DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

AUG 20 2001

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The Honorable Jon S. Corzine
United States Senator
208 White Horse Pike
Suite 18-19
Barrington, New Jersey 08007

Dear Senator Corzine:

Thank you for your letter of July 3, 2001, on behalf of your constituent, Ms. Carol Lydick of Allentown, New Jersey. Ms. Lydick is concerned about the accurate labeling of allergens in foods, genetically modified foods, and pharmaceuticals. She suffers from Celiac disease, which causes intolerance to the protein component of the gluten in wheat, barley, rye, and oats. She also has intolerances to soybean, corn, dairy, and fluoride. Ms. Lydick is concerned that foods contain "hidden" ingredients that are not declared on the label.

The Food and Drug Administration (FDA or the Agency) appreciates the difficulties faced by persons with food allergies and food intolerances. We have enclosed a Notice to Manufacturers that FDA distributed to food manufacturers, trade associations, and other food industry groups. It outlines steps to ensure that allergens are declared on food labels.

In the Notice, we ask manufacturers to examine their product formulations for known allergens and to be sure to declare the presence of these ingredients in the ingredient statement on the label. Please note that wheat is included in the list of common allergens. We believe that the inclusion of wheat in the list will help enable persons who have Celiac disease to avoid many products containing gluten.

By way of background, the Federal Food, Drug, and Cosmetic (FD&C) Act requires, in virtually all cases, that labels of food fabricated from two or more ingredients bear a declaration of each ingredient, by its common or usual name,

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in descending order of predominance by weight in the ingredient statement. There are two very narrow exemptions from this ingredient-labeling requirement. The first is provided in section 403(i) of the FD&C Act. It states that spices, flavorings, and certain colorings may be declared collectively without naming each one.

The second is provided in Title 21, Code of Federal Regulations § 101.100(a). It states that incidental additives, such as processing aids that are present at insignificant levels and that do not have a technical or functional effect in the finished food, do not have to be declared on the label. Since evidence suggests that some allergenic substances can cause serious allergic responses in some individuals upon ingestion of very small amounts, FDA's Notice advised manufacturers that an allergen cannot be determined to be present at an insignificant level and therefore does not qualify for an exemption.

FDA has been working with industry and consumer groups to raise awareness about the presence of allergens in foods and to identify practical approaches for the labeling of allergens. Addressing food allergen issues has been identified as a priority this year by FDA's Center for Food Safety and Applied Nutrition (CFSAN). Specifically, CFSAN plans to develop a strategy for exploring clearer labeling of food allergens and just recently held a public meeting on August 13, 2001.

Importantly, CFSAN has received and is currently reviewing petitions that raise concerns similar to those of Ms. Lydick. We have forwarded her correspondence to the docket for this matter for inclusion in the record (Docket #00P-1322). Please be assured that we will consider all comments before making a final decision on this issue. For your information, we have also enclosed a recent article entitled, "Food Allergen Awareness: An FDA Priority".

Regarding Ms. Lydick's interest in the labeling of bioengineered foods, FDA does not require that bioengineered foods and foods containing bioengineered ingredients be labeled as such. On January 18, 2001, FDA issued draft guidance for the voluntary labeling of products indicating whether they were produced through bioengineering or contain bioengineered ingredients (copy enclosed). The public comment

period on the draft guidance closed on March 19, 2001, and FDA is in the process of evaluating the more than 55,000 comments received.

In a related matter, on January 18, 2001, FDA published a proposed rule (copy enclosed) to require that developers of bioengineered plant varieties notify FDA of their intention to market such products. FDA has proposed that specific information be submitted to help determine whether the foods pose potential safety, labeling, or adulteration issues. In addition, the Agency has made a commitment to ensuring that consumers have access to information about new bioengineered food products in a timely fashion, and thus plans to make more information about these foods available on FDA's website.

The comment period for the proposed rule closed on May 3, 2001, and the Agency is in the process of evaluating the more than 50,000 comments received. More information on food biotechnology can be found on CFSAN's at http:\\www.cfsan.gov/~lrd/biotechm.html.

Finally, to address Ms. Lydick's concerns about the labeling of pharmaceuticals, The FD&C Act generally does not require the declaration of inactive ingredients on the labels of prescription drugs. However, by regulation, FDA has required that labels of non-oral dosage forms of prescription drug products identify the products' inactive ingredients and, in the case of products for parenteral injection, that the labels indicate the proportion of the inactive ingredients.

As information becomes available to FDA indicating a relationship between a particular inactive ingredient and a potential hazard to consumers, appropriate steps may be taken either to require labeling to contain information about the relationship or to prohibit the use of those ingredients in prescription drugs. This was the basis for the ruling on FD&C Yellow No. 5, a potential sensitizing agent for many individuals. FDA published a final regulation in the Federal Register of June 26, 1979, stating that foods and certain drugs for human use which contain FD&C Yellow No. 5 must bear a label declaration to that effect.

In addition, prior to having her prescriptions filled, Ms. Lydick may wish to have her physician or pharmacist contact the manufacturer of the drug to ascertain the inactive

ingredients. Also, she may wish to contact the manufacturer herself. Finally, the best source of information locally may be a referral from her physician to a dietetic specialist.

Thanks again for contacting us concerning this matter. If you have further questions, please let us know.

Sincerely,

Kristina Harper

Melinda K. Plaisier
Associate Commissioner
for Legislation

Enclosures

U. S. Food and Drug Administration
Center for Food Safety and Applied Nutrition
February-March 2001

Food Allergen Awareness: An FDA Priority

New initiatives focus on allergens in 2001.

Authors

Reprinted from *Food Safety Magazine* February-March 2001 issue

(Also available in PDF format)

As part of the public health mission to keep food safe, the U. S. Food and Drug Administration (FDA) is increasing its activity on food allergen awareness. FDA's 2001 allergen priorities for the Center for Food Safety and Applied Nutrition (CFSAN) describe new initiatives.[1] For example, a major goal is to provide guidance to industry and regulators on how to manage allergens through appropriate manufacturing and labeling practices.

For sensitive individuals, the presence of allergens in food is potentially life-threatening. Currently, there is no cure for food allergy. The only successful method to manage food allergy is avoidance of foods containing the allergen. Fortunately, most consumers are aware of their specific sensitivities and can avoid foods that might result in a life-threatening situation. For example, a person with a peanut allergy may find it easy to avoid whole peanuts. Formulated foods, however, present a separate challenge. In such cases, the individual relies on accurate ingredient labeling. The FDA, food manufacturers and special interest groups are working to increase public awareness of the seriousness of allergic reactions and to assure that allergens are appropriately labeled in food products.[2] For example, one of the U. S. Department of Health and Human Services' "Healthy People 2010" initiatives for the coming decade is to reduce the number of deaths due to anaphylaxis caused by food allergens.[3]

Allergic reactions are reported to be caused by a large variety of foods, and in theory, any food protein is capable of causing an anaphylactic reaction.[4] Agency allergen awareness efforts currently focus on the eight foods that are most frequently implicated in serious allergic responses: milk, eggs, fish, wheat, tree nuts, legumes

(particularly, peanuts and soybeans), crustaceans and mollusks.[1] Allergenic proteins in these eight foods are estimated to cause 90% of the allergic reactions in the U. S.[5] Some of these foods, such as milk and eggs, are often used as added ingredients in formulated products. Low amounts of these proteins may elicit a response and reactions may vary from mild to life-threatening, depending on a person's particular sensitivity. (Other substances, such as FD&C Yellow No. 5, sulfites and carmine/cochineal extract, also may cause allergic or allergic-type reactions.)

The number of allergic individuals in the U. S. is unknown. Estimates suggest, however, that 1.5% of the adult population and 5% of children younger than three years old have some form of food allergy.[6] One estimate of the number of fatal food anaphylaxis cases in the U. S. is 125 per year.[4]

THE INGREDIENT LABEL: ALERT FOR THE ALLERGY-SENSITIVE PERSON

The Federal Food, Drug, and Cosmetic Act (FD&C) requires, in virtually all cases, a complete listing of all the ingredients of a food on the food label. In certain cases, such as with allergens, public health concerns have been noted as FDA took steps to require particular wording in an ingredient statement. For example, 21 *Code of Federal Regulations* (CFR) 102.22 requires the food source identification for protein hydrolysates, e. g. "hydrolyzed wheat gluten," and "hydrolyzed soy protein."[7] Failure to list an ingredient on the food label, particularly an allergen, has resulted in product recalls. A recent review of FDA food recall actions for undeclared allergens such as peanuts, egg, or milk revealed an increase in recalls during the last decade. Recall activity increased from an average of 35 per year at the beginning of the last decade to an average of 90 per year during the last four years of the same decade (Figure 1).

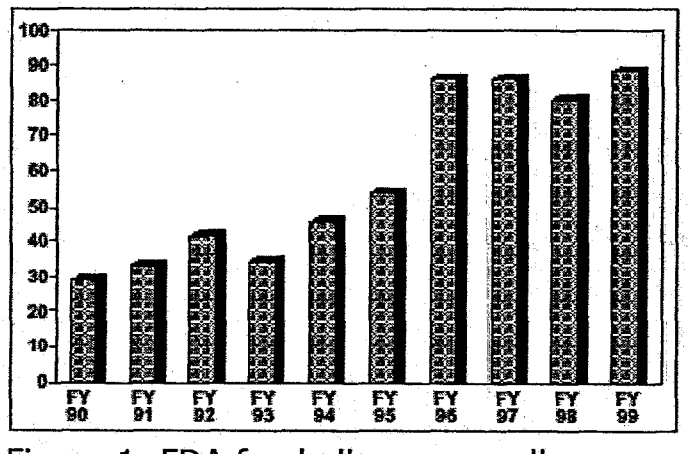

Figure 1. FDA food allergen recalls.

Additionally, FDA has received a number of reports of consumers who experienced adverse reactions following exposure to an allergenic substance in foods. Many of these exposures occurred because the presence of the allergenic substance in the food was not declared on the food label. This public health concern has prompted FDA

to develop an initiative on food allergen awareness.

In the spirit of the 1990 Nutrition Labeling and Education Act (NLEA), FDA's activities during the past 10 years have encouraged consumers to read the product label. While it is understood that an added ingredient must be declared in the ingredient statement, food manufacturers must pay particular attention to instances in which inadvertent introduction of allergens can potentially occur because of the firm's production practices; for example, rework addition, product carryover due to use of common equipment, production scheduling or allergenic product above exposed product lines.

In 1996, FDA issued a notice to the food industry alerting manufacturers and trade associations, requesting assistance in addressing the major public health problem of undeclared allergens in food.[8,9] FDA commented on current labeling requirements, voluntary labeling practices used by industry and various options such as additional rulemaking to alert consumers to the presence of allergens. In particular, the FDA noted the importance of declaring allergens even when present in very low amounts.

COLLECTIVE NAMING AND INCIDENTAL INGREDIENTS

The 1996 notice describing FDA's policy for food allergens outlined "exemptions" under the law for the labeling of ingredients, including food allergens on food packaging, and noted the use of precautionary statements such as "may contain" on food ingredient labeling. The "exemptions" are of two types: One focuses on collective naming of spices, flavors and colors, and the other on declaration of incidental additives such as processing aids.[10,11]

The first exemption refers to collective naming of flavors, certain colors (color additives exempt from certification in 21 *CFR* Part 73) and spices. Although these terms may be used on the food label, they are not completely descriptive. Food labels with collectively named additives may confuse individuals who wish to avoid allergenic substances, particularly when the allergenic substance is not clearly labeled. On several occasions, the FDA has clarified publicly that the FD&C Act allows spices, flavors, and colors to be declared collectively without naming each one. In some instances, these ingredients contain subcomponents that are allergens. Therefore, FDA recommends that processors declare allergenic ingredients in a spice or in a flavor. This might be accomplished by either declaring the allergenic ingredient by its common or usual name in the ingredient list as a separate ingredient or parenthetically following the term spice, flavor or color, or as a separate declaration immediately below the list of ingredients indicating the presence of the allergen. In addition, for some food labeling decisions, it is also clearly advantageous to the allergic consumer for the manufacturer to voluntarily declare any allergenic source from which an ingredient may be derived, such as soy, milk and eggs.

The second "exemption," incidental additives, refers to food substances that are exempt from labeling on an ingredient statement because they are used at or find

their way into food at insignificant levels and do not have any technical or functional effect in that food. In this case, each individual food firm makes an assessment of the food ingredients that may be introduced during food processing into their final food product and then determines the ingredient label. This can lead to errors in judgment by the food industry or others involved in food handling as to what ingredients should be declared on the food label. While FDA believes that every food firm makes a sincere effort to label the ingredients in their food products completely, it is also clear that firms do miss including allergenic ingredients on their food labels. This happens at times because subtle changes in food processing aids, such as filtering substances, may introduce allergenic components into the manufactured food and a company may simply not realize the addition of such an allergen to the final food product. The agency stated in its 1996 notice that ingredients that are food allergens do not meet the requirements for incidental additives and therefore are not exempt from ingredient declaration.[8,9] When these labeling errors are found by consumers or the food industry, the food label is usually corrected. At times, these errors also result in a recall of a company's products if they reach the marketplace.

PRECAUTIONARY LABELING STATEMENTS

The 1996 notice also addressed the use of precautionary labeling statements.[8,9] Statements such as "may contain peanuts" or "made on shared equipment" are voluntarily placed on food packaging labels by food manufacturers. These statements tend to express the manufacturers' concern that their food products could possibly contain other food ingredients not listed on the food label in the final food products. It is not clear whether the "may contain (ingredient)" is or is not present in this particular food package. The agency is gathering data on the extent of use of "may contain (ingredient)" and other precautionary labeling statements and intends to address their use in the future.

FOOD ALLERGEN INITIATIVES AND POLICY DEVELOPMENT

Beginning in 2000, CFSAN made increasing consumer and industry awareness to the presence of allergens in foods a high priority. In meeting the 2000 goal of increased awareness, CFSAN representatives held meetings at 14 locations in which they made presentations on allergen risks and labeling requirements.[12] CFSAN increased allergen awareness for those groups who provide food products to the public, as well for parents who may not be familiar with the challenges of caring for children who have a food sensitivity. These productive exchanges provided FDA with an opportunity to gather information for helpful consumer messages from individuals who, personally, or through their children, experienced allergic responses. For example, consumers suggested the use of certain terms to call attention to the presence of an allergen, i. e. use "milk" in the ingredient statement, if the formulation contains caseinate, or "egg" if the food contains albumin. The agency also sought to gain insight into industry allergen management practices and control methods. As part of the 2000 effort, FDA and state health departments began working cooperatively to establish uniform inspection procedures for food allergens.

Continuing these efforts with the 2001 CFSAN priorities, CFSAN plans to proceed with consumer and industry education efforts and to develop a strategy for clearer labeling of food allergens on the food label. Priorities include publishing a draft Compliance Policy Guide on manufacturing and labeling practices, issuing a field allergen inspection guide and providing training for FDA field offices. While emphasis is on the eight food allergens, FDA plans to publish a proposed rule to require declaration of carmine/cochineal extract on product labels.

OTHER RESEARCH ACTIVITIES

Survey. A national assessment of the extent of food allergenicity would be helpful to clarify who and to what extent consumers experience allergic reactions to food. The agency is studying ways to accomplish this survey and is seeking suggestions from those who are interested. One approach that is being considered is to use eight or nine regions of the country to determine, through hospital emergency room discharge codes, how many people have food allergen problems and anaphylaxis during the course of a year and how much of this anaphylaxis is caused by food. Investigating hospital discharge codes has been discussed in medical literature, but these studies have involved only isolated parts of the nation.[13]

Food Allergen Test Kits. Detecting the allergenic protein components of the eight major allergenic foods is the subject of much research and development. The developers of tests that can detect minute levels of these proteins have to produce antibodies for these proteins from animal sources. Once an antibody is isolated, barriers such as cross-reactivity to substances other than the desired proteins have to be addressed. Results must be reproducible and kits must be effective to detect these proteins in different foods.

A number of test kits are manufactured in this country for commercial use. Although there is not a test kit for each allergen in the food supply, kits are available for peanut, milk and egg protein. Other test kits for allergenic proteins are under development. The FDA is participating with the National Food Processors Association (NFPA) in establishing a peanut protein standard. A peanut flour standard is being developed that will be used to establish a common relationship or scale for the peanut protein test kits currently on the market. Although plans include standard development for other allergenic proteins, much work is needed to develop test kits and common standards for these proteins.

Food Allergen Thresholds. As mentioned above, quantitative food allergen thresholds are currently unknown. Although available data suggest that it is not possible to determine the amount of allergenic protein necessary to elicit an allergic reaction, discussions in public forums offer the hope that future research will determine a safe level for undeclared allergens in food.[14] FDA welcomes receiving any human data that might be available to help determine possible limits for the effects of allergenic proteins in sensitive populations.

OTHER INITIATIVES

Importantly, FDA recognizes the efforts of the food industry in addressing the presence of food allergens. For example, major industry representatives are supporting CFSAN priorities and have signaled development of a voluntary allergen labeling program.[15] Industry's senior management has made a commitment to managing allergens by training employees on allergens and plant-specific control procedures, evaluating rework procedures, working with ingredient suppliers to identify and label all allergenic ingredients in their products, requiring documentation of equipment cleaning and sharing best allergen practices with other corporations.

Information sharing among interested parties will go a long way to address the public health problem of food allergens. CFSAN anticipates that in 2001 public exchanges will continue through workshops as well as comments received on any guidance that issues. We look forward to constructive activities.

By Kenneth J. Falci, Ph.D., Kathy L. Gombas and Elisa L. Elliot, Ph.D.
Series Editor: Catherine "Kitty" Bailey, M.Ed.

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***Kathy L. Gombas** is the Deputy Director of the Division of HACCP Programs, CFSAN, FDA. Her division provides technical expertise and leadership in areas of food safety programs and HACCP to support the development of agency policies, regulations, standards and training.*

***Elisa L. Elliot, Ph.D.**, is a microbiologist in the Division of HACCP Programs, CFSAN, FDA, with lead responsibility for the food safety portion of the U. S. DHHS Healthy People 2010 initiative. She began her 11-year career with FDA as a researcher developing methods for* Vibrio *species.*

REFERENCES

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Guidance for Industry

Voluntary Labeling Indicating Whether Foods Have or Have Not Been Developed Using Bioengineering

Draft Guidance

This guidance document is being distributed for comment purposes only.

Draft released for comment January 2001.

Comments and suggestions regarding this draft document should be submitted by to Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with Docket Number 00D-1598. For questions regarding this draft document contact Catalina Ferre-Hockensmith, (202) 205-4168.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Food Safety and Applied Nutrition

Guidance for Industry

Voluntary Labeling Indicating Whether Foods Have or Have Not Been Developed Using Bioengineering

Draft Guidance

This draft guidance represents FDA's current thinking on voluntary labeling of foods indicating whether foods have or have not been developed using bioengineering. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such an approach satisfies the requirements of applicable statutes and regulations. The draft guidance is being distributed for comment purposes in accordance with FDA's Good Guidance Practices (65 FR 56468, September 19, 2000).

BACKGROUND

In the Federal Register of May 29, 1992 (57 FR 22984), FDA published its "Statement of Policy: Foods Derived from New Plant Varieties" (the 1992 policy). The 1992 policy applies to foods developed from new plant varieties, including varieties that are developed using recombinant deoxyribonucleic acid (rDNA) technology (which is often referred to as "genetic engineering" or "biotechnology"). This guidance document refers to foods derived from plant varieties that are developed using rDNA technology as "bioengineered foods." In addition, because the Federal Food Drug, and Cosmetic Act (the act) defines food as articles used for food or drink for man or other animals, this

guidance document applies to animal feeds as well as to human foods. The 1992 policy provides guidance to industry on scientific and regulatory issues related to bioengineered foods and solicited written comments from interested persons. The policy includes guidance on questions to be answered by developers of foods from new plant varieties, to ensure that the new products are safe and comply with applicable legal requirements. It also encourages continuation of the general practice of the food industry to consult with the agency about the safety of new foods, e. g., bioengineered foods.

In the 1992 policy, FDA also addresses the labeling of foods derived from new plant varieties, including plants developed by bioengineering. The 1992 policy does not establish special labeling requirements for bioengineered foods as a class of foods. The policy states that FDA has no basis for concluding that bioengineered foods differ from other foods in any meaningful or uniform way, or that, as a class, foods developed by the new techniques present any different or greater safety concern than foods developed by traditional plant breeding.

To fully understand the agency's mandate and authority in requiring labeling of foods, one must refer to the Federal Food, Drug, and Cosmetic Act (the act) to determine the extent to which the agency is charged with governing labeling of foods. Section 403 governs the labeling of foods. Under section 403(a)(1), a food is misbranded if its labeling is false or misleading in any particular. Section 201(n) of the act provides additional guidance on how labeling may be misleading. It states that labeling is

misleading if it fails to reveal facts that are material in light of representations made or suggested in the labeling, or material with respect to consequences that may result from the use of the food to which the labeling relates under the conditions of use prescribed in the labeling, or under such conditions of use as are customary or usual. While the legislative history of section 201(n) contains little discussion of the word "material," there is precedent to guide the agency in its decision regarding whether information on a food is in fact material. Historically, the agency has generally interpreted the scope of the materiality concept to mean information about the attributes of the food itself. FDA has required special labeling on the basis of it being "material" information in cases where the absence of such information may: 1) pose special health or environmental risks (e.g., warning statement on protein products used in very low calorie diets); 2) mislead the consumer in light of other statements made on the label (e.g., requirement for quantitative nutrient information when certain nutrient content claims are made about a product); or 3) in cases where a consumer may assume that a food, because of its similarity to another food, has nutritional, organoleptic, or functional characteristics of the food it resembles when in fact it does not (e.g., reduced fat margarine not suitable for frying).

Although the 1992 policy does not require special labeling for bioengineered foods, the agency advised in that policy that labeling requirements that apply to foods in general also apply to foods produced using biotechnology. Section 403(i) of the act requires that each food bear a common or usual name or, in the absence of such a name, an appropriately

descriptive term. In addition, under section 201(n), the label of the food must reveal all material facts about the food. Thus:

- If a bioengineered food is significantly different from its traditional counterpart such that the common or usual name no longer adequately describes the new food, the name must be changed to describe the difference.

- If an issue exists for the food or a constituent of the food regarding how the food is used or consequences of its use, a statement must be made on the label to describe the issue.

- If a bioengineered food has a significantly different nutritional property, its label must reflect the difference.

- If a new food includes an allergen that consumers would not expect to be present based on the name of the food, the presence of that allergen must be disclosed on the label.

In the Federal Register of April 28, 1993 (58 FR 25837), the agency requested data and information on certain labeling issues that had arisen from the labeling guidance in the 1992 policy. In 1999, the agency announced that it would hold three public meetings (64 FR 57470; October 25, 1999). The purpose of those meetings was for the agency to share its current approach and experience over the

previous five years regarding bioengineered foods, to solicit views on whether FDA's policies should be modified, and to gather information to be used to assess the most appropriate means of providing information to the public about bioengineered products in the food supply. The agency received more than 50,000 written comments about its policy regarding safety and labeling of bioengineered foods. The theme related to labeling in those comments and the testimony at the meetings was that there are very strongly held but divergent views as to whether bioengineered foods should be required to bear special labeling. However, there was general agreement that providing more information to consumers about bioengineered foods would be useful. A number of comments supported the need for guidance from FDA regarding appropriate ways that industry could voluntarily provide information on a food label about bioengineering.

FDA has reviewed information in the comments received in response to the 1992 policy and the 1993 information request as well as the comments from the 1999 meetings. Most of the comments that addressed labeling requested mandatory disclosure of the fact that the food or its ingredients was bioengineered or was produced from bioengineered food. However, these comments did not provide data or other information regarding consequences to consumers from eating the foods or any other basis for FDA to find under section 201(n) of the act that such a disclosure was a material fact. Many of the comments expressed concern about possible long term consequences from consuming bioengineered foods, but they

did not contend that any of the bioengineered foods already on the market have adverse health effects. The comments were mainly expressions of concern about the unknown. The agency is still not aware of any data or other information that would form a basis for concluding that the fact that a food or its ingredients was produced using bioengineering is a material fact that must be disclosed under sections 403(a) and 201(n) of the act. FDA is therefore reaffirming its decision to not require special labeling of all bioengineered foods.

The agency is providing the following guidance to assist manufacturers who wish to voluntarily label their foods as being made with or without the use of bioengineered ingredients. While the use of bioengineering is not a material fact, many consumers are interested in the information, and some manufacturers may want to respond to this consumer desire. The guidance was developed using information from the comments and from focus groups, as well as other resources, and is intended to help ensure that labeling is truthful and not misleading.

GUIDANCE

In determining whether a food is misbranded, FDA would review label statements about the use of bioengineering to develop a food or its ingredients under sections 403(a) and 201(n) of the act. Under section 403(a) of the act, a food is

misbranded if statements on its label or in its labeling are false or misleading in any particular. Under section 201(n), both the presence and the absence of information are relevant to whether labeling is misleading. That is, labeling may be misleading if it fails to disclose facts that are material in light of representations made about a product or facts that are material with respect to the consequences that may result from use of the product. In determining whether a statement that a food is or is not genetically engineered is misleading under sections 201(n) and 403(a) of the act, the agency will take into account the entire label and labeling.

Statements about foods developed using bioengineering

FDA recognizes that some manufacturers may want to use informative statements on labels and in labeling of bioengineered foods or foods that contain ingredients produced from bioengineered foods. The following are examples of some statements that might be used. The discussion accompanying each example is intended to provide guidance as to how similar statements can be made without being misleading.

- "Genetically engineered" or "This product contains cornmeal that was produced using biotechnology."

The information that the food was bioengineered is optional and this kind of simple statement is not likely to be misleading. However, focus group data indicate that

consumers would prefer label statements that disclose and explain the goal of the technology (why it was used or what it does for/to the food) (Ref. 1). Consumers also expressed some preference for the term "biotechnology" over such terms as "genetic modification" and "genetic engineering" (Ref. 1).

- "This product contains high oleic acid soybean oil from soybeans developed using biotechnology to decrease the amount of saturated fat."

This example includes both required and optional information. As discussed above in the background section, when a food differs from its traditional counterpart such that the common or usual name no longer adequately describes the new food, the name must be changed to describe the difference. Because this soybean oil contains more oleic acid than traditional soybean oil, the term "soybean oil" no longer adequately describes the nature of the food. Under section 403(i) of the act, a phrase like "high oleic acid" would be required to appear as part of the name of the food to describe its basic nature. The statement that the soybeans were developed using biotechnology is optional. So is the statement that the reason for the change in the soybeans was to reduce saturated fat.

- "These tomatoes were genetically engineered to improve texture."

In this example, the change in texture is a difference that may have to be described on the label. If the texture improvement makes a significant difference in the finished product, sections 201(n) and 403(a)(1) of the act would require

disclosure of the difference for the consumer. However, the statement must not be misleading. The phrase "to improve texture" could be misleading if the texture difference is not noticeable to the consumer. For example, if a manufacturer wanted to describe a difference in a food that the consumer would not notice when purchasing or consuming the product, the manufacturer should phrase the statements so that the consumer can understand the significance of the difference. If the change in the tomatoes was intended to facilitate processing but did not make a noticeable difference in the processed consumer product, a phrase like "to improve texture for processing" rather than "to improve texture" should be used to ensure that the consumer is not misled. The statement that the tomatoes were genetically engineered is optional.

- "Some of our growers plant tomato seeds that were developed through biotechnology to increase crop yield."

The entire statement in this example is optional information. The fact that there was increased yield does not affect the characteristics of the food and is therefore not necessary on the label to adequately describe the food for the consumer. A phrase like "to increase yield" should only be included where there is substantiation that there is in fact the stated difference.

Where a benefit from a bioengineered ingredient in a multi-ingredient food is described, the statement should be worded so that it addresses the ingredient and

not the food as a whole; for example, "This product contains high oleic acid soybean oil from soybeans produced through biotechnology to decrease the level of saturated fat." In addition, the amount of the bioengineered ingredient in the food may be relevant to whether the statement is misleading. This would apply especially where the bioengineered difference is a nutritional improvement. For example, it would likely be misleading to make a statement about a nutritionally improved ingredient on a food that contains only a small amount of the ingredient, such that the food's overall nutritional quality would not be significantly improved.

FDA reminds manufacturers that the optional terms that describe an ingredient of a multi-ingredient food as bioengineered should not be used in the ingredient list of the multi-ingredient food. Section 403(i)(2) of the act requires each ingredient to be declared in the ingredient statement by its common or usual name. Thus, any terms not part of the name of the ingredient are not permitted in the ingredient statement. In addition, 21 CFR 101.2(e) requires that the ingredient list and certain other mandatory information appear in one place without other intervening material. FDA has long interpreted any optional description of ingredients in the ingredient statement to be intervening material that violates this regulation.

Statements about foods that are not bioengineered or that do not contain ingredients produced from bioengineered foods

Terms that are frequently mentioned in discussions about labeling foods with respect to bioengineering include "GMO free" and "GM free." "GMO" is an acronym for "genetically modified organism" and "GM" means "genetically modified." Consumer focus group data indicate that consumers do not understand the acronyms "GMO" and " GM" and prefer label statements with spelled out words that mean bioengineering (Ref. 1).

Terms like "not genetically modified" and "GMO free," that include the word "modified" are not technically accurate unless they are clearly in a context that refers to bioengineering technology. "Genetic modification" means the alteration of the genotype of a plant using any technique, new or traditional. "Modification" has a broad context that means the alteration in the composition of food that results from adding, deleting, or changing hereditary traits, irrespective of the method. Modifications may be minor, such as a single mutation that affects one gene, or major alterations of genetic material that affect many genes. Most, if not all, cultivated food crops have been genetically modified. Data indicate that consumers do not have a good understanding that essentially all food crops have been genetically modified and that bioengineering technology is only one of a number of technologies used to genetically modify crops. Thus, while it is accurate to say that a bioengineered food was "genetically modified," it likely would be inaccurate to state that a food that had not been produced using biotechnology

was "not genetically modified" without clearly providing a context so that the consumer can understand that the statement applies to bioengineering.

The term "GMO free" may be misleading on most foods, because most foods do not contain organisms (seeds and foods like yogurt that contain microorganisms are exceptions). It would likely be misleading to suggest that a food that ordinarily would not contain entire "organisms" is "organism free."

There is potential for the term "free" in a claim for absence of bioengineering to be inaccurate. Consumers assume that "free" of bioengineered material means that "zero" bioengineered material is present. Because of the potential for adventitious presence of bioengineered material, it may be necessary to conclude that the accuracy of the term "free" can only be ensured when there is a definition or threshold above which the term could not be used. FDA does not have information with which to establish a threshold level of bioengineered constituents or ingredients in foods for the statement "free of bioengineered material." FDA recognizes that there are analytical methods capable of detecting low levels of some bioengineered materials in some foods, but a threshold would require methods to test for a wide range of genetic changes at very low levels in a wide variety of foods. Such test methods are not available at this time. The agency suggests that the term "free" either not be used in bioengineering label statements or that it be in a context that makes clear that a zero level of bioengineered

material is not implied. However, statements that the food or its ingredients, as appropriate, was not developed using bioengineering would avoid or minimize such implications. For example,

- "We do not use ingredients that were produced using biotechnology;"
- "This oil is made from soybeans that were not genetically engineered;" or
- "Our tomato growers do not plant seeds developed using biotechnology."

A statement that a food was not bioengineered or does not contain bioengineered ingredients may be misleading if it implies that the labeled food is superior to foods that are not so labeled. FDA has concluded that the use or absence of use of bioengineering in the production of a food or ingredient does not, in and of itself, mean that there is a material difference in the food. Therefore, a label statement that expresses or implies that a food is superior (e.g., safer or of higher quality) because it is not bioengineered would be misleading. The agency will evaluate the entire label and labeling in determining whether a label statement is in a context that implies that the food is superior.

In addition, a statement that an ingredient was not bioengineered could be misleading if there is another ingredient in the food that was bioengineered. The claim must not misrepresent the absence of bioengineered material. For example, on a product made largely of bioengineered corn flour and a small amount of

soybean oil, a claim that the product "does not include genetically engineered soybean oil" could be misleading. Even if the statement is true, it is likely to be misleading if consumers believe that the entire product or a larger portion of it than is actually the case is free of bioengineered material. It may be necessary to carefully qualify the statement in order to ensure that consumers understand its significance.

Further, a statement may be misleading if it suggests that a food or ingredient itself is not bioengineered, when there are no marketed bioengineered varieties of that category of foods or ingredients. For example, it would be misleading to state "not produced through biotechnology" on the label of green beans, when there are no marketed bioengineered green beans. To not be misleading, the claim should be in a context that applies to the food type instead of the individual manufacturer's product. For example, the statement "green beans are not produced using biotechnology" would not imply that this manufacturer's product is different from other green beans.

Substantiation of label statements

A manufacturer who claims that a food or its ingredients, including foods such as raw agricultural commodities, is not bioengineered should be able to substantiate that the claim is truthful and not misleading. Validated testing, if available, is the

most reliable way to identify bioengineered foods or food ingredients. For many foods, however, particularly for highly processed foods such as oils, it may be difficult to differentiate by validated analytical methods between bioengineered foods and food ingredients and those obtained using traditional breeding methods. Where tests have been validated and shown to be reliable they may be used. However, if validated test methods are not available or reliable because of the way foods are produced or processed, it may be important to document the source of such foods differently. Also, special handling may be appropriate to maintain segregation of bioengineered and nonbioengineered foods. In addition, manufacturers should consider appropriate recordkeeping to document the segregation procedures to ensure that the food's labeling is not false or misleading. In some situations, certifications or affidavits from farmers, processors, and others in the food production and distribution chain may be adequate to document that foods are obtained from the use of traditional methods. A statement that a food is "free" of bioengineered material may be difficult to substantiate without testing. Because appropriately validated testing methods are not currently available for many foods, it is likely that it would be easier to document handling practices and procedures to substantiate a claim about how the food was processed than to substantiate a "free" claim.

FDA has been asked about the ability of organic foods to bear label statements to the effect that the food (or its ingredients) was not produced using biotechnology.

On December 21, 2000, the Agriculture Marketing Service of the U.S. Department of Agriculture (USDA) published final regulations on procedures for organic food production (National Organic Program final rule; 65 FR 80548). That final rule requires that all but the smallest organic operations be certified by a USDA accredited agent and lays out the requirements for organic food production. Among those requirements is that products or ingredients identified as organic must not be produced using biotechnology methods. The national organic standards would provide for adequate segregation of the food throughout distribution to assure that non-organic foods do not become mixed with organic foods. The agency believes that the practices and record keeping that substantiate the "certified organic" statement would be sufficient to substantiate a claim that a food was not produced using bioengineering.

References

1. Levy, A.S., Derby, B.M., "Report on Consumer Focus Groups on Biotechnology", Consumer Studies Team, Center for Food Safety and Nutrition, Food and Drug Administration, Washington, D.C., 2000

withdrawn, the dates of these actions, and the reasons for these actions.

(10) Other relevant data and information that the Director, CBER, determines are necessary for the appropriate consideration of the public health and scientific issues, including relevant ethical issues, raised by human gene therapy or xenotransplantation.

10. Section 601.53 is added to subpart F to read as follows:

§ 601.53 Submission of certain data and information related to human gene therapy or xenotransplantation for public disclosure.

(a) A sponsor of an IND shall submit to FDA for public disclosure in a redacted version the submissions identified in paragraphs (b)(1) through (b)(5) of this section. Each submission shall include all applicable information identified as disclosable in § 601.52, but shall be redacted to remove or obscure all information considered confidential as a trade secret, certain confidential commercial information, such as information regarding commercial licensing agreements or the identification of suppliers, and names and other personal identifiers of patients and, except as specifically provided in this section, names and personal identifiers of any third party, such as physicians or hospitals, must be redacted.

(b) The following shall be submitted in a suitably redacted version and in duplicate at the time points noted:

(1) Information as defined under § 601.52 at the time of initial IND submission.

(2) Any amendment documenting changes or additions to the information as defined under § 601.52 at the time the amendment goes into effect.

(3) IND safety reports at the time of submission of the initial report to FDA.

(4) The annual report, within 60 days of the anniversary date that the IND went into effect, in accordance with § 312.33 of this chapter.

(5) Other information upon the specific request of the Director, CBER.

(c) The submissions identified in paragraph (b) of this section shall be submitted in a form readily separable from the original unabridged submission to FDA and clearly marked on each page of the redacted version as suitable for public disclosure.

(d) Any copies of copyrighted material shall be submitted in a single appendix to each redacted version. Copyrighted materials whose copyright is not owned by the applicant shall not be included in any other section of the redacted versions. A bibliography of copyrighted materials contained in the appendix shall be included as part of each redacted version.

(e) Any data or information submitted to FDA as a redacted version for public disclosure in accordance with paragraph (a) of this section shall be accompanied by the following statement signed by a responsible individual:

The information contained herein has been redacted for public disclosure. The only material removed from these records is: Confidential commercial or trade secret information exempt from disclosure under the Freedom of Information Act (5 U.S.C. 552 (b)(4)) and the Food and Drug Administration's implementing regulations (21 CFR 20.61); names and other personal identifiers of patients and, except as specifically provided in the regulations, names and other personal identifiers of any third party.

I declare, under the penalty of perjury, that the foregoing is true and correct.

Dated: December 20, 2000.

Jane E. Henney,

Commissioner of Food and Drugs.

Donna E. Shalala,

Secretary of Health and Human Services.

[FR Doc. 01–1048 Filed 1–17–01; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Parts 192 and 592

[Docket No. 00N–1396]

RIN 0910–AC15

Premarket Notice Concerning Bioengineered Foods

AGENCY: Food and Drug Administration, HHS.

ACTION: Proposed rule.

SUMMARY: The Food and Drug Administration (FDA) is proposing to require the submission to the agency of data and information regarding plant-derived bioengineered foods that would be consumed by humans or animals. FDA is proposing that this submission be made at least 120 days prior to the commercial distribution of such foods. FDA is taking this action to ensure that it has the appropriate amount of information about bioengineered foods to help to ensure that all market entry decisions by the industry are made consistently and in full compliance with the law. The proposed action will permit the agency to assess on an ongoing basis whether plant-derived bioengineered foods comply with the standards of the Federal Food, Drug, and Cosmetic Act (the act).

DATES: Submit written comments on the proposed rule by April 3, 2001. Submit written comments on the information collection provisions by February 20, 2001.

See section XIV of this document for the proposed effective date of a final rule based on this document.

ADDRESSES: Submit written comments to the Dockets Management Branch (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit written comments on the information collection provisions to the Office of Information and Regulatory Affairs, OMB, New Executive Office Bldg., 725 17th St. NW., rm. 10235, Washington, DC 20503, Attn: Desk Officer for FDA.

FOR FURTHER INFORMATION CONTACT:

Regarding human food issues: Linda S. Kahl, Center for Food Safety and Applied Nutrition (HFS–206), Food and Drug Administration, 200 C St. SW., Washington, DC 20204, 202–418–3101.

Regarding animal feed issues: William D. Price, Center for Veterinary Medicine (CVM) (HFV–200), Food and Drug Administration, 7500 Standish Pl., Rockville, MD 20855, 301–827–6652.

SUPPLEMENTARY INFORMATION:

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consultation involved FLAVR SAVR™ tomatoes.[2] In developing FLAVR SAV™ tomatoes, Calgene used rDNA technology to introduce an antisense polygalacturonase gene, which was derived from tomatoes, and the kanamycin resistance gene (the *kan*^{r} gene), which encodes the enzyme aminoglycoside-3′-phosphotransferase II (APH(3′)II). The enzyme APH(3′)II confers resistance to the clinically used antibiotics kanamycin and neomycin in the selection of new plant varieties developed using rDNA technology. The use of APH(3′)II raised several issues that had not previously been evaluated by the agency in the context of food safety. The initial consultation between the agency and Calgene about the intended use of APH(3′)II, which in this instance resulted in the filing and approval of a food additive petition (59 FR 26700, May 23, 1994), was an effective mechanism to fully explore and resolve these issues.

The resolution of these and other scientific issues entailed the use of nontraditional approaches to the evaluation of food safety. For example, traditional evaluation of the safety of a food additive frequently includes toxicological tests conducted in accordance with the principles outlined in the agency's "Toxicological Principles for the Safety Assessment of Direct Food Additives and Color Additives Used in Food" (Redbook (Ref. 3)).[3] In addition to guidance on when certain tests may be appropriate, the Redbook includes specific recommendations on the protocols for conducting such tests.

In contrast, issues raised during the consultations on APH(3′)II and the FLAVR SAVR™ tomato required evaluation of data generated using procedures that had only rarely been used in the evaluation of food safety. For example, Calgene used "Southern blots" to determine which DNA sequences had been transferred to FLAVR SAVR™ tomatoes, "Northern blots" to demonstrate the intended technical effect in FLAVR SAVR™ tomatoes, and "Western blots" to determine the amount of APH(3′)II present in FLAVR SAVR™ tomatoes. The use of nontraditional strategies in the evaluation of food safety likely will become the norm as the use of rDNA technology expands, and further consultations between industry and the agency would foster the identification and design of reasonable test procedures to evaluate the composition and safety of whole foods.

Consultations are an appropriate forum for industry and the agency to address proactively issues that are relevant to bioengineered foods, and developers have actively consulted with FDA about their products since the issuance of the 1992 policy. In June 1996, FDA provided guidance to industry on procedures for these consultations (the 1996 procedures (Ref. 5)).[4] Under that process, a developer who intends to commercialize a bioengineered food meets with the agency to identify and discuss relevant safety, nutritional, or other regulatory issues regarding the bioengineered food prior to marketing it. Depending on the experience the agency and the developer have with the kind of modification being considered, a developer may initiate such a consultation early or late in the development of the food. When the developer believes that it has accumulated adequate data or information to address any issues raised during the consultation, the developer begins the "final consultation" by submitting to FDA a summary of its scientific and regulatory assessment of the food. To date, the agency has completed its evaluation of data or other information from more than 45 such consultations (Ref. 6). FDA believes that, to date, all developers of bioengineered foods commercially marketed in the United States have consulted with the agency prior to marketing the food.

FDA continues to believe that the consultation process is appropriate for bioengineered foods. Accordingly, this proposed rulemaking includes FDA's recommendation that developers consult with the agency to identify and discuss relevant safety, nutritional, or other regulatory issues regarding a bioengineered food (see proposed § 192.10 and section VI of this document).

C. Public Meetings

In 1999, FDA announced that the agency would hold three public meetings, each in a different region of the United States (64 FR 57470, October 25, 1999). The purpose of those meetings was for the agency to share its current approach and experience over the past 5 years regarding bioengineered foods, to solicit views on whether FDA's policies or procedures should be modified, and to gather information to be used to assess the most appropriate means of providing information to the public about bioengineered products in the food supply. In the notice announcing the public meetings (64 FR 57470), FDA requested comments on specific questions regarding bioengineered foods. As a result of those meetings and the request for comments, the agency subsequently received more than 35,000 written comments about its policy regarding bioengineered foods.

At those meetings, and in the comments, FDA heard three messages very clearly. First, there does not appear to be any new scientific information that raises questions about the safety of bioengineered foods currently being marketed. Second, some of the public is concerned about FDA's existing guidance and regulatory approach to overseeing the safety of these products. These concerns include whether FDA's guidance and regulatory approach will be adequate for future developments and whether firms will continue to inform FDA about new bioengineered foods under the present program. In addition, there was a concern that the current regulatory process lacks transparency (e.g., because FDA discloses each consultation about a bioengineered food only at the end of the process). Third, there are very strongly held but divergent views as to whether bioengineered foods should bear special labeling. However, there was general agreement that providing more information to consumers about bioengineered foods would be useful[5] (Ref. 8).

II. Legal Authority

FDA is responsible for ensuring that all foods[6] in the American food supply conform to the applicable provisions of the law. The act provides FDA with broad authority to regulate the safety and wholesomeness of food. In particular, the act prohibits the adulteration of food under section 402 of the act (21 U.S.C. 342) and the misbranding of food under section 403

[2] This consultation was concluded in May 1994 (59 FR 26647 at 26700, May 23, 1994).

[3] In 1993, the Center for Food Safety and Applied Nutrition (CFSAN) released a revised Redbook for public comment (58 FR 16536, March 29, 1993). Following its evaluation of comments on each draft chapter of the Redbook, CFSAN is making revised chapters available on its Internet site (Ref. 4).

[4] In October 1997, FDA made administrative revisions to these procedures to reflect reorganizations within the Office of Premarket Approval, CFSAN, and the Center for Veterinary Medicine (CVM). In this document, FDA refers to these procedures as "the 1996 procedures" to reflect the year that the agency made them available.

[5] In May 2000, FDA announced that it intended to issue for public comment draft labeling guidance to aid manufacturers who wish to voluntarily label their products as made with or without the use of bioengineering or bioengineered ingredients (Ref. 7). The development of that draft guidance is outside the scope of this document.

[6] There are certain exceptions to this jurisdiction pertaining to meat, poultry, and egg products that are not relevant to this rulemaking.

soy beans for allergenicity, they found that people allergic to Brazil nuts were also allergic to the bioengineered soy (Refs. 9 and 10). Given the potential consequences to sensitive consumers of eating soy products containing a Brazil nut allergen, such a food would likely be considered misbranded within the meaning of sections 201(n) and 403(a)(1) of the act, unless the presence of the new allergen were disclosed to consumers.

Further, in certain circumstances, labeling may not be adequate or practical to ensure that consumers are aware of the presence of unexpected allergens. FDA would likely consider such food containing an unexpected allergen to be adulterated within the meaning of section 402(a)(1) of the act because the unexpected allergen rendered the food possibly injurious to health. With alterations of this type, FDA should be made aware of the modification and have an opportunity to assess whether and how the food could legally be marketed. Specifically, FDA should have the opportunity to consider whether any labeling proposed by the developer would ensure that the engineered food is not misbranded within the meaning of sections 201(n) and 403(a)(1) of the act, and whether, even with labeling, the food would be adulterated because it may be injurious to health within the meaning of section 402(a)(1) of the act.

Compositional changes in foods created through breeding may also present regulatory status issues. Although traditional breeding techniques can be used to alter significantly the compositional characteristics of food, rDNA technology enhances that ability because rDNA technology enables breeders to make targeted changes in plant components such as proteins and other constituents. For example, rDNA techniques would facilitate a breeder's ability to modify a soy plant so that the composition of oil derived from the plant would more closely resemble that of a tropical oil than that of conventional soy oil. In these circumstances, the name "soy oil" would likely not be suitable for the oil derived from the altered soy plant because the composition of the new oil is significantly different from what is customarily understood to be "soy oil". Thus, a new common or usual name would likely be required for this new oil to ensure that the oil is not misbranded under section 403(i)(1) of the act. FDA should be made aware of compositional changes of this type so that the agency may consider whether a new common or usual name is required and, if so, what that new name should be.

Additionally, rDNA technology has recently begun to be used to introduce multiple genes to generate new metabolic pathways (Ref. 11). New metabolic pathways are intended to result in the synthesis of substances not normally present in the host plant. Such modifications may alter the composition of the food in a significant manner that may raise nutritional or safety issues or that would require use of a new common or usual name.

In addition to enabling breeders to introduce desired new characteristics into foods, all breeding methods used to develop new plant varieties have a potential for unintentionally introducing undesired new characteristics into foods (57 FR 22986). Broadly speaking, a breeding method's potential for introducing unintended changes to the characteristics of a food results either from bringing into a food plant extraneous genetic material encoding trait(s) additional to the desired trait(s), or from introducing mutations (such as deletions, amplifications, insertions, rearrangements, or DNA base-pair changes) into the plant's native genetic material that alter some characteristic(s) of the food.

The most commonly used breeding method is a "narrow cross," which is hybridization between varieties of the same species. Hybridization between related species or genera that cannot be cross-fertilized is a "wide cross." Wide crosses are useful for expanding the range of genetic source material that can be introduced into food crops, but are performed relatively infrequently because of technical and logistical difficulties. Both wide and narrow crosses will introduce into plants extraneous genetic material along with the genetic material encoding the desired traits. Breeders then attempt to remove any undesired traits through extensive backcrossing.

Plant breeders also use mutagenic techniques to modify plants. These techniques include random mutagenesis using a mutagenic agent and somaclonal variation. (Somaclonal variation refers to the process of growing a plant up from tissue culture and observing for phenotypic changes, which are often due to chromosomal rearrangements or other mutations.) Both techniques can introduce undesirable mutations along with possible desirable mutations. As with hybridization, breeders perform backcrosses to eliminate any undesirable traits. Cell fusion poses similar issues to those posed by wide crosses (because it generally is performed between cells of different species of plants) and posed by somaclonal variation (because it involves growing a plant up from tissue culture).

Recombinant DNA technology greatly reduces the likelihood of introducing extraneous genetic material, as compared with hybridization, because it enables breeders to introduce only the gene or genes of interest, with little or no extraneous deoxyribonucleic acid (DNA). However, it shares with mutagenesis techniques a potential for introducing unintended effects through mutations. In part, this is because rDNA technology involves growing plants from tissue culture, which can exhibit somaclonal variation, and, more significantly, because breeders using this technology generally cannot control the location in the plant genome at which genetic material will insert when introduced into a plant. Thus, with rDNA technology, the introduced genetic segment may insert into a genetically active chromosomal location. Such insertion may disrupt or inactivate an important gene or a regulatory sequence that affects the expression of one or several genes, thereby potentially affecting adversely the safety of the food or raising other regulatory issues. Such an occurrence is referred to as an insertional mutation.

FDA believes that in the future, plant breeders will increasingly use rDNA techniques to achieve more complicated compositional changes to food, sometimes introducing multiple genes residing on multiple vectors to generate new metabolic pathways. FDA expects that with the increased introduction of multiple genes, unintended effects may become more common. For example, rice modified to express pro-vitamin A was shown to exhibit increased concentrations of xanthophylls (Ref. 11), and rice modified to reduce the concentration of a specific protein was found to exhibit an increased concentration of prolamine (Ref. 12).

FDA believes that the use of rDNA techniques in plant breeding may lead to unintended changes in foods that raise adulteration or misbranding questions. These unintended changes may cause a food to be adulterated because the food may be rendered injurious to health within the meaning of section 402(a)(1) of the act, or, in the absence of a new common or usual name, cause the food to be misbranded under section 403(i)(1) of the act. Because of its role in ensuring the safety of the U.S. food supply, FDA needs to be aware of the modifications to food source plants from the application of rDNA technology and any unintended effects in food that result so that the agency can evaluate whether the foods

to be utilized by plant breeders to an increasingly greater extent.

The confluence of the increasingly broader use of rDNA techniques to develop foods for human and animal use and the globalization of the world's food supply also suggest that FDA needs to be aware of the various foods developed using rDNA technology. Currently, approximately 45 percent of the United States' plant-derived food is imported, and that percentage continues to increase. The agency expects that rDNA techniques may, over time, be used increasingly by plant breeders and developers in countries that export foods to this country. In such circumstances, the accuracy of FDA's knowledge about the presence in the U.S. food supply of foods developed using rDNA techniques is likely to decrease. In addition, the awareness of particular food allergies is not uniform throughout the world because the diets of some populations do not contain sufficiently large amounts of a food such that the allergic potential has been demonstrated; in these circumstances, it is particularly important that FDA be aware of imported foods modified using rDNA techniques that may unexpectedly contain a substance that is an allergen.

For all these reasons, FDA believes that the food products of rDNA technology are appropriately made subject to greater regulatory scrutiny by FDA in the form of enhanced agency awareness of all such foods intended for commercial distribution. This increased agency awareness will ensure that at this stage of this continuously evolving technology, all market entry decisions about new bioengineered foods, including those intended for import into the United States, are made consistently and in full compliance with the law. Similarly, in order for the agency to evaluate fully and consistently the possible regulatory consequences of the alterations made possible using rDNA technology, FDA must be made aware of the bioengineered foods entering commercial distribution.

Section 701(a) of the act (21 U.S.C. 371(a)) authorizes the Secretary of the Department of Health and Human Services (the Secretary) to issue regulations for the efficient enforcement of the act; under section 903(d)(2) of the act (21 U.S.C. 393(d)(2), the Secretary is responsible for executing the act, including section 701(a), through the Commissioner of Food and Drugs. The authority under section 701(a) of the act to issue regulations under the act extends to both regulations that supplement a specific statutory mandate as well as regulations that are justified by the statutory scheme as a whole. (See *National Confectioner's Association* v. *Califano*, 569 F.2d 690, 693 (D.C. Cir. 1978), citing *Toilet Goods Association* v. *Gardner*, 387 U.S. 158, 163 (1967).) In assessing a regulation issued under section 701(a), it is important to consider both the statutory purpose as well as the practical aspects of the situation, including the possible enforcement problems that may be encountered by FDA. (See *National Confectioner's Association* v. *Califano*, 569 F.2d 690, 693 (D.C. Cir. 1978), citing *Toilet Goods Association* v. *Gardner*, 387 U.S. 158, 163 (1967).)

To ensure that FDA has the maximum amount of information about foods from bioengineered plants, the agency has tentatively concluded that, prior to initiation of commercial distribution in the United States of a bioengineered food, FDA must be notified of the intent to market such food, including foods intended for import into the United States. Notification will ensure that the agency is aware of all bioengineered foods entering commercial distribution that are subject to FDA's jurisdiction and will help to ensure that all market entry decisions by the industry are made consistently and in full compliance with the law. This will permit the agency to assess on an ongoing basis whether foods developed using rDNA technology comply with the standards of the act. FDA believes that it is essential that all those developing and marketing bioengineered foods participate fully and completely in the proposed notification program. Therefore, the agency is proposing that the notification program that is described in this document be mandatory.

Accordingly, for the reasons set forth above concerning the special circumstances of bioengineered foods, to enforce the act efficiently, and in particular, to administer efficiently the act's various provisions that relate to food as such provisions apply to bioengineered food, including section 301 of the act (21 U.S.C. 331) and sections 402, 403, and 409 of the act, FDA is proposing regulations to require that the agency be notified at least 120 days prior to the initiation of commercial distribution in the United States of a bioengineered food. The elements of FDA's proposed program are discussed in detail below.

III. Scope

FDA is proposing to require the submission to the agency of data and information regarding plant-derived bioengineered foods that would be consumed by humans or animals. FDA's proposal also includes a recommendation that prospective notifiers participate in a presubmission consultation program. The regulations regarding bioengineered foods that would be consumed by humans would be codified in new part 192. The regulations regarding bioengineered foods that would be consumed by animals would be codified in new part 592. The proposed regulations regarding bioengineered foods that would be consumed by animals parallel the proposed regulations regarding bioengineered foods that would be consumed by humans. For ease of discussion, in this proposed rule, FDA describes each of the regulations that would be codified in part 192, without describing the parallel regulations in part 592. Following this discussion, FDA describes areas of importance in the proposed animal feed regulations (section XI of this document).

IV. Definitions

FDA is proposing to codify five definitions that are associated with the proposed notification program (proposed § 192.1). These terms are bioengineered food, commercial distribution, notifier, premarket biotechnology notice (PBN or notice), and transformation event. FDA invites comments on these proposed definitions. FDA is particularly interested in comments on the proposed definitions of bioengineered food and transformation event. Specifically, FDA is requesting comment on whether these proposed definitions are consistent with the agency's intent (described in section V of this document) that the proposed notification program apply to a particular subset of plant-derived foods. Such comments may result in a modification to the proposed definitions.

Under the proposed definitions, a required PBN may be submitted by any person who is responsible for the development, distribution, importation, or sale of a bioengineered food. Based on the agency's experience, FDA expects that it ordinarily will be the seed developers and purveyors who notify the agency about a bioengineered food.

V. Requirement for Premarket Biotechnology Notice

FDA is proposing to require a submission to the agency of data and information regarding a plant-derived bioengineered food at least 120 days prior to the commercial distribution of the food (proposed § 192.5). The proposed regulation would include a bioengineered food derived from a new

(proposed § 192.10). The proposed recommendation describes procedures for requesting consultation and the public disclosure provisions that likely would apply to records that FDA maintains about the consultation. Under § 192.10(f), a notifier must state his view as to whether the fact that he is consulting with FDA, or any or all of the data or information that he submits to FDA, is exempt from disclosure under the Freedom of Information Act (FOIA) and must explain the basis for any such exemption claim. The recommendation to consult with FDA derives from the 1992 policy, the 1996 procedures, and FDA's experience under the 1996 procedures. FDA discusses the details of this proposed recommendation immediately below.

Using rDNA technology, bioengineered plants such as corn are now being developed for non-food uses. Examples of such applications include the transfer of genes that encode pharmaceutical proteins, oral vaccines, and enzymes that would be used for non-food industrial applications. In some cases, such as most of the pharmaceutical proteins, the final product would be a highly purified component of the plant commodity. In other cases, such as some oral vaccines, the final product would be a minimally processed plant commodity. In some cases, there may be a potential for a bioengineered plant commodity that is not intended for use in food to enter the food supply inadvertently. FDA encourages developers of bioengineered plants that are not intended for use in food or feed, but that theoretically could enter the food or feed supply, to participate in the consultation program described in this proposed rule. This participation would ensure that developers have given careful consideration to the procedures needed to ensure that their products do not inappropriately get into the food supply, and are aware of the legal implications if their products do.

A. Presubmission Consultation Program

FDA is proposing to recommend that a prospective notifier participate in a presubmission consultation program (proposed § 192.10(a)). Under the program (proposed § 192.10(b)), a prospective notifier would write to FDA and ask to consult about a bioengineered food. FDA would establish an administrative file for each consultation and would meet with a prospective notifier upon request. Although FDA may provide written feedback during the consultation, that feedback would not release the prospective notifier from the proposed requirement to notify FDA about the bioengineered food at least 120 days before commercialization of the food. The proposed presubmission consultation program derives from the 1992 policy, the 1996 procedures, and FDA's experience under the 1996 procedures.

B. Public Disclosure

FDA is proposing to provide information about the availability for public disclosure of: (1) The fact that a developer is consulting with FDA (proposed § 192.10(c)) and (2) the data or information in the file that FDA would establish for a presubmission consultation (proposed § 192.10(d)). The regulations would inform all parties of the fact that FDA must act in response to a request under FOIA for information on presubmission consultations, and must disclose, or protect from disclosure, the applicable record(s) in accordance with § 20.61 (21 CFR 20.61) (proposed § 192.10(c)(2) and (d)(1)).

In light of the significant public interest in bioengineered foods and in FDA's oversight of these foods, FDA believes that it is important for developers to be informed that FOIA may entitle the public to know that the developer has provided data or information to FDA about a bioengineered food and to receive a copy of those data or information. Likewise, FDA believes that it is equally important for the public to know that the fact that a developer is consulting with FDA may be exempt from disclosure under FOIA and that some or all of the data or information that are submitted to FDA during a presubmission consultation could be exempt from public disclosure.

Under FOIA, data or information that are submitted to the Federal Government are available for public disclosure unless those data or information fall within an established exemption of FOIA. The exemption that is most relevant to data or information provided to FDA during a presubmission consultation is "exemption 4," which applies to "trade secrets and commercial or financial information obtained from a person and privileged or confidential." (5 U.S.C. 552(b)(4)). FDA has issued regulations implementing exemption 4 of FOIA in § 20.61.

FDA believes that, in most cases, the fact that a developer is consulting with FDA would not constitute confidential commercial information. For example, most plants developed using rDNA technology are considered "regulated articles" under regulations of USDA's APHIS (7 CFR part 340), which regulates the introduction of certain "genetically engineered" plants. At some stage of research and development of a regulated article, a developer requests from APHIS a determination of the article's regulatory status, and, consistent with FOIA requirements, APHIS discloses that request. Thus, by virtue of the APHIS process, the fact that the developer is developing the plant and its food product would usually already be disclosed.

FDA also believes that, in most cases, most of the data or information provided to FDA during a presubmission consultation would not constitute a trade secret or confidential commercial information. For example, only a handful of the submissions that FDA has received under its current consultation program identified specific data or information that the developer claimed to be exempt under § 20.61. Nevertheless, there could be circumstances where a developer initiates a presubmission consultation about a product that has not previously been disclosed to the public and has grounds to claim that the fact of the consultation should not be available for public disclosure. In such circumstances, disclosing any data or information in the applicable submission would reveal the existence of the submission. Thus, as long as the existence of the consultation is exempt from disclosure, all data or information in the submission would necessarily be exempt from disclosure.

C. Standard Procedures

FDA is proposing that a prospective notifier ask FDA in writing for an opportunity to consult about a bioengineered food (proposed § 192.10(e)). A written request would provide clarity about the subject of the consultation.

FDA is proposing to require that a prospective notifier who initiates a consultation inform FDA whether, in his view, the fact of the consultation with FDA is confidential, and whether, in his view, any or all of the provided data or information is confidential (proposed § 192.10(f)(1)). FDA also is proposing to require that a prospective notifier who claims confidentiality for the existence or content of a presubmission consultation explain the basis for that claim (proposed § 192.10(f)(2)). FDA is proposing these requirements because of the significant public interest in bioengineered foods. These requirements would ensure that FDA is aware of the prospective notifier's position regarding the availability for public disclosure of the existence and content of the

take place through a meeting or through a telephone conference). FDA is highlighting the opportunity to discuss the bioengineered food by a mechanism other than a face-to-face meeting to minimize the potential that a small business or academic research group would elect not to participate in the program due to the cost of travel. Given the agency's experience under the current consultation process, FDA is confident that a meaningful dialogue can often be accomplished without a face-to-face meeting.

VII. Premarket Biotechnology Notice: Administrative Information

FDA is proposing to codify certain administrative information that would apply to a PBN (proposed § 192.20). The proposed administrative information includes information about where to send a PBN, the number of copies to send, how to include information in a foreign language, how to refer to data or information that are already in FDA's files, how to obtain guidance on scientific issues, and the prerogative of a notifier to withdraw a PBN from FDA's consideration. Many of these administrative aspects of the proposed notification program are consistent with procedures already in place for the food additive petition program (§ 171.1 (21 CFR 171.1)). FDA discusses the details of these administrative aspects of the proposed notification program immediately below.

A. Submissions to CFSAN for Use in Human Food, Animal Feed, or Both

FDA is proposing that a notifier send a PBN regarding a bioengineered food to CFSAN (proposed § 192.20(a)). As necessary and appropriate, CFSAN would coordinate FDA's evaluation of the PBN with CVM. The proposed regulation is consistent with the approach that FDA recommended in the 1996 procedures, an approach that has worked well.

B. Paper Copies

FDA is proposing that a prospective notifier send to the agency an original paper version and one paper copy of a PBN (including any amendments) (proposed § 192.20(b)(1)). A notifier would have an option to submit one additional paper copy or, under proposed 192.20(c)(1), to submit an electronic copy that is formatted in a manner that makes it suitable for FDA to use while evaluating the PBN. The number of paper copies required by the regulation is consistent with the number of paper copies that FDA currently requires for other premarket submissions, such as a food additive petition. A requirement for multiple paper copies generally serves the purpose of providing a copy of the submission to multiple scientific reviewers. However, as discussed below, FDA also is recommending that a notifier submit an electronic copy of a PBN that is formatted in a manner that makes it suitable for FDA to use in evaluating a PBN. Because scientific reviewers could accomplish their review by accessing the electronic copy, under the proposed rule, a notifier who submits an electronic evaluation copy would submit one less paper copy. FDA would retain the original paper version at CFSAN, while the paper copy would be retained at CVM. Comments may result in a modification to the proposed requirement to submit a single paper copy.

Under the regulation, the paper copy would be the official version at FDA. This provision would clarify the status of an electronic copy that FDA also is proposing to require [11] (see proposed § 192.20(c)(1) and section VII.C of this document).

FDA is proposing that a notifier who claims that specific data or information in the PBN are confidential must prepare and submit one paper copy of the PBN that does not contain any of those data or information (proposed § 192.20(b)(2)). Consistent with the EFOIA proposed rule, the notifier would prepare this redacted paper copy in a manner that clearly identifies the location and relative size of deleted information. As discussed previously regarding a presubmission consultation (see section VI.C of this document), the redacted copy would be very useful as it would communicate very clearly which data or information the notifier considers to be exempt from disclosure.

C. Electronic Copies

FDA is proposing to include in the regulation a recommendation that a notifier submit an electronic copy (the evaluation copy) that is formatted in a manner that makes it suitable for FDA to use while evaluating the PBN (proposed § 192.20(c)(1)). Because technology is advancing at a rapid pace, the regulation would inform notifiers how to obtain information about the appropriate format of the electronic copy rather than specify that format. Under the regulation, a notifier would provide such an electronic copy of both the original PBN and of any amendments to the PBN. FDA is recommending the submission of an electronic evaluation copy to take advantage of the fact that contemporary technology makes it possible for notifiers to send, and FDA to evaluate, submissions of data or information in electronic form, and the availability of an electronic evaluation copy has the potential to improve the efficiency of FDA's review. To encourage manufacturers to submit an electronic evaluation copy, a notifier who submits such a copy would submit a total of two, rather than three, paper copies.

FDA also is proposing to require that a notifier submit an electronic copy (the disclosure copy) that is formatted in a manner that makes it suitable for FDA to use to make a PBN available to the public in an electronic reading room (proposed § 192.20(c)(2)). As would be the case with the electronic evaluation copy, the regulation would inform notifiers how to obtain information about the appropriate format of the electronic copy and a notifier would be required to provide such an electronic copy of both the original PBN and of any amendments to the PBN. Consistent with the EFOIA proposed rule, a notifier would delete data or other information claimed to be confidential from the electronic copy in a manner that clearly identifies the location and relative size of deleted information. FDA is proposing to require an electronic disclosure copy to facilitate the agency's compliance with EFOIA, which includes provisions regarding the availability of records in electronic form and the establishment of "electronic reading rooms." As discussed in the EFOIA proposed rule, section 4 of EFOIA (5 U.S.C. 552(a)(2)(D)) adds a new category of records that agencies must make available in their public reading rooms. This new category consists of copies of records that have been released to any person under FOIA and that, because of their subject matter, the agency determines have become or are likely to become the subject of subsequent requests for substantially the same records. In light of the significant public interest in bioengineered foods and in FDA's oversight of these foods, FDA has tentatively concluded that it is likely that each submitted PBN would be requested under FOIA multiple times.

The preparation of an electronic copy formatted in a manner that makes it suitable for FDA to use to make a PBN available to the public in an electronic reading room will require use of computer technology. Although the use

[11] Under 21 CFR 11.1(c), an electronic record that meets the requirements of 21 CFR part 11 may be used in lieu of a paper record, unless paper records are specifically required. However, CFSAN is not prepared, at this time, to accept an electronic record as the official record because CFSAN does not yet have specific guidance for the submission of records only in electronic form.

notifier's view that the bioengineered food is as safe as comparable food and that the intended use of the bioengineered food is in compliance with all applicable requirements of the act (proposed § 192.25(a)(1)). Applicable requirements of the act would include, for example, the requirement under section 409(a) and 402(a)(2)(C) of the act for FDA review and approval of a food additive and the requirement under section 201(n) and 403 of the act that labeling for the food be appropriate. FDA also is proposing that a notifier state that to the best of the notifier's knowledge, the PBN is a representative and balanced submission that includes information, unfavorable as well as favorable, pertinent to the evaluation of the safety, nutritional, or other regulatory issues that may be associated with the bioengineered food (proposed § 192.25(a)(2)). FDA is proposing that the notifier attest to these statements because, under the act, developers of new foods have a responsibility to ensure that the foods they offer to consumers are safe and in compliance with all requirements of the act (57 FR 22984 at 22985).

FDA is proposing the standard "as safe as" because this is the standard that the agency currently uses to evaluate a notice that is submitted under the 1996 procedures. Because the proposed standard is a comparative standard ("as safe as"), it takes into account circumstances such as the existence of naturally occurring toxicants in many plants (e.g., solanine that occurs naturally in potatoes). As discussed below (see section VIII.G.1 and proposed § 192.25(g)(1)), FDA also is proposing that the notifier provide a justification for selecting a particular food or foods as the "comparable food" to which the notifier will compare the bioengineered food.

2. Statements Regarding the Availability of Data and Information for FDA's Review

FDA is proposing to require that a notifier agree to make relevant data or information that are not included in the PBN available to FDA upon request while FDA is evaluating the PBN or for cause (proposed § 192.25(a)(3)). FDA is proposing this requirement to ensure that the agency will have access to relevant data or other information if safety questions arise after the bioengineered food enters commercial distribution. This proposed requirement will also continue a practice that began under the 1996 procedures.

FDA also is proposing that a notifier agree to two procedures for making such data or information available to FDA (proposed § 192.25(a)(4)). The first procedure is to allow FDA to review and copy these data or information at a specified address during customary business hours. The second procedure is to send these data or information to FDA. FDA is proposing that a notifier agree to both of these two procedures to provide flexibility and efficiency to both the notifier and the agency.

3. Statement Regarding Public Disclosure

FDA is proposing that a notifier inform FDA as to whether the notifier claims that the existence of a PBN, or any or all of the data or information in the PBN, is exempt from disclosure under the FOIA and explain the basis for that claim (proposed § 192.25(a)(5)). FDA is proposing these requirements in light of the significant public interest in bioengineered foods. These requirements would ensure that FDA is aware of the notifier's position regarding the availability for public disclosure of the existence and content of a PBN. In addition, FDA believes that these requirements would alert a notifier that the data or information contained in a PBN are available for disclosure unless the applicable criteria for exemption are satisfied.

As discussed more fully below, this proposed rule assumes that the existence and content of a PBN is available for public disclosure unless the notifier establishes that the existence of the notice constitutes confidential commercial information or that specific data or information in the PBN constitute a trade secret or confidential commercial information. Thus, the proposed rule acknowledges that there could be circumstances in which the existence or content (or a portion of the content) of a PBN would be eligible for an exemption from public disclosure.

B. Part II: Synopsis

FDA is proposing that the first section of a PBN be a synopsis (proposed § 192.25(b)) that includes the same information that FDA is recommending for inclusion in a presubmission consultation (see proposed § 192.10(f)(3) and section VI.C of this document). The synopsis would be a concise document that describes the bioengineered food in a manner that is suitable for preparing a publicly accessible list of PBN's (see proposed § 192.40(c)(1)(i) and section X.A of this document).

C. Part III: Status at Other Federal Agencies and Foreign Governments

FDA is proposing that a notifier inform FDA of the status of any prior or ongoing evaluation of the bioengineered plant, or food derived from such a plant, by USDA/APHIS and EPA (proposed § 192.25(c)(1) and (c)(2)). The proposed regulation is consistent with the recommendations in a report issued in April 2000 by the National Research Council (the 2000 NRC Report) (Ref. 14). That report recommended, among other things, that FDA, EPA, and USDA/APHIS establish a process to ensure appropriate and timely exchange of information between agencies about bioengineered pest-protected plants. Under the regulation, FDA would be aware of any issues still pending at those agencies, that are relevant to FDA's evaluation of the bioengineered food in question. When necessary and appropriate, FDA would contact APHIS, EPA, or both agencies about their evaluation of the bioengineered plant.

In addition, as discussed previously in this notice, the purpose of this notification program is to provide FDA with the information necessary to determine whether there are legal status questions concerning a bioengineered food so as to permit FDA to carry out its enforcement responsibilities. This would include its responsibilities to enforce section 402(a)(2)(B) of the act, which addresses foods containing illegal pesticide residues.[13] If the EPA regulatory process regarding the bioengineered food is not yet complete and a tolerance or exemption from tolerance has not been established, the food would not be in full compliance with the law. Accordingly, in these circumstances, FDA would inform a notifier that the agency does not consider the notifier's PBN to satisfy the requirement for premarket notice (see proposed § 192.30(e) and section IX.C.5 of this document).

FDA also is proposing that a notifier inform FDA as to whether the bioengineered food is or has been the subject of review by any foreign government and, if so, describe the status of that review (proposed § 192.25(c)(3)). Foreign countries have instituted various regulatory requirements for bioengineered foods. Information about the status of a notifier's submission(s) to foreign

[13] Under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), EPA registers pesticides, including those introduced into food via bioengineering; under section 408 of the act (21 U.S.C. 346a), EPA sets a tolerance or grants an exemption from a tolerance for pesticide residues in food. FDA has the statutory responsibility to enforce these tolerances or exemptions; under section 402(a)(2)(B), a food is adulterated if it contains a pesticide residue that exceeds an established tolerance or for which there is no tolerance or exemption from the requirement for a tolerance.

considerably depending upon the chemical, physical, and physiological properties of the substance and its estimated dietary exposure.

FDA is proposing that a notifier include either: (1) An estimate of dietary exposure to substances introduced into, or modified in, the food (proposed § 192.25(f)(3)(i)); or (2) a statement that explains the basis for the notifier's conclusion that an estimate of dietary exposure to these substances is not needed to support safety (proposed § 192.25(f)(3)(ii)). As discussed in the 1992 policy (57 FR 22984 at 22998), many substances that would be introduced into, or modified in, a bioengineered food would be present in the bioengineered food at a relatively low level. For example, since 1994, developers have completed more than 45 consultations about bioengineered foods, most of which contain newly introduced or modified enzymes (Ref. 6). In most cases, an estimate of dietary exposure to these enzymes was not critical to the safety assessment. However, this is not always the case, even for enzymes that would be present in food at a low level. For example, in the case of the enzyme APH(3')II, FDA relied, in part, on the estimated dietary exposure to APH(')II in concluding that active APH(3')II in food would not interfere with the clinical efficacy of the orally administered antibiotic, kanamycin (59 FR 26700 at 26703). Thus, the particular circumstances will determine whether an actual estimate of dietary exposure to a substance that is introduced into a food plant is needed to support the notifier's view that the bioengineered food is as safe as comparable food.

3. Allergenicity

FDA is proposing that a notifier include a discussion of the available data or information that address the potential that a protein introduced into the food will be an allergen (proposed § 192.25(f)(4)). The proposed regulation is consistent with the 1996 procedures, which recommend that a notifier provide FDA with information regarding any known or suspected allergenicity and a discussion of the available information about the potential for the bioengineered food to induce an allergic response. Because scientific methods to assess this issue are evolving, in the proposed regulation FDA is recommending that a notifier contact FDA about the agency's current thinking on this topic.

FDA is developing guidance for evaluating the potential allergenicity of proteins introduced into bioengineered foods and intends to make that draft guidance available for public comment in the near future. The draft guidance will be based in part on recommendations made by scientific experts who attended a public scientific conference on food allergy and bioengineered foods that FDA, EPA, and USDA jointly hosted on April 18 and 19, 1994 (the 1994 allergenicity conference (Ref. 17)).[17]

4. Other Safety Issues

It is impracticable for FDA to either anticipate all classes of substances that could be introduced into food or provide specific guidance about each of those classes of substances. Therefore, FDA is proposing that a notifier provide a discussion of data or information relevant to other safety issues that may be associated with the substances introduced into, or modified in, the food (proposed § 192.25(f)(5)). This requirement would cover any issues that are not explicitly addressed in proposed § 192.25(f)(1), (f)(2), (f)(3), and (f)(4) regarding substances introduced into, or modified in, the food. Such issues could include, for example, the digestibility or toxicity of an introduced protein. FDA expects that such issues would be identified during presubmission consultations on specific foods.

G. Part VII: Data and Information About the Food

FDA is proposing that a notifier provide data or information about the bioengineered food (proposed § 192.25(g)). These data or information would include a justification for selecting a particular food(s) as "comparable food" (proposed § 192.25(g)(1)); a discussion of historic uses of the comparable food(s) (proposed § 192.25(g)(2)); data or information comparing the composition and characteristics of the bioengineered food to those of comparable food(s), with emphasis on significant nutrients, naturally occurring toxicants and antinutrients, and any intended changes to the composition of the food (proposed § 192.25(g)(3)); any other information relevant to the safety, nutritional, or other regulatory assessment of the bioengineered food (proposed § 192.25(g)(4)); and a narrative that explains the basis for the notifier's view that the bioengineered food is as safe as comparable food(s) and that the bioengineered food is otherwise in compliance with all applicable requirements of the act (proposed § 192.25(g)(5)). In general, the proposed requirements derive from the 1992 policy, the 1996 procedures, and FDA's experience under the 1996 procedures. FDA discusses the details of this proposed regulation immediately below. FDA requests comment on the proposed submission requirements regarding the food. Such comments may result in a modification to the proposed submission requirements.

1. Comparable Food

FDA is proposing that the notifier provide a justification for selecting a particular food or foods as the "comparable food" to which the notifier will compare the bioengineered food (proposed § 192.25(g)(1)). The proposed requirement is based on the 1992 policy and FDA's experience under the 1996 procedures.

Ordinarily, the comparable food would be the parental variety or commonly consumed varieties of the parent plant (57 FR 22984 at 22996 and Ref. 5)). However, when the intended effect of the transformation is to change the composition of the food, it may be appropriate to also compare the composition and characteristics of the bioengineered food to that of another commonly consumed food. For example, if an oilseed crop is modified to produce an oil that has a higher content of a particular fatty acid than commonly consumed varieties, it may be appropriate to also compare the composition and characteristics of the bioengineered food to that of a food that contains that fatty acid. FDA expects that any issues associated with the appropriate selection of comparable food(s) would be identified during presubmission consultations on specific products.

2. Historic Uses of the Comparable Food

FDA is proposing that the notifier provide a discussion of historic uses of the comparable food(s) to which the notifier will compare the bioengineered food (proposed § 192.25(g)(2)). Several

[17] The goal of the 1994 allergenicity conference was to foster a scientific dialogue to assess information that was available at that time regarding the characteristic properties of food allergens and the methods that are available to assess allergenicity. The scientists who participated in this conference noted that serum from an individual who is sensitive to a known allergenic source can be used to assess the allergenic potential of proteins derived from that source. These scientists acknowledged that there are no direct methods to assess allergenicity of proteins from sources that are not known to produce food allergy. However, they suggested that the possibility that a new protein will cause an allergic reaction can, to some degree, be evaluated by comparing its similarity to characteristics of known food allergens. If a protein does not have characteristics of known food allergens, the potential that the protein would cause an allergic reaction is minimized. Because exceptions have been reported for the observed characteristics of allergens, and no one factor is fully predictive, the scientists recommended that an assessment of allergenicity be based on all available information.

materials promptly), under the regulation, FDA could send a letter or telefax to the notifier explaining that the agency had received, but not filed, the PBN and the reasons therefor.

Under proposed § 192.30(a)(1), CFSAN will inform CVM about any PBN that it files. Regardless of whether the bioengineered food would be used in human food, food for animals, or both, this inter-Center communication will ensure that both Centers are aware of all bioengineered foods that are nearing commercialization.

B. Acknowledgment Letter

FDA is proposing to send, within 15 working days of filing a notice, a letter to the notifier (or, when applicable, the notifier's agent) informing the notifier of the date on which FDA filed the PBN (proposed § 192.30(b)). As a practical matter, such a letter would acknowledge receipt as well as inform the notifier of the date of filing.

C. Response Letter

FDA is proposing to respond to a notifier within 120 days of filing a notice (proposed § 192.30(c)). Because all submissions will be sent to CFSAN, CFSAN would issue the response to the notifier, regardless of whether the intended use of the bioengineered food is in human food, food for animals, or both. A response from CFSAN would make clear that CFSAN was aware of, and thus had been notified about, all bioengineered foods, regardless of their intended use.

As with any correspondence, the particular circumstances will determine the full text of the agency's letter. However, the agency believes that a letter would likely fall into one of four general categories (proposed § 192.30(d)(1), (d)(2), (d)(3), and (d)(4)). FDA discusses each of these four categories immediately below.

1. General Categories for FDA's Response

a. *Letter that extends FDA's evaluation.* FDA is proposing that the agency could inform a notifier that the agency is extending its evaluation of the premarket notice by 120 days (proposed § 192.30(d)(1)). Under the regulation, in this letter FDA would also inform the notifier that the agency expects that the bioengineered food will not be marketed during the extended evaluation period.

Ordinarily, FDA expects to send a final response to a notifier within 120 days, particularly if a prospective notifier discusses relevant scientific and regulatory issues with FDA, prior to submitting a PBN about a bioengineered food (see proposed § 192.10 and section VI of this document). However, there are several circumstances that could prevent the agency from completing its evaluation within that time period. For example, FDA may need to extend the review time if a notifier did not participate in the presubmission consultation program; the issues raised by a particular bioengineered food could be particularly novel and complex; parts of a submission could require clarification, amplification, or correction; or the submission could be poorly written or be of such poor scientific quality that it precludes timely evaluation by the agency.

As discussed previously, FDA is issuing this proposed rule to ensure that it has the appropriate amount of information about bioengineered foods and to help to ensure that all market entry decisions by the industry are made consistently and in full compliance with the law. The goal of this rulemaking would not be achieved if a bioengineered food entered commercial distribution before FDA had completed its evaluation of the applicable notice.

b. *Letter that the notice does not provide a basis.* FDA is proposing that the agency have an option to inform a notifier that the premarket notice does not provide a basis for the notifier's view that the bioengineered food is as safe as comparable food or is otherwise lawful (proposed § 192.30(d)(2)). In so doing, FDA would inform the notifier of the reasons for this conclusion. Under the regulation, in this letter FDA would also inform the notifier that the agency expects that the bioengineered food will not be marketed.

FDA has had experience with another food program, the proposed notification program for GRAS substances, in which some submitted notices do not provide a basis for the notifier's view that the intended use of a substance is lawful (Ref. 18). The underlying reasons why the applicable notices have not provided a basis for a GRAS determination have been quite varied. Likewise, there could be various reasons why a premarket notice does not provide a basis for the notifier's view that the bioengineered food is as safe as comparable food or is otherwise lawful. For example, the notice may not provide a basis for the notifier's view that a substance introduced into the bioengineered food is not an unapproved food additive or that the bioengineered food would not be misbranded. As another example, the notice may not provide a basis to conclude that a bioengineered food that contains an unusually high level of a naturally occurring toxicant would not be adulterated. As a third example, if the poor quality of a notice makes it difficult for the agency to fully evaluate the notice, regardless of the time period available, FDA may inform the notifier of the inadequacies of the notice rather than extend its evaluation of the notice for another 120 days.

If a notice about a bioengineered food does not provide a basis to conclude that a bioengineered food is as safe as comparable food or is otherwise lawful, that food could be adulterated or misbranded and should not be marketed. If a notifier initiates commercial distribution of a bioengineered food after being informed that the applicable notice is not adequate, FDA will carefully and completely review the legal status of the applicable food and will use all available options to ensure that the food is fully in compliance with all provisions of the act. In particular, in such circumstances, the agency fully intends to bring to bear the complete range of its authorities and resources, including its authority under section 704 of the act (21 U.S.C. 374) to conduct inspections and investigations, collect samples, and perform analyses, as well as its authority under sections 705 and 903 of the act (21 U.S.C. 375 and 393) to engage in publicity and public education. When the agency concludes through the application of these resources that a food is adulterated, misbranded, or otherwise not in full compliance with the act, FDA will utilize the act's legal sanctions, as appropriate, including in rem seizure of violative foods and injunction proceedings against, or criminal prosecution of, those responsible for distributing such foods.

c. *Letter that FDA has no questions.* If, based on its evaluation of a notice, FDA has no questions regarding the notifier's view that the bioengineered food is as safe as comparable food and is otherwise lawful, FDA would inform a notifier of that fact (proposed § 192.30(d)(3)). Because the evaluation of food safety is a time-dependent judgment that is based on general scientific knowledge as well as specific data and information about the food, FDA would qualify its statement to clarify that the agency has no questions "at this time." This proposed response is similar to the letters that FDA has issued in response to submissions received under the 1996 procedures.

d. *Letter that a notifier has withdrawn the notice.* Under proposed § 192.20(g), if a notifier requests that FDA cease to evaluate a PBN, FDA would retain the PBN in its files and classify the PBN as "withdrawn." In such a circumstance,

The proposed regulation commits to make available the "text" of the agency's letter and the agency's memorandum, rather than a "copy" of these records, to enable FDA to satisfy the regulations by a mechanism other than providing a physical copy of these records (e.g., by providing an electronic copy on the Internet). Consistent with current procedures for updating an easily accessible inventory of notices received for another foods program (i.e., the GRAS notification program; see Ref. 18), FDA expects to add the text of applicable agency letters and memoranda to the easily accessible file on an approximately monthly basis. The proposed regulation to make this information easily accessible to the public is responsive to the input that FDA received at the public meetings that it convened in 1999, and to the comments that FDA received as a result of those meetings.

As discussed previously (proposed § 192.30(c)(1) and section IX.C.1 of this document), a notifier could receive a letter that informs the notifier that FDA is extending its evaluation of the premarket notice by 120 days. Under the proposed regulation to make the agency's response to a PBN easily accessible to the public, such an extension letter would be easily accessible to the public. When FDA issues a final letter regarding the applicable notice, it is likely that the agency would replace the extension letter with the final letter rather than making both letters easily accessible. The fact that the notifier had received an extension letter would still be readily apparent (e.g., because the date of the final response letter would be more than 120 days from the date of the extension letter). In addition, it is likely that FDA's final response letter would acknowledge the fact that the agency had sent a letter extending its evaluation.

XI. Proposed Regulations Regarding Bioengineered Foods That Would Be Used in Animal Feed

FDA is proposing to require the submission to the agency of data and information regarding bioengineered plant-derived foods that would be used in animal feed. FDA's proposal also includes a recommendation that prospective notifiers participate in a presubmission consultation program. In general, these proposed regulations regarding bioengineered foods intended to be fed to animals (proposed part 592) parallel the agency's proposed regulations for human food (proposed part 192). The following discussion addresses areas of importance in the proposed animal feed regulations (proposed part 592).

The number of different species encompassed by the term "animal," as used in the act, is extraordinarily broad. CVM has regulatory authority over the food consumed by all nonhuman species, ranging from those raised in aquaculture, such as lobster and fish, to pets, birds, and the traditional classes of farm animals like cattle, swine, and horses. These animals may consume parts of a bioengineered plant that are not eaten by people. For example, cattle and other herbivores eat the forage portion of the corn plant (stalk and leaves), which has no human food applications. In addition, animals may eat the byproducts or residues left over from the production of human foods. For example, soybean meal, which is a source of dietary protein widely used in animal diets, is a byproduct from the production of soybean oil, which is primarily used in human foods. As another example, broken rice, which is not desirable for human food, is a major pet food ingredient.

Undesirable substances can concentrate in the byproducts or residues left over from the production of human foods. For example, gossypol, a naturally occurring toxicant in cotton, concentrates in cottonseed meal, which is a byproduct obtained during the manufacture of cottonseed oil. The presence of gossypol limits the use of cottonseed meal in animal feed. As another example, some substances that can cause enlargement of the thyroid naturally occur in rapeseed plants and are concentrated in the meal (commonly called canola meal) that is a byproduct obtained during the manufacture of low erucic acid rapeseed oil (comonly called canola oil). These compounds must remain at a low level for the canola meal to be useful in animal feed.

In some cases, bioengineered foods could make up most of an animal's diet, which the animal could consume for its entire lifespan. For example, in a single year a high-producing dairy cow could eat as much as 6,000 pounds of a nutritional supplement containing added energy and protein. This supplement could contain up to 80 percent corn grain and 20 percent soybean meal. The same dairy cow could also consume as much as 4,380 pounds of fermented corn forage and ears (i.e., whole plant corn silage in that same year). Fattening beef cattle could eat a diet based on 10 percent whole plant corn silage, 80 percent corn grain, and 9 percent soybean meal. A typical swine diet contains 74 percent corn grain and 23 percent soybean meal, while broiler chicks might eat a ration that is 58 percent corn grain and 35 percent soybean meal. Because these foods may comprise such a large percentage of an animal's diet, an undesirable substance that is introduced into a bioengineered food, even at a low level, has the potential to adversely affect an animal that eats the food.

Because of these factors, notifiers in assembling a PBN to address bioengineered foods to be consumed by animals should pay particular attention to the intended use of the bioengineered food, including the species expected to consume it; the function and level of all introduced or modified substances; and any changes in the composition and characteristics of the food. FDA has concluded that the notices should contain adequate information about any potential safety issues for all substances introduced into, or modified in, the food. Concerns associated with any changes in the composition or characteristics of the bioengineered food should also be addressed. Notifiers should be aware that in some cases, animal diets are formulated using different nutritional parameters than those used by human nutritionists. For example, when a diet is formulated for cattle, nutritionists utilize parameters such as neutral detergent fiber and acid detergent fiber in evaluating the suitability of a potential ingredient. Notices for bioengineered plants intended to be fed to animals should incorporate these differences in how ingredients are evaluated for their nutritional content.

XII. Paperwork Reduction Act

This proposed rule contains information collection provisions that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (the PRA) (44 U.S.C. 3501–3520). A description of these provisions is given below with an estimate of the annual reporting and recordkeeping burden. Included in the estimate is the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing each collection of information.

FDA invites comments on: (1) Whether the proposed collection of information is necessary for the proper performance of FDA's functions, including whether the information will have practical utility; (2) the accuracy of FDA's estimate of the burden of the proposed collection of information, including the validity of the methodology and assumptions used; (3) ways to enhance the quality, utility, and clarity of the information to be

food and food for animals, FDA's assumption results in a conservative estimate of the reporting and recordkeeping burden.

Because FDA's analysis assumes that all notices will encompass both human food and food for animals, and because all notices are submitted to CFSAN, regardless of the intended use, FDA is estimating the recordkeeping and reporting burden only for the regulations issued in Part 192. FDA is making no separate estimate of the recordkeeping and reporting burden for the regulations issued in Part 592 because this burden is subsumed within the burden estimated for part 192.

A. Hourly Burden to Prepare a Report (Proposed §§ 192.20(a) through (b)(1) and § 192.25)

FDA contacted five firms that had made one or more submissions under FDA's existing procedures, which are summarized in a guidance first issued in 1996 (the 1996 procedures (Ref. 5)). FDA asked each of these firms for an estimate of the hourly burden to prepare a submission under the current process. Three of these firms subsequently provided the requested information. Based on this information, FDA is estimating that the average time to prepare a submission under the 1996 procedures is 150 hours.

The proposed rule would include some reporting requirements that are not described in the 1996 procedures. After considering the amount of time that firms need, on average, to prepare a submission under the 1996 procedures, and after considering the relative contribution of the additional parts, FDA is estimating that a firm would need 32 to 48 additional hours to prepare the additional sections. For the purpose of this analysis, FDA selected the average of these estimates (i.e., 40 additional hours).

FDA is estimating that the hourly burden to prepare a PBN is the sum of the hours that a firm currently spends, on average, to prepare a submission under the 1996 procedures and the additional hours that a firm would spend, on average, to prepare a submission that addresses requirements that are not described under the 1996 procedures. This sum is 150 hours plus 40 hours, or 190 hours.

B. Hourly Reporting Burden Associated With Confidential Information in a Report (Proposed § 192.20(b)(2)(i) and (b)(2)(ii)

FDA expects that most of the data or information in a PBN will be available for public disclosure. However, a few firms that made submissions under the 1996 procedures included information that they considered to be confidential. To ensure that FDA is aware of confidential information, under the proposed rule a notifier must identify any confidential information in the PBN. FDA is estimating that two PBN's per year would contain confidential information and that it would take a notifier 2 hours to identify this information. Under the proposed rule, a notifier who includes confidential information must prepare and submit an additional paper copy that has been edited to delete confidential information (i.e., a redacted copy). FDA is estimating that it would take a notifier 5 hours to prepare the redacted copy. FDA's estimates of the hourly reporting burden associated with confidential information are based on its familiarity with submissions received under the 1996 procedures, including the content and organization of those submissions. In most cases, the confidential information is present in limited locations within a given submission.

C. Hourly Reporting Burden Associated With Electronic Copies of the Report (Proposed §§ 192.20(c)(1) and (c)(2)

Under the proposed rule, a notifier ordinarily would submit an electronic copy that would be in a format that is suitable for FDA to use to make the PBN available in an electronic reading room (e.g., html format). FDA is estimating that it would take 8 hours to format the electronic disclosure copy. Because a notifier who includes confidential information must redact this copy, FDA is estimating that it would take an additional 4 hours to do the redacting and that this would occur in 2 of the 20 notices submitted per year. Thus, FDA is estimating that it would take a total of 8.4 hours, on average, to prepare the electronic disclosure copy. FDA's estimate of the hourly reporting burden associated with an electronic copy is based on its understanding of the attributes of commonly used software programs that likely would be used to prepare the electronic copy.

Under the proposed rule, a notifier may request a waiver from the proposed requirement to submit an electronic disclosure copy, e.g., because the notifier does not have access to the technology that is needed to prepare such a copy. Because a notifier who requests a waiver need only write an explanation of why he is requesting the waiver, FDA estimates that it would take 0.5 hours to request a waiver. Because most firms who have already consulted with FDA regarding bioengineered foods are large firms who likely would have access to the appropriate technology, FDA is assuming that a request for a waiver will be a rare event, and may not happen at all. Therefore, in this estimate of the hourly burden to prepare a notice, FDA is making the conservative assumption that all firms will submit an electronic disclosure copy, with an hourly burden of 8 hours, and that no firms will request a waiver, which would have a reduced burden of only 0.5 hours.

In addition, in the proposed rule FDA is recommending that a notifier submit an electronic copy that would be formatted in a manner that is suitable for FDA to use to evaluate the PBN (e.g., portable document format (PDF)). A notifier who submits an electronic evaluation copy would submit one less paper copy. FDA is estimating that it would take 8 hours to format the electronic evaluation copy.

D. Hourly Reporting Burden Associated With English Language Translations, Authorization to Incorporate Information by Reference, and Withdrawal (Proposed § 192.20(d), (e), and (g)

Under the proposed rule, a notifier who includes information in a foreign language must include an English translation that is verified to be accurate and complete. Based on its experience, FDA is estimating that it would take 20 hours to prepare such a translation and that this would happen very rarely (i.e., once every 2 years). However, FDA has limited experience with the hourly burden associated with English language translations and specifically requests comment on this estimate.

Under the proposed rule, a notifier who wishes to incorporate by reference a submission made by another party must include a signed statement from that party, authorizing the notifier to incorporate the information by reference, unless the referenced submission is publicly available (e.g., under the FOIA). FDA is estimating that it would take 2 hours to obtain the signed statement and that this would happen very rarely (i.e., once every 2 years). FDA's estimate is based on its experience with incorporation by reference in another food program (i.e., the food additives program).

Under the proposed rule, a notifier who wishes to withdraw a PBN from FDA's consideration must do so in writing. Because this can be done by a simple letter, FDA is estimating that it would take 1 hour. FDA also is estimating that this would happen very rarely (i.e., once every 2 years).

that would otherwise have been identified and resolved through consultation with the agency. For example, the food may contain an unexpected allergen or an unapproved food additive, or may be so significantly different from its conventional counterpart that special labeling would be required to enable consumers to identify the difference.

Bioengineering enables developers to expand greatly the range of sources of genes to introduce into foods. Genes code for proteins, and virtually all known food allergens are proteins. Therefore, by transferring a gene from one foodplant to another (and thereby essentially transferring a protein from one food to another) one may transfer the allergenic properties of the first food to the second. Because food allergies can result in serious harm, including anaphylactic shock and death, it is important to know the allergenic profile of food from a plant that is to be used as the source of a gene to be transferred to another foodplant.

It is also possible for a protein that has never been in food before to become an allergen once people become exposed to it in the diet. Therefore, it is also important to know whether a protein from a traditionally nonfood source has characteristics associated with allergenic proteins.

Similarly, because bioengineering enables developers to introduce genetic material from a wider range of sources than has traditionally been possible, there is a greater likelihood that a developer using bioengineering to modify a foodplant may introduce genetic material whose expression results in a substance that is significantly different from substances historically consumed in food. Such a substance may require premarket approval as a food additive because it may not be GRAS.

It is also possible with bioengineering that the newly introduced genetic material may be inserted into the chromosome of a foodplant in a location that causes the food derived from the plant to have higher levels of toxins than normal, or lower levels of a significant nutrient. In the former case, the food may not be safe to eat, or may require special preparation to reduce or eliminate the toxic substance. In the latter case, the food may require special labeling, so that consumers would know that they were not receiving the level of nutrients they would ordinarily expect from consuming a comparable food. It is important therefore for developers to evaluate bioengineered foods from new plant varieties to determine whether the composition of the food has been altered.

The additional provisions of the proposed rule, beyond what was requested by the 1996 procedures, aid in ensuring that relevant safety questions are addressed by the developer. The submission of a narrative of the developer's reasons for concluding that the bioengineered food is as safe as comparable food and its justification of the choice of comparable foods by the notifier will aid in ensuring that all potential safety issues have been considered. Discussion of unsuitable uses will provide FDA the opportunity to ensure that foods that would not be suitable for particular applications are not marketed for those applications. Submission of a redacted copy will aid the agency in protecting confidential information in the notice and in responding to FOIA requests. Submission of an electronic disclosure copy would facilitate the agency's making the PBN available in an electronic reading room.

2. Costs

For developers who would have gone through FDA's consultation process, the costs associated with the proposed required process would include only costs of the additional provisions of the proposed rule. The required process will be modeled on the experience and knowledge gained from the current consultation process, but there will be a number of new provisions that will have costs for notifiers. First, the rule would require a narrative explaining how the notifier concluded the bioengineered food is as safe as comparable food and that the food is in compliance with the act. Second, notifiers who inform FDA about a bioengineered food that contains a gene that encodes resistance to an antibiotic must specifically discuss the issues associated with the use of that gene. Although this provision was not in the 1992 policy or the 1996 procedures, in 1998 FDA released draft guidance for public comment. Since 1998, most notifiers who are in this situation have included this discussion in their submissions; in addition, many plant varieties are being developed without genes that encode resistance to an antibiotic. Therefore, FDA is considering that the requirement to discuss genes that encode resistance to an antibiotic be a cost of the proposed rule for only one submission per year (that is, FDA is estimating that only one relevant submission would have omitted this discussion without the rule). Third, notifiers must submit a written justification of their choice of foods that are comparable to the bioengineered food and the historic uses of these comparable foods. Fourth, if the bioengineered food is unsuitable for any applications or uses, notifiers must submit a description of these applications or uses. Because inappropriate uses are seldom an issue, FDA is considering that this issue would arise approximately once every 3 years. Fifth, if the submission includes confidential information, notifiers must submit redacted copies. Because very few submissions under the current process have included confidential information, FDA is considering that approximately one or two copies per year will contain confidential materials. Sixth, notifiers must ordinarily would submit an electronic copy suitable for making the PBN available in an electronic reading room, but could request a waiver if they have access to the technology that would be needed to prepare the copy.

FDA contacted five firms that had made one or more submissions under the 1996 procedures. FDA asked each of these firms for an estimate of the hourly cost associated with preparing a submission under the current process. Three of these firms subsequently provided the requested information. One firm estimated an average cost of $125 per hour; another firm estimated an average cost of $48 per hour; a third firm estimated an average cost of $60 per hour. Based on this information, FDA is estimating that the average cost to prepare a submission under the 1996 procedures is approximately $78 per hour.

The agency estimated the cost of a notice as the time needed multiplied by $78, the average cost associated with the person responsible for preparing a notice. Since 1994, FDA has received approximately eight submissions per year, but the agency expects this number of submissions to increase because of the increasing use of the technology. Because most firms who have consulted with FDA under the current process are large firms who likely would have access to the technology that would be needed to prepare an electronic disclosure copy, in this analysis FDA is estimating that no firms would request a waiver from the proposed requirement to submit such a copy. Therefore, total costs for these additional provisions are expected to be between $16,604 and $67,444 per year.

1. Transcript of the Meeting of FDA's Food Advisory Committee, Herndon, VA, April 6, 7, and 8, 1994.

2. Transcript of the Joint Meeting of FDA's Food Advisory Committee and Veterinary Medicine Advisory Committee, November 2 and 3, 1994.

3. Table of Contents, "Toxicological Principles for the Safety Assessment of Direct Food Additives and Color Additives Used in Food" (Also known as "Redbook I"), FDA, Bureau of Foods (Now CFSAN), 1982. May be Purchased From: National Technical Information Services (NTIS), 5285 Port Royal Rd., Springfield, VA 22161, 703–487–4650, NTIS Order Number PB83–170696.

4. Table of Contents, "Toxicological Principles for the Safety of Food Ingredients; Redbook 2000," available at http://vm.cfsan.fda.gov.

5. "Guidance on Consultation Procedures: Foods Derived From New Plant Varieties," available at http://vm.cfsan.fda.gov.

6. "Foods Derived From New Plant Varieties Derived Through Recombinant DNA Technology; Final Consultations Under FDA's 1992 Policy," available at http://vm.cfsan.fda.gov.

7. Press Release, U.S. Department of Health and Human Services, "FDA to Strengthen Pre-market Review of Bioengineered Foods," May 3, 2000, available at http://vm.cfsan.fda.gov.

8. Transcripts from Public Meetings Held on November 18, 1999, Chicago, IL, November 30, 1999, Washington, DC, and December 13, 1999, Oakland, CA; at http://www.fda.gov.

9. Nordlee, J. A. et al., "High Methionine Brazil Nut Protein Binds Human IgE," *Journal of Allergy and Clinical Immunology*, vol. 93, number 1, part 2, p. 209, 1994.

10. Nordlee, J. A. et al., "Identification of Brazil-Nut Allergen in Transgenic Soybeans," *New England Journal of Medicine*, vol. 334, pp.688–728, 1996.

11. Ye, X. et al., "Engineering the Provitamin A (Beta-Carotene) Biosynthetic Pathway into (Carotenoid-Free) Rice Endosperm," *Science* vol. 287: pp. 303–05, 2000.

12. Kubo, Tomoaki, "Potential of Foods From Which Unfavorable Component Have Been Removed," Topic 10, Joint FAO/WHO Expert Consultation on Foods Derived from Biotechnology, Biotech 00/12, 29 May-2 June 2000, available at www.who.int/fsf/GMfood/consultation) May2000/biotech) 00) 12.pdf.

13. Agriculture Biotechnology: Permitting, Notification, and Deregulations, U.S. Department of Agriculture, Animal Plant Health and Inspection Service, available at http://www.aphis.usda.gov.

14. Genetically Modified Pest-Protected Plants: Science and Regulation. Committee on Genetically Modified Pest-Protected Plants, Board on Agriculture and Natural Resources, National Research Council, National Academy Press, Washington, DC 20055, available at http://www.nap.edu/.

15. "Guidance for Industry: Use of Antibiotic Resistance Marker Genes in Transgenic Plants," available at http://vm.cfsan.fda.gov.

16. "Report on Consultations Regarding Use of Antibiotic Resistance Marker Genes in Transgenic Plants," available at http://vm.cfsan.fda.gov.

17. Transcript of "Conference on Scientific Issues Related to Potential Allergenicity in Transgenic Food Crops," Annapolis, MD, April 18 and 19, 1994, Document TR–1, summary available at http://vm.cfsan.fda.gov.

18. Inventory of GRAS Notices, available at http://vm.cfsan.fda.gov.

List of Subjects

21 CFR Part 192

Administrative practice and procedure, Food additives, Food labeling, Foods, Reporting and recordkeeping requirements.

21 CFR Part 592

Administrative practice and procedure, Animal feeds, Animal foods, Food additives, Food labeling, Reporting and recordkeeping requirements.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, it is proposed that Title 21 CFR, Chapter I be amended as follows:

1. Add part 192 to read as follows:

PART 192—PREMARKET NOTICE CONCERNING BIOENGINEERED FOOD

Sec.

192.1 Definitions: What terms do I need to know?
192.5 Requirement for premarket biotechnology notice.
192.10 Recommendation for presubmission consultation.
192.20 Premarket biotechnology notice: Administrative information.
192.25 Premarket biotechnology notice—required parts: What must I include in a premarket biotechnology notice?
192.30 FDA evaluation and response: What will I get back from FDA and how long will it take?
192.40 Public disclosure.

Authority: 21 U.S.C. 331, 342, 343, 348, 371.

PART 192—PREMARKET NOTICE CONCERNING BIOENGINEERED FOOD

§ 192.1 Definitions: What terms do I need to know?

(a) A *bioengineered food* means food derived from a plant that is developed using a transformation event.

(b) *Commercial distribution* means introduction, or delivery for introduction, into interstate commerce for sale or exchange for consumption in any form by humans or other animals.

(c) A *notifier* is the person who submits a premarket biotechnology notice under this part. Any person who is responsible for the development, distribution, importation, or sale of a bioengineered food may be a notifier.

(d) A *premarket biotechnology notice* (PBN) is a submission to FDA regarding a bioengineered food that is intended to enter commercial distribution. Under this part, a PBN includes all data and information in the original submission and in any amendments to the original submission.

(e) *Transformation event* means the introduction into an organism of genetic material that has been manipulated in vitro. For the purpose of this part, "organism" refers to plants.

§ 192.5 Requirement for premarket biotechnology notice.

(a) *What foods must I notify FDA about?* You must notify FDA about any bioengineered food, including a bioengineered food derived from a new plant variety modified to contain a pesticidal substance, that will enter commercial distribution unless all of the following conditions are satisfied:

(1) The bioengineered food derives from a plant line that represents a transformation event that has been addressed in a PBN previously submitted to FDA;

(2) The use or application of the bioengineered food has been addressed in a notice previously submitted to FDA; and

(3) A letter from FDA demonstrates that FDA has evaluated the use or application of the bioengineered food and has no questions about it. This would include a letter issued between May 1, 1994, and the effective date of this rule.

(b) *Must the data or other information that I submit to support my PBN be generated from a particular plant line?* The data or other information that you submit to FDA regarding a bioengineered food must be generated from a plant line whose derivation can be traced to the transformation event that is the subject of the notice and that contains the genetic material introduced via the transformation event.

(c) *When do I submit my PBN?* You must submit your PBN at least 120 days before the bioengineered food is marketed.

§ 192.10 Recommendation for presubmission consultation.

(a) *Is there a program that provides an opportunity for me to consult with FDA about a bioengineered food before I submit a PBN?* FDA has established a presubmission consultation program to enable a prospective notifier to identify and discuss relevant safety, nutritional, or other issues regarding a bioengineered food before submitting a PBN about that food. FDA recommends that you participate in this program.

at the address listed previously or look on OPA's home page on the Internet.

(2) *Disclosure copy.* (i) Unless waived under paragraph (c)(2)(ii) of this section, you must submit an electronic copy that is formatted in a manner that makes it suitable for FDA to use to make your PBN available to the public in an electronic reading room. This includes an electronic copy of your original PBN and of any amendments that you make to your PBN. If you claim that specific data or other information in the PBN are confidential, you must remove such data or information from the disclosure copy in a manner that clearly identifies the location and relative size of deleted information. To obtain current information about the technical format of this disclosure copy, write to OPA at the address listed previously or look on OPA's home page on the Internet.

(ii) You may request that FDA waive the requirement for an electronic disclosure copy, e.g., if you do not have access to the appropriate technology for formatting such a copy. FDA will grant or deny your request according to its merits.

(d) *May I submit any data or other information, such as a reprint of a published scientific article, in a foreign language?* If you submit any material in a foreign language, you must provide an English translation that is verified to be complete and accurate.

(e) *May I incorporate data or other information that are already retained in FDA's files by referring to them?* (1) If you previously submitted a file to FDA, you may incorporate that file by referring FDA to it.

(2) If someone else previously submitted a file to FDA, the procedure that you may use to incorporate that file into your PBN depends on whether the file is publicly available (e.g., the file is in an electronic reading room or is otherwise available under FOIA).

(i) If the file is publicly available, you may incorporate that file by referring FDA to it.

(ii) If the file is not publicly available, you may incorporate that file by referring FDA to it if the person who submitted the file authorizes you to do so in a signed statement and you include that signed statement in your PBN.

(f) *How can I get additional information that will help me to prepare a PBN?* You can obtain current guidance regarding specific technical issues by writing to OPA at the address listed previously or by looking on OPA's home page on the Internet.

(g) *May I withdraw a PBN from FDA consideration after I send it?* (1) At any time during FDA's evaluation of a PBN, you may request that FDA cease to evaluate it. Your request would not preclude you from submitting a future PBN about the same bioengineered food.

(2) If you request that FDA cease to evaluate your PBN, FDA will retain your PBN in its files and classify your PBN as "withdrawn."

§ 192.25 Premarket biotechnology notice—required parts: What must I include in a premarket biotechnology notice?

A PBN has seven parts. You must include all of the information described in each part, or explain why it does not apply to the bioengineered food.

(a) *Part I.* In your PBN, you must provide a letter that a responsible official of your organization, or your attorney or agent, dates and signs. In this letter, you inform FDA that you are submitting a PBN under § 192.25, state your position or title, and attest to the following:

(1) It is your view that:

(i) The bioengineered food is as safe as comparable food; and

(ii) The intended use of the bioengineered food is in compliance with all applicable requirements of the Federal Food, Drug, and Cosmetic Act (the act).

(2) You agree to make relevant data or other information that are not included in your PBN available to FDA upon request, either while FDA is evaluating your PBN or for cause.

(3) You agree to two procedures for making relevant data or other information that are not included in your PBN available to FDA by:

(i) Allowing FDA to review and copy these data or information at a specified address during customary business hours; or

(ii) Sending a copy of these data or information to FDA.

(4)(i) Your view as to whether the existence of your PBN, or any or all of the data or other information in your PBN, is exempt from disclosure under the FOIA (i.e., is confidential); and

(ii) If you claim that the existence of the PBN, or any or all of the data or other information in the PBN, is confidential, you must explain the basis for your claim.

(5) To the best of your knowledge, the PBN is a representative and balanced submission that includes information, unfavorable as well as favorable, pertinent to the evaluation of the safety, nutritional, or other regulatory issues that may be associated with the bioengineered food.

(b) *Part II.* In your PBN, you must provide the following synopsis:

(1) *Section 1.* Your name and address;

(2) *Section 2.* The name of the bioengineered food that is the subject of the PBN and the plant species from which it is derived;

(3) *Section 3.* The distinctive designation(s) that you use to identify the applicable transformation event(s);

(4) *Section 4.* A list of the identity(ies) and source(s) of introduced genetic material;

(5) *Section 5.* A description of the purpose or intended technical effect of the transformation event. This includes expected significant changes in the composition or characteristic properties of food derived from the plant as a result of the transformation event, regardless of whether these changes result from the insertion of new genes or from a modification in the expression of endogenous genes;

(6) *Section 6.* A description of the applications or uses of the bioengineered food; and

(7) *Section 7.* A description of any applications or uses that are not suitable for the bioengineered food.

(c) *Part III.* In your PBN, you must describe the status of the bioengineered food at other Federal agencies and foreign governments.

(1) *Status at the U.S. Department of Agriculture, Animal and Plant Health Inspection Service (APHIS).* A statement as to whether the bioengineered food plant has been the subject of an initiated or completed authorization, or petition for nonregulated status by APHIS, under 7 CFR 340.

(2) *Status at the U.S. Environmental Protection Agency (EPA).* A statement as to whether any plant pesticide residue in the bioengineered food is or has been the subject of a consultation with, or review by, EPA and, if so, a description of the status of that consultation or review.

(3) *Status at foreign governments.* A statement as to whether the bioengineered food is or has been the subject of review by any foreign government and, if so, a description of the status of that consultation or review.

(d) *Part IV.* In your PBN, you must provide the following data or other information about the method of development of the food:

(1) *Section 1.* Characterization of the parent plant including scientific name, taxonomic classification, mode of reproduction, and pertinent history of development.

(2) *Section 2.* Construction of the vector used in the transformation of the parent plant. This includes a thorough characterization of the genetic material intended for introduction into the parent plant and a discussion of the transformation method, open reading frames, and regulatory sequences.

(2) In general, FDA will use the information submitted in Part II of each PBN (i.e., the information described in § 192.25(b) of this part) to prepare this list and will update this list on an approximately monthly basis.

(c) *Would the data or other information in my PBN (including an amendment to my PBN, or any data or information that I incorporate by reference) be available to the public?* (1) Ordinarily, the data or other information in your PBN are available for public disclosure, in accordance with § 20.61 of this chapter, as of the date that FDA files the PBN.

(2) If you believe that any or all of the data or other information in your PBN is confidential, it is your responsibility to say so. The way to do this is in the letter that you send in Part I of your PBN (§ 192.25(a)(4)). In addition, under § 192.20(b) and (c), it is your responsibility to provide copies of your PBN that do not contain any data or other information that you claim are confidential.

(3) If you claim that any or all of the data or other information in your PBN is confidential, FDA will evaluate your claim. FDA will disclose the data or information in your PBN unless FDA determines that your claim demonstrates that the criteria for exemption from disclosure in § 20.61 of this chapter are satisfied.

(4) If FDA determines that any or all of the data or other information in your PBN is confidential as of the date that we file it, those data or information would be available for public disclosure, in accordance with § 20.61 of this chapter, when the criteria for exemption from disclosure in § 20.61 of this chapter are no longer satisfied.

(5) As long as the existence of your PBN is confidential, then the data or other information in your PBN would not be available for public disclosure.

(d) *How could the public obtain disclosable data and information in my PBN?* Under the FOIA, the public could obtain the disclosable data or other information in your PBN or an amendment to your PBN, or that you incorporate by reference into your PBN, by looking for these data and information in FDA's electronic reading room or by asking FDA to send them a copy of these data and information.

(e) *Would the agency's evaluation of my PBN be available to the public?* FDA will make the following information easily accessible to the public (e.g., by placing the information on the Internet or in a paper or electronic file that is available at FDA for public review and copying):

(1) The text of any letter issued by the agency under § 192.30(c).

(2) The text of the agency's completed evaluation of any notice submitted under this part.

2. Add part 592 to read as follows:

PART 592—PREMARKET NOTICE CONCERNING BIOENGINEERED FOOD

Sec.

592.1 Definitions: What terms do I need to know?
592.5 Requirement for premarket biotechnology notice.
592.10 Recommendation for presubmission consultation.
592.20 Premarket biotechnology notice: Administrative information.
592.25 Premarket biotechnology notice—required parts: What must I include in a premarket biotechnology notice?
592.30 FDA evaluation and response: What will I get back from FDA and how long will it take?
592.40 Public disclosure.

Authority: 21 U.S.C. 331, 341, 343, 348, 371.

§ 592.1 Definitions: What terms do I need to know?

(a) *A bioengineered food* means food derived from a plant that is developed using a transformation event.

(b) *Commercial distribution* means introduction, or delivery for introduction, into interstate commerce for sale or exchange for consumption in any form by humans or other animals.

(c) A *notifier* is the person who submits a premarket biotechnology notice under this part. Any person who is responsible for the development, distribution, importation, or sale of a bioengineered food may be a notifier.

(d) *A premarket biotechnology notice* (PBN) is a submission to FDA regarding a bioengineered food that is intended to enter commercial distribution. Under this part, a PBN includes all data and information in the original submission and in any amendments to the original submission.

(e) *Transformation event* means the introduction into an organism of genetic material that has been manipulated in vitro. For the purpose of this part, "organism" refers to plants.

§ 592.5 Requirement for premarket biotechnology notice.

(a) *What foods must I notify FDA about?* You must notify FDA about any bioengineered food, including a bioengineered food derived from a new plant variety modified to contain a pesticidal substance, that will enter commercial distribution unless all of the following conditions are satisfied:

(1) The bioengineered food derives from a plant line that represents a transformation event that has been addressed in a PBN previously submitted to FDA;

(2) The use or application of the bioengineered food has been addressed in a notice previously submitted to FDA; and

(3) A letter from FDA demonstrates that FDA has evaluated the use or application of the bioengineered food and has no questions about it. This would include a letter issued between May 1, 1994, and the effective date of this rule.

(b) *Must the data or other information that I submit to support my PBN be generated from a particular plant line?* The data or other information that you submit to FDA regarding a bioengineered food must be generated from a plant line whose derivation can be traced to the transformation event that is the subject of the notice and that contains the genetic material introduced via the transformation event.

(c) *When do I submit my PBN?* You must submit your PBN at least 120 days before the bioengineered food is marketed.

§ 592.10 Recommendation for presubmission consultation.

(a) *Is there a program that provides an opportunity for me to consult with FDA about a bioengineered food before I submit a PBN?* FDA has established a presubmission consultation program to enable a prospective notifier to identify and discuss relevant safety, nutritional, or other issues regarding a bioengineered food before submitting a PBN about that food. FDA recommends that you participate in this program.

(b) *How does the presubmission consultation program work?* In this program, you inform FDA about the bioengineered food. FDA encourages you to discuss with us safety, nutritional, or other issues that may be associated with the bioengineered food. FDA will establish an administrative file for your consultation. Although FDA may provide written feedback during the consultation, that feedback would not release you from the requirement in § 592.5 to notify FDA about the bioengineered food as described in §§ 592.20 and 592.25.

(c) *Would the fact that I am consulting with FDA be confidential?* (1) In most cases, the fact that you are consulting with FDA would not be confidential.

(2) If you claim that the fact that you are consulting with FDA is confidential, FDA will evaluate your claim. If FDA is asked, under the Freedom of Information Act (FOIA), about whether you are consulting with us, FDA will

access to the appropriate technology for formatting such a copy. FDA will grant or deny your request according to its merits.

(d) *May I submit any data or other information, such as a reprint of a published scientific article, in a foreign language?* If you submit any material in a foreign language, you must provide an English translation that is verified to be complete and accurate.

(e) *May I incorporate data or other information that are already retained in FDA's files by referring to them?* (1) If you previously submitted a file to FDA, you may incorporate that file by referring FDA to it.

(2) If someone else previously submitted a file to FDA, the procedure that you may use to incorporate that file into your PBN depends on whether the file is publicly available (e.g., the file is in an electronic reading room or is otherwise available under FOIA).

(i) If the file is publicly available, you may incorporate that file by referring FDA to it.

(ii) If the file is not publicly available, you may incorporate that file by referring FDA to it if the person who submitted the file authorizes you to do so in a signed statement and you include that signed statement in your PBN.

(f) *How can I get additional information that will help me to prepare a PBN?* You can obtain current guidance regarding specific technical issues by writing to OSC at the address listed previously or by looking on CVM's home page on the Internet.

(g) *May I withdraw a PBN from FDA consideration after I send it?* (1) At any time during FDA's evaluation of a PBN, you may request that FDA cease to evaluate it. Your request would not preclude you from submitting a future PBN about the same bioengineered food.

(2) If you request that FDA cease to evaluate your PBN, FDA will retain your PBN in its files and classify your PBN as "withdrawn."

§ 592.25 Premarket biotechnology notice—required parts: What must I include in a premarket biotechnology notice?

A PBN has seven parts. You must include all of the information described in each part, or explain why it does not apply to the bioengineered food.

(a) *Part I.* In your PBN, you must provide a letter that a responsible official of your organization, or your attorney or agent, dates and signs. In this letter, you inform FDA that you are submitting a PBN under § 192.25 and attest to the following:

(1) It is your view that:

(i) The bioengineered food is as safe as comparable food; and

(ii) The intended use of the bioengineered food is in compliance with all applicable requirements of the the Federal Food, Drug, and Cosmetic Act (the act).

(2) You agree to make relevant data or other information that are not included in your PBN available to FDA upon request, either while FDA is evaluating your PBN or for cause.

(3) You agree to two procedures for making relevant data or other information that are not included in your PBN available to FDA by:

(i) Allowing FDA to review and copy these data or information at specified address during customary business hours; or

(ii) Sending a copy of these data or information to FDA.

(4)(i) Your view as to whether the existence of your PBN, or any or all of the data or other information in your PBN, is exempt from disclosure under the FOIA (i.e., is confidential); and

(ii) If you claim that the existence of the PBN, or any or all of the data or other information in the PBN, is confidential, you must explain the basis for your claim.

(5) To the best of your knowledge, the PBN is a representative and balanced submission that includes information, unfavorable as well as favorable, pertinent to the evaluation of the safety, nutritional, or other regulatory issues that may be associated with the bioengineered food.

(b) *Part II.* In your PBN, you must provide the following synopsis:

(1) *Section 1.* Your name and address;

(2) *Section 2.* The name of the bioengineered food that is the subject of the PBN and the plant species from which it is derived;

(3) *Section 3.* The distinctive designation(s) that you use to identify the applicable transformation event(s);

(4) *Section 4.* A list of the identity(ies) and source(s) of introduced genetic material;

(5) *Section 5.* A description of the purpose or intended technical effect of the transformation event. This includes expected significant changes in the composition or characteristic properties of food derived from the plant as a result of the transformation event, regardless of whether these changes result from the insertion of new genes or from a modification in the expression of endogenous genes;

(6) *Section 6.* A description of the applications or uses of the bioengineered food; and

(7) *Section 7.* A description of any applications or uses that are not suitable for the bioengineered food.

(c) *Part III.* In your PBN, you must describe the status of the bioengineered food at other Federal agencies and foreign governments.

(1) *Status at the U.S. Department of Agriculture, Animal and Plant Health Inspection Service (APHIS).* A statement as to whether the bioengineered food plant has been the subject of an initiated or completed authorization, or petition for nonregulated status by APHIS, under 7 CFR part 340.

(2) *Status at the U.S. Environmental Protection Agency (EPA).* A statement as to whether any plant pesticide residue in the bioengineered food is or has been the subject of a consultation with, or review by, EPA and, if so, a description of the status of that consultation or review.

(3) *Status at foreign governments.* A statement as to whether the bioengineered food is or has been the subject of review by any foreign government and, if so, a description of the status of that consultation or review.

(d) *Part IV.* In your PBN, you must provide the following data or other information about the method of development of the food:

(1) *Section 1.* Characterization of the parent plant including scientific name, taxonomic classification, mode of reproduction, and pertinent history of development.

(2) *Section 2.* Construction of the vector used in the transformation of the parent plant. This includes a thorough characterization of the genetic material intended for introduction into the parent plant and a discussion of the transformation method, open reading frames, and regulatory sequences.

(3) *Section 3.* Characterization of the introduced genetic material, including the number of insertion sites, the number of gene copies inserted at each site, information on deoxyribonucleic acide (DNA) organization within the inserts, and information on potential reading frames that could express unintended proteins in the transformed plant.

(4) *Section 4.* Data or other information related to the inheritance and genetic stability of the introduced genetic material.

(5) *Section 5.* A discussion, as necessary, of other relevant data or other information about the method of development.

(e) *Part V.* In your PBN, you must discuss any newly inserted genes that encode resistance to an antibiotic. FDA recommends that you contact FDA about the agency's current thinking on this topic.

(f) *Part VI.* In your PBN, you must provide the following data or other information about substances (other than DNA, ribonucleic acid (RNA), or

(3) If you claim that any or all of the data or other information in your PBN is confidential, FDA will evaluate your claim. FDA will disclose the data or information in your PBN, unless FDA determines that your claim demonstrates that the criteria for exemption from disclosure in § 20.61 of this chapter are satisfied.

(4) If FDA determines that any or all of the data or other information in your PBN is confidential as of the date that we file it, those data or information would be available for public disclosure, in accordance with 20.61 of this chapter, when the criteria for exemption from disclosure in § 20.61 of this chapter are no longer satisfied.

(5) As long as the existence of your PBN is confidential, then the data or other information in your PBN would not be available for public disclosure.

(d) *How could the public obtain disclosable data and information in my PBN?* Under the FOIA, the public could obtain the disclosable data or other information in your PBN or an amendment to your PBN, or that you incorporate by reference into your PBN, by looking for these data and information in FDA's electronic reading room or by asking FDA to send them a copy of these data and information.

(e) *Would the agency's evaluation of my PBN be available to the public?*

FDA will make the following information easily accessible to the public (e.g., by placing the information on the Internet or in a paper or electronic file that is available at FDA for public review and copying):

(1) The text of any letter issued by the agency under § 192.30(c) of this chapter.

(2) The text of the agency's completed evaluation of any notice submitted under this part.

Dated: September 22, 2000.

Jane E. Henney,

Commissioner of Food and Drugs.

Donna E. Shalala,

Secretary of Health and Human Services.

[FR Doc. 01–1046 Filed 1–17–01; 8:45 am]

BILLING CODE 4160–01–F

DEPARTMENT OF THE TREASURY

Internal Revenue Service

26 CFR Part 1

[REG–107047–00]

RIN 1545–AY02

Hedging Transactions

AGENCY: Internal Revenue Service (IRS), Treasury.

ACTION: Notice of proposed rulemaking and notice of public hearing.

SUMMARY: This document contains proposed regulations relating to the character of hedging transactions. These proposed regulations reflect changes to the law made by the Ticket to Work and Work Incentives Improvement Act of 1999. The proposed regulations affect businesses entering into hedging transactions. This document also provides notice of a public hearing on these proposed regulations.

DATES: Written or electronically generated comments must be received by April 25, 2001. Requests to speak (with outlines of oral comments to be discussed) at the public hearing scheduled for May 16, 2001, at 10 a.m., must be submitted by April 25, 2001.

ADDRESSES: Send submissions to: CC:M&SP:RU (REG–107047–00), room 5226, Internal Revenue Service, POB 7604, Ben Franklin Station, Washington, DC 20044. Submissions may be hand delivered between the hours of 8 a.m. and 5 p.m. to: CC:M&SP:RU (REG–107047–00), Courier's Desk, Internal Revenue Service, 1111 Constitution Avenue NW., Washington, DC. Alternatively, taxpayers may submit comments electronically via the Internet by selecting the "Tax Regs" option on the IRS Home Page, or by submitting comments directly to the IRS internet site at *http://www.irs.gov/tax_regs/regslist.html*. The public hearing will be held in the IRS auditorium, 1111 Constitution Ave., NW., Washington, DC.

FOR FURTHER INFORMATION CONTACT: Concerning the regulations, Jo Lynn Ricks, (202) 622–3920; concerning submissions of comments, the hearing, and/or to be placed on the building access list to attend the hearing, contact Lanita Vandyke, (202) 622–7180 (not toll-free numbers).

SUPPLEMENTARY INFORMATION:

Paperwork Reduction Act

The collection of information contained in this notice of proposed rulemaking has been reviewed and approved by the Office of Management and Budget in accordance with the Paperwork Reduction Act of 1995 (44 U.S.C. 3507(d)) under control numbers 1545–1403 and 1545–1480.

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a valid control number assigned by the Office of Management and Budget.

Books or records relating to a collection of information must be retained as long as their contents may become material in the administration of any internal revenue law. Generally, tax returns and tax return information are confidential, as required by 26 U.S.C. 6103.

Background

This document contains proposed amendments to 26 CFR part 1 under section 1221 of the Internal Revenue Code (Code). Prior to amendment in 1999, section 1221 generally defined a capital asset as property held by the taxpayer other than: (1) Stock in trade or other types of assets includible in inventory; (2) property used in a trade or business that is real property or property subject to depreciation; (3) certain copyrights (or similar property); (4) accounts or notes receivable acquired in the ordinary course of a trade or business; and (5) U.S. government publications.

In 1994, the IRS published in the **Federal Register** (59 FR 36360) final Treasury regulations under section 1221 providing for ordinary character treatment for most business hedges. The regulations generally apply to hedges that reduce risk with respect to ordinary property, ordinary obligations, and borrowings of the taxpayer and that meet certain identification requirements. (§ 1.1221–2). In 1996, the IRS published in the **Federal Register** (61 FR 517) final regulations on the character and timing of gain or loss from hedging transactions entered into by members of a consolidated group. The final regulations published in 1994 and 1996 are collectively referred to as the Treasury regulations in this preamble.

On December 17, 1999, section 1221 was amended by section 532 of the Ticket to Work and Work Incentives Improvement Act of 1999 (113 Stat. 1860) to provide ordinary gain or loss treatment for hedging transactions and consumable supplies. Section 1221(a)(7) provides ordinary treatment for hedging transactions that are clearly identified as such before the close of the day on which they were acquired, originated, or entered into.

The statute defines a hedging transaction generally to include a transaction entered into by the taxpayer in the normal course of business primarily to manage risk of interest rate, price changes, or currency fluctuations with respect to ordinary property, ordinary obligations, or borrowings of the taxpayer. § 1221(b)(2)(A)(i) and (ii). The statutory definition of hedging transaction also includes transactions to manage such other risks as the Secretary may prescribe in regulations. Section 1221(b)(2)(A)(iii). Further, the statute

JON S. CORZINE
NEW JERSEY

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(856) 757–5353

July 3, 2001

Dr. Bernard Schwetz
Acting Deputy Commissioner
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

Dear Acting Commissioner Schwetz:

My office has received a letter from Carol Lydick concerning food allergies. In an effort to be responsive to my constituent, I am forwarding this correspondence for y our review.

Please respond to Barbara Wallace in my Barrington office. Thank you for your attention to this matter.

Sincerely,

Jon S. Corzine
United States Senator

JSC:baw

01. 3510

Carol Lydick
11 Poe Lane
Allentown, NJ 08501
Phone: 609-259-7916 - Fax: 609-259-0562
Lydickj@awol.com

Senator Jon S. Corzine
208 White Horse Pike, Suite 18
Barrington, New Jersey 08007

Re: HFA-305 FDA,
Dockets Management Group

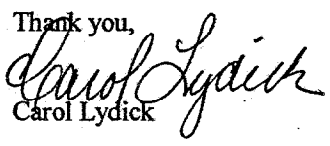
Accurate Food Labels. I suffer from Celiac Disease and other food intolerances, such as soybean, corn, dairy and fluoride. My grandson has such severe peanut and soy allergies, that he cannot attend school because even touch (someone handling a implement after eating a peanut containing product) or airborne peanut particles cause asthma and ultimately anaphylactic shock. My daughters in law, and her children, suffer intolerances of milk, watermelon, strawberries oranges, bananas and chocolate. We also have others who have Celiac Disease in the family, and with better diagnostics, we are discovering more and more people who have these allergies/intolerances of foods which often manifest as other illnesses and immune disorders (cancer, fibromyalgia, chronic fatigue, etc.)

Finding suitable food is so difficult. Often we find ourselves suffering from problems, only to discover when calling the manufacturer, there are hidden ingredients in the foods that have triggered an attack. This is especially life threatening for those who have peanut allergies and other anaphylactic responses, and although the results are less immediate, it can be life threatening for people with Celiac Disease.

Pharmaceutical Companies. People in the vitamin and health food industry seem to have develop the concept of food allergies and their consequences to the sufferers. Most label their products with at least the top 8 allergens that might be in their products. Recently we found that my grandson was given an inhaler to prevent soy-induced asthma, and it had soy in the composition of the product. This was not listed on the label and when we tried to get the information, it was not readily available. One would think that pharmaceutical companies would be even more cautious do to the very nature of their business. Unfortunately, pharmaceuticals are most often made with products that are the cause of most allergies, as their base, such as wheat, soy, and corn. These are not listed on the product and when one calls that company they find that the representatives don't know. They hide behind the statement that "We receive our fillers from a variety of manufacturers and do not know what is in it." All manufacturers should be required to list ingredients and in seems inconceivable to me that a drug company would put unknown ingredients into their product. Yet this appears to be the practice.

Genetically Modified Foods. There is now great danger to those of us with food allergies in attempts to modify foods by using products to which many are allergic/intolerant. This is a crisis in the making. Once these foods are released into the food chain, it will be difficult, if not impossible to stop. It will be impossible to know if one will pick up an apple, grape or a bowl of Rice Crispies and not go into anaphylactic shock from an unknown allergen. I am totally against mixing these food types, because of the above reasons. If this was done, it must be carefully labeled even down to the knowledge of the farmer, buyer, manufacturer, and on up to the consumer. I believe this is a dangerous practice, which Europe rejects and I feel that we here in the US should also put strict limits on the practice.

Thank you,



Carol Lydick