selection, growth, removal from cell culture, processing, packaging, and labeling of the final product. Developers of such products should contact CVM at animalfood-premarket@fda.hhs.gov to discuss submissions and setting up consultation meetings. Food manufacturers have an obligation to ensure that the foods they market are safe and lawful. CVM has information on its regulatory programs for animal foods at Animal Food & Feeds | FDA.
- **USDA-FSIS** ensures domestic and imported meat (including Siluriformes fish), poultry, and egg products are safe, wholesome, and properly labeled. FSIS reviews and approves products of new technologies, including products made from modified animals and products made from animal cells. For animal cell products derived from amenable species (livestock, poultry, and Siluriformes fish (catfish)) and intended for human food, FSIS oversees the harvesting from cell culture, processing, packaging, and labeling of the final product. Further information about this program can be found at FSIS Compliance Guideline Procedures for New Technology Notifications and Protocols | Food Safety and Inspection Service (usda.gov). **USDA-VS** will ensure safe importation of livestock, birds and their hatching eggs, and certain fish (not including salmon); cell lines from such animals; animal pests; and veterinary biologics. Developers should consult with USDA-VS to understand the permitting requirements for the importation of live animals.
- **USDA-FDLD** will oversee bioengineered labeling if resulting food for human consumption contains detectable modified genetic material produced with recombinant DNA technologies and cannot be created through conventional breeding or found in nature. Consult with USDA-FDLD to see whether your food product may require a BE disclosure. Information can be found at National Bioengineered Food Disclosure Standard.

For a complete list of an agency's roles and responsibilities, see Table 2.

TABLE 4: CASE STUDY EXAMPLES OF ANIMALS, ANIMAL CELLS, AND ANIMAL PRODUCTS PRODUCED WITH BIOTECHNOLOGY

	GROWTH TRAITS IN A FOOD ANIMAL THAT IS NOT REGULATED BY FSIS	POPULATION SUPPRESSION IN A PEST ANIMAL	CELLS FROM AMENABLE SPECIES FOR HUMAN FOOD	CELLS FROM NON-AMENABLE SPECIES FOR HUMAN FOOD	CELLS FROM ANY SPECIES FOR ANIMAL FOOD
Examples of each product type	*Fast growing Salmon*	*Self-limiting mosquito*	*Pig*	*Salmon*	*Pet Food*
EPA					
OPP		X			
FDA					
CFSAN			X	X	
CVM	X				X
USDA					
FSIS			X		
VS	*				
FDLD	X		X[1]		

[1] For final food products subject to the Federal Food, Drug, and Cosmetic Act that contain detectable modified genetic material.

* Certain fish, not including salmon.

Case study examples of microorganisms produced with biotechnology, microbial cells, and microbial products produced with biotechnology (Table 5).

In Table 5 below,

- **EPA-OPP** regulates the sale, distribution, and use of all pesticides including those produced through genetic engineering and evaluates risks to humans and the environment from exposure to pesticides, including dietary exposure to pesticide residues in human and animal food. EPA-OPP requires developers to register pesticides in order to sell or distribute a pesticide product with particular conditions of use. EPA-OPP requires the establishment of a pesticide tolerance (maximum residue levels) or tolerance exemption for residues of a pesticide in or on both domestic and imported foods (for humans and animals). EPA-OPP requires Experimental Use Permits (EUPs) for field testing. Experimental tests are typically presumed not to need an EUP when conducted on a cumulative total of 10 acres or less of land or one surface acre or less of water per pest tested. However, for genetically engineered microorganisms, the applicant must notify EPA-OPP when testing is 10 acres or less of land or one surface acre or less of water in order to confirm an EUP is not required.
- **EPA-OPPT** evaluates human health and environmental safety of the microorganism and chemicals derived from the microorganism. The developer must submit a notice to EPA prior to commercial manufacture of a new chemical or new microorganism, before engaging in a significant new use of an existing chemical or microorganism, or prior to use of a new microorganism in research and development activities resulting in environmental release. Prior to commercial manufacture, EPA must make a risk determination and take steps to address risk before the new microorganism can enter commerce. For research and development activities resulting in environmental release of a new microorganism, EPA must review and approve any proposed activities prior to commencement of field trials.

- **FDA-CFSAN** operates both mandatory (for food additives or color additives) and voluntary programs that oversee the safety of substances added to food (including substances from microbes, or any other source). FDA has information about these programs at Food Ingredients & Packaging | FDA. Food manufacturers have an obligation to ensure that the foods they market are safe and lawful.
- **FDA-CVM** offers several regulatory programs through which firms can submit information regarding the safety and regulatory status of a product in animal food, including products of microbes. FDA has information about these programs on its website at Animal Food & Feeds | FDA. Food manufacturers have an obligation to ensure that the foods they market are safe and lawful.
- **USDA-BRS** will ensure safe shipment, contained production, and/or confined field release of microorganisms that are plant pathogens or could pose a plant pest risk, or are biocontrol organisms for plant pests. To import a modified microbe, move a modified microbe interstate, or conduct a field trial, you will need a permit from USDA-BRS. Information can be found at Biotechnology Permits.

For a complete list of an agency's roles and responsibilities, see Table 2.

TABLE 5: CASE STUDY EXAMPLES OF MICROORGANISMS PRODUCED WITH BIOTECHNOLOGY, MICROBIAL CELLS, AND MICROBIAL PRODUCTS PRODUCED WITH BIOTECHNOLOGY

	INTERGENERIC MICROORGANISM FOR ENVIRONMENTAL RELEASE	CONTAINED PRODUCTION OF AN INTERGENERIC MICROORGANISM NOT EXCLUDED UNDER TSCA [1]	CONTAINED PRODUCTION OF A FOOD INGREDIENT IN A MICROORGANISM	CONTAINED PRODUCTION OF A DIETARY SUPPLEMENT IN A MICROORGANISM	FIELD TESTING OR COMMERCIAL USE OF A MICROORGANISM USED AS A PESTICIDE
Examples of each product type	*Nitrogen-fixing soil bacteria*	*Intergeneric yeast modified for ethanol production*	*Vanillin produced by bacteria*	*Vitamin D produced in yeast*	*Bacillus thuringiensis*
EPA					
OPP					X
OPPT	X[1]	**X**			
FDA					
CFSAN			X	X	
CVM		X[5]	X	X[2]	
USDA					
BRS[3]	X	X[4]	X[4]	X[4]	X

[1]EPA's OPPT regulates chemicals, including microorganisms, under TSCA excluding those intended for use in food, food additives, drugs, cosmetics, medical devices, tobacco, nuclear material, firearms, or pesticides (but not pesticide intermediates).
[2] If the ingredient is used in animal food.
[3] BRS permit is required if the microorganisms are plant pathogens or could pose a plant pest risk, or biocontrol organisms for a plant pest that could pose a plant pest risk.
[4] BRS permit is required for contained production if the organisms are being imported or moved interstate.
[5] If byproducts of fermentation, such as devitalized biomass or dried distillers grains, are used in animal food.