



July 22, 2022

Rani Thomas  
Senior Regulatory Affairs Manager  
Grain Processing Corporation  
1600 Oregon Street  
Muscatine, IA 52761

Re: Docket No. FDA-2020-P-1875

Dear Ms. Thomas:

This letter responds to your citizen petition dated November 20, 2020, requesting that the Food and Drug Administration (FDA or we) “amend 21 CFR § 101.9(c)(6)(i) Nutrition Labeling of Food to include Isomaltodextrin as Dietary fiber under the Resistant Maltodextrin category in the Nutrition Facts label on foods and beverages and dietary supplements.” See Citizen Petition from Rani Thomas, Grain Processing Corporation, submitted to the Division of Dockets Management, Food and Drug Administration, dated November 20, 2020 (“Petition”), at page 1.

In accordance with 21 CFR 10.30(e)(3), we are denying your Petition for the reasons stated below.

### **I. FDA’s Actions Regarding Dietary Fiber**

In the *Federal Register* of May 27, 2016, we published a final rule entitled, “Food Labeling: Revision of the Nutrition and Supplement Facts Labels” (81 FR 33742). The final rule, among other things, defines dietary fiber as “non-digestible soluble and insoluble carbohydrates (with 3 or more monomeric units), and lignin that are intrinsic and intact in plants; isolated or synthetic non-digestible carbohydrates (with 3 or more monomeric units) determined by FDA to have physiological effects that are beneficial to human health” (see 21 CFR 101.9(c)(6)(i)). In the final rule, we identified seven isolated or synthetic non-digestible carbohydrates that have a physiological effect that is beneficial to human health. We also stated that any interested person may seek to amend the listing of added fibers through the existing citizen petition process in 21 CFR 10.30.<sup>1</sup>

In the *Federal Register* of March 2, 2018 (83 FR 8997), we announced the availability of a final guidance document entitled, “Scientific Evaluation of the Evidence on the Beneficial

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<sup>1</sup> For up-to-date information on the additional non-digestible carbohydrates that FDA has determined may be added to the definition of dietary fiber, see “Questions and Answers on Dietary Fiber,” available at [http://www.fda.gov/food/food-labeling-nutrition/questions-and-answers-dietary-fiber#synthetic\\_fibers](http://www.fda.gov/food/food-labeling-nutrition/questions-and-answers-dietary-fiber#synthetic_fibers).

Physiological Effects of Isolated or Synthetic Non-digestible Carbohydrates Submitted as a Citizen Petition (21 CFR 10.30)” (“final guidance”). This final guidance describes our recommendation on the scientific evidence needed, and the approach for evaluating the scientific evidence, on the physiological effects of isolated or synthetic non-digestible carbohydrates added to foods that are beneficial to human health. We also stated in this final guidance that we intend to evaluate the strength of the evidence to determine whether there is a beneficial physiological effect of an added non-digestible carbohydrate using the publicly available studies from which scientific conclusions can be drawn (final guidance at page 14).

In the *Federal Register* of June 15, 2018 (83 FR 27894), we announced the availability of a related final guidance document entitled, “The Declaration of Certain Isolated or Synthetic Non-Digestible Carbohydrates as Dietary Fiber on Nutrition and Supplement Facts Labels” (“enforcement discretion guidance”) that identifies eight additional isolated or synthetic non-digestible carbohydrates – including resistant maltodextrin/dextrin – that we intend to propose adding to the list of isolated or synthetic non-digestible carbohydrates that meet our regulatory definition of “dietary fiber” in 21 CFR 101.9(c)(6)(i).<sup>2</sup> We stated in this guidance that, based on our review of citizen petitions submitted to FDA, comments that we had received, and our independent evaluation of the available scientific data, we had tentatively determined that these eight additional isolated or synthetic non-digestible carbohydrates have physiological effects that are beneficial to human health. Therefore, we also stated our intent to exercise enforcement discretion for the declaration of these eight isolated or synthetic non-digestible carbohydrates as a dietary fiber on Nutrition Facts and Supplement Facts labels.

A document entitled, “Review of the Scientific Evidence on the Physiological Effects of Certain Non-Digestible Carbohydrates” (“science review document”), in which we summarized the scientific evidence regarding biomarkers and physiological endpoints related to human health for these eight non-digestible carbohydrates, accompanied this enforcement discretion guidance.<sup>3</sup> In this science review document, we described resistant maltodextrin/dextrin as a glucose oligosaccharide composed of non-digestible oligosaccharides of glucose molecules that are joined by digestible linkages and non-digestible  $\alpha$ -1,2 and  $\alpha$ -1,3 linkages. We also discussed our review of the scientific evidence for resistant maltodextrin (RMD) and resistant dextrin (RD) (i.e., indigestible dextrin) related to at least one physiological endpoint that is beneficial to human health.

Briefly, we identified four studies that evaluated the effect of RMD/RD consumption on calcium absorption or retention. As we explained in the science review document, increased intestinal absorption of minerals having public health significance, such as calcium, is a physiological effect that is beneficial to human health. In addition to being a nutrient of public health significance, calcium is required on the Nutrition Facts label (21 CFR 101.9(c)(8)(ii)).

We found that the strength of the evidence supports a beneficial physiological effect of RMD/RD in increasing calcium absorption and body retention, as well as bone formation. Therefore, the evidence from which scientific conclusions could be drawn supports our decision to propose to

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<sup>2</sup> These eight isolated or synthetic non-digestible carbohydrates include some broader categories, e.g., mixed plant cell wall fibers.

<sup>3</sup> Available at <https://www.fda.gov/media/113659/download>.

amend the list of nondigestible carbohydrates that meet the definition of dietary fiber to include RMD/RD as a dietary fiber. Thus, we stated that we intended to exercise enforcement discretion for declaring the amount of RMD/RD as dietary fiber until we complete rulemaking.<sup>4</sup>

## **II. The Petition's Requested Action**

The Petition asks that we “amend 21 CFR § 101.9(c)(6)(i) ... to include Isomaltodextrin as Dietary fiber under the Resistant Maltodextrin category in the Nutrition Facts label ...” (Petition at page 1). The Petition asserts that isomaltodextrin (IMD) should be added to the list of dietary fibers in 21 CFR § 101.9(c)(6)(i) on the grounds that IMD “is a Resistant Maltodextrin (with 3 or more monomeric units) that is the same as the substance recognized by FDA as Dietary Fiber” (Petition at page 1). The petition further states that “IMD is very similar in structure and digestibility to the approved Dietary fibers in the Resistant Maltodextrin category and therefore be [sic] considered as Resistant Maltodextrin/Dextrin” (Petition at page 2). The petition provides the characterization of IMD; the manufacturing process and a process flow diagram; a structural comparison of IMD, maltodextrin, RMD, and RD; data on the in-vitro digestibility of IMD; and information regarding a Generally Recognized as Safe (GRAS) review of IMD.

## **III. FDA's Evaluation of the Evidence Submitted**

We reviewed your petition under the final guidance. In the final guidance, we provided background information on how we define dietary fiber, and we reiterated that as part of this definition, a dietary fiber must be shown to have physiological effects that are beneficial to human health. We also reiterated that by defining dietary fiber based on a physiological effect that is beneficial to human health, we would ensure that the dietary fiber declared on the nutrition label would assist consumers in maintaining healthy dietary practices (final guidance at page 4; see also 81 FR 33742 at 33858). We further stated that “[t]he physiological effects of specific isolated or synthetic non-digestible carbohydrates from foods or other sources that are added to foods can only be ascertained by evaluating the non-digestible carbohydrates individually” (final guidance at page 5).

Although IMD might be structurally similar to RD and RMD, the chemical structure of IMD lacks some of the non-digestible bond linkages that are present in RMD/RD.<sup>5</sup> It is unclear to what extent the lack of specific non-digestible bond linkages (i.e., beta-bonds and  $\alpha$ -1,2 linkages) in IMD, and the different percentages of other non-digestible and digestible bonds in IMD relative to those in RMD/RD, would be expected to result in similar or different physiological effects among these substances. The petition provides no information that would allow us to evaluate whether these differences in chemical structure may result in similar or different

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<sup>4</sup> See FDA's “Questions and Answers on Dietary Fiber,” available at <https://www.fda.gov/food/food-labeling-nutrition/questions-and-answers-dietary-fiber>.

<sup>5</sup> The final guidance addresses the scientific evaluation of synthetic non-digestible carbohydrates and isolated non-digestible carbohydrate ingredients that are produced as a result of processing of foods and other sources, to the extent that the ingredients in and of themselves have a specific chemical structure (carbohydrate composition and non-digestible bond linkages) (final guidance at page 5). Available at <https://www.fda.gov/media/101183/download>.

physiological effects that are beneficial to human health (e.g., increase of calcium absorption, among other relevant beneficial physiological effects identified in the scientific literature<sup>6</sup>).<sup>7</sup>

With respect to the 2015 GRAS notification for IMD<sup>8</sup> referred to in the petition (Attachment A at page 9), a GRAS notification focuses on safety – not on issues pertaining to nutrition or potential health benefits.<sup>9</sup> As we stated in the Nutrition Facts label final rule, “A dietary fiber that is GRAS does not necessarily meet the definition of dietary fiber for purposes of nutrient declaration.”<sup>10</sup> Similarly, the data provided in the petition with respect to the digestibility of IMD (Attachment A at pages 8-9) and the reference cited in the Petition for an in-vitro assay system that simulates the physiological conditions for starch digestion<sup>11</sup> do not provide evidence of a beneficial physiological effect on human health that is sufficient for FDA to propose to amend 21 CFR 101.9(c)(6)(i) to include IMD in the regulatory definition of “dietary fiber.”<sup>12</sup>

Lastly, the amount of dietary fiber to be declared on the Nutrition Facts label is no longer based on analytical methods, such as AOAC analytical methods (81 FR 33852). Therefore, IMD having “greater than 80% dietary fiber as measured by approved methods” is no longer the basis for meeting the dietary fiber definition for labeling purposes, but rather that the isolated or synthetic non-digestible carbohydrates (with 3 or more monomeric units) has been determined by FDA to have physiological effects that are beneficial to human health.

As previously mentioned, FDA’s final guidance describes our recommendations on the approach for evaluating the scientific evidence related to beneficial physiological effects of isolated or synthetic non-digestible carbohydrates added to foods. We specifically stated that “interested parties should submit all publicly available human studies on a specific isolated or synthetic non-digestible carbohydrate as part of a citizen petition, regardless of the studies’ findings. Publicly available studies include those studies that are in manuscript form and can be available for the public to review. We may identify additional relevant intervention studies through a literature search. We intend to focus our review primarily on articles reporting human intervention studies because these studies can provide evidence from which scientific conclusions can be drawn

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<sup>6</sup> There are a number of beneficial physiological effects associated with the consumption of non-digestible carbohydrates. Some examples include attenuation of blood glucose and/or insulin, and cholesterol concentrations; reduced energy intake; and improved laxation (i.e., the elimination of fecal waste) (81 FR 33742 at 33856, 33858; IOM, 2001; IOM, 2002).

<sup>7</sup> As explained in the Nutrition Facts label final rule (81 FR 33742 at 33853), an isolated or synthetic non-digestible carbohydrate only needs to demonstrate one beneficial physiological effect.

<sup>8</sup> See Agency Response Letter GRAS Notice No. GRN000610. Available at <https://www.fda.gov/food/gras-notice-inventory/agency-response-letter-gras-notice-no-grn-000610>

<sup>9</sup> See, e.g., 81 FR 33852 at 33854 (“[T]he GRAS review system evaluates ingredients for their safety, rather than beneficial physiological effects.”)

<sup>10</sup> See 81 FR 33854. See also 81 FR 33856 (“[E]ven if a manufacturer self-determines that a fiber is GRAS...whether the fiber has a beneficial physiological effect to health is a separate question.”)

<sup>11</sup> O’Dea K and Muir JG. Measurement of resistant starch; factors affecting the amount of starch escaping digestion in vitro. *Am J Clin Nutr* 1992; 56:123-7.

<sup>12</sup> Animal and *in vitro* studies can be used to generate hypotheses, investigate biological plausibility of hypotheses, or to explore a mechanism of action of a specific food component through controlled animal diets. However, these studies do not provide information from which scientific conclusions can be drawn regarding the beneficial physiological effects in humans of a food component, such as added non-digestible carbohydrates (final guidance at page 8). Available at <https://www.fda.gov/media/101183/download>.

about the beneficial physiological effect of a specific isolated or synthetic non-digestible carbohydrate in humans” (final guidance at page 6).

Given the petition’s position on the similarity of IMD and RMD/RD, the petition does not provide information with regard to conducting a literature search, the results of a literature search, or summaries of relevant human intervention studies. The petition also does not include the results of any publicly available human intervention studies to support the requested action.

We were unable to review your petition using the recommendations identified in our final guidance because you did not submit data on the physiological effects of IMD and thus did not provide scientific evidence to demonstrate that the consumption of IMD has a physiological effect that is beneficial to human health. While FDA recognizes that IMD is similar in structure to RMD/RD, as noted earlier, there are also differences among these substances, particularly with respect to the percentages of digestible and non-digestible glycosidic linkages. The petition does not provide data to demonstrate that, despite these differences, IMD would have the same beneficial physiological effects as RMD/RD.

#### **IV. Conclusion**

Based on our consideration of the scientific evidence and other information submitted with the petition, we conclude that we are unable to evaluate whether the consumption of IMD has a physiological effect that is beneficial to human health. Consequently, we do not plan to propose to amend the list of nondigestible carbohydrates that meet the definition of dietary fiber to include IMD as a dietary fiber. Therefore, in accordance with 21 CFR 10.30(e)(3), we are denying your petition. You are welcome to resubmit your petition if you are able to provide FDA with data and scientific evidence demonstrating that the strength of the evidence supports that IMD has a beneficial physiological effect on human health.

Sincerely,

Claudine Kavanaugh, PhD, MPH, RD  
Director  
Office of Nutrition  
and Food Labeling  
Center for Food Safety  
and Applied Nutrition