I. What is Biotechnology?

A. One generally applicable definition is "the use of living organisms to make new products."

B. Biotechnology is not new. For thousands of years, people have been using living organisms in food production. Traditional plant breeding is an example of such use, as is using bacteria to convert milk into yogurt.

1. What is new and what has made "biotechnology" a modern term are the new powerful techniques that have been developed in basic genetic research. These new techniques provide the ability specifically and selectively alter organisms.

2. Until recently, molecular biologists have not been able to study the DNA and genes in cells. In the last ten or fifteen years, however, scientists have made several breakthroughs that have allowed them to study genes in more detail. They have found that DNA can be "cut" and attached to another piece DNA.

3. This has led to the familiar terminology "gene splicing" or "recombinant DNA" technology. Each means the same thing—the ability to take a piece of DNA from one source and attach it to DNA from another source, allowing scientists to isolate a gene from one organism and introduce it into another organism to confer a desirable trait. Scientists can easily transfer genes from one source into bacteria, plants, or animals of totally different origin (see Attachment, "What's Coming to the Table?").


A. Overview. The policy is premised on the fundamental legal notion that the agency's existing statutory authority for regulating the safety and labeling of food is sufficient to ensure the safe and non-misleading marketing and use of food from plant varieties derived from biotechnology (see "FDA's Proposed Policy Regarding Foods Derived From New Plant Varieties," 57 Fed. Reg. 22,984 (May 29, 1992)). The policy consistent with FDA's longstanding, albeit informal, approach to the regulation of products biotechnology (see "Statement of Policy for Regulating Biotechnology Products," 51 Fed. Reg. 23,31 (June 26, 1986)).

B. Scope of the Policy.

1. The policy deals only with single gene transfers.

2. The policy does not address foods and food ingredients regulated by FDA that are derived from algae, microorganisms, and other nonplant organisms. Foods produced by fermentation when microorganisms are necessary components of the food, or foods derived from animals that are subject to FDA's authority (including seafood), are not included in the policy statement.

3. The policy does not cover new drugs, new animal drugs, or pesticide chemicals.
The policy relies upon a "decision-tree" approach to assess the safety of foods derived from new plant varieties and focuses primarily on six "decision-tree" models to aid in determining the regulatory status of products. These decision-trees outline a series of questions related to the safety and nutritional value of a food derived from the new plant variety and are intended to provide general guidance to breeders and developers. The decision-trees, or "flow charts," reflect the current state of scientific information, but are not intended to serve as regulatory requirements and may require modification.

2. The decision-trees are designed to help determine whether a new plant variety is as safe and nutritious as its parental variety. The safety scheme focuses on the characteristics of the new plant variety, the characteristics of the host and donor species, the nature of the genetic change, the identity and function of newly introduced substances, and the unintended effects that may accompany the genetic change. Specifically, the decision-trees call for an evaluation of the following end points:

   a) toxicants known to be characteristic of the host and donor species;
   b) the potential that food allergens will be transferred from one source to another;
   c) the concentration and bioavailability of important nutrients for which a crop is ordinarily consumed;
   d) the safety and nutritional value of newly introduced proteins; and
   e) the identity composition and nutritional value of modified carbohydrates, fats, and oils.

There are only three possible outcomes in the various decision-trees: "no concerns"—"new variety not acceptable," and "consult FDA" (see decision-tree flow chart attachment).

D. Regulatory Status of Foods Produced by Biotechnology.


   a) Relying on existing statutory authority, FDA has carved out a policy which should allow "the lion's share of foods" to avoid food additive status and, thus, also avoid premarket approval requirements.
   b) The policy provides that the safety of biotechnology derived food will be regulated primarily under FDA's postmarket, food adulteration authority.
   c) The section will be applied to any substance that occurs unexpectedly in the food. This includes naturally occurring toxicants whose level is unintentionally increased by the genetic modification, as well as unexpected toxicants that first appear in the food as a result of genetic engineering techniques.
   d) Such substances will be regarded by FDA as food adulterants under section 402(a)(1) only if the levels present in the food may render the food injurious to health. So regulated, such a substance (and its purveyors) is subject to enforcement action if it proves to be an adulterant (FDCA § 402(a)(1), 21 U.S.C. § 342(a)(1)).

2. Food additive or generally recognized as safe (GRAS) status. a) FDA will apply the food additive and GRAS rubrics to the regulation of all intended expression products or products present in foods derived from new plant varieties.

   b) "Intended" products include proteins or substances produced by the action of protein enzymes. These substances include carbohydrates, fats, and oils. When such a substance is present in the food at levels "generally comparable to or greater than" those in the genetically engineered food, FDA believes there is unlikely to be a safety question sufficient to affect the presumed
GRAS status of the nongenetically derived food. Similarly, minor variations in molecular structure will not affect the GRAS status of the food (the agency does not define "minor").

c) Nevertheless, where the intended expression product (the protein, carbohydrate, fat, oil, or other substance) in a food differs significantly in structure, function, or composition from substances found currently in food, the substances may not be GRAS and may require premarket approval as a food additive.

d) Most important is the agency's conclusion that transferred genetic materials (nucleic acids) are presumed to be GRAS (and therefore exempt from premarket approval requirements) because they are present in the cells of every living organism, including plants. The practical effect of this conclusion would be to shift agency scrutiny from the source of the organism to the effects of the organism in food.

Summary: FDA's safety concerns.

a) The policy clarifies FDA's concerns regarding genetically engineered plants. Those concerns appear to be primarily with assessing the safety and propriety of intended effects of genetic engineering.

b) Implicit in the adopted scheme is that good manufacturing practices will decrease unintended risks to an acceptable, and easily enforceable, minimum.

c) It is important to note that there are few "bright lines" in the agency's policy; there is still the question of how serious the agency is about narrowly interpreting, and applying, its food additive authority.

E. Jurisdiction.

1. In announcing its policy, FDA states that it intends to work closely with the Environmental Protection Agency (EPA) in minimizing duplication in the regulation of genetically engineered crops. The agency explains that substances that are pesticides are to be regulated by EPA, but cautions that FDA's authority can reach any nonpesticide substance introduced into a new plant variety that is expected to become a component of food. The agency further advises that FDA and EPA intend to consult closely on jurisdictional questions as well as on scientific matters.

According to FDA, EPA will address food safety issues associated with a pesticide, including marker genes, under its regulatory jurisdiction. The agency also advises that any food safety questions beyond those associated with the pesticide, such as those raised by unexpected or unintended compositional changes, will be regulated by FDA.

EPA will have jurisdiction over substances that are intended to kill insects; substances intended to protect plants from viral, fungal, or bacterial infection; and substances that are plant regulators. FDA will have jurisdiction over substances intended to alter the nutritional composition of food, substances intended to enhance the plant's resistance to chemical herbicides, and substances intended to alter the flavor or texture of food.

FDA categorically states in its policy that it does not consider the activities it may take with respect to foods from new plant varieties, other than the promulgation of food additive regulations, as constituting agency action under the National Environmental Policy Act of 1969 (NEPA, Pub. L. No. 91-190, 83 Stat. 852 (1970) (codified at 42 U.S.C. §§ 4321-4361 (1988))).
111. Labeling Issues Regarding Genetically Modified Food

A. Overview.

1. FDA believes that unless real consequences ensue from biotechnologically-produced food, the fact that certain consumers may want information regarding whether the food is produced by biotechnology does not justify labeling.

2. The agency states in its policy that appropriate labeling is necessary to inform consumers only if a food derived from a new plant variety differs from its traditional counterpart in such a manner that the common or usual name no longer applies to the new food, or if a safety or usage issue exists to which consumers must be alerted.

3. For example, the agency cites the hypothetical of a tomato injected with a peanut protein, resulting in the documented potential to cause an allergic reaction in a susceptible population. Under such circumstances, FDA concludes that a label declaration would be necessary to alert consumers who are allergic to peanuts to avoid the tomato.

4. This approach reflects the agency's longstanding view that knowledge about the methods used in the development of a new plant variety is not "material" information that needs to be disclosed, and that the agency is unaware of any information showing that foods derived from such methods differ from other foods in any meaningful way necessitating a labeling-disclosure.

B. Conveying Meaningful Information to the Consumer Regarding Genetically Altered Food.

1. Section 403(i) of the FDCA requires that a food bear on its label the common or usual name of the ingredients from which it is "fabricated" (FDCA § 403(i), 21 U.S.C. § 343(i)). The purpose of this section, as recognized in 1938, was-and remains—to ensure that the consumer obtains "reasonable information regarding the composition of the foods he buys" (S. REP. No. 361, 74th Cong., 1st Sess.; C.W. DUNN, FEDERAL FOOD, DRUG, AND COSMETIC ACT 247 (1938)).

2. In spite of the fact that significant changes in the genetic composition of food have been perfected for years, no one has seriously suggested that altered genetic materials constitute ingredients from which a given food is fabricated.

3. This common sense interpretation of the requirements of section 403(i) is consistent with the literal language of the section that clearly excludes from compliance with the requirements of the section those ingredients for which it would be impracticable, or for which it would result in deception or unfair competition to so identify. This interpretation also is consistent with the agency's regulations exempting incidental additives and other ingredients from the scope of section 403(i) (see 21 C.F.R. § 101.100 (1995)).

4. FDA relies upon the use of "common or usual" names to communicate meaningful information to consumers (see 21 C.F.R. pt. 102). These regulations provide that the name of a food must accurately identify or describe in simple and direct terms the basic nature of the food (see 21 C.F.R. § 102.5(a)). The key criterion is that the name of a product should not be misleading to the consumer and should be informative as possible about the composition of the food or food ingredient involved.

5. A fruit or vegetable modified by novel, or for that matter nonnovel, techniques would be appropriately labeled within the meaning of section 403(i) if the significant aspect of the modification regarding the composition of the food were identified. For example, a tomato developed to have a high level of vitamin C could be appropriately labeled "high vitamin C tomato." In this case, the consumer is fully informed as to the substance of the compositional change in the food that he or she may purchase (FDCA § 403(i), 21 U.S.C. § 343(i)).

6. FDA can require that source and function information be included in the common or usual name ("high vitamin C tomato modified with peanut gene"). FDA traditionally has appreciated the consumer's need and concern about receiving source and function information. In many situations,
the agency provides for source information as a part of the ingredient name where such information is essential
to adequately describe the basic nature of the food ingredient. Thus, gluten, a principal protein component of
com and of wheat, must be identified in ingredient list as either "com gluten" (21 C.F.R. § 184.1321) or "wheat
gluten" (21 C.F.R. § 184.1322). The identification of source is essential for gluten because, as the agency has
explained, persons with celiac disease are unable to ingest gluten from wheat without intestinal upset, but are
able to ingest gluten from com without side effects (see Final Rule on GRAS Status of Wheat Gluten and Com
Gluten, 50 Fed. Rec., 8997 (Mar. 6, 1985)). In such a case, FDA reasonably considers source information to be
part of the ingredient's common or usual name.

7. There are any number of situations, however, in which the agency has decided that source information is not a
necessary part of the common or usual name of a food or food ingredients (see, e.g., 56 Fed. C, Reg. 28,603
(June 21, 1991) (FDA proposed rule regarding food labeling,)).

8. Only in those cases where such information has a material bearing on the purchase of a food or NN-here
consumers may be misled without such information is FDA likely to take steps to require such information. The
controlling factors in agency decision making in this area are that the information should be either important to
understanding the value of a given biotechnology derived food or determining whether the food may present
significant adverse health consequences without such information (56 Fed. Reg. at 28,604).

C. Is the Fact that a Food is the Product of Biotechnology a "Material Fact" Within the Meaning of Section 201(n) of the
FDCA (FDCA § 201(n), 21 U.S.C. § 321(n))?  

1. Section 403(a) of the FDCA prohibits labeling which is "false or misleading in any particular" (FDCA § 403(a), 21
U.S.C. § 343(a)). The term "misleading" is defined in section 201(n) of the FDCA:

In determining whether the labeling is misleading, it should be taken into account (among other things) not only representations made or suggested ... but also the extent to which the labeling fails to reveal facts material in the light of such representations or material with
respect to consequences which may result from the use of the article to which the labeling or
advertising relates (FDCA § 201(n), 21 U.S.C. § 321(n)).

One of the best articulations of the agency's interpretation of the interplay between section 403(a) and 201(n) is
found in the agency's final rule "Irradiation in the Production, Processing and Handling, of Food" (51 Fed. Reg.
13,376 (Apr. 18, 1986)). Sources of irradiation intended for use in processing food are included in the statutory
definition of "food additive" (see FDCA § 201(s), 21 U.S.C. § 321(s)). In approving certain safe food additive
uses of irradiation, FDA was confronted with the issue as how an irradiated food should be labeled. The agency
concluded that there was adequate statutory authority under sections 403(a) and 201(n) to require a retail label
statement on foods that had been irradiated, even though there was no concern about the safety of such treated
foods (FDCA §§ 403(a), 201(n); 21 U.S.C. §§ 343(a), 321(n)).

In reaching this conclusion, the agency considered whether the changes brought about by the safe use of
irradiation are "material facts" in the context of section 201(n). An important consideration in the agency's
analysis was that irradiation may not change the food visually, and that in the absence of a statement that a food
has been irradiated, the implied representation to consumers is that the food has not been processed. The agency
reasoned that the omission of information that a food has been processed may be material to consumers. The
agency noted that other processes are not material because the fact of processing is either obvious to the
consumer or conveyed to the consumer through labeling or packaging (e.g., frozen, canned).
IV. Summary.

A. By setting regulatory priorities and establishing a general approach for dealing with the food safety and nutrition issues presented by genetically derived plant varieties, the new FDA policy ensures movement and progress toward the lawful marketing of such products.

B. Nevertheless, a number of uncertainties remain in how FDA will apply the policy:

1. How will the agency respond to issues involving more than single gene transfers?

2. How will the next administration perceive the emphasis on section 402(a) of the FDCA as the primary vehicle of regulatory control (FDCA §402(a), 21 U.S.C. § 342(a))?

3. Will some generic labeling statement eventually be recommended to accompany modified foods?

C. A constant in the agency's policy will likely be the substantive criteria for showing the safety and wholesomeness of a genetically engineered plant variety. It appears that manufacturers, with some assurance, may rely on long-range plans for data collection. Although the mechanism that will be applied in evaluating such data—either under section 402(a) rubric, food additive rubric, or some combination of the two—may change, the likely agency concerns appear to be identified with a degree of permanence that has been lacking in this area until now.

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FIGURE 2. SAFETY ASSESSMENT OF NEW VARIETIES: THE HOST PLANT*

1. Does the host plant have a history of safe use?
   - YES
   - NO

2. Do characteristics of the host species, related species, or progenitor lines warrant analytical or toxicological tests?
   - YES
   - NO

3. Do test results provide evidence that toxicant levels in the new plant variety do not present a safety concern?
   - YES
   - NO

4. In the concentration and bioavailability of important nutrients in the new variety within the range ordinarily seen in the host species?
   - YES
   - NO

5a. No concerns

5b. New variety not acceptable

5c. Consult FDA

FIGURE 3. SAFETY ASSESSMENT OF NEW VARIETIES: THE DONOR(S)*

1. Is the food from the donor commonly allergenic?
   - YES
   - NO

2. Can it be demonstrated that the allergenic determinant has not been transferred to the new variety of host?
   - YES
   - NO

3. Do characteristics of the donor species, related species, or progenitor lines warrant analytical or toxicological tests?
   - YES
   - NO

4. Do test results provide evidence that toxicant levels in the new variety do not present a safety concern?
   - YES
   - NO

5. New variety not acceptable

6. No concerns

7. Consult FDA on protocols for allergenicity testing and/or labeling

FIGURE 4. SAFETY ASSESSMENT OF NEW VARIETIES: PROTEINS INTRODUCED FROM DONOR(S)

10

Is the newly introduced protein present in food derived from the plant?

- YES -> 11
- NO

11

Is the protein derived from a food source, or substantially similar to an edible protein?

- YES
- NO -> 14

14

Consult FDA

11

Is the food from the donor commonly allergenic?

- YES
- NO -> 17b

17b

Consult FDA on protocols for allergenicity testing and/or labeling

11

Can it be demonstrated that the allergenic determinant has not been transferred to the new variety of host?

- YES
- NO -> 17a

17a

No concerns

12

Is the introduced protein reported to be toxic?

- YES -> 17c
- NO

17c

Consult FDA

13

Will the intake of the donor protein in the new variety be generally comparable to the intake of the same or similar protein in donor or other food?

- YES
- NO

15

Does the biological function of the introduced protein raise any safety concern, or is the introduced protein reported to be toxic?

- YES
- NO

16

Is the introduced protein likely to be a macroconstituent in the human or animal diet?

- YES -> 17d, e
- NO

17d, e

Consult FDA

FIGURE 5. SAFETY ASSESSMENT OF NEW VARIETIES: NEW OR MODIFIED CARBOHYDRATES

Have any structural features or functional groups been introduced into the carbohydrate that do not normally occur in food carbohydrates?

YES

18

Has there been an intentional alteration in the structure, composition, or level of carbohydrates in the new variety?

YES → Consult FDA

NO

19

Have there been any alterations that could affect digestibility or nutritional qualities in a carbohydrate that is likely to be a macroconstituent in the diet?

YES → Consult FDA

NO

20a

No concerns
