

# FDA Issues Dietary Fiber Guidance and Scientific Review of 26 Fibers

November 30, 2016

Food, Beverage, and Dietary Supplements

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On November 22, FDA issued two long-anticipated dietary fiber documents that inform its May 2016 revisions<sup>1</sup> to the nutrition information required to appear on food labels: the Draft Guidance for Industry: Scientific Evaluation of the Evidence on the Beneficial Physiological Effects of Isolated or Synthetic Non-digestible Carbohydrates Submitted as a Citizen Petition (21 CFR 10.30) (Draft Guidance)<sup>2</sup> and the Science Review of Isolated and Synthetic Non-Digestible Carbohydrates (Science Review).<sup>3</sup> FDA also provided a webpage with Questions and Answers for Industry on Dietary Fiber (Dietary Fiber Q&A).<sup>4</sup>

FDA will accept comments on the Draft Guidance until January 23, 2017 (60 days after the date of publication) and on the Science Review until January 9, 2017 (45 days after the date of publication).

FDA has not extended the current compliance timeframe of July 26, 2018<sup>5</sup> for revising the declaration of dietary fiber (where applicable), but states in its associated Dietary Fiber Q&A that it is committed to exploring options to address the timing issue if it is unable to update the list of dietary fibers in time for companies to relabel or reformulate before July 26, 2018.

## Background

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As part of its revisions to the nutrition label for foods and dietary supplements released in May 2016, FDA, for the first time, defined “dietary fiber” as non-digestible soluble and insoluble carbohydrates (with three or more monomeric units), and lignin that are intrinsic and intact in plants, and isolated or synthetic non-digestible carbohydrates (with three or more monomeric units) that FDA determines to have a physiological effect that is beneficial to human health.

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<sup>1</sup> See *FDA Issues Final Rules on Changes to Nutrition Labels*, Covington Client Alert (May 23, 2016), available [here](#).

<sup>2</sup> *Draft Guidance: Scientific Evaluation of the Evidence on the Beneficial Physiological Effects of Isolated or Synthetic Non-digestible Carbohydrates Submitted as a Citizen Petition (21 CFR 10.30): Guidance for Industry* (Nov. 2016), available [here](#).

<sup>3</sup> *Science Review of Isolated and Synthetic Non-Digestible Carbohydrates* (Nov. 2016), available [here](#).

<sup>4</sup> *Questions and Answers for Industry on Dietary Fiber*, FDA.gov, available [here](#).

<sup>5</sup> This is the compliance date for manufacturers with \$10 million or more in annual food sales. For manufacturers with less than \$10 million in annual food sales, the compliance date is July 26, 2019.

In the final rule, FDA stated that it had reviewed over 20 isolated or synthetic non-digestible carbohydrates (NDCs), but concluded that, based on the information available to FDA at that time, only seven<sup>6</sup> met its definition of dietary fiber. FDA promised to, and has now issued, its Scientific Review of 26 NDCs as well as the Draft Guidance on how it will review the scientific information in citizen petitions seeking approval of potential dietary fibers.

## **Draft Guidance on How FDA Will Review the Scientific Evidence in Dietary Fiber Petitions**

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The Draft Guidance includes additional information on “intact and intrinsic” dietary fibers and sets out FDA’s three-step process for evaluating the scientific information submitted in a fiber petition.

### **“Intrinsic and intact” Dietary Fiber Includes Fibers Produced Using Mechanical Processes**

The Draft Guidance confirms that dietary fiber includes: the fiber in fiber-containing foods that are produced using mechanical processes (e.g., milling) if the food contains other nutrients normally found in the food (cereal bran, cocoa powder, flours, vegetable purees or pomace, vegetable protein extracts, parts of a food (e.g., outer coat of peas); and NDCs (e.g., resistant starch) that are created during the normal processing of food (e.g., flaked corn cereal)).

FDA distinguishes these “intrinsic and intact” dietary fibers from “isolated or synthetic” NDCs, which include: foods or parts of foods that have been processed and result in a food with an increased concentration of NDCs that no longer contain or contain lower amounts of nutrients, such as vitamins and minerals; and NDCs that are obtained from non-food sources, such as stems, branches, and trunks of trees, inedible hulls and husks, seaweed, and fungus. FDA will only consider “isolated or synthetic” NDCs to meet the definition of dietary fiber if they have a beneficial physiological effect and will likely approve most NDCs as dietary fiber through the citizen petition process.

### **FDA’s 3-Step Scientific Evaluation Process for Dietary Fiber Petitions**

FDA states that the purpose of its Draft Guidance is to provide its current thinking on the information needed in a dietary fiber petition and the approach it will take in reviewing the scientific evidence presented in a petition. The Draft Guidance explains FDA’s three step process for evaluating the evidence submitted in a fiber petition, which includes: (1) identifying scientific articles that evaluate the physiological effects of a synthetic or isolated non-digestible carbohydrate; (2) eliminating those studies from which no scientific conclusions can be drawn about the carbohydrate; and (3) evaluating the strength of the scientific evidence to determine whether the carbohydrate sufficiently supports a beneficial physiological effect to human health.

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<sup>6</sup> These are beta-glucan soluble fiber, psyllium husk, cellulose, guar gum, pectin, locust bean gum, and hydroxypropylmethylcellulose.

### Step 1: Identifying Scientific Articles

FDA expects a petition to include “all publicly available human studies on a specific . . . carbohydrate . . . regardless of the studies’ findings.”<sup>7</sup> Notwithstanding this requirement, FDA will rely primarily on randomized, controlled human intervention studies in assessing whether an NDC meets its definition of dietary fiber, because these studies provide the strongest evidence of a link between an NDC and a beneficial physiological effect. FDA is unlikely to extrapolate results from intervention studies on selected populations to different populations because doing so may not be scientifically valid.

Regarding whether FDA will consider non-intervention studies in its assessment, the Draft Guidance states that FDA: is not aware of any observational studies directed at beneficial physiological effects of NDCs; will use review articles and similar publications only to identify additional studies; and will use animal and *in vitro* studies as background information regarding mechanisms of action.

### Step 2: Evaluating Human Intervention Studies

The Draft Guidance explains that FDA will first review all the studies to identify relevant human intervention studies and then evaluate such studies to determine whether it can draw any scientific conclusions regarding the NDCs beneficial physiological effects. In order for FDA to draw scientific conclusions, the study should:

- Use the NDC in its isolated form and not in combination with other NDCs.
- Evaluate a specific endpoint shown to have a beneficial physiological effect (currently, FDA has identified the following endpoints: lowering blood glucose<sup>8</sup>, lowering cholesterol levels, lowering blood pressure, improved laxation and bowel function<sup>9</sup>, increased mineral absorption in the intestinal tract, reduced energy intake<sup>10</sup> (for example, due to the fiber promoting a feeling of fullness)).
- Use healthy study subjects.<sup>11</sup>

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<sup>7</sup> Draft Guidance at 6.

<sup>8</sup> FDA does not consider studies of glycemic index (GI) to be sufficient to demonstrate attenuation of blood glucose levels because GI does not provide information on how an isolated or synthetic NDC affects the glycemic response of a food or a beverage that contains nutrients (e.g., starch) that affect blood glucose levels. *Id.* at 10.

<sup>9</sup> FDA recognizes reduced transit time of food through the intestinal tract, increased rates of defecation (e.g., stools per day), ease of defecation, and reduced complaint of defecation. FDA’s view is that an increase in fecal weight does not necessarily indicate improved bowel function but will consider it in its reviews only to evaluate changes in laxation. *Id.*

<sup>10</sup> FDA views reduced energy intake from food consumption, rather than satiety, a physiological benefit, but FDA will consider changes in satiety in its review to understand the mechanism by which a potential reduction in energy intake might occur. *Id.*

<sup>11</sup> FDA will consider studies that include individuals at risk of developing a disease (e.g., elevated LDL cholesterol levels, metabolic syndrome, or abnormal glucose tolerance test) or who have an unrelated diseases (e.g., individuals with osteoporosis and being evaluated for attenuation of blood glucose levels). *Id.* at 11. FDA will only extrapolate from studies conducted with diseased subjects if doing so is

- Include an appropriate control group.
- Have baseline values that are not significantly different between the control and intervention groups.
- Be of a sufficient duration.<sup>12</sup>
- Use appropriate statistical analysis<sup>13</sup>
- Be relevant to the general U.S. population.<sup>14</sup>

FDA will eliminate studies from which it cannot draw scientific conclusions, but is open to evaluating other beneficial physiological endpoints if scientific evidence exists to support their inclusion.

### Step 3: Evaluating the Strength of the Scientific Evidence

To evaluate the strength of the scientific evidence, FDA intends to consider: (1) the number of studies; (2) the number of subjects per group in each study; (3) whether the outcomes of the studies demonstrate a statistically significant difference between the intervention and control groups ( $p < 0.05$ ); (4) whether the results supporting the beneficial physiological effect have been replicated; (5) the relevance of the body of scientific evidence to the U.S. population or target subgroup; and (6) the overall consistency of the totality of the information (e.g., the level of agreement among the studies from which scientific conclusions can be drawn about the NDC and physiological benefit).

### **Considerations for Stakeholders**

As a note of caution, FDA states in its Dietary Fiber Q&A that if, after the compliance date, an NDC is not included in its definition of “dietary fiber” but is included in the product’s declaration of dietary fiber, the product would be misbranded. This approach applies to NDCs under consideration by FDA in pending citizen petitions.

Stakeholders may wish to provide comments and information regarding: additional beneficial physiological endpoints; the use of NDCs in combination as a single ingredient and the relevance of scientific studies demonstrating physiological benefits of the combined NDC ingredient rather than separate studies of each NDC; confirmation on study duration for the

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scientifically appropriate because: (1) the mechanism(s) for the mitigation or treatment effects measured in the diseased populations are the same as the mechanism(s) for risk reduction effects in non-diseased populations; and (2) the added non-digestible carbohydrate affects these mechanisms in the same way in both diseased and healthy people. *Id.*

<sup>12</sup> To demonstrate cholesterol lowering effects, FDA considers 3 weeks to be the minimum study duration. To demonstrate bowel function, FDA considers 1 week to be the minimum to allow for a sufficient amount of time for collecting stool samples. *Id.*

<sup>13</sup> FDA expects, for example, that if a study conducts statistical analyses among more than two study groups, the data should be analyzed by a test designed for multiple comparisons (e.g., Bonferroni, Duncan). *Id.* at 12–13.

<sup>14</sup> FDA explains that differences in nutrition, diet, and beneficial physiological effects between the United States and the country where a study was done may mean that the study results cannot be extrapolated to the U.S. population. *Id.* at 13.

other beneficial physiological endpoints (e.g., lowering blood glucose, lowering blood pressure, increased mineral absorption in the intestinal tract, and reduced energy intake); examples of other study populations that might be at risk of developing diseases that would be acceptable study groups; potential impacts on end users of NDCs still under review in a citizen petition, and options for how FDA can announce that a NDC was “approved” as dietary fiber to allow its use before it is officially added to the definition through rule-making.

Finally, stakeholders could provide FDA options to address the timing issue, given that FDA has stated it would explore such options if it is unable to update the list of dietary fibers by July 26, 2018.

Comments on FDA’s Draft Guidance should be submitted by January 23, 2017.

### **FDA’s Science Review of 26 Isolated or Synthetic NDCs**

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Along with the Draft Guidance, FDA issued its Science Review of 26 isolated or synthetic NDCs. FDA chose these 26 NDCs<sup>15</sup> because they were “the most common ones being added to food and declared on the Nutrition Facts as dietary fiber.” FDA’s Science Review follows the three-step review process outlined in its Draft Guidance and includes a summary of each study that met FDA’s review criteria (i.e., from which FDA could draw scientific conclusions) and a list of studies that FDA did not consider because they did not meet the agency’s review criteria.

Notably, while the Science Review does exclude certain studies that FDA concluded did not meet its review criteria, FDA does not include a final assessment or provide any comments on the strength of the scientific evidence it reviewed for any of the 26 NDCs. FDA has posted several citizen petitions it has received that request approval as dietary fibers. FDA is requesting additional scientific information on the 26 NDCs in its Science Review (and any others) and feedback on the physiological endpoints it used in its Science Review and other possible beneficial physiological endpoints. Given that FDA did not include any of the 26 NDCs in the final definition of dietary fiber, these NDCs may not meet FDA’s definition unless it receives additional information not included in its Science Review that the NDC provides a physiological benefit (that has been replicated in more than one study).

FDA has stated it will move expeditiously to review and approve any additional dietary fibers based on the information it receives in this comment period and in citizen petitions and will most likely provide its decision collectively for all the NDCs currently under its review.

Comments on FDA’s Science Review must be received by January 9, 2017

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<sup>15</sup> The 26 NDCs include: Gum Acacia; Alginate; Apple Fiber; Bamboo Fiber; Carboxymethylcellulose; Corn Hull Fiber; Cottonseed Fiber; Galactooligosaccharides; Inulin/Oligofructose/Synthetic Short Chain Fructooligosaccharides; Karaya Gum; Oat Hull Fiber; Pea Fiber; Polydextrose; Potato Fibers; Pullulan; Rice Bran Fiber; High Amylose Corn/Maize Starch (Resistant Starch 2); Retrograded Corn Starch (Resistant Starch 3); Resistant Wheat and Maize Starch (Resistant Starch 4); Soluble Corn Fiber; Soy Fiber; Sugar Beet Fiber; Sugar Cane Fiber; Wheat Fiber; Xanthan Gum; Xylooligosaccharides

Covington & Burling LLP continues to monitor developments in food labeling requirements, and in particular, FDA's actions on dietary fiber, added sugars, and other actions related to FDA's revisions to nutrition information. If you have any questions concerning food labeling developments discussed in this alert or other food regulatory matters or would like assistance in preparing comments to FDA on the issues describe above, please contact any of the following attorneys in our Food & Drug Practice group or visit our [food, beverage and dietary supplements practice](#) website:

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