COMMENTS AND AGENCY'S RESPONSES ON THE PUBLIC HEARING ON THE LABELING OF FOOD MADE FROM AQUADVANTAGE SALMON

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On September 21, 2010, FDA held a public hearing on the labeling of food from AquAdvantage Salmon,[1] a genetically engineered (GE) Atlantic salmon. See 75 FR 52602 (Aug. 26, 2010). The purpose of the hearing was for FDA to explain the relevant legal principles for food labeling and solicit information and views from interested persons on the application of these principles to the labeling of food derived from AquAdvantage Salmon. FDA invited the public to provide information relevant to FDA's consideration of whether there are material differences between food from AquAdvantage Salmon and food from non-GE, farm-raised Atlantic salmon. FDA received over 30,000 responses to the public hearing, each containing one or more comments. The comments were from consumers, consumer groups, trade associations, advocacy groups, farmers, fishermen, industry, grocery stores, environmental organizations, academic institutions, states, cities, medical professionals, and schools.

[1] AquAdvantage Salmon are the triploid, hemizygous, all-female Atlantic salmon from the E0-1α lineage genetically engineered (GE) Atlantic salmon that are the subject of New Animal Drug Application (NADA)141-454 sponsored by AquaBounty Technologies, Inc. (ABT). They are a subset of ABT salmon, which are any GE Atlantic salmon from the E0-1α lineage, irrespective of ploidy, zygosity, or gender (i.e., the set of salmon that includes diploid GE salmon that may be used as broodstock as well as AquAdvantage Salmon or other triploid GE salmon). The NADA is for approval of the α-form of the *opAFP-GHc2* recombinant DNA construct at the α-locus in the EO-1α line of Atlantic salmon under the conditions of use specified in the application. For ease of reference, this document refers to the construct as the AquAdvantage construct.

Many of the comments addressed issues other than the subject of the hearing, and included topics such as the well-being of GE animals, and statements opining that FDA should not approve the new animal drug application (NADA) related to AquAdvantage Salmon. Most of these comments expressed concern about or opposition to GE salmon. Also, many of the comments expressed concern about perceived environmental risks related to its production. Because these comments are outside the scope of the public hearing, they will not be addressed in this document, and are covered in FDA's response to comments regarding the AquAdvantage Salmon environmental assessment. Members of the public concerned about those issues should look at that document for FDA's response.

[http://www.fda.gov/AnimalVeterinary/DevelopmentApprovalProcess/GeneticEngineering/GeneticallyEngineeredAnimals/ucm466220.htm]

Many of the comments requested that FDA require that the labeling of food derived from AquAdvantage Salmon indicate that the food was produced using genetic engineering.

At the public hearing, FDA explained the relevant legal principles for food labeling and invited the public to share its views on the application of this framework to the labeling of food derived from AquAdvantage Salmon. In particular, FDA requested public comment on two questions. These questions follow below along with summaries of substantive comments submitted in response to the questions, grouped by topic, and FDA's reply to those comments.

Question 1. Which facts about the AquAdvantage Salmon seem most pertinent for FDA's consideration of whether there are any "material" differences between foods from this salmon and foods from other Atlantic salmon? (Keep in mind that the use of genetic engineering does not, in and of itself, constitute a "material" difference under the law.)

(Topic 1: Does AquAdvantage Salmon require labeling for health risk purposes?) Several comments stated that food from AquAdvantage Salmon should be labeled to indicate it is GE because it poses special health risks to consumers by introducing hormones and allergens into the diet, and by exposing consumers to greater antibiotic residues and environmental toxins. One comment stated that FDA has previously required that food products be labeled to warn consumers of potential health risks, citing as examples the required disclosure of risks of gastro-intestinal (GI) effects of olestra and warning labels on unpasteurized juice.

(Response) FDA has determined that food from AquAdvantage Salmon is as safe as food from other, non-GE, farm-raised Atlantic salmon. See FOI Summary, Section IX. In assessing the safety of food from a GE animal, the risk issues involved in determining food safety can be divided into two overall categories: (1) whether there is any direct toxicity, including allergenicity, via food consumption of the expression product of the article (or direct effects); and (2) where there is potential indirect toxicity associated with both the article and its expressed product (or indirect effects).[2] If the expression product

[2] FDA, Guidance for Industry: Regulation of Genetically Engineered Animals Containing Heritable Recombinant DNA Constructs (2009), available at: ;

is shown to be safe, and the composition of edible tissues from the GE animal is shown to be as safe as those from animals of the same or comparable type that are commonly and safety consumed, then FDA views this as evidence that food derived from the GE animal is safe.

For this application, CVM looked at whether there are any differences between food from AAS and other, non-GE comparator Atlantic salmon, and whether food from AAS is as safe as food from other, non-GE comparator Atlantic salmon. FOI Summary, Section IX A.

The first step in determining whether there were any changes in composition as a result of the introduction of the AquAdvantage construct, or whether AAS was more allergenic than other Atlantic salmon, was to determine whether AAS is in fact Atlantic salmon. In order to make this determination, CVM evaluated data and information from all of the available studies used by the agency to determine the identity of fish as described by the agency's Regulatory Fish Encyclopedia (RFE).[3] Based on this evaluation, CVM determined that AAS meets the identity criteria for Atlantic salmon as established by FDA's RFE for Atlantic salmon under both molecular criteria established for the RFE. FOI Summary, Section IX B.

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http://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/ucm113903.pdf
Codex Alimentarius Commission (CAC) (2008). Guideline for the Conduct of Food Safety Assessment of Foods Derived from Recombinant-DNA Animals (Codex Alimentarius Commission). CAC/GL 68-2008. Available at http://www.codexalimentarius.net/download/standards/11023/CXG_068e.pdf.

[3] The RFE is a searchable compilation of data in several formats that assists with the accurate identification of fish species that was developed by FDA scientists at the Seafood Products Research Center (SPRC, Seattle District), and the Center for Food Safety and Applied Nutrition (CFSAN) to help federal, state, and local officials and purchasers of seafood identify species substitution and economic deception in the marketplace (available at http://www.fda.gov/Food/FoodScienceResearch/RFE/). Data in the RFE includes high-resolution photographs of the whole fish and marketed products (fillets and steaks), tissue protein patterns determined by isoelectric focusing electrophoresis gels, and mitochondrial DNA sequence determined by DNA barcoding.

Direct effects. With respect to direct effects, which refer to those effects that arise from consumption of edible products from AquAdvantage Salmon including the construct or its gene expression product, CVM's analysis focused on effects associated with the Chinook salmon growth hormone and other hormones that could be affected by changes in growth hormone expression in food derived from AquAdvantage Salmon. The agency identified no additional food consumption risks with respect to hormones.

Some commenters stated that one study appeared to show that AquAdvantage Salmon have a higher level of IGF1 than non-GE salmon. IGF1 is an endogenous hormone associated with expression and circulating levels of growth hormone, and thus is a normal component of food derived from animals. It has been considered as a potential hazard for human consumption following increased growth hormone levels in food producing animals. The agency has previously issued an analysis of the potential risk that IGF1 may pose, which is available on our website.[4] For AquAdvantage Salmon, evaluation of data showed that one mature diploid GE salmon (as opposed to the triploid, GE AquAdvantage Salmon) exhibited an increased level of IGF1 in comparison to mature diploid comparator Atlantic salmon.

FDA conducted a margin of exposure assessment (MOE) in order to determine whether the observed differences are biologically relevant. MOE assessments are often performed to determine whether exposures to a particular substance or component of the food(s) under consideration fall within the range of daily exposures or are different from those in the comparator group and, if so, whether the difference is expected to result in an

[4] FDA, Report on the Food and Drug Administration's Review of the Safety of the Recombinant Bovine Somatotropin (2009), available at http://www.fda.gov/AnimalVeterinary/SafetyHealth/ProductSafetyInformation/ucm130321.htm

adverse outcome. For purposes of this assessment, CVM considered whether exposure to IGF1 at the maximum concentration identified in the one outlier mature diploid GE salmon fell within the range of daily exposures to IGF1 or is different from exposure to IGF1 from the sponsor control fish such that the difference is expected to result in an adverse outcome. FDA determined that the resulting maximum estimated level of consumed IGF1 was well within levels of exposure from other dietary sources of IGF1 and poses no additional risk. FOI Summary, Section IX C 1 a iii.[5]

Indirect effects. With respect to indirect effects, which are those effects that might arise as the result of changes that occur following the insertion of the rDNA construct in AquAdvantage Salmon, the agency reviewed a compositional analysis of edible tissues and concluded that no biologically relevant differences were observed in the general (e.g., proximates, including total protein and total fat) or detailed (e.g., specific amino acids, vitamins, fatty acids, ratios of fatty acids, including omega-3 and omega-6 fatty acids) composition of food from AquAdvantage Salmon and non-GE, farm-raised Atlantic salmon. FOI Summary, Section IX G.

With respect to endogenous allergenicity, FDA evaluated whether the edible tissue from ABT salmon is more allergenic than the non-GE comparator. The allergenic potency of triploid GE salmon, including AquAdvantage Salmon, is not statistically different from that of non-GE comparator salmon. Initial evaluation of the results suggested that there may be an increase in the relative allergenic potency in the GE diploid salmon compared to sponsor control salmon. Out of an abundance of caution,

[5] For more information on IGF-1 levels in AquAdvantage Salmon, see Response to Public Comments to the Veterinary Medicine Advisory Committee (VMAC Comment Response), II A viii., and Freedom of Information Summary Section IX.C 1 a iii.

however, the agency judged that it would want additional data and information to draw a conclusion on the relative allergenic potency of diploid ABT salmon. FDA also noted that individuals allergic to salmon will avoid all salmon. For this reason, small changes in the levels of endogenous allergens would likely have little or no public health impact.[6] However, AquAdvantage Salmon does not present an additional risk of allergic reaction to salmon-allergic individuals and is unlikely to cause allergic cross-reactions in those who are not salmon-allergic.

Other health risks. Some comments said that health risks (such as bacteria resistant to antibiotics, allergic reactions, poisoning) from the use of antibiotics on farm-raised salmon will be greater for GE salmon. There are no data indicating that AquAdvantage Salmon require more antibiotics than non-GE, farm-raised Atlantic salmon under the aquaculture conditions being used. Absent the presence of bacterial disease, AquaBounty should not have a need to use antibiotics. For more information see VMAC Comment Response II B iii.

One comment stated that FDA has required that olestra and unpasteurized juice bear additional labeling because of health risks. In the case of fresh juice products, FDA concluded that the possible presence of pathogens in untreated fresh juice was a material fact because it could result in illness, and therefore the agency required that labeling of fruit and vegetable juice products that have not been processed to prevent, reduce, or eliminate pathogenic microorganisms include a warning statement. 63 FR 37030 (July 8,

[6] CVM consulted Dr. Dean Metcalfe, Chief, Laboratory of Allergic Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, on general scientific matters related to endogenous allergens in foods known to be allergenic. In his consultation with FDA Dr. Metcalfe emphasized this point regarding individuals who are allergic to salmon avoiding consumption of all salmon. See FOI Summary Section IX.C.2.b.v and Appendix 2.

1998); 21 CFR 101.17(g). There is no similar risk of illness from AquAdvantage Salmon. Unlike unpasteurized juice, there is no greater risk of illness from consuming AquAdvantage Salmon, than its non-GE, farm-raised counterpart. In the case of olestra, FDA concluded that there was a reasonable certainty of no harm from the use of olestra in savory snacks and that there was no evidence of adverse health consequences from the possible effects of olestra on the gastro-intestinal (GI) system.[7] 61 FR 3118, 3158-59 (Jan. 30, 1996). The agency concluded, however, that certain consequences of consuming foods containing olestra were "material" facts that required disclosure in a statement on the label of foods containing olestra. Id. at 3160-62.[8] Furthermore, based on the data evaluated, there is no difference in consequences from consumption of AquAdvantage Salmon versus non-GE, farm-raised Atlantic salmon and there is, therefore, no comparable material fact pertaining to effect of consumption that must be disclosed on the label of AquAdvantage Salmon.

With regard to a commenter's assertion that studies of GE fish generally suggest a higher tolerance to toxins in the environment, the website cited by the commenter to support this assertion simply speculates that GE fish might have such a tolerance; it does not cite any scientific data to support this hypothesis. Moreover, the researcher who suggests this risk and is interviewed on the cited website concludes that, in case there is

[7] FDA concluded that, while olestra may cause certain GI effects, including loose stools, these effects were not adverse effects because they do not threaten health. For example, effects described as ''diarrhea'' were not diarrhea in the medical sense because they were not associated with water loss or electrolyte imbalance. 61 FR 3118, 3158 (Jan. 30, 1996). Rather, loose stools and other GI effects experienced as a consequence of consuming foods containing olestra were deemed "material" facts in part so consumers would be able to associate olestra with the GI symptoms it may cause and to preclude unnecessary concerns and inappropriate medical treatment. Id. at 3159.

[8] FDA later reviewed additional data and information collected after the use of olestra was approved and based on that data and information determined that the statement was no longer necessary. 68 FR 46364 (Aug. 5, 2003).

any such risk, "[u]ntil further notice, transgenic [i.e., GE] fish should be bred in closed systems on land." See http://cordis.europa.eu/fetch?CALLER=EN_NEWS&ACTION=D&RCN=31252. The agency notes that as part of the conditions established in the approval, AquAdvantage Salmon may only be bred and raised in the physically contained, land-based tanks at the AquaBounty facilities in Prince Edward Island, Canada and Panama, as specified in the NADA. As a result, AquAdvantage Salmon are not exposed to any toxins that might exist in the open environment.

(Topic 2: Is the Food Production Process material information?) Several comments expressed the belief that the fact that AquAdvantage Salmon is genetically engineered is material information and that FDA, therefore, should require additional labeling of food from AquAdvantage Salmon. Some of these comments stated that when FDA required labeling to indicate that foods are irradiated the agency had adopted an interpretation of "material" that includes information about food manufacturing production methods.

(Response) As noted in the Federal Register notice for the public hearing, whether a food has or has not been produced using genetic engineering, in and of itself, is not a material fact within the meaning of the Federal Food, Drug, and Cosmetic Act (FD&C Act). 75 FR 52602 (Aug. 26, 2010); see also 57 FR 22984 (May 29, 1992); Alliance for Bio-Integrity v. Shalala, 116 F. Supp. 2d 166 (D.D.C. 2000); Stauber v. Shalala, 895 F. Supp. 1178 (W.D. Wis. 1995). Moreover, as also noted in the Federal Register notice for the public hearing, FDA cannot require labeling of foods based solely on differences in the

production process if the resulting products are not materially different due solely to the production process. 75 FR 52602 (Aug. 26, 2010); see Alliance for Bio-Integrity, 116 F. Supp. 2d at 179, 179 n. 10 (explaining that the FD&C Act does not require disclosure of a food's method of production without regard to its effect on the product); U.S. v. Ninety-Five Barrels (More or Less) Alleged Apple Cider Vinegar, 265 U.S. 438, 445 (1924) (same).

Regarding the labeling of irradiated foods, 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. Where a material change in the food's characteristics has been identified additional labeling is required [9] Id. 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.

(Topic 3: Is genetic engineering material to purchasing decisions?) Numerous comments stated that many consumers want food from GE salmon to be labeled as such, because for these consumers, genetic engineering is a material fact affecting purchasing decisions. Comments also stated that FDA has interpreted consumer preferences, both religious and cultural, as "material" when it required food labels to indicate the source of protein hydrolysates (e.g., plant or animal based). One of these comments stated that the Karuk, a Native American tribe, revere salmon as part of their culture, and the Karuk do not want to eat GE salmon.

(Response) FDA regulates food labeling under the FD&C Act, and other laws, as applicable. The FD&C Act does not expressly require food labeling indicating that a food has or has not been produced using genetic engineering. Under the FD&C Act, food labeling may not be false or misleading. 21 U.S.C. 343(a)(1). Labeling is misleading if it does not reveal facts that are material in light of representations made or suggested in the labeling, or with respect to consequences that may result from the use of the food to

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

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).

Consumer preference, alone, does not make something about a food "material" within the meaning of the FD&C Act and, by itself, is not a permissible basis for FDA to require labeling. Alliance for Bio-Integrity, 116 F. Supp. 2d at 178–79 (finding that consumer interest, alone, is not a sufficient basis upon on which FDA can require food labeling); Stauber, 895 F. Supp. 1178 (W.D. Wis. 1995) (same); see also Int'l Dairy Foods Ass'n v. Amestoy, 92 F.3d 67, 74 (2d Cir. 1996) (holding that consumer interest, alone, was not a sufficient government interest to compel food labeling).

For these reasons, while the agency recognizes some consumers are interested in knowing that food from AquAdvantage Salmon is produced using genetic engineering, such consumer interest, alone, is not a material fact within the meaning of the FD&C Act, and is not a sufficient basis upon which FDA can require additional labeling.

Regarding the labeling for the source of protein hydrolysates, in a proposed rule on food labeling and declaration of ingredients, FDA proposed that labeling indicating the source of a protein hydrolysate was necessary for a number of tentative reasons. 56 FR 28592, 28599-00 (June 21, 1991). First, FDA tentatively found that because the source of a protein hydrolysate has a significant effect on the ingredient's compositional and functional properties, inclusion of the source in the name of a protein is necessary to adequately describe the nature of the ingredient. Id. at 28599-00. In addition, the agency tentatively found that the source of a protein hydrolysate would be information of material importance for people who wish to avoid certain foods based on religious or cultural reasons. Id. at 2600. Lastly, the agency tentatively found that labeling indicating

the source of a protein hydrolysate would be necessary in order to for consumers who may be allergic to the source of a protein hydrolysate to identify and avoid such foods. Id. Accordingly, the agency did not propose to require labeling indicating the source of a protein hydrolysate based on consumer preference alone. Nevertheless in the final rule on food labeling and declaration of ingredients, FDA's basis for requiring such labeling was that source declaration was necessary to describe the basic nature of the ingredient, and because individuals who are allergic to a specific food need to know when it is present as an ingredient in order to make informed purchase decisions. 58 FR 2850, 2867 (Jan. 6, 1993). Accordingly, the agency ultimately did not adopt religious or cultural preferences as a basis for requiring food labeling indicating the source of protein hydrolysates.

(Topic 4: Does AquAdvantage Salmon no longer meet consumers' understanding of Atlantic salmon?) A comment stated that AquAdvantage Salmon falls outside consumers' understanding of what Atlantic salmon is because AquAdvantage Salmon has genetic material from non-salmon fish (ocean pout) and non-GE, Atlantic salmon does not and, furthermore, this added genetic material is an ingredient that should be reflected on the label.

(Response) The comment did not provide data with respect to consumers' understanding of Atlantic salmon or its assertion that AquAdvantage Salmon falls outside of any such understanding.

FDA considered the extent to which AquAdvantage Salmon differ from appropriate comparators with respect to the criteria for Atlantic salmon in FDA's Regulatory Fish Encyclopedia and food composition. FDA determined that AquAdvantage Salmon meets criteria that have been established for Atlantic salmon in FDA's Regulatory Fish Encyclopedia. No biologically relevant differences were observed in the general (e.g., proximates, including total protein and total fat) or detailed (e.g., specific amino acids, fatty acids, ratios of fatty acids) composition of food from AquAdvantage Salmon and their appropriate comparators; and AquAdvantage Salmon pose no additional allergenic risk than other non-GE, farm-raised Atlantic salmon. FOI Summary, Section IX. Therefore, FDA concludes that AquAdvantage Salmon falls within common or usual name, "Atlantic salmon," and that the essential nature of the salmon has not changed as a result of the introduction of the AquAdvantage construct. To the extent consumers misperceive food from AquAdvantage Salmon as being different from its non-GE, farm-raised counterpart such that the common name "Atlantic salmon" no longer adequately describes it or, as otherwise being significantly different from non-GE, farm-raised Atlantic salmon, such misperception does not constitute a sufficient basis upon which FDA can require additional labeling. See e.g., Stauber, 895 F. Supp. at 1193 ("If . . . the [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.").

With respect to a commenter's contention that the introduction of a genetic construct into AquAdvantage Salmon represents an added ingredient that should be listed on the label of food derived from the salmon, FDA has previously stated that substances

that are inherent components of a food, such as recombinant DNA constructs, are not ingredients that must be individually identified in labels of foods containing them. See Agency Summary Memorandum re: Consultation With Calgene, Inc., Concerning Flavr Savr™ Tomatoes, http://www.fda.gov/Food/Biotechnology/Submissions/ucm225043.htm.

(Topic 6: Biological differences) Some comments indicated that AquAdvantage Salmon differs significantly from non-GE, farm-raised Atlantic salmon in allergenicity, hormone levels, amino acids, fatty acids, vitamins, minerals, and total content of protein and fat.

(Response) There are no biologically relevant differences between food from AquAdvantage Salmon and non-GE, farm-raised Atlantic salmon. The general composition (i.e., proximates, vitamins, minerals and individual fatty acids and amino acids) of AquAdvantage Salmon does not differ in any biologically meaningful way from that of non-GE, farm-raised Atlantic salmon. No biologically relevant differences were observed in the general (e.g., proximates, including total protein and total fat) or detailed (e.g., specific amino acids, fatty acids, ratios of fatty acids) composition of food from AquAdvantage Salmon and their appropriate comparators, including non-GE, farm-raised Atlantic salmon. Analysis of a statistical difference in vitamin B6 levels demonstrated no impact on safety or nutrition, and thus is not biologically relevant.[10]

FDA previously addressed issues concerning hormone levels and allergenicity in Topic1. The agency has concluded that there are no biologically relevant differences

[10] For more information on vitamin B6 levels, see VMAC comment response, II A vi, and FOI Summary Section IX C 2 a iii b ii.

between food from AquAdvantage Salmon and food from their appropriate comparators, including non-GE, farm-raised Atlantic salmon.

Question 2. If FDA determined there are "material" differences, how would that difference be described on a food label in a way that is truthful and non-misleading? (Keep in mind that it is the difference in composition, or in functional, organoleptic or other material properties that must be described, not the underlying production process.)

(Topic 7: Proposed label statements) One comment suggested a label statement to indicate the sources and functions of the introduced genetic material: "Contains genetic material from Chinook salmon (a growth hormone) and ocean pout (enhancing action of other genes)." Another comment suggested that the statement include the purpose of the process similar to the irradiation statements: "treated with radiation to control spoilage," "treated with radiation to extend shelf life," or "treated with radiation to inhibit maturation." Such a statement could read: "Genetically engineered with ocean pout and Chinook salmon to increase growth rate." Another suggestion was: "Genetically engineered to include growth hormone and antifreeze genes from unrelated species."

(Response) None of the comments to the public hearing provided data or other information to substantiate a finding that there is a material difference between food from AquAdvantage Salmon and food from non-GE, farm-raised Atlantic salmon that must be disclosed on the label. Without a finding of a material difference, FDA cannot require additional labeling of food from AquAdvantage Salmon. Moreover, the comments did

not provide any data or other information to substantiate how the suggested statements would be understood by consumers.

As noted in the Federal Register notice for the public hearing, whether a food has or has not been produced using genetic engineering, in and of itself, is not a material fact within the meaning of the Federal Food, Drug, and Cosmetic Act (FD&C Act). 75 FR 52602 (Aug. 26, 2010); see also 57 FR 22984 (May 29, 1992); Alliance for Bio-Integrity v. Shalala, 116 F. Supp. 2d 166 (D.D.C. 2000); Stauber v. Shalala, 895 F. Supp. 1178 (W.D. Wis. 1995). Moreover, as also noted in the Federal Register notice for the public hearing, FDA cannot require labeling of foods based solely on differences in the production methods if the resulting products are not materially different due to the production method. 75 FR 52602 (Aug. 26, 2010); see Alliance for Bio-Integrity, 116 F. Supp. 2d at 179, 179 n. 10 (explaining that the FD&C Act does not require disclosure of a food's method of production without regard to its effect on the product); U.S. v. Ninety-Five Barrels (More or Less) Alleged Apple Cider Vinegar, 265 U.S. 438, 445 (1924) (same). Stauber, 895 F. Supp. at 1193 ("If . . . the [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.").