DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

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Andrew Kimbrell
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660 Pennsylvania Ave., S.E.
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Washington, D.C. 20003

Re: Docket No. FDA-2011-P-0723

Dear Mr. Kimbrell:

This letter responds to your citizen petition (petition), submitted on behalf of the Center for Food Safety. Your petition requests that the Food and Drug Administration ("FDA," "agency," or "we") "require that foods that are genetically engineered organisms, or contain ingredients derived from genetically engineered organisms – collectively referred to as 'Foods derived from GE sources'- be labeled under the Federal Food, Drug, and Cosmetic Act" (the FD&C Act) and "that FDA revisit its interpretation of 'material' facts in light of intervening evidence since the agency enacted its 'Statement of Policy: Foods Derived from New Plant Varieties' in 1992" (1992 Policy).[1] Pet. at 2. Your petition asserts that FDA is required to mandate such food labeling under the FD&C Act and the failure to require such labeling is arbitrary and capricious and thereby in violation of the Administrative Procedures Act (APA). Id. More specifically, you request that: (1) FDA rescind its 1992 Policy and issue a new policy declaring that a production process is "material" under section 201(n) of the FD&C Act [21 U.S.C. § 321(n)] " if it results in a change to a food at the molecular or genetic level because a significant share of consumers would find it relevant to their purchasing decisions"; and (2) FDA issue new regulations that require additional labeling for all foods produced using genetic engineering, including provisions defining the terms " genetic engineering" and "genetically engineered food," that the nutrition facts panel include a listing of the genetically engineered ingredients, and that the label of the food provide notices specifying the food is genetically engineered or sourced from genetically engineered foods.[2] Pet. at 2-3.

[1] Statement of Policy: Foods Derived From New Plant Varieties, 57 FR 22984 (May 29, 1992). In this letter we refer to this document as "the 1992 Policy."

[2] FDA interprets your citizen petition as requesting these actions for foods derived from genetically engineered plants based on the action requested and the scientific data and information cited in your petition. Your petition requests that FDA rescind its 1992 Policy, which only applies to foods derived from new plant varieties. Further, the scientific data and information relied upon in your petition only pertain to genetically engineered plants.

DECISION SUMMARY

After careful review of your citizen petition, we are denying your petition in accordance with Title 21 Code of Federal Regulations (CFR) 10.30(e)(3) (21 CFR 10.30(e)(3)) for the reasons explained in this response. In summary, your petition does not provide a sufficient basis for FDA to rescind or otherwise deviate from its 1992 Policy with respect to the labeling of foods derived from genetically engineered plants or otherwise require additional labeling for such foods.[3] The petition does not provide evidence sufficient to show that foods derived from genetically engineered plants, as a class, differ from foods derived from non-GE plant varieties in any meaningful or uniform way, or that as a class, such foods present any different or greater safety concerns than foods developed by traditional plant breeding. The petition does not provide evidence sufficient to show that the genetic engineering of plants in the development of foods constitutes a material fact under the FD&C Act. Therefore, without a finding of materiality, under the FD&C Act FDA cannot require that all foods derived from genetically engineered plants, as a class, be labeled as having been genetically engineered. Further, while we appreciate consumer interest in the labeling of food derived from genetically engineered plants, consumer interest alone does not provide a sufficient basis to require labeling disclosing whether a food has been produced with or without the use of such genetic engineering. Absent a sufficient basis to require such labeling, the agency cannot compel food manufacturers to label their foods with information regarding whether such foods were produced through the use of genetic engineering.[4]

I. RELEVANT LEGAL AND POLICY BACKGROUND

A. Statutory Framework for Regulation of Food under the FD&C Act

The FD&C Act provides FDA with authority to regulate and ensure the safety of foods and food additives. In addition, the FD&C Act imposes obligations on developers of food to ensure that the foods they offer to consumers are safe and comply with applicable requirements. Under section 402(a)(1) of the FD&C Act [21 U.S.C. 342(a)(1)], a food shall be deemed adulterated, and thus unlawful, if it bears or contains an added poisonous or deleterious substance that may render the food injurious to health or if it bears or contains a naturally occurring substance such that the quantity of said substance renders it injurious to health.

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[3] FDA uses the terms "genetically engineered" or "genetic engineering" throughout this response to refer to a food that has been derived from a new plant variety developed using modern biotechnology. Modern biotechnology means the application of *in vitro* nucleic acid techniques, including recombinant deoxyribonucleic acid (DNA) and direct injection of nucleic acid into cells or organelles, or fusion of cells beyond the taxonomic family, that overcome natural physiological reproductive or recombinant barriers and that are not techniques used in traditional breeding and selection. E.g., Codex Alimentarius Commission, "Principles for the Risk Analysis of Foods Derived from Modern Biotechnology (Adopted 2003. Amendment 2008.) CAC/GL 44-2003, available at: http://www.codexalimentarius.org/download/standards/10007/CXG_044e.pdf

[4] We received and reviewed the many written comments to the petition. The comments included original e-mails, letters, form letters and letters with multiple signatures; however, the majority were nearly identical form letters which presented the writers' opinions but did not provide any additional supporting data (i.e., studies or research papers) or other information not already considered by the agency. For these reasons, the comments received in the docket do not add anything to the arguments raised in the petition and therefore we did not address them in our response.

Further, section 409 of the FD&C Act [21 U.S.C. 348] establishes premarket requirements for substances that are "food additives." A "food additive" is defined, under section 201(s) of the FD&C Act [21 U.S.C. 321(s)], in relevant part, as follows:

> [A]ny substance the intended use of which results or may reasonably be expected to result, directly or indirectly, in its becoming a component or otherwise affecting the characteristics of any food . . . if such substance is not generally recognized, among experts qualified by scientific training and expertise to evaluate its safety, as having been adequately shown through scientific procedures (or, in the case of a substance used in food prior to January 1, 1958, through either scientific procedures or experience based on common use in food) to be safe under the conditions of its intended use," subject to certain exceptions.

Section 409(b)(1) of the FD&C Act [21 U.S.C. 348(b)(1)]. Section 301(a) of the FD&C Act [21 U.S.C. 331(a)] prohibits, in relevant part, any person from introducing or delivering for introduction into commerce any food that is adulterated. Foods that are adulterated under section 402(a)(1) of the FD&C Act are subject to enforcement actions, including seizure, injunction, and criminal prosecution in certain situations.[5]

In addition to the statutory and regulatory framework for food and food additives from a safety perspective (i.e., adulteration), the agency also regulates the labeling of food products under related authorities (i.e., misbranding) as discussed further below.

B. Food Labeling

Under section 403(a)(1) of the FD&C Act [21 U.S.C. 343(a)(1)], a food is misbranded if its labeling "is false or misleading in any particular." Both the presence and absence of information in food labeling can be misleading. Section 201(n) of the FD&C Act [21 U.S.C. 321(n)] further defines misleading labeling, particularly with respect to the absence of information in labeling. Specifically, section 201(n) provides 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. The FD&C Act does not specifically define the term "material" within the context of section 201(n). In requiring food labeling based on section 201(n), the agency has interpreted the scope of "materiality" to mean information about the attributes of the food itself.[6]

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[5] See authorities in section 304 of the FD&C Act [21 U.S.C. 334] (seizure), section 302 of the FD&C Act [21 U.S.C. 332] (injunction), and section 303 of the FD&C Act [21 U.S.C. 333] (criminal penalties).

[6] You acknowledge in your petition that, though the FD&C Act does not specifically define the term "material" within the context of section 201(n), the legislative history of the 1938 FD&C Act reveals that the materiality requirement was intended to have the same meaning as a corresponding paragraph in false advertising bill (the Wheeler-Lea Act). Pet. at 13. Further, you assert that the language of the Wheeler-Lea Act has been traced back to the 1938 Restatement of Torts § 538, "which defined a fact to be material 'if its existence or nonexistence is a matter to which a reasonable man would attach importance in determining his choice of action in a transaction in question.'" Id. We disagree that mere interest to a reasonable man determines materiality. To the contrary, as you acknowledge elsewhere in your petition, the "legislative history [of the 1938 FD&C Act] is silent as what type of fact is material." Id. There is in fact no evidence in the conference report you cite to support the inference that

FDA has found information to be material and required additional labeling in cases where the absence of such information may: (1) pose special health risks for some people (e.g., warning statements 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); or (3) mislead the consumer 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 that is not suitable for frying).[7]

C. The 1992 Policy

In the 1992 Policy, FDA clarified its interpretation of the FD&C Act with respect to foods derived from new plant varieties, including plants developed by new methods of genetic modification such as rDNA techniques. 57 FR 22984 (May 29, 1992). FDA explained that foods, such as fruits, vegetables, grains, and their byproducts, derived from new plant varieties developed by the new methods of genetic modification are regulated within the existing framework of the FD&C Act, FDA's implementing regulations, and current practice. Id. Further, the agency explained that its regulatory approach to foods developed using new methods of genetic modification is the same at its approach to foods developed by older methods of genetic modification (i.e., traditional plant breeding). Under the 1992 Policy (which represents the agency's current views), the regulatory status of a food "is dependent on objective characteristics of the food and the intended use of the food (or its components)" and not on the fact that a new method is used to produce or develop the food. Id. at 22984-85.

In developing the 1992 Policy, FDA considered both the science and the law to determine how foods derived from new plant varieties should be evaluated under the FD&C Act. Based on the statutory definition of "food additive," FDA determined that it is the intended or expected introduction of a substance into food that makes the substance potentially subject to regulation as a food additive. Id. at 22990. Thus, with respect to recombinant DNA (rDNA) technology, FDA determined that it is the transferred genetic material (nucleic acids) and the intended expression product or products present in food that would be potentially subject to regulation as a food additive. With respect to transferred genetic material (nucleic acids), the agency explained that generally it did not anticipate that transferred genetic material would itself be subject to food additive regulation because nucleic acids are present in the cells of every living organism, including every plant and animal used for food by humans or animals, and nucleic acids do not raise a safety concern as a component of food. Id.

With respect to intended expression products or products present in foods derived from new plant varieties, the agency explained that it expected that such products would typically be proteins or substances produced by the action of enzymes, such as carbohydrates, fats, and oils, and when the substance present in the food is one that is already present at generally comparable or greater levels in currently consumed foods, there is unlikely to be a safety question sufficient to call into question the presumed GRAS status of such naturally occurring substances. Id.

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materiality in the context of section 201(n) was intended by Congress to have the same meaning as the term "material" under the Wheeler-Lea Act. We therefore find this argument to be without merit.

[7] FDA, Guidance for Industry: Voluntary Labeling Indicating Whether Foods Have or Have Not Been Derived from Genetically Engineered Plants (2015), available at: www.fda.gov/foodguidances

Thus, the agency reasonably concluded that the substances in foods derived from new plant varieties that are similar to those substances in traditional foods with a long history of use, when present at comparable or lower levels, are likely to pose no safety questions.

The agency was also aware of the theoretical possibility that a food developer may develop a food derived from a genetically engineered plant with an intended expression product that differs significantly in structure, function, or composition from substances in traditional food, and in such cases, the intended expression product may not be GRAS. Id. Because the use of *all* introduced substances cannot be considered to be categorically GRAS or categorically a food additive, and given that the statutory framework places an obligation on developers of food to make their own judgments about the regulatory status of food prior to marketing, the agency decided the best approach to regulatory oversight of this emerging area of technology was to provide companies with guidance concerning the review of such introduced substances and to encourage developers to consult with FDA. The agency encouraged developers of food from new plant varieties produced through genetic engineering to consult with the agency to ensure that all safety questions were resolved prior to commercialization. In that way, if FDA found that a certain introduced substance warranted a food additive review, it could discuss its concerns with the developer to ensure that the appropriate regulatory review and approval process is followed.

The 1992 Policy explains that in determining whether new plant varieties are as safe and nutritious as their parental varieties, certain characteristics of the new plant variety should be considered, including "characteristics of the host and donor species, the nature of the genetic change, the identity and function of the newly introduced substances, and unexpected or unintended effects that accompany the genetic change." 57 FR 22984 at 22992. The assessment takes into account questions about known toxicants, potential of the food to contain food allergens, the concentration and bioavailability of important nutrients, the safety and nutritional value of newly introduced proteins, and the identity, composition and nutritional value of modified carbohydrates, or fats and oils. Id.[8]

Among the issues discussed in the 1992 Policy, FDA addressed labeling of foods derived from new plant varieties. FDA explained that it considered new methods of genetic modification, including rDNA techniques, to be extensions at the molecular level of traditional methods that will be used to achieve the same goals as traditional plant breeding. Id. at 22991. Further, the agency stated it was not aware of any information showing that foods derived by these new methods differed in any meaningful or uniform way, or, as a class, presented any different or greater safety concern than foods developed by traditional plant breeding. Id. Accordingly, FDA concluded that the method used in the development of a new plant variety (including the use of new techniques including recombinant DNA techniques) is normally not material information within the meaning of section 201(n) of the FD&C Act and would not usually be required to be disclosed in labeling of food. Id. However, the agency noted that if a food derived from a new plant variety differs from its traditional counterpart such that the

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[8] The approach to food safety assessment described in the FDA's 1992 policy and used in its voluntary pre-market biotechnology consultations is consistent with the approach to safety assessment for foods from GE plants laid out by Codex Alimentarius (Codex Alimentarius Commission, 2003).

common or usual name no longer applies to the food, or if a safety or usage issue exists to which consumers must be alerted, such information must be disclosed in the food's labeling. Id.

FDA's interpretation of its labeling authority with respect to foods derived from genetically engineered plants, as explained in the 1992 Policy, was upheld by the United States District Court for the District of Columbia in Alliance for Bio-Integrity v. Shalala, 116 F. Supp. 2d 166, 170 (D.D.C. 2000).

D. Alliance for Bio-Integrity v. Shalala and Other Cases Involving Challenges Based on Consumer Interest

Many of the contentions made in your citizen petition are similar to claims raised in Alliance for Bio-Integrity v. Shalala, 116 F. Supp. 2d 166, 170 (D.D.C. 2000) (hereinafter ABI). In ABI, a group of plaintiffs challenged the 1992 Policy for, among other things, FDA's failure to require additional labeling for foods derived from genetically engineered plants, asserting that the failure to require such additional labeling violated the FD&C Act and was arbitrary and capricious and thereby in violation of the APA. Id. at 170; 178-79. Specifically, the plaintiffs challenged FDA's interpretation of the term "material" within the meaning of section 201(n) of the Act, contending that the use of genetic engineering is a "material fact" based in part on consumer interest in labeling indicating whether foods have been genetically engineered. Id.

In response, the agency thoroughly explained its development of the 1992 Policy, along with the many factors the agency evaluated, in a Memorandum in Support of a Motion for Summary Judgment (Docket No. 92N-1039). Specifically, FDA explained that in developing the 1992 Policy, the agency considered intended and unintended or unexpected changes in foods derived from genetically engineered plants and evaluated several factors, including, in relevant part, the: (1) safety of the introduced genetic material; (2) introduction of new substances in the food such as proteins, carbohydrates, fats, or oils that differ significantly in composition from such substances as they are currently found in food; (3) potential for significant nutritional changes; (4) potential for new or increased toxicants, increased anti-nutrients, decreased nutrients, or other unintended changes in the foods; and (5) potential for allergenicity relating to the introduction of proteins new to specific foods. (Mem., p. 2-5). In addition, FDA explained that it had sought the input and expertise of scientists from around the world, and analyzed reports in the scientific literature, including an evaluation of plants modified through both new and traditional means. (Mem., p. 3).

FDA explained that, based on this extensive review, it had concluded that safety concerns due to the use of genetic engineering in food-producing plants are no different for genetically engineered foods, as a class, than for foods derived from traditionally bred plants. (Mem. p. 3-4). FDA further explained that it had concluded that the use of genetic engineering in plants has not resulted in the production of proteins, carbohydrates, fats, or oils that are substantially different from substances that have been contained in foods for thousands of years. (Mem. p. 4). Having determined that there was no scientific basis for concluding that, as a class, foods derived from genetically engineered plants pose inherent risks or safety consequences to consumers or differ in a material way from their traditional counterparts, FDA concluded that there was no statutory basis to require additional labeling for all foods derived from genetically engineered plants. (Mem. p. 23).

The District Court in ABI rejected the plaintiffs' claims and upheld FDA's interpretation of the term "material" within the meaning of section 201(n) of the Act, holding that, "without a determination that, as a class, rDNA derived food pose inherent risks or safety consequences to consumers, or differ in some material way from their traditional counterparts, the FDA is without authority to mandate labeling." ABI, 116 F. Supp. 2d at 178 n.8 (emphasis in original). The court rejected the plaintiffs' argument that consumer demand was a material fact under section 201(n) of the FD&C Act:

> More specifically irksome to the Plaintiffs, the FDA does not read § 201(n) to authorize labeling requirements solely because of consumer demand. The FDA's exclusion of consumer interest from the factors which determine whether a change is "material" constitutes a reasonable interpretation of the statute. Moreover, it is doubtful whether the FDA would even have the power under the [FD&C Act] to require labeling in a situation where the sole justification for such a requirement is consumer demand.
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> Plaintiffs fail to understand the limitation on the FDA's power to consider consumer demand when making labeling decisions because they fail to recognize that the determination that a product differs materially from the type of product it purports to be is a factual predicate to the requirement of labeling. Only once materiality has been established may the FDA consider consumer opinion to determine whether a label is required to disclose a material fact. . . . . "[i]f [a] product does not differ in any significant way from what it purports to be, then it would be misbranding to label the product as different, even if consumers misperceived the product as different."

Id. at 179 (internal citation and quotation marks omitted).

The District Court also rejected the plaintiffs' argument that the use of genetic engineering in plants is a material fact that requires food labeling, finding that FDA's determination that foods derived from GE sources, as a class, do not require labeling disclosing that such foods were produced with use of genetic engineering was not arbitrary and capricious, and noting that the FD&C Act does not require disclosure of how a food is produced without regard to its effect on the product:

> Disclosure of the conditions or methods of manufacture has long been deemed unnecessary under the law. The Supreme Court reasoned in 1924, "When considered independently of the product, the method of manufacture is not material. The act requires no disclosure concerning it." U.S. v. Ninety-Five Barrels (More or Less) Alleged Apple Cider Vinegar, 265 U.S. 438, 445, 44 S. Ct. 529, 68 L.Ed. 1094 (1924)

ABI, 161 F.Supp. 2d at 179n. 10.

You assert in your petition that this case "is inapposite and was wrongly decided," and as such the Agency should not rely on the precedent set by the ABI court. Pet. at 15. Specifically,

you assert that the court erred in giving the 1992 Policy *Chevron* deference,[9] because the 1992 Policy was not an agency rule carrying the force of law. Id. However, this argument is incorrect. The ABI court did not give *Chevron* deference to the 1992 Policy but, rather, gave deference to the agency's interpretation of "food additive" in the context of section 201(s) and "material" in the context of section 201(n) of the FD&C Act. Thus, with regard to the Agency's interpretation of materiality, the ABI court noted:

> The FDCA, 21 U.S.C. § 321(n), grants the FDA limited authority to require labeling. In general, foods shall be deemed misbranded if their labeling "fails to reveal facts . . . material with respect to consequences which may result from the use of the article 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." 21 U.S.C. § 321(n). Plaintiffs challenge the FDA's interpretation of the term "material." Thus, the question is again one of statutory interpretation. As is apparent from the statutory language, Congress has not squarely addressed whether materiality pertains only to safety concerns or whether it also includes consumer interest. Accordingly, interpretation of the § 321(n)'s broad language is left to the agency. *Cf. Community Nutrition Inst. v. Block*, 242 U.S. App. D.C. 28, 749 F.2d 50, 54 (D.C. Cir. 1984) ("[T]he relatively unspecific nature of the labeling standard which Congress has prescribed . . . suggests that this is an area in which courts must give great deference to the Secretary [of Agriculture]'s judgments.").

ABI, 161 F. Supp. 2d at 178. Moreover, the ABI court recognized that the 1992 Policy was not a substantive rule having the force and effect of law,[10] but rather that "[b]ecause the Statement is a policy statement merely announcing a GRAS presumption," concluding that "the omission of formal notice-and-comment procedures does not violate the Administrative Procedure Act." ABI, at 173.

In Stauber v. Shalala, 895 F. Supp. 1178 (W.D. Wis. 1995), plaintiffs argued that FDA was required to mandate labeling of food products derived from cows treated with recombinant bovine growth hormone drug (rbST) approved for use in dairy cows to enhance milk production to reflect such fact. Id. at 1193. Specifically, plaintiffs argued that widespread consumer demand for such labeling was a "material fact" within the meaning of section 201(n) of the FD&C Act and, therefore, required labeling. Id. The court rejected this argument. Acknowledging FDA's receipt of thousands of letters from consumers urging FDA to deny approval of rBST or to require labeling of rBST products, the court nonetheless affirmed FDA's longstanding interpretation regarding materiality:

> Regarding widespread consumer demand, plaintiffs are incorrect in their assertion that by itself consumer opinion could suffice to require labeling. . . . In the absence of evidence of a material difference between rbST-derived milk and ordinary milk, the use of consumer demand as the rationale for labeling would violate the [FD&C Act].

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[9] *See Chevron, U.S.A. v. Natural Resources Defense Council*, 467 U.S. 837(1984).

[10] Contrary to your assertions, nowhere in its opinion does the ABI court refer to the 1992 Policy as both a rule and a statement of policy; therefore, we find this argument to be without merit. Pet. at 15.

Id.

In another case involving the labeling of products from cows treated with rbST, the Second Circuit similarly held that consumer interest alone is not a sufficient government interest to compel labeling. International Dairy Foods Ass'n v. Amestoy, 92 F.3d 67, 74 (2d Cir. 1996). In Amestoy, dairy manufacturers challenged the constitutionality of a Vermont statute requiring them to identify products that were derived from dairy cows treated with rbST. Id. at 69. Reversed on appeal, the Second Circuit held that the labeling requirement was unconstitutional because the requirement was solely based on "strong consumer interest and the public's right to know." Id. at 73. The court noted that it was not aware of any case "in which consumer interest alone was sufficient to justify requiring a product's manufacturers to publish the functional equivalent of a warning about a production method that has no discernable impact on a final product." Id. (internal citations omitted).

As the above referenced cases illustrate, courts have repeatedly and correctly rejected the notion that consumer interest alone is sufficient to constitute a material fact under section 201(n) of the FD&C Act. The FD&C Act plainly does not require disclosure of the method of production without regard to its effect on the product. However, manufacturers are free to disclose such information in the labeling of their products provided such disclosures are truthful and not misleading. The agency offers a voluntary premarket plant biotechnology consultation process to assist in this regard.

E. Voluntary Premarket Plant Biotechnology Consultation Program

Food manufacturers have an obligation under the FD&C Act to ensure that the foods they offer consumers are safe and otherwise in compliance with applicable legal requirements. See e.g., 21 U.S.C. § 342 et seq.; see also 57 Fed. Reg. 104 (May 29, 1992). To help crop developers meet their obligation to market only safe and lawful foods, FDA operates a voluntary premarket plant biotechnology consultation program pursuant to which firms submit to FDA a summary of the safety and nutritional assessment that the developer conducted and then FDA considers, based on agency scientists' evaluation of the available information, whether any unresolved issues exist regarding the food derived from the new plant variety that would necessitate legal action by the agency if the product were introduced into commerce (FDA, 1997). Such consultations focus on the pre-market food safety and other testing performed by developers of genetically engineered crops. We will address the consultation program in more detail later in this response.

II. Analysis

You raise a number of issues in your petition about the development of GE foods and FDA's policy regarding the labeling of such foods. You maintain that FDA should or is otherwise required to compel additional labeling for foods derived from GE sources because: (1) genetic engineering is "radically different" from conventional plant breeding and therefore poses unknown human health risks; (2) genetic engineering in plants causes adverse environmental impacts; (3) consumers are interested in such labeling and absent such labeling are misled; (4) and for other reasons, including the patentability of foods derived from GE sources and the

regulation of foods derived from GE sources in other countries. We address each of these claims below.

A. Genetic Engineering in Plants

Genetic engineering in plants is a production method that is comparable to other methods of genetic modification used in plant breeding. Plant breeding is the science of combining desirable genetic traits (such as unique economic, environmental, nutritional or aesthetic characteristics) into new plant varieties that can be used in agriculture. (57 FR 22984, Sleper, 2006). Genetic modification of plant varieties through DNA manipulation is not unique to genetic engineering and also occurs in traditional methods of plant breeding. The term "genetic modification," within the context of plants, is an umbrella term, encompassing a broad array of methods used to alter the genetic composition of a plant, including traditional hybridization and plant breeding as well as more modern rDNA techniques (National Research Council, 2004, p. ix, 17-18; National Research Council , 2014;). Genetic modification techniques in plants have been used for thousands of years in the domestication of crops (National Research Council , 2004; Doebley et al., 2006). For example, the generation of triticale, a crop used for both human food and animal food, was developed through the interspecies crossing of wheat and rye (National Research Council , 2004, p. 3). Accordingly, plant genetic engineering may be considered an extension at the molecular level of traditional methods that are used to achieve the same goals pursued with traditional plant breeding (FDA, 1992). Some crops have been genetically modified for a particular purpose through traditional plant breeding techniques and genetic engineering. For example, crops resistant to imidazolinone herbicide have been produced through both traditional plant breeding techniques (Tan, 2005) and genetic engineering techniques.[11]

Your petition makes broad generalizations regarding genetic engineering, asserting that there are "profound" or "radical" differences between plant breeding and genetic engineering, that foods derived from GE sources do not have the history of safe use as compared to foods developed through traditional breeding practices, and therefore such foods are unsafe. Pet. at 9. In support of these assertions, you cite one article on the Consumers Union Internet site (CU article) and internal FDA memoranda that represent working papers and that are not final Agency positions. We reviewed the CU article cited in your petition.[12] Page 1 of the CU article refers to how the process of genetic engineering differs from the process of conventional plant breeding and states that conventional breeding, "…seeks to achieve expression of genetic material which is already present within a species." The CU article indicates that there are limited exceptions to this distinction between conventional breeding and genetic engineering, such as the gene transfer processes of species hybridization, wide crosses and horizontal gene transfer. The CU article also notes that scientists may, "…insert custom-designed genes that do not exist in nature." Page 7 of the CU article discusses horizontal gene transfer (the potential for genes to inadvertently be passed from one species to another, such as the transfer of DNA from plants to soil microorganisms) including the natural defense mechanisms used to prevent such

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[11] Food and Drug Administration to Angela McKean, BASF PlantScience, LLC, 2012; available at: http://www.fda.gov/Food/FoodScienceResearch/GEPlants/Submissions/ucm296341.htm.

[12] Your petition cites pages 1 and 7 of "Genetic Engineering is Not an Extension of Conventional Plant Breeding; How Genetic Engineering Differs from Conventional Breeding, Hybridization, Wide Crosses and Horizontal Gene Transfer" published by Consumers Union on its Internet site.

transfer from occurring. Although the CU article discusses the different mechanisms by which DNA is transferred in genetic engineering and conventional breeding the CU article does not establish that the foods derived from either conventional breeding or genetic engineering are necessarily different from each other in terms of safety or other factors relevant to how the food would be used.

While not specifically cited in your petition, we note that although the CU article asserts that genetic engineering vastly differs from conventional plant breeding, it states that the differences between plants produced through genetic engineering and conventional breeding are normative and philosophically based, rather than scientific.[13] The CU article mistakenly then goes on to state that in regards to labeling, FDA has the authority to require that any documentable change should be labeled (p. 10 of the article). We disagree, because unless the change to a food is material under 403(a) and 201(n) of the Act, labeling is not required.

Whether differences between conventional plant breeding and genetic engineering are subjectively described by some as "profound" or "radical" is immaterial with respect to the regulatory status of a food, including its labeling. For example, your petition argues that there are "profound" or "radical" differences between the various techniques used as part of conventional plant breeding versus genetic engineering. The labeling of food, whether produced through conventional breeding or genetic engineering, is based on material changes to the food's characteristics under 403(a) and 201 (n) of the Act—not on individual views regarding the extent to which food production methods differ. The internal FDA memoranda cited in your petition (Pet. at 9) were drafted by individual FDA scientists during development of the 1992 Policy. As with the development of any new policy, FDA scientists considered, among other things, intended and unintended or unexpected effects related to foods derived from genetic engineering in plants. Contrary to the suggestions in your petition, these scientists were not making conclusions regarding the safety of all substances that may be derived from genetic engineering in plants and used in food. Instead, they were considering theoretical possibilities and debating the most effective way to apply the provisions of the FD&C Act to such substances. This is part of the normal deliberative process but does not cabin that process. As the dates of the memoranda show, they do not reflect FDA's final position; they were prepared months before FDA finalized its position and issued its policy statement in May, 1992. Moreover, these excerpts include a select few comments out of the entire 44,000-page record related to the development of FDA's 1992 Policy and these comments were ultimately addressed in FDA's 1992 Policy, as explained by the Agency in Alliance for Bio-Intergrity v. Shalala (2000), 116 F. Supp. 2d. 166 at 177-78.

The simple fact that a plant is produced by one method over another does not necessarily mean that there will be a difference in the safety or other characteristics of the resulting foods. The determining factor is the final food product and its objective characteristics in comparison to its traditional counterpart, not the process used to produce the plant from which the food was derived (National Research Council, 2004, p. 63). Along the same lines, the regulatory status of a food, irrespective of the method by which it is developed, is dependent upon objective characteristics of the food and the intended use of the food (or its components) (FDA, 1992).

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[13] Specifically, the article states, "Whether these differences are "significant" or "insignificant", however, is a value question and a philosophical question, not a scientific question." (p. 10 of the article)

Food labeling, including the required disclosure of material information under Sections 403(a) and 201 (n) of the Act, is also based on characteristics of the food itself and is not dictated by whether the method (e.g., conventional plant breeding) used to produce the food has historically produced safe food. FDA notes that the case of the Lenape potato is contrary to the assertion in your petition that there is necessarily a history of safe use associated with organisms derived by traditional plant breeding practices. The Lenape potato, developed using conventional breeding techniques, was found after commercialization to have elevated solanine content in the tubers and was removed from the market (National Research Council, 2004). The case of the Lenape potato is an example demonstrating that it is the objective characteristics of the food, and not the method used to develop it, that are determinative of a food's safety.

FDA's 1992 Policy makes clear that foods from genetically engineered plant varieties must meet the same safety and regulatory requirements as food from non-genetically engineered plants. Although foods from GE plants may not have been on the market for the length of time as plants produced through conventional plant breeding techniques that does not mean that all resulting foods are any less safe. To date, we have completed over 155 consultations for GE plant varieties. The numbers of consultations completed, coupled with the rigor of the evaluations demonstrate that foods from GE plants can be as safe as comparable foods produced using conventional plant breeding.[14]

B. The Safety of Foods Derived From Genetically Engineered Plants

In your petition, you make a number of assertions regarding or questioning the safety of foods derived from GE sources. More specifically, you assert that genetically engineered foods are unsafe because they present unknown health consequences, including an increase in levels of toxicants, allergens, and antibiotic resistance. Pet. at 9-10. You state that "unlike time-tested conventional food varieties, which have had centuries to manifest long-term health impacts, the scientific community and our government are still uncovering new and significant information about the human health . . . impacts of GE foods." Pet. at 11). You cite three studies to support these conclusions along with internal FDA memoranda. We have carefully reviewed these studies, and we find them insufficient to support a categorical determination that foods derived from genetically engineered plants, as a class, pose different or greater safety risks than foods developed through traditional plant breeding, as discussed below.

1. Evaluation of the Information Submitted

a. Antibiotic resistance and other adverse or unknown health effects

You refer to an article by Nap et al. (1992) as support for your assertion that foods derived from GE sources may cause antibiotic resistance. Pet at 9. While scientists have expressed concern about the use of antibiotic resistance genes in GE plants, your petition fails to acknowledge that certain antibiotic resistance genes have been found to be safe for use in the production of GE plants. For example, the Nap, et al. article cited in your petition reviews the

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[14] Food and Drug Administration. "Biotechnology Consultations on Food from GE Plant Varieties." July 19, 2015, Available at: www.fda.gov/bioconinventory, accessed November 5, 2015.

safety of GE plants resistant to the antibiotic kanamycin and concludes that the use of kanamycin-resistance in GE plants is safe. As part of their review, the authors considered the properties and applications of kanamycin, the existence of kanamycin resistance in bacteria, possible spread of kanamycin resistance and consumption of kanamycin-resistant plant material. The article concludes that the kanamycin resistance trait is already ubiquitous in nature and that this trait is unlikely to provide any selective advantage to organisms outside the laboratory indicating that the use of the kanamycin resistance marker is unlikely to meaningfully spread resistance to kanamycin. Further, the article concludes that at no point will there be any interference with modern antibiotic therapies and that any interference with veterinary uses of kanamycin will be negligible. While your petition expresses concern about the possibility of GE plants contributing to antibiotic resistance your petition does not take into account the findings in the study you cite, which indicate that kamanycin resistance can be safely used in GE plants.

Moreover, in 1994, FDA approved a food additive petition regarding the use of kanamycin resistance in certain GE plants. See 59 Fed. Reg. 98 (May 23, 1994). FDA approved the protein aminoglycoside 3'-phosphotransferase II (APH(3')II) as a processing aid for use in the development of new varieties of tomato, oilseed rape and cotton . Id. APH(3')II provides resistance to the antibiotic kanamycin. In its safety assessment of APH(3')II, FDA considered safety issues associated with the use of an antibiotic resistance genes in plants. As part of its review, FDA considered the direct effects of ingestion of APH(3')II and the biological activity of APH(3')II (i.e., the effect of the enzyme on the therapeutic efficacy of orally administered antibiotics). The agency also evaluated whether there are any safety concerns from potential transfer of the gene encoding APH(3')II when it is used to produce new varieties of tomato, oilseed rape, and cotton. Further, FDA considered whether antibiotic therapy would be compromised by potential transfer of the kanamycin resistance gene to intestinal microorganisms and whether the kanamycin resistance gene might be transferred to soil microorganisms, thereby increasing the level of antibiotic-resistant organisms in the environment.

FDA also consulted the agency's Food Advisory Committee about the use of kanamycin resistance in tomato; specifically, the possibility that the kanamycin resistance gene might be transferred to microorganisms in the GI tract and in the environment. See 59 Fed. Reg. 50 (March 15, 1994), reference 1. The committee members concluded that transfer of the kanamycin resistance gene consumed as a component of tomatoes to microorganisms in the GI tract was highly unlikely based on published data in the scientific literature. Similarly, the committee members judged that the potential for transfer of the kanamycin resistance gene from plants to microorganisms in the environment is highly unlikely based on the members' knowledge of mechanisms of gene transfer. In addition, members of the committee pointed out that the rate at which such transfer could take place, if at all, was of so small a magnitude that,

coupled with the high prevalence of kanamycin resistant organisms already present in the environment, it would not cause a significant environmental impact. [15]

FDA concluded that the potential transfer of the kanamycin resistance gene, as well as other antibiotic resistance marker genes, from crops to microorganisms should be evaluated on a case-by-case basis and that the use of the kanamycin resistance gene does not pose safety concerns in terms of increase in the population of antibiotic-resistant pathogens due to the potential for horizontal transfer of the gene (59 FR 26700). Taking into consideration concerns about antibiotic resistance and the food safety of the APH(3')II protein, FDA concluded that the use of APH(3')II as a processing aid in the development of new varieties of tomato, oilseed rape and cotton varieties is safe(59 FR 26700).

You refer to an article by Rowland (2002) (Pet ref. 26) as support for your assertion that foods derived from GE sources present unknown or adverse health consequences. Your petition notes that, according to Rowland, toxicity assessment typically involves exposing laboratory animals to high levels of isolated chemicals, and that "complex mixtures of complex chemicals" such as novel foods derived from GE sources, cannot be administered to animal subjects in this conventional manner. You petition cites only a portion of the Rowland article and fails to point out that the author further explains how scientists have overcome these difficulties. Specifically, Rowland (2002) states:

> "In an attempt to rationalize the safety evaluation process and circumvent the difficulties in toxicological assessment of food materials, the Organization for Economic Cooperation and Development (1993) developed the concept of substantial equivalence, which subsequently has been discussed and developed (World Health Organization, 1995). The concept is that if it can be demonstrated that the novel food is essentially similar to its conventional counterpart, then it is likely to be no more or less toxic than the latter. Hence, there is no need for extensive toxicological testing. It is widely applied by regulatory agencies throughout the world, including North America, Japan, Europe and Australia, in the safety assessment of novel foods."

In addition, in 2003, the Codex Alimentarius published its "Guideline for the Conduct of Food Safety Assessment of Foods Derived from Recombinant-DNA Plants." (Codex Alimentarius Commission, 2003) which utilizes the concept of substantial equivalence and the comparative approach to safety assessment described by Rowland (2002). In conclusion, the difficulties you assert with the use of laboratory animals to test whole foods have been overcome by the development of a comparative safety assessment based on the concept of substantial

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[15] Some members of the committee, while convinced by the information presented at the meeting that the transfer of the kanamycin resistance gene from tomato plants to microorganisms in the soil was improbable, expressed concern regarding the use of the kanamycin resistance gene in other crops that may be grown on a wide scale. Some committee members were concerned that a determination of safety with regard to the use of the kanamycin resistance gene in tomato might signal to producers that it is now permissible to use the kanamycin resistance gene in other crops. In light of such concerns, these committee members advised that use of the kanamycin resistance gene in other crops should be evaluated on a case-by-case basis. Indeed, subsequent uses of the kanamycin resistance gene, and other antibiotic resistance genes, have been evaluated for safety on a case-by-case basis (59 FR 26700).

equivalence. This approach was agreed upon internationally over 10 years ago through the Codex Alimentarius Commission.

You refer to a Canadian study (Aris and LeBlanc, 2011) purporting to evaluate maternal and fetal exposure to the pesticides glyphosate and its metabolite aminomethyl phosphoric acid (AMPA), glufosinate and its metabolite 3-methylphosphinicopropionic acid (3-MPPA) and Cry1Ab protein, as support for your assertion that foods derived from GE sources present unknown or adverse health consequences. Pet at 10-11. You claim the study's findings cast doubt on the position that the genetically engineered Bt toxin would be broken down by human digestive systems before entering the bloodstream. The study reports that glyphosate and glufosinate herbicides were detected in sera of nonpregnant women and that 3-MPPA and Cry1Ab were detected in sera of pregnant women, their fetuses and nonpregnant women (Aris and LeBlanc, 2011). According to the study, all subjects were healthy, there were no adverse perinatal outcomes and all neonates were of appropriate size for gestational age. The study concludes that more studies on the presence of pesticide-associated genetically engineered foods in maternal, fetal and non-pregnant women's blood are needed and that the results reported in the study provide baseline data for future studies (Aris and LeBlanc, 2011).

Several comments were published in the scientific literature in response to this study (Blacker, 2011; Goldstein, 2012; Mueller, 2012). These comments raise serious questions about the methods used in the study, thereby calling into question the validity of the study's findings. The published comments raised questions regarding (1) whether the subjects in the study actually consumed foods from GE plants and, if so, how much; (2) whether the methodology used to detect Cry1Ab was validated for use in measuring Cry1Ab in human sera; (3) whether the analytical method for Cry1Ab detects only Cry1Ab and not also Cry1Ac; (4) the fact that N-acetylglufosinate, which was not measured, is the major metabolite associated with the use of glufosinate on glufosinate-tolerant crops (3-MPPA, which was measured, is more commonly associated with the use of glufosinate on non-glufosinate-tolerant (i.e., non-GE) crops); (5) methodological questions about the manner in which 3-MPPA was measured potentially resulting in an overestimation of 3-MPPA levels; and (6) whether the pesticide residues detected were related to the use of GE plants at all (the three pesticides -glyphosate, glufosinate and Cry1Ab- considered in the study are also used in agriculture that does not involve GE plants).

As mentioned above, the substances measured in the Aris and LeBlanc (2011) study are pesticides or pesticide metabolites. FDA regulates foods derived from genetically engineered crops in conjunction with EPA (and USDA) under the Coordinated Framework for the Regulation of Biotechnology.[16] Pesticides, including those genetically engineered into food crops, are regulated primarily by EPA, which reviews the safety of pesticides and sets tolerances (or establishes exemptions from the requirement of a tolerance) for pesticides. EPA has concluded the Bt proteins, including Cry1Ab, approved for use in food do not pose adverse effects on human health.[17,18]

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[16] 51 FR 23302 (Jun. 26, 1986).

[17] Environmental Protection Agency (October 2001). "Biopesticides Registration Action Document - *Bacillus thuringiensis* Plant-Incorporated Protectant." Available at http://www3.epa.gov/pesticides/chem_search/reg_actions/pip/1-overview.pdf

[18] In citation 27 you state, "In approving Bt corn, FDA had previously relied on the industry's assurances that the Bt toxin would be broken down during digestion." Your citation incorrectly asserts that FDA evaluates the safety of

b. Draft internal FDA memoranda

Your petition also refers to excerpts from internal FDA memoranda written during the development of the 1992 Policy, as support for your assertion that foods derived from GE sources, as a class, could cause an increase in levels of toxicants, allergens, loss of nutrients, and antibiotic resistance. Pet. at 9 – 10.[19] As discussed above, these memoranda were drafted by individual FDA scientists during the development of FDA's 1992 Policy and do not represent a final or otherwise official agency position. Contrary to the suggestions in your petition, these scientists were not making conclusions regarding the safety of all substances that may be derived from genetic engineering in plants and used in food. Instead, they were considering theoretical possibilities and debating the most effective way to apply the provisions of the FD&C Act to such substances. Your petition only refers to certain excerpts from these memoranda and overlooks other critical information discussed in the memoranda and record to draw broad and misrepresentative conclusions regarding foods derived from GE sources. These excerpts include a select few comments out of the entire 44,000-page record and these comments were ultimately addressed in FDA's 1992 Policy.

c. Boggs case and "demonstrably true" assertion

Your petition also asserts that the labeling requested in your petition is required for foods derived from GE sources even if safety risks or differences for such foods are uncertain but are "demonstrably true." Pet. at 11. In support of this assertion, you cite International Dairy Foods Ass'n v. Boggs (Boggs), 622 F.3d 628 (6th Cir. 2010). As explained further below, this argument is misplaced.

In Boggs, dairy process or trade organizations challenged as unconstitutional a State labeling regulation that prohibited dairy processors from making labeling claims about the absence of recombinant or artificial hormones in their milk products (composition claims) and required processors to include a disclaimer when making similar claims about their production processes (production claims) . 622 F. 3d at 632, 634-35. The district court upheld the State's restriction on composition claims, finding that any such claims would be inherently misleading. See id. at 636. The Court of Appeals for the Sixth Circuit, analyzing the State's restriction on composition claims using the four-part analysis set forth in Central Hudson Gas & Electric Corp. v. Public Service Commission, 447 U.S. 557 (1980), reversed. Applying the first step under Central Hudson, it determined that the commercial prohibited speech in question was not

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pesticides such as the Bt protein. As explained in this section, the food safety assessment of pesticides, such as the Bt proteins, falls under the regulatory purview of EPA.

[19] FDA notes that in three cases you reference FDA memoranda but do not provide copies of the memoranda cited. In citation 19 of your petition you cite a page in *Environmental Politics Casebook: Genetically Modified Foods* but neither you nor the publication provides identifying information for the memoranda cited. In citation 21, you did not include a copy of the reference you cite as "Food and Drug Administration, Comments on proposed approach to unknown and unexpected toxicants (undated)." In citation 23, you did not include a copy of the document that you cite as "Food and Drug Administration Draft Appendix: Specific Considerations in the Safety Assessment of Foods and Feeds Derived from Genetically Modified Plants (Dec. 12, 1991)." Along the same lines, the references "Food and Drug Administration, Comments on proposed approach to unknown and unexpected toxicants (undated)" and "Food and Drug Administration Draft Appendix: Specific Considerations in the Safety Assessment of Foods and Feeds Derived from Genetically Modified Plants (Dec. 12, 1991)" are not included in the list of "Materials Relied Upon By Petitioners" submitted with your petition. See 21 CFR 10.20(c)(1)(iii).

inherently misleading , Although the Court recognized that there may be no way to differentiate naturally occurring hormones from rbST in milk, cows that are never treated with rbST cannot produce milk that contains rbST and, therefore, the composition claim "rbST free" is "demonstrably true." Id. at 637. [20] Id.

The decision, accordingly, did not address whether the FD&C Act requires labeling disclosing that foods are derived from GE sources (or even labeling of dairy products from cows treated with rbST)[21] where safety risks for such foods are "uncertain" but "demonstrably true," as asserted in your petition. Instead, the Court was presented only with the question whether a State can prohibit certain labeling that is not misleading.

Moreover, while a fact may be "demonstrably true," this, alone, does not establish that such fact is required to be disclosed in food labeling under section 201(n) of the FD&C Act. The determining factor is the characteristics of the final food product and whether such food presents material differences or safety concerns in comparison to its traditional counterpart, not the process under which such food was developed (National Research Council, 2004, p. 63). Indeed, if a food "product does not differ in any significant way from what it purports to be, then it would be misbranding to label the product as different," particularly based on unsubstantiated and speculative risks. See Stauber, 895 F. Supp. at 1193.

2. Voluntary Premarket Plant Biotechnology Consultation Process

In your petition you also suggest that the voluntary premarket plant biotechnology consultation process between FDA and crop developers is not adequate for determining whether foods from genetically engineered plants are safe. Pet. at 9-11. Your petition essentially argues that FDA is not in a position to know whether there are safety problems with individual foods in the absence of "government-mandated, independent, peer-reviewed scientific testing of GE foods." Pet. at 11. You claim that the FDA consultation program is inadequate to establish the safety of foods from GE plants based on certain language included in letters that we send to developers. Many of your assertions are based on the use of genetic engineering in the production of food, and not about an individual food product's safety.

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[20] The Court of Appeals further evaluated the State's regulation under the remaining Central Hudson factors and found the State's restriction on commercial speech to be unconstitutional after concluding that the restriction did not directly advance the State's asserted interest. Id. at 639.

[21] With respect to your petition's claims regarding evidence demonstrating a compositional difference between milk from cows treated with rbST and milk from untreated cows, we note that before approving rbST, FDA's Center for Veterinary Medicine (CVM) conducted an extensive review of the data and information on the safety and effectiveness of rbST, and determined, among other things, that food products from cows treated with rbST are safe for consumption by humans. See: FOI Summary POSILAC®, 1993; see also Stauber, 895 F. Supp. 1178. Subsequently, CVM completed a comprehensive review of the human food safety sections of the investigational new animal drug file and master file supporting the rbST approval and determined, in relevant part, that there are no new scientific concerns regarding the safety of milk from cows treated with rbST. The agency's report on the review of the safety of rBST can be found in the following webpage: http://www.fda.gov/AnimalVeterinary/SafetyHealth/ProductSafetyInformation/ucm130321.htm. We note that, in the 1994 "Interim Guidance on the Voluntary Labeling of Milk and Milk Products from Cows that Have Not Been Treated with Recombinant Bovine Somatotropin," FDA stated there is no significant [compositional] difference between milk from treated and untreated cows because there is no way to differentiate analytically between naturally occurring BST and rBST in milk. 59 Fed. Reg. 6279, 6290.

We appreciate the opportunity presented here to explain the consultation program in greater depth than is reflected in our letters to crop developers (or firms). The voluntary premarket plant biotechnology consultation process is rigorous and follows the safety principles articulated in the 1992 Policy. As previously discussed in this response, food manufacturers are required to market only safe and otherwise lawful foods. Consequently, such firms conduct testing and analysis to ensure the safety of their products. FDA's reliance on data submitted by crop developers as part of the plant biotechnology consultation process is no different from the agency's traditional interactions with sponsors or developers of other FDA-regulated products. For example, the sponsor of a new food additive,[22] a new dietary ingredient,[23] conducts the safety studies (or contracts with a third party to have the studies completed) and FDA evaluates the results of those studies.

The voluntary premarket plant biotechnology consultation process is a way to help firms ensure that they are meeting their legal obligation to market only safe and otherwise lawful foods. As part of the consultation process, a firm submits data and information to us from the safety and nutritional assessment(s) that the firm conducts and we then consider whether any unresolved issues exist that would necessitate regulatory action if the product were introduced into commerce (FDA, 1997). If such foods are found to contain an unapproved food additive or a plant incorporated protectant for which there is no applicable tolerance or tolerance exemption, separate pre-market approval for the use of the additive or plant incorporated protectant by the relevant governing federal agency (e.g., FDA, Environmental Protection Agency, etc.) would be required before such foods could be lawfully marketed.

The data and information submitted to FDA as part of the consultation process are evaluated by FDA scientists from our Center for Food Safety and Applied Nutrition and our Center for Veterinary Medicine. The teams are comprised of staff with scientific credentials in disciplines including chemistry, nutrition, toxicology, animal science, and molecular biology. Additional scientific expertise is added as needed based on the product being considered. The scientific approach used in evaluation of consultation submissions is consistent with the approach described in the relevant Codex Alimentarius guidelines (Codex Alimentarius Commission, 2003; FDA, 2015; FDA, 2006).

We will, as necessary, request from the firm additional data and information if insufficient data and information have been provided to address safety and/or legality of the product. We also consider any additional data and scientific information available in the literature. To date, we have completed consultations addressing the safety and nutrient content of foods from more than 155 GE plant varieties,[24] meaning that FDA is satisfied that there are no outstanding safety or other issues relevant to the review and that we had no questions about the developer's determination that food from the new variety is as safe as that from its conventional counterpart. The numbers of consultations completed, coupled with the rigor of the evaluation,

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[22] "Guidance for Industry: Questions and Answers about the Petition Process." Available online: http://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/ucm253328.htm#answerF.

[23] "Draft Guidance for Industry: Dietary Supplements: New Dietary Ingredient Notifications and Related Issues." http://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/ucm257563.htm.

[24] See Biotechnology Consultations on Food from GE Plant Varieties (last updated July 19, 2015), available at http://www.fda.gov/bioconinventory.

demonstrate that foods from GE plants are indeed examined for food/feed safety prior to marketing.

C. Environmental Impacts

In your petition you assert that FDA should or must require additional labeling for food from GE crops based on environmental reasons. Specifically, you assert that GE crops cause a "myriad [of] environmental impacts." Pet. at 12. In addition, you assert that FDA has supplemental statutory authority under the National Environmental Policy Act (NEPA) to base substantive decisions like mandatory labeling on environmental concerns. Pet. at 16. Moreover, you cite Environmental Defense Fund v. Mathews, 410 F. Supp. 336 (D.D.C. 1976), as supporting the proposition that NEPA requires FDA to "base substantive decisions like mandatory labeling on environmental impacts" Pet. at 16. Finally, you assert that FDA must take into account certain environmental considerations when making its substantive decisions, including a decision on whether to mandate additional labeling for foods derived from GE crops. Id.

First, "it is now well settled that NEPA itself does not mandate particular results, but simply prescribes the necessary process." Robertson v. Methow Valley Citizens Council, 490 U.S. 332, 333 (1989). Environmental Defense Fund v. Mathews, 410 F. Supp. 336 (D.D.C. 1976), upon which you rely, is not to the contrary. Although the Court in that case held that FDA must consider environmental factors in its decision-making, and that NEPA provides FDA with authority to base its substantive decisions on environmental considerations, it further held that NEPA does not ***require*** FDA to do so (i.e., base its substantive decisions on environmental considerations).[25] *Id.* at 338.

Moreover, your assertions related to environmental impacts are flawed for a number of reasons. First, you provided no information to support your assertions that GE crops cause adverse environmental impacts and, therefore, that a categorical determination regarding the environmental impacts of all genetically engineered crops is warranted. Moreover, Monsanto Co. et al, v. Geertson Seed Farms, 561 U.S. 139 (2010) (hereinafter Geertson), upon which you rely, does not support the proposition that *all* genetically engineered crops, as a class, cause adverse environmental impacts. Pet. at 16.

Geertson involved a challenge to a decision by the Department of Agriculture's (USDA) Animal and Plant Health Inspection Service (APHIS) to deregulate a variety of genetically engineered alfalfa. In that case, the Supreme Court held only that the plaintiffs had standing because the harms they cited—namely economic harms related to a risk of "gene flow" between genetically engineered alfalfa and non-genetically engineered alfalfa—were sufficient "to satisfy the injury-in-fact prong of the constitutional standing analysis." Id. at 154-155. However, the Court did not consider whether the risk of "gene flow" extended to *all* genetically engineered crops. See id. at 156. Accordingly, the opinion does not support your assertion that foods

[25] "This is not to say that NEPA requires FDA's substantive decisions to favor environmental protection over other relevant factors. Rather, it means that NEPA requires FDA to consider environmental factors in its decision-making process and supplements its existing authority to permit it to act on those considerations. It permits FDA to base a decision upon environmental factors, when balanced with other relevant considerations." Environmental Defense Fund v. Mathews, 410 F. Supp. at 338.

derived from GE crops require the additional labeling because such crops, as a class, cause adverse environmental impacts or harms.

Lastly, to the extent that your petition suggests that FDA failed to comply with NEPA in developing the 1992 Policy, such an argument is also flawed. NEPA directs federal agencies to consider the consequences of "major federal actions significantly affecting the quality of the human environment." 42 U.S.C. § 4332(2)(C).[26] As the ABI court found, FDA's 1992 Policy does not constitute a "major federal action" requiring preparation of an environmental impact statement or environmental assessment under NEPA because the policy is reversible, maintains the substantive status quo, and takes no overt action. ABI, 116 F. Supp. 2d at 173-175. For these reasons, we conclude that the information you provide in your citizen petition is insufficient to establish that all genetically engineered crops, as a class, cause adverse environmental impacts and such impacts require that all foods derived from such crops bear additional labeling under the FD&C Act.

D. Consumer Interest

Your petition makes a number of assertions related to consumer interest in knowing whether foods are derived from genetically engineered plants.[27] Your petition asserts that there is widespread and substantial consumer demand for labeling indicating whether foods have been genetically engineered, consumers make purchase decisions based on food production processes, consumers have a right to know[28] (through food labeling) whether foods have been genetically engineered, and consumer interest for such information constitutes a "material fact" within the meaning of section 201(n) of the FD&C Act. Pet. at 12-13, 17, 18-19.

Your petition attempts to identify additional reasons related to consumer interest to support your position that all foods derived from GE plants are required under the FD&C Act to bear the labeling requested in your petition. Pet. at p. 12. More specifically, your petition asserts

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[26] The Council for Environmental Quality (CEQ) has issued regulations implementing NEPA that apply to all agencies of the Federal government and are codified in 40 CFR Parts 1500-1508. The CEQ regulations provide for the evaluation of the environmental effects of a major federal action in an environmental impact statement (EIS), an environmental assessment (EA), or a claim of categorical exclusion (CE). 40 CFR §§ 1508.4, 1508.9, 1508.11.

[27] Your petition contends, among other things, that mandatory labeling of foods derived from GE sources is necessary to prevent economic fraud. You assert that the majority of consumers are wary if not opposed to buying foods derived through genetic engineering and that consumers do not expect that their foods will be genetically engineered. You argue that failure to label in this situation is a form of economic fraud. We find this argument to be without merit. Economic fraud traditionally involves altering physical properties of food to make it appear better than it is (e.g., high fructose corn syrup added to real maple syrup), or the deceptive labeling and packaging of foods (e.g., false country-of-origin labeling on seafood products) to increase market value. However, your claim of economic fraud is not based on surreptitious physical alteration or deceptive practices but rather failure to include information that happens to be of interest to you: that is not a basis on which FDA can compel labeling. Further, the agency is not aware of any scientific evidence indicating that foods derived from genetically engineered sources, as a class, otherwise differ from conventional foods in any meaningful or uniform way. Accordingly, the agency cannot conclude that foods derived from genetically sources require additional labeling or that the absence of such labeling would be tantamount to economic fraud.

[28] Your petition cites to case law in support of a constitutional and common law consumer "right-to-know." However, as a preliminary matter, we note that there are constitutional and statutory limitations in this regard. Namely, consumer interest is not a basis on which to compel mandatory labeling under the authority of the FD&C ActThis argument is addressed further in Section 2b.

that "substantial consumer demand for the labeling of GE foods, as evidenced by consumer opinion polls and consumers' willingness to pay for non-GE foods, underscores that there are numerous reasons that the failure to label GE foods is misleading to consumers," including potential and unknown health risks, adverse environmental impacts, animal welfare, faith, political concerns, and social justice. Pet. at p. 12. However, as discussed above, your petition does not provide a sufficient basis for FDA to conclude that all foods derived from GE plants, as a class, pose different or greater safety concerns than foods developed through traditional plant breeding. Such reasons, alone, do not justify requiring the food labeling requested in your petition as these issues do not do not relate to attributes of foods derived from GE plants or the consequences of use of such foods.

In support of your assertion that substantial consumer demand indicates that the failure to label foods derived from GE sources is misleading to consumers, you submitted exhibits containing survey poll data; however, you did not provide any information to support your assertion that absent the labeling requested in your petition consumers are somehow misled or deceived. While consumer interest, alone, is not a material fact under section 201(n) of the FD&C Act and does not provide a sufficient basis upon which the agency can require food labeling, we evaluated these exhibits and find them to have significant limitations that call into question the validity of the reported findings, as discussed below.

1. *Evaluation of the Information Submitted*

   a. *Inappropriate wording of questions or answers and method of information collection*

Some of the questions posed to respondents in the surveys cited in your petition were worded or framed in a manner that emphasized only one point of view when referring to genetically engineered foods, such as questions asking whether such foods "should be labeled" (Thomson Reuters 2010, Pet. ref. 15; Consumer Reports 2008, Pet ref. 16; MSNBC 2011, Pet ref. 17; and Washington Post 2010, Pet Ref. 18). In addition, one of the response choices in Ref. 18, "Yes, I have a right to know what I am eating," is an example of another statement that cues respondents to only the ideological position that one is entitled to know what one is eating. The wording of such statement is "loaded" in the sense that the statements predispose respondents to a particular answer rather than to balanced answers or leads respondents to answer according to the intent of the wording. According to survey literature, this type of wording can increase the endorsement of the stated viewpoint and thereby result in response bias (Narayan and Krosnick, 1996). Consequently, the reported number of respondents supporting labeling is likely to be an exaggeration of the true attitude of respondents on this topic.

In addition, the wording of these questions tends to create social desirability bias, where responses do not necessarily represent respondents' true opinions because respondents want to create a favorable impression (Holbrook, Green, and Krosnick, 2003). Research has shown that telephone surveys, such as two of the surveys submitted as exhibits to the petition (Reuters, 2010; Consumer Reports, 2009) are among the types of surveys that are more vulnerable to social desirability bias where some respondents report inaccurately because they feel they should respond based on what they believe are the interviewers' (or questions') expectations.
Both issues ("loaded" wording and social desirability bias) are likely to have made the extent of

consumer support or desire for the labeling appear to be higher than it would have been if the surveys did not suffer from these methodological issues.

In addition, the report of the Washington Post 2010 poll states that it is a non-scientific user poll, and results are not statistically valid. The report has at least two flaws: questions are not phrased neutrally (are "loaded"); and a survey sample that is not representative of the general population. As the report states, "(T)his is a non-scientific user poll. Results are not statistically valid and cannot be assumed to reflect the views of Washington Post users as a group or the general population." In addition, the question wording only presented one point of view ("should … be labeled"). Therefore, the report cannot be considered representative of opinions of Americans and does not provide support to the petition. For these reasons, we cannot assume the results reflect the views of Washington Post users as a group or the general population.

b. *Statistical validity of results*

Some of the polls were conducted on a very small group or a geographically limited group of respondents. For example, Mendenhall and Evenson, (2002), Pet. Ref. 20, report findings from a telephone survey of 54 primary household food shoppers in New Haven, CT. The study conducted by Tegene, et al (2003), Pet. Ref. 22, had a sample size of 172 adults in Des Moines, IA and St. Paul, MN. Rousu et al, (2004), Pet. Ref. 21 conducted their survey with only 44 consumers in Des Moines, IA. Finally, Noussair's (2004), Pet. Ref. 24, study was conducted in France with 97 French consumers. Sample size and geographic representation are important features of any empirical study in which the goal is to draw statistical inferences about an overall population from the results from the sample.

According to the survey literature, inadequate coverage of a survey's sample of the population that the survey is intended to represent can lead to misleading or biased estimates of population opinions (e.g., Lohr 2008). Where the sample size and geographic representation of a study is small or limited, the results of the study cannot reasonably be imputed to large general population. In addition, small sample size can cause imprecision in survey results because of potentially large margin of error in the estimates (e.g., Fowler 2014). In the present case, the petition asserts that, based on the above-mentioned references, there is "a significant share of consumers" who would find the declaration relevant to their purchasing decisions (petition, pg. 2). Due to the limited sample sizes and geographic representation, however, the referenced results cannot be considered as either reflecting the opinions of "a significant share of consumers," or providing relatively precise estimates of the magnitudes or directions of such opinions.

In addition to the limited sample size or geographical location, the study by Rousu, et al., (2004) had another significant limitation. Specifically, the study asked participants to select between three different products (vegetable oil, potatoes, and corn tortilla chips) and to state prices participants would be willing to pay for each product. The label for each product included statements indicating that the food did not contain a certain amount of genetically engineered ingredients ((1) a "certified non-GM" statement; (2) a "1% GM-tolerant" statement; and (3) a "5% GM-tolerant label"). In this study GE food was not clearly defined. Results showed that prices participants were willing to pay were not different between the three labels, except between the "non-GM" and "1% GM-tolerant" labels on the chip product. There is no evidence,

however, that the study included a food label that does not state anything about its GE attribute. The lack of a control or baseline means that the study could not have provided comparisons between a food product that is labeled as having not been genetically engineered versus a food product without any such labeling. Accordingly, it is questionable whether the study accurately measures whether and how much price premium participants would have been willing to offer for foods derived from non-GE sources over foods derived from GE sources.

The study by McKluskey et al. (2001) was conducted in Japan with 400 Japanese customers at a local grocery cooperative. Respondents were asked, among other things, their willingness to pay for tofu containing genetically modified soybeans and noodles made from genetically modified wheat. Since the study was not conducted with U.S. consumers, it is not clear whether the findings could apply to U.S. consumers given the cross-country differences reported in Chern et al. (2003).

The study by Noussair, et al. (2004) (Pet. Ref 36) found that 42% of its participants were willing to buy a "genetically modified" biscuit product if its price was inexpensive. The authors noted that "the results contrast with surveys that indicate overwhelming opposition to GM foods." (Noussair, et al, 2004, pg. 1, abstract). The study was conducted with a small number of French consumers in a particular geographical region. Furthermore, as Chern et al., (2013) shows, there may be cross-country differences in consumer attitudes and willingness-to-pay regarding foods derived from GE sources. Due to the three issues stated above, this study cannot be used to yield valid conclusions regarding U.S. consumer' attitude toward foods derived from GE sources. In all cases, the small respondent group size, and limited geographic location do not allow any conclusions to be representative of all U.S. consumers and therefore cannot be projected to the general U.S. population.

c. Validity of contingent valuation results

The study by Chern et al. (2003), (Pet. Ref. 36), estimated consumer willingness-to-pay for selected GE vegetable oil and salmon. In particular, one student survey was conducted with 175 upper class students at Ohio University with varying levels of information about foods derived from GE sources. In addition, a phone survey was conducted with 256 U.S. adults selected using a random digit dialing method. There existed noticeable inconsistencies in estimated willingness to pay between different studies. According to the authors, the 2003 estimate of the willingness-to-pay "definitely need[s] further validation" and the 2002 estimate "need[s] to be validated with a larger sample size." Therefore, given the uncertainties around these estimates, we do not consider such estimates reliable.

The surveys used a simplified version of the contingent valuation method, in which individuals are asked to state their willingness to pay for a hypothetical product or change in a policy. Contingent valuation is a survey-based method often used to place a monetary value on environmental goods and services not usually bought and sold in the marketplace, such as air pollution (Carson, 2000). A review of recent contingent valuation research suggests that many results are biased and inconsistent (Hausman, 2012). In particular, this literature raises doubts about whether participants in such studies can comprehend the issue about which they are asked to express a monetary value or use appropriate and relevant considerations in generating the size

of the monetary value (see, e.g., Svedsäter, 2003).[29] Furthermore, when contingent valuation surveys are considered as opinion polls on possible government actions (as is in this petition), they do not have much information to contribute to inform public policy (Diamond and Hausman, 1994). One of the reasons is that people may not already have the preference they are asked to express and thus, construct the preference as intended by a contingent valuation study (Diamond and Hausman, 1994). Accordingly, reliance on contingent valuation surveys in government decision making is often misguided (Diamond and Hausman, 1994).

The extent that contingent valuation estimates can be used as a measure of individuals' preference with respect to an issue is thus debatable. In addition, social desirability bias is another issue that can limit the usefulness of contingent valuation estimates as a measure of people's demand for a hypothetical policy or course of action. Under social desirability, people's responses to survey questions do not necessarily represent their true opinions because they want to create a favorable impression of themselves during the survey (Holbrook, Green and Krosnick, 2003). Therefore, we do not consider the submitted references as reliable indicators of the extent of consumer interest in GE labeling in the United States.[30]

3. The Information Submitted Does Not Support the Proposed Labeling Requirements

a. Limitations on empirical evidence and case law

As described above, there are significant limitations concerning the information you submitted, rendering it insufficient to conclude that consumers understand genetic engineering or that there is widespread or strong desire or demand for the type of labeling requirement you propose. In addition, none of the information you submitted addresses consumer deception related to the labeling of foods derived from GE sources. In other words, you provided no empirical evidence to support your assertion that absent the labeling requested in your petition for foods derived from GE sources, consumers are misled about material facts regarding such foods.

While FDA appreciates consumers' interests, consumer interest alone does not constitute a material fact under section 201(n) of the FD&C Act and is not a sufficient basis upon which FDA can require additional labeling for foods.[31] See ABI, 116 F. Supp. 2d 166 ; Stauber, 895 F.

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[29] In considering the validity of consumer survey data measuring consumers' willingness to pay for certain food labeling, the D.C. Circuit recently noted that such data poses vulnerabilities "as consumers tend to overstate their willingness to pay; after all, the data sound possibly useful, and giving a 'Yes' answer on the survey doesn't cost a nickel." American Meat Institute v. United States Dept. of Agriculture, 760 F.3d 18, 24-25 (D.C. Cir, 2014).

[30] Moreover, we note that if the Agency were to endorse your argument that consumer interest constitutes a material fact within the meaning of section 201(n) of the FD&C Act, there is no logical end to the amount of information that would be required on the labeling of any given product. That is to say, if consumer interest alone were decisive, labeling would be impossibly long and of little practical use. In addition, it is difficult to conceive of a non-arbitrary way for the Agency to establish any threshold "level" of consumer interest sufficient to prompt the implementation of new labeling requirements to circumvent such a problem.

[31] As stated by the court in Stauber, "[r]egarding widespread consumer demand, plaintiffs are incorrect in their assertion that by itself consumer opinion to suffice to require labeling. . . . In the absence of evidence of a material difference . . . the use of consumer demand as the rationale for labeling would violate the [FD&C Act]." Stauber, 895 F. Supp. at 1193. Similarly, as explained by the court in ABI, "[p]lantiffs fail to understand the limitation on the FDA's power to consider consumer demand when making labeling decisions because they fail to recognize that the determination that a product differs materially from the type of product it purports to be is a factual predicate to

Supp. 1178 ; Amestoy, 92 F.3d at 73 (holding that consumer interest alone is not a sufficient government interest on which to compel labeling). Absent a material change or difference in foods derived from GE plants, as a class, the FD&C Act does not require labeling indicating that such foods have been developed through genetic engineering. ABI, 116 F. Supp. 2d at 179 n. 8 ("[W]ithout a determination that, as a class, rDNA-derived foods pose inherent risks or safety consequences to consumers, or [otherwise] differ in some material way from their traditional counterparts, the FDA is without authority to mandate labeling.")

b. Commercial free speech protection under the First Amendment

We are also mindful of the First Amendment's protection of commercial speech, and requirement that the government generally must have a sufficient basis to regulate it. See e.g., Virginia Pharmacy Bd. v. Virginia Citizens Consumer Council, Inc., 425 U.S. 748 (1976) (holding that the First Amendment protects commercial speech from unwarranted governmental regulation); Central Hudson Gas & Electric Corp. v. Public Service Commission, 447 U.S. 557, 565 (1980) ("If communication is neither misleading nor related to unlawful activity, the government's power is more circumscribed. The State must assert a substantial interest to be achieved by restrictions on commercial speech."); Zauderer v. Office of Disciplinary Counsel, 471 U.S. 626, 651 (1985) ("[U]njustified or unduly burdensome disclosure requirements might offend the First Amendment by chilling protected commercial speech."). Your petition does not provide a sufficient basis for FDA to compel the labeling requested in your petition for all foods derived from GE sources as your petition does not provide a basis for FDA to conclude that such foods, as a class, present different or greater safety concerns than foods developed by traditional plant breeding, or otherwise differ from other foods in any meaningful or uniform way.

Most of the assertions in your petition regarding consumer interest or consumer's right to know do not relate to characteristics of foods derived from GE sources or their consequences of use, and instead rely solely upon consumer interest. Consumer interest alone is not a sufficient justification to compel labeling for all foods derived from GE sources, particularly where such foods, as a class, do not present any different or greater safety risks or otherwise differ from other foods in any meaningful or uniform way. See e.g., Amestoy, 92 F.3d at 73-74 (holding that consumer interest alone was not a strong enough government interest to compel food labeling regarding a food's production method, and that, absent "some indication that . . . information bears on a reasonable concern for human health or safety or some other sufficiently substantial governmental concern, the manufacturers cannot be compelled to disclose it").

c. Additional considerations regarding materiality

In addition, while describing a food's method of production in the food's labeling may influence a consumer's purchase decisions because of their own views about the use of such technology, the FD&C Act does not require disclosure of how a food is produced without regard to its effect on the resulting product. As the ABI court noted, "[d]isclosure of the conditions or methods of manufacture has long been deemed unnecessary under the law." ABI, 116 F. Supp.

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the requirement of labeling. Only once materiality has been established may the FDA consider consumer opinion to determine whether a label is required to disclose a material fact. . . . If, however, the product does not differ in any significant way from what it purports to be, then it would be misbranding to label the product as different, even if consumers misperceived the product as different." ABI, 116 F. Supp. 2d at 179 (internal citations omitted).

2d at 179, 179 n. 10 (*citing* Ninety-Five Barrels (More or Less) Alleged Apple Cider Vinegar, 265 U.S. at 445).[32] Moreover, the agency has not found a sufficient basis to conclude that consumers would be misled absent labeling indicating that a food has been developed through genetic engineering.

Section 201(n) of the FD&C Act describes when the absence of information may be misleading. Specifically, 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" (21 U.S.C. 321(n)). FDA has not found that genetically engineered foods as a class warrant additional labeling under section 201(n) because we have not found a sufficient basis to conclude that such foods present any different or greater safety concerns than food developed by traditional plant breeding or that such foods differ from other foods in any meaningful or uniform way. Indeed, if a food product "does not differ in any significant way from what it purports to be, then it would be misbranding to label the product as different, even if consumers misperceived the product as different." ABI, 116 F. Supp. 2d at 179 (quoting Stauber, 895 F. Supp. 1178 at 1193).

For these reasons, FDA does not agree with your assertions that the method used to produce a food, without regard to its effect on the food, is a material fact. Otherwise, any and all differences in food production methods could require food labeling solely based on consumer interest, regardless of whether the production method alters the attributes of the food or its consequences of use. Such an outcome would be inconsistent with the courts' findings in ABI and in Stauber. Moreover, consumer interest in the information or issues described in your petition may be addressed through voluntary labeling indicating whether a food was produced using genetic engineering, and manufacturers may provide such information in the labeling of their foods, provided that such labeling is truthful and not misleading.[33]

C. OTHER ARGUMENTS

1. Patentability

You assert in your petition that foods derived from genetically engineered sources using recombinant DNA technology must differ meaningfully from their conventional counterparts because they are patentable. Pet. at 16-17. You also contend that to be patentable, a food derived from a genetically engineered source must be "new" and "novel." Id. Thus, you assert that a food product or its production method that is patentable cannot be both "novel" for patent purposes yet "substantially equivalent" to an existing product or process and, therefore, foods derived from genetically engineered sources should be labeled in the manner requested in your petition. As discussed below, this assertion conflates two separate standards—factors for consideration in determining patentability and factors for determining whether a food is required to bear labeling disclosing material facts within the meaning of the FD&C Act. While novelty

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[32] *See also* Ninety-Five Barrels (More or Less) Alleged Apple Cider Vinegar, 265 U.S. at 445 ("When considered independently of the product, the method of manufacture is not material. The [A]ct requires no disclosure concerning it.").

[33] FDA, Guidance for Industry: Voluntary Labeling Indicating Whether Foods Have or Have Not Been Derived from Genetically Engineered Plants (2015), available at: www.fda.gov/foodguidances

may be an aspect of patentability, the fact that a food product or its method of production is considered novel within the context of patent law does not mean that, as a result, such food product is required to bear labeling disclosing its method of production under the FD&C Act.

Plant varieties have been patentable since long before the use of genetic engineering to produce new plant varieties. Indeed, the first plant patent was issued in 1931.[34] The laws governing patents are not the same as those governing the labeling of foods under the FD&C Act. Patent laws are codified in different statutes, articulate different standards, and serve different purposes.[35] In general, the main purpose of a patent is "to promote creation" or advancement "by offering inventors exclusive rights for a limited period as an incentive for their inventiveness and research efforts."[36] Patentability generally is dependent upon a number of factors, including novelty, utility, and non-obviousness, as set forth in particular patent laws.[37]

The provisions of the FD&C Act related to food labeling generally set forth different standards and serve different purposes from those associated with patentability. The factors considered in determining whether a food or its process of development is patentable are not the same as those considered in determining whether the labeling for a food is required to bear certain information, including whether such labeling fails to reveal a material fact within the meaning of section 201(n) of the Act. The fact that a seed or a production method for a food can be subject to a patent is not dispositive as to whether the labeling for the food fails to reveal a material fact within the meaning of section 201(n) of the FD&C Act. As discussed above, the determining factor, within this context, is the final food product and whether such food presents material differences or safety concerns in comparison to its traditional counterpart; not whether the food or its method of manufacture or development is subject to a patent. See National Research Council, 2004, p. 63; ABI, 116 F. Supp. 2d 166, 178-79; Stauber v. Shalala, 895 F. Supp. 1178, 1193-94 (W.D. Wis. 1995). Accordingly, even if the method of developing a food were patentable, absent a material difference between the food and its traditional counterpart, the food generally would not be required to bear additional labeling regarding its method of development under section 201(n) of the Act.[38]

For these reasons, we do not agree that genetically engineered foods using recombinant DNA technology are required to bear additional labeling under the FD&C Act solely because such foods, or the technologies used to produce such foods are patentable.

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[34] Plant Patent 1 (PP1), U. S. Patent and Trademark Office, August 18, 1931.

[35] Federal patent power stems from a specific constitutional provision which authorizes Congress to "promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries." Art. I § 8, cl. 8; see also Graham v. John Deere Co., 383 U.S. 1 (1966). Patent laws "promote this progress by offering inventors exclusive rights for a limited period as an incentive for their inventiveness and research efforts." Diamond v. Chakrabarty, 447 U.S. 303, 307 (citing Kewanee Oil Co. v. Bicron Corp., 416 U.S. 470, 480-81 (1974); Universal Oil Co. v. Globe Co., 332 U.S. 471, 484 (1944).

[36] Ass'n for Molecular Pathology v. Myriad Genetics, Inc, 133 S.Ct. 2107, 2116 (2013); Diamond, 447 U.S. at 307 (internal citations omitted).

[37] See e.g., John Deere Co., 383 U.S. at 12.

[38] ABI, 116 F. Supp. at 179, 179 n. 10 ("Disclosure of the conditions or methods of manufacture has long been deemed unnecessary under the law) (citing Ninety-Five Barrels (More or Less) Alleged Apple Cider Vinegar, 265 U.S. at 445); *see also* Ninety-Five Barrels (More or Less) Alleged Apple Cider Vinegar, 265 U.S. at 445 ("When considered independently of the product, the method of manufacture is not material. The [A]ct requires no disclosure concerning it.").

4. Other Food Labeling Requirements

a. Other FDA food labeling requirements

i. Irradiation

In your petition, you indicate that FDA's determination that the production method of genetic engineering does not constitute a "material fact" under section 201(n) of the FD&C Act conflicts with the agency's past interpretation of its statutory authority with respect to other food production processes. Specifically, your petition cites FDA's 1986 rule for the use of irradiation for the treatment of foods (51 FR 13376 (Apr. 18, 1986)) to support this proposition. We disagree. In 2007, we proposed to amend irradiation labeling regulations to limit mandatory labeling to only those irradiated foods in which the irradiation causes a material change in the food's characteristics (e.g., organoleptic, nutritional, or functional properties), or a material change in the consequences that may result from the use of the food under the conditions of use prescribed in the label and labeling or under customary or usual conditions (see 72 FR 16291 (Apr. 4, 2007)).

In the proposed rule, we clarified that historically, the agency has generally interpreted the scope of the materiality concept to mean information about the characteristics of the food. Id. Further, we explained that the need for irradiation labeling must be determined on a case-by-case basis because the effect of irradiation on the properties of concern depends on the particular food, the dose of irradiation, the type of irradiation, and other parameters. We also explained that many changes caused by irradiation, such as the effects of irradiation that kill or weaken insects and microorganisms, are of little significance, as the composition of the food will remain within normal variations of non-irradiated foods. Id. at 16293-94. Thus, under the proposed rule, the fact that a food has been irradiated would not by itself require disclosure on a food label as long as the irradiation has not caused a material change in the food's characteristics.[39] Where a material change in the food's characteristics has been identified, additional labeling indicating that material change would be required.[40] While this proposed rule has not yet been finalized, it represents our most recent position regarding the use of irradiation in the treatment of food and the requirements under sections 403(a) and 201(n) of the FD&C Act for labeling such foods.

ii. Protein hydrolysates

In addition, your petition refers to a 1991 proposed rule on food labeling and declaration of ingredients (56 FR 28592, 28600 (June 21, 1991)) as supporting your contention that FDA's policy for the labeling of food derived from GE plants is inconsistent with previous agency

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[39] For example, see the discussion of irradiated bananas versus irradiated spices at 72 FR 16291, 16294 (Apr. 4, 2007).

[40] The additional labeling would also include a statement that the food had been irradiated because, in the absence of such labeling, the food could appear to consumers to be unprocessed (e.g., "fresh") when, in fact, it was not. Concerns about consumer misperception of a food's freshness underlie any distinction that FDA has previously made between the labeling requirements for a "process" method as opposed to a "production" method, but such concerns are not present in the instance of genetic engineering. As discussed elsewhere, foods from genetically engineered sources do not, as a class, differ from their non-GE counterparts.

interpretations of its statutory authority with respect to other food production processes. Specifically, you cite FDA's tentative finding in the 1991 proposed rule that the food source of a protein hydrolysate is information of material importance for a person who desires to avoid certain foods for religious or cultural reasons. Id. We disagree with this proposition as well.

In the 1991 proposed rule on food labeling, FDA explained that because the source of a protein hydrolysate has a significant effect on its compositional and functional properties, inclusion of the source in the name of a protein hydrolysate is essential to adequately describe the nature of the ingredient Id. The agency further stated that comments to the agency's 1989 Advance Notice of Proposed Rulemaking, which solicited public comment on a wide range of food labeling issues, including the labeling of protein hydrolysates (54 FR 32610 (Aug. 8, 1989)), showed that consumers are interested in being able to identify the food source of a protein hydrolysate, for, in part, religious or cultural reasons. Recognizing these comments, the agency stated its *tentative* finding that source declaration of a protein hydrolysate is of material importance for consumers who desire to avoid certain foods for religious or cultural reasons (56 FR 28592 (June 21, 1991)).

However, in the 1993 final rule on food labeling and declaration of ingredients the agency did not include, as one of its bases to mandate source declaration for protein hydrolysates that such information is a material fact for religious or cultural reasons (see 58 FR 2850 (Jan. 6, 1993). The bases for the final rule are as follows: 1) the source declaration as part of the common or usual name of protein hydrolysates is necessary to describe the basic nature of the ingredient because of the inherent differences in the nature of the source protein; and 2) the inclusion of the protein source in the common or usual name of protein hydrolysates is a material fact under section 201(n) of the FD&C Act because this information is required by allergic individuals in order to make purchase decisions. Id. In addition, several comments to the agency's 1991 proposal to require source declaration of protein hydrolysates stated that source declaration should be limited to the terms "animal" or "vegetable" and that these generic terms would be sufficient for individuals wishing to avoid certain foods for religious or cultural reasons. Id. at 2867. In the 1993 final rule, the agency responded to these comments and stated that generic terms like "animal" or "vegetable" do not adequately describe the basic nature or characterizing properties of the protein hydrolysate nor distinguish between the several types of source proteins in each class of ingredients. Id. The agency further explained that the declaration of the food source of a protein hydrolysate is essential to describe the basic nature of the protein hydrolysate, and that the food source is a significant determinant in the hydrolysate's eventual use in a food. Id.

Therefore, the agency's bases for mandating source declaration for protein hydrolysates are related to characteristics of the food or its consequences of use, and although consumers' desire for source declaration of protein hydrolysates for religious or cultural reasons is also satisfied, that is an ancillary effect rather than a statutorily identified basis for the labeling requirement.

Consistent with the agency's previous determinations, FDA sees no legal basis to require that foods derived from genetically engineered sources, as a class, be labeled to indicate that such foods have been produced through genetic engineering. Your petition does not provide sufficient evidence or factual information that would change this analysis.

b. Foreign labeling requirements

You assert in your petition that, internationally, widespread mandatory labeling for foods derived from genetically engineered sources shows United States policy to be outdated. You state that many countries require genetically engineered foods to be labeled and that we must, therefore, require the labeling of such foods.

Laws regarding the regulation of foods from genetically engineered sources may differ from country to country. FDA regulates foods under the FD&C Act and other applicable laws. Foods derived from genetically engineered plants are regulated within the existing framework of the FD&C Act, FDA's implementing regulations, and current practice, utilizing an approach that is identical in principle to that applied to foods developed by traditional plant breeding. 57 FR 22984. Under the FD&C Act, the method used in the development of a new plant variety is not material information within the meaning of section 201(n) of the FD&C Act.[41] The fact that other countries may have different labeling laws or that U.S. manufacturers may label their products to comply with foreign labeling laws is not dispositive as to whether a food is required to bear additional labeling under the FD&C Act.

You also state that, at the Codex Committee on Food Labeling in May 2010, the United States had dwindling international support for its position on the labeling of genetically engineered foods. In May 2011, the Thirty-Ninth Session of the Codex Committee on Food Labelling (CCFL) completed the *Compilation of Codex Texts Relevant to Labelling of Foods Derived from Modern Biotechnology (Compilation Document).*[42] The general objective of the CCFL is to develop labeling guidance to enhance consumer protection and facilitate trade. The Codex Alimentarius Commission adopted the *Compilation Document* in July, 2011.

The *Compilation Document* provides no new guidance to countries on the question of mandatory versus voluntary labeling of foods produced using modern biotechnology. The *Compilation Document* confirms that Codex labeling texts developed for foods generally, also apply to genetically engineered foods and that such foods are not necessarily different simply due to their method of production. The *Compilation Document* does not endorse one labeling approach over others, nor does it distinguish among them. Rather, it reminds Codex members that their laws and regulations should be consistent with already adopted Codex provisions.

III. Conclusion

For the reasons discussed above, we conclude that your petition does not provide sufficient grounds for the agency to rescind or otherwise deviate from its 1992 Policy with respect to the labeling of foods derived from genetically engineered plants or otherwise require

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[41] See also ABI, 116 F. Supp. 2d at178-79 ("Disclosure of the conditions or methods of manufacture has long been deemed unnecessary under the law.") (citing Ninety-Five Barrels (More or Less) Alleged Apple Cider Vinegar, 265 U.S. at 445) ("When considered independently of the product, the method of manufacture is not material. The [A]ct requires no disclosure concerning it."); Stauber, 895 F. Supp. at1193-94.

[42] Codex Alimentarius Commission, 39th Session., Compilation of Codex Texts Relevant to Labelling of Foods Derived from Modern Biotechnology., U.N. Doc. CAC/GL 76-2011 (May 2011), available: http://www.codexalimentarius.org/standards/list-of-standards/

additional labeling for foods produced using genetic engineering. FDA is therefore denying your petition in accordance with 21 CFR 10.30(e)(3).

If you have any questions please contact the Office of Nutrition, Labeling, and Dietary Supplements at telephone number 240-402-2371.

Sincerely,

Leslie Kux
Associate Commissioner for Policy

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