FDA U.S. FOOD & DRUG ADMINISTRATION
CENTER FOR FOOD SAFETY & APPLIED NUTRITION

January 9, 2020

Jianhua Zhu, Ph.D.
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Re: Docket Number FDA-2019-P-2239

Dear Dr. Zhu:

This letter is in response to your citizen petition dated May 3, 2019, requesting that the Food and Drug Administration (FDA or we) "amend 21 CFR § 101.9(c)(6)(i) so that it includes "isomalto-oligosaccharides" in the list of dietary fibers that meet the definition of dietary fiber." (Citizen Petition from Dr. Jianhua Zhu, Ph.D., BioNeutra North America Inc., submitted to the Division of Dockets Management, Food and Drug Administration, dated May 3, 2019 ("Petition") at page 1).

We note that this is the second citizen petition you have submitted requesting that FDA amend 21 CFR 101.9(c)(6)(i) to include isomaltooligosaccharides ("IMO") among the isolated or synthetic non-digestible carbohydrates that have been determined by FDA to have physiological effects that are beneficial to human health and therefore include IMO in the calculation of the amount of dietary fiber on the Nutrition Facts label. We denied your first citizen petition (see Docket No. FDA-2016-P-4275; dated December 5, 2016) ("original petition"), as explained in a letter ("original denial letter") from FDA to Dr. Jianhua Zhu, dated June 13, 2018.[1]

You indicate that your petition contains the translation of three articles[2] that were cited in your original petition (Petition at page 2). The original petition did not include the verified translations of these articles as required by FDA's regulation in 21 CFR 10.20(c)(2).[3] In addition, you indicate that your petition includes "scientific evidence to support the relationship between IMO consumption and blood cholesterol levels" (Petition at page 2). Your original

[1] U.S. Food and Drug Administration, Denial Letter to BioNeutra North America Inc. (June 13, 2018), available at https://www.regulations.gov/document?D=FDA-2016-P-4275-0057.

[2] Liu S, Ling Y, and Tsai CE. Biotechnically synthesized oligosaccharides and polydextrose reduce constipation and putrefactive metabolites in the human. *Nutritional Sciences Journal* 1994;19:221-232; Lee M, Lee K, and Ly S. Improving effects of fructooligosaccharide and isomaltooligosaccharide contained in sponge cakes on the constipation of female college students. *Journal of the Korean Society of Food Science and Nutrition* 2003;32:621-626; Lin S, Lim P, Wang H and Hsiao C. Effects of isomaltooligosaccharide chiffon cake on serum biochemical parameters, constipation, and fecal putrefactive metabolites in hyperlipidemic subjects. *Nutritional Sciences Journal* 2005;30:108-115.

[3] As stated in 21 CFR 10.20(c)(2), "If a part of the material submitted is in a foreign language, it must be accompanied by an English translation verified to be complete and accurate, together with the name, address, and a brief statement of the qualifications of the person making the translation. A translation of literature or other material in a foreign language is to be accompanied by copies of the original publication."

petition was based solely on the grounds that IMO has a beneficial physiological effect on laxation, and therefore you did not previously include or discuss studies that evaluated health outcomes related to blood cholesterol. Thus, your petition differs from your original petition in that your petition describes the results of human intervention studies in which the relationship between IMO consumption and laxation and/or blood cholesterol were evaluated.

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.[4]

In accordance with 21 CFR 10.30(e)(3), we are denying your petition. This letter sets out the basis for our determination that the strength of the evidence does not show that the consumption of IMO has a physiological effect that is beneficial to human health.

I. FDA's Consideration of the Scientific Evidence

Your petition requests that FDA add IMO to the list of dietary fibers in 21 CFR 101.9(c)(6)(i) on the grounds that IMO has physiological effects that are beneficial to human health based on evidence you submitted that "evaluated the relationship between IMO consumption and laxation and/or blood cholesterol" (Petition at page 3).

In the *Federal Register* of March 2, 2018 (83 FR 8997), we announced the availability of a

1. final guidance document entitled "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)" ("final guidance"). This final guidance describes our views 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. It also discusses the inclusion of studies on diseased populations under certain circumstances as part of our evaluation of the totality of the scientific evidence, provides detail on the physiological endpoints that we consider when reviewing the scientific evidence, and provides detail regarding factors we consider when evaluating the strength of the scientific evidence.

We reviewed your petition and your original petition using the factors identified in the final guidance. In our previous review of your original petition, we evaluated whether the consumption of IMO has the beneficial physiological effects that you had identified as grounds

[4] For up-to-date information on the additional non-digestible carbohydrates that FDA intends to propose 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.

for adding IMO to the list of dietary fibers; these effects included "favorable and consistent effects of isomaltooligosaccharides on laxation, as indicated by improvements (*i.e., increases*) in defecation frequency and increases in fecal weight" (original petition at page 2). We concluded that the strength of the scientific evidence did not show that the consumption of IMO has a physiological effect that is beneficial to human health (original denial letter at page 6).

In our review of your current petition, we note that your petition addresses the potential physiological effects of IMO consumption on blood cholesterol, in addition to those potential effects related to laxation. Your petition also affirms your intention to include two of the endpoints that FDA had specifically stated were appropriate indicators of laxation, defecation frequency (number of stools/day) and fecal weight per day (based on stool collections over multiple days), as well as subjective symptoms related to laxation (see Petition at page 3). This response letter addresses the additional data and information provided in the current petition that was not included in your original petition and provides our current determination on the overall strength of the scientific evidence.

Laxation

In our original denial letter,[5] we stated that we could draw scientific conclusions from three human intervention studies that evaluated the effect of IMO on laxation.[6] We also stated that we could not draw scientific conclusions from three studies because the subjects used enemas and/or laxatives[7] (Chen et al., 2001; Yen et al., 2011) or the study lacked a control group and statistical analysis (Qing et al., 2003).[8]

Your petition identifies five studies[9] that you consider to be relevant in demonstrating a beneficial physiological effect of IMO consumption on laxation (Petition at page 6). Four of

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[5] See *supra* note 1.

[6] BioNeutra Inc. [unpublished]. Double-blind, randomized, placebo controlled study to investigate the effects of VitaSugar™/VitaFiber™-IMO in healthy adults: final report. (Study Identification Number: 11VBHB). Edmonton (AB): BioNeutra Inc. 2012; Bouhnik Y, Raskine L, Simoneau G et al. The capacity of non-digestible carbohydrates to stimulate fecal bifidobacteria in healthy humans: a double-blind, randomized, placebo-controlled, parallel-group, dose-response relation study. *American Journal of Clinical Nutrition* 2004; Kaueko T, Kohmoto T, Kikuchi H et al. Effects of isomalto-oligosaccharides intake on defecation and intestinal environment in healthy volunteers. *Journal of Home Economics of Japan* 1993. See *supra* note 1 for full study descriptions.

[7] We also noted: "The subjects in these studies were permitted to use enema treatments upon request, if spontaneous defecation was incomplete, or if spontaneous defecation did not occur within three days. We disagree with the petitioner that scientific conclusions can be drawn from these studies because the use of enema treatments during the fecal collection period does not allow for adequate collection of fecal samples for the measuring of spontaneous defecation without the use of enemas. Therefore, the independent effect of IMO consumption on laxation could not be evaluated." See *supra* note 1, at 3.

[8] Chen HL, Lu YH, Lin JJ et al. Effects of isomalto-oligosaccharides on bowel functions and indicators of nutritional status in constipated elderly men. *Journal of American College of Nutrition* 2001;20:44-49; Yen CH, Tseng YH, Kuo YW et al. Long-term supplementation of isomalto-oligosaccharides improved colonic microflora profile, bowel function, and blood cholesterol levels in constipated elderly people--a placebo-controlled, diet-controlled trial. *Nutrition* 2011;27:445-450; Qing G, Yi Y, Guohong J et al. Study on the regulative effect of isomaltooligosaccharides on human intestinal flora. *Journal of Hygiene Research* 2003;32:54-55.

[9] BioNeutra Inc, 2012; Bouhnik et al., 2004; Kaneko et al., 1993; Yen et al., 2011; Chen et al., 2001.

these studies[10] were included in your original petition, and the fifth study[11] (which was not included in your original petition) previously had been identified and evaluated by FDA (original denial letter at page 3). Thus, your petition contains no new data regarding the effects of IMO on laxation that had not previously been considered and evaluated by FDA.[12] In our previous evaluation of the five relevant studies identified in your petition, we determined that the strength of the scientific evidence did not support a finding of a beneficial effect of IMO consumption on laxation (original denial letter at page 5).

Your petition includes a "Summary of Findings" (Petition at page 10), in which the studies by Chen et al. (2001) and Yen et al. (2011) are addressed. These studies were included with your original petition and were previously evaluated by FDA. Your petition also refers to the letters submitted as part of the Top Health Ingredients citizen petition (Docket number FDA-2019-P-1640) regarding the use of laxative/enema treatments in the studies by Chen et al. (2001) and Yen et al. (2011) (Petition at page 8 and 9). Both letters concluded that the use of laxative/enema treatments in the studies reported by Yen et al. (2011) and Chen et al. (2001) had no bearing on the study results because the number of laxative/enema treatments used were not statistically different between the control and experimental phases of the study. The studies by Yen et al. (2011) and Chen et al. (2001) were non-randomized studies that were conducted in nursing home residents with chronic constipation, and subjects were permitted to use laxative and/or enema treatments during the intervention. In Yen et al. (2011), the authors noted that "enema usage was not tightly controlled in this study and they could be administered on request of subjects who had relied on them for a long period of time." As noted above, we stated in our original denial letter that scientific conclusions could not be drawn from the studies by Yen et al. (2011) and Chen et al. (2001) because the use of enema treatments during the fecal collection period does not allow for adequate collection of fecal samples for the measuring of spontaneous defecation without the use of enemas; therefore, the independent effect of IMO on laxation could not be evaluated (original denial letter at page 3).

In our final guidance, we discuss the importance of having a sufficient amount of time for collecting stool samples.[13] There is considerable variability in colonic function (e.g., transit time), both within and between individuals.[14] For most healthy subjects (e.g., individuals without constipation), five days allows for passage of most material for the measuring of spontaneous defecation (i.e., without the use of enemas); however, individuals with constipation may have prolonged transit.[15] In the studies by Chen et al. (2001) and Yen et al. (2011), the use

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[10] BioNeutra Inc, 2012; Kaneko et al., 1993; Yen et al., 2011; Chen et al., 2001.

[11] Bouhnik et al., 2004.

[12] We agree that scientific conclusions could not be drawn from Lee et al. (2003) or Lin et al. (2005) (Petition at page 6) because the study lacked an appropriate control group and statistics were not conducted between treatment and control groups, and the study did not evaluate valid measures of laxation, respectively.

[13] U.S. Food and Drug Administration, 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) (February 2018), available at https://www.fda.gov/media/101183/download.

[14] Wyman JB, Heaton KW, Manning AP et al. Variability of colonic function in healthy subjects. *Gut* 1978;19:146-150.

[15] Camilleri M, Thompson WG, Fleshman JW et al. Clinical management of intractable constipation. *Annals of Internal Medicine* 1994;121:520-528; Evans RC, Kamm MA, Hinton JM et al. The normal range and simple

of laxative and/or enema treatments throughout the fecal collection period does not allow for an adequate duration of collection, without the use of laxative/enema treatments, for the measuring of spontaneous defecation. Without an adequate collection period, excluding the use of laxative/enema treatments, the independent effect of IMO cannot be evaluated due to the effect of laxative/enema treatments on laxation.[16]

In addition to the inadequate collection time without the use of laxative/enema treatments, statistically comparing the number of laxative/enema treatments between study phases, particularly in these small (n = 7 and n = 13), unblinded, and non-randomized[17] studies that were not well controlled (e.g., laxative/enema treatments were administered if spontaneous defecation did not occur in three days and/or as requested by the subjects, and different types of laxative/enema treatments were permitted), would not necessarily negate a potential confounding effect of these treatments on measures of laxation. Furthermore, the number of laxative/enema treatments used throughout the study periods was reported, but the use of these treatments during each fecal collection period was not reported. Therefore, it is unclear if the usage (e.g., frequency, type, timing, and/or dose) of laxative/enema treatments during the fecal collection periods at the end of each study phase was different between the treatment and control phases of the studies, which is important due to the acute nature of the effects of laxative/enema treatments. In addition, in the study by Yen et al. (2011), different types of laxative/enema treatments were permitted which could affect their impact on measures of laxation (e.g., frequency of bowel movements and fecal output), as different laxative/enema treatments vary in their onset and mechanisms of action (i.e., how they act and how long they take to act).[18] There are also different factors that can impact the effect of enemas (e.g., amount of applied fluid and substances included such as glycerol).[19] The design of these studies did not allow for the control of these different variables related to the use of laxative/enema treatments, which can affect their impact on laxation. For these reasons, we have not changed our view that conclusions cannot be drawn from studies if enemas and/or laxatives are used during the fecal collection period, as the independent effect of IMO consumption on laxation cannot be evaluated in such studies (original denial letter at page 3).

In our final guidance, we also discuss studies conducted in subjects who have a disease, condition, undergo a surgical procedure, or receive a treatment that could influence the physiological effect being studied. The subjects in Chen et al. (2001) and Yen et al. (2011) were elderly nursing home residents, with chronic constipation and long-term use of laxative/enema

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diagram for recording whole gut transit time. *International Journal of Colorectal Disease* 1992;7:15-17; Lembo A & Camilleri M. Chronic constipation. *The New England Journal of Medicine* 2003;349:1360-8.

[16] Dinning PG, Hunt L, Lubowski DZ et al. The impact of laxative use upon symptoms in patients with proven slow transit constipation. *BioMed Central Gastroenterology* 2011;11:1-7.

[17] Blinding and randomization reduce the likelihood of potential bias and minimize the effects of other variables or confounders on the results. Confounders are factors that are associated with both the physiological benefit in question and the intervention, and if not controlled for, prevent an investigator from being able to conclude that an outcome was caused by an intervention. U.S. Food and Drug Administration, *supra* note 13.

[18] Portalatin M, Winstead N. Medical management of constipation. *Clinics in Colon and Rectal Surgery* 2012;25: 12–19.

[19] Klaschik E, Nauck F, Ostgathe C. Constipation – modern laxative therapy. *Supportive Care in Cancer* 2003;11:679-685.

treatments,[20] who were permitted to receive laxative/enema treatments throughout the studies. We cannot draw scientific conclusions from such studies unless evidence is available that allows for extrapolation to subjects who have not received a treatment that could influence the endpoint being measured. Due to the lack of evidence demonstrating that IMO consumption has a beneficial physiological effect on laxation in subjects who are not using laxative/enema treatments, extrapolation of the results from Chen et al. (2001) and Yen et al. (2011) is not scientifically appropriate.

Blood Cholesterol

Your petition identifies five studies that evaluated the effect of IMO consumption on blood cholesterol[21] (Petition at page 11). In discussing two of these studies (BioNeutra Inc. Report, 2012 and Chen et al., 2001), you state that no statistically significant differences were found in total- and LDL-cholesterol between subjects in the IMO treatment groups versus those in the control groups in either study (Petition at page 11). FDA agrees that neither of these studies demonstrated a beneficial physiological effect of IMO consumption on blood cholesterol. With regards to the study by Wang et al. (2001), your petition concludes that subjects who consumed IMO had a significant reduction in total- and LDL-cholesterol compared to subjects in the control group (Petition at page 12). However, we disagree with this assessment. With regard to total cholesterol, we are unable to draw conclusions about the effects of IMO in the study by Wang et al. (2001) because statistical comparisons of the baseline values between groups were not reported;[22] therefore, it is not clear whether baseline values between the treatment and control groups in this study were statistically significantly different from each other. With regard to LDL-cholesterol, after four weeks there was no statistically significant difference in LDL-cholesterol between the IMO consumption group and the control group ($P > 0.05$), as reported in Wang et al. (2001). On page 12 of your petition, you reference the statistical analysis that was submitted in the Top Health Ingredients citizen petition (Docket number FDA-2019-P-1640). However, the Top Health Ingredients petition lacks sufficient details describing the analysis, so we are unable to determine whether an appropriate analysis was performed. Therefore, we are unable to draw conclusions from the analysis and unable to draw scientific conclusions about the effects of IMO consumption on total cholesterol in the study by Wang et al. (2001).

In discussing the study by Yen et al. (2011),[23] your description of the results for total- and LDL-cholesterol is consistent with FDA's discussion in the denial letter dated June 13, 2018, in

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[20] This population may have numerous lifestyle characteristics that differ from the general U.S. population (e.g., diet, exercise, medication use, and long-term use of laxative/enema treatments) and can impact laxation. As you noted in your petition (Petition at page 16), this population may have impaired mobility/ability to exercise, and poor chewing ability affecting dietary intake of certain foods, which can both impact laxation.

[21] BioNeutra Inc, 2012; Chen H et al., 2001; Wang HF, Lim PS, Kao MD et al. Use of isomalto-oligosaccharide in the treatment of lipid profiles and constipation in hemodialysis patients. *Journal of Renal Nutrition* 2001; 11:73-79; Yen et al., 2011; and Lin et al., 2005.

[22] When comparing the mean baseline total and LDL-cholesterol between the treatment and control groups, the values for LDL-cholesterol, but not total cholesterol, were numerically similar (131.5 ± 48.5 and 131.0 ± 39.9 mg/dL, respectively). Therefore, conclusions could be drawn for the effects of IMO on LDL-cholesterol, but not for total cholesterol.

[23] See *supra* note 8.

response to the citizen petition submitted by Top Health Ingredients.[24] In that letter, we concluded that the study by Yen et al. (2011) showed mixed results, with a beneficial effect of IMO vs. placebo on total- and LDL-cholesterol during one phase of the study, but no statistically significant effect on total- and LDL-cholesterol in another phase of the study.

You also provided a translation of the study by Lin et al. (2005).[25] This study was a randomized, double-blind, parallel study in hyperlipidemic college students (mean age = 17 years). Participants consumed chiffon cake with either IMO (n = 22; 10 g of IMO; baseline total- and LDL-cholesterol = 220.7 ± 24.2 and 139.9 ± 33.0 mg/dL, respectively) or sucrose (control, n = 20; 0 g of IMO; baseline total- and LDL-cholesterol = 215.0 ± 12.1 and 139.4 ± 11.9 mg/dL, respectively). After six weeks, total-cholesterol (201.7 ± 21.1 vs. 217.8 ± 15.6 mg/dL) and LDL-cholesterol (121.9 ± 27.1 vs 142.2 ± 15.7 mg/dL) were statistically significantly lower in the IMO group compared to the control group ($P < 0.05$ for both).

II. Strength of the Scientific Evidence

We evaluated the strength of the scientific evidence by considering various factors, such as the number of studies and sample sizes of each study, dose response data if available, the types of foods tested, the relevance of the body of scientific evidence to the U.S. population or target subgroup, and the overall consistency of the total body of evidence. Based on this evidence, we evaluated whether the findings presented in the relevant clinical studies demonstrated that there is a beneficial physiological effect of IMO consumption to human health and, therefore, whether to propose to include IMO as a dietary fiber in the dietary fiber definition.

Laxation

As mentioned above, in evaluating your original petition, we previously concluded that the strength of the scientific evidence did not support a finding of a beneficial effect of IMO consumption on laxation (original denial letter at page 5).[26] We also noted above that your petition (i.e., your second petition that we are evaluating in this letter) contained no new data regarding the effects of IMO on laxation that had not previously been considered and evaluated by FDA. Our conclusion—that we are unable to draw scientific conclusions from the studies by Chen et al. (2001) and Yen et al. (2011) because the independent effect of IMO cannot be evaluated, for the reasons discussed above—has not changed. Therefore, the overall strength of the scientific evidence in the petition remains the same as in the original petition with respect to laxation, and our conclusion that the strength of the scientific evidence does not support a finding of a beneficial effect of IMO consumption on laxation has not changed.

Blood Cholesterol

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[24] U.S. Food and Drug Administration, Denial Letter to Top Health Ingredients Inc. (June 13, 2018), available at https://www.regulations.gov/document?D=FDA-2016-P-1180-0046.

[25] See *supra* note 2.

[26] See *supra* note 1.

With regard to the effect of IMO on blood cholesterol, there were five publicly available studies (BioNeutra Inc. Report, 2012; Chen et al., 2001; Lin et al., 2005; Wang et al., 2001; Yen et al., 2011) from which scientific conclusions could be drawn. In the one study in healthy individuals, conducted in Canada, (BioNeutra Inc. Report, 2012) (n = 19; mean age = 42 years; mean baseline cholesterol = 4.81-4.91 mmol/L[27]), there was no statistically significant effect of IMO consumption (36 or 54 g/day) on total- or LDL-cholesterol. Three studies (n = 7 to 20) were conducted in Taiwan in non-healthy individuals, e.g., hyperlipidemic individuals, elderly nursing home residents with chronic constipation, and hemodialysis patients with uremic dyslipidemia. One of these studies (Lin et al., 2005; mean age = 17 years) reported a statistically significant lowering of total- and LDL-cholesterol with IMO consumption (10 g/day). Two of these studies (Chen et al., 2001; Wang et al., 2001; mean age = 75 and 64 years, respectively) demonstrated that there was no statistically significant effect of IMO consumption (24 or 30 g/day) on total- or LDL-cholesterol, and one study (Yen et al., 2011; mean age = 83 years) had mixed results (22 g/day; one comparison showed a statistically significant lowering of total- and LDL-cholesterol with IMO and one comparison showed no statistically significant effect on total- and LDL-cholesterol).[28] In summary, three of the five studies (BioNeutra Inc. Report, 2012; Chen et al., 2001; Wang at al., 2001) showed no statistically significant effect of IMO on total- and/or LDL-cholesterol, including the study in healthy individuals. One study in hyperlipidemic individuals (Lin et al., 2005) showed a beneficial effect of IMO on total- and LDL-cholesterol, and one study in elderly nursing home residents with chronic constipation (Yen et al., 2011) showed mixed results, with a beneficial effect on total- and LDL-cholesterol compared with one control period, but no statistically significant effect compared with the other control period. Further, the one study conducted in individuals that were the most representative of the general U.S. population (BioNeutra Inc. Report, 2012)[29] found no statistically significant effect of IMO on total- and LDL-cholesterol. We considered whether there was a plausible explanation for the inconsistencies between studies that found a statistically significant effect and studies that found no statistically significant effect. We were unable to find a plausible explanation for the inconsistency in the findings or to consider those studies that did not find a statistically significant effect as being less relevant to or less important in determining the strength of the total body of evidence. Consequently, we have determined that the strength of the scientific evidence does not support a finding of a beneficial effect of IMO consumption on blood cholesterol.

III. Conclusion

Based on our consideration of the scientific evidence and other information submitted with the petition, and other pertinent scientific evidence and information, we conclude that the strength of the evidence does not show that the consumption of IMO 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 IMO as a dietary

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[27] To convert cholesterol values in mmol/L to mg/dl, multiply by 38.7.

[28] Baseline cholesterol values were not reported in Chen et al., 2001 and Yen et al., 2011. In Wang et al., 2001, mean baseline total cholesterol was 210 mg/dL and 205 mg/dL in the IMO and control groups, respectively.

[29] This study was conducted in Canada in males and females who were 18-65 years of age and generally healthy. Other studies cited in the petition were conducted in Taiwan in subjects who were hemodialysis patients (Wang et al., 2001), constipated elderly men (Chen et al., 2001), constipated elderly men and women (Yen et al., 2011), and hyperlipidemic college students (Lin et al., 2005).

fiber based on this scientific evidence. Therefore, in accordance with 21 CFR 10.30(e)(3), we are denying your petition.

We recognize, of course, that new scientific information may become available that demonstrates a beneficial physiological effect associated with the consumption of IMO. Although we are denying your petition, we would consider a new petition from you concerning the consumption of IMO that is based on new scientific information.

Sincerely,

Claudine Kavanaugh, Ph.D., M.P.H., R.D.
Director
Office of Nutrition
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