



Masayasu Takada, Ph.D.
Nihon Shokuhin Kako Co., Ltd.
30 Tajima Fuji
Shizuoka, JAPAN
417-8530

Re: GRAS Notice No. GRN 000711

Dear Dr. Takada:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 000711. We received Nihon Shokuhin Kako Co., Ltd (NSK)'s notice on June 13, 2017, and filed it on July 5, 2017. NSK submitted an amendment to the notice on September 20, 2017. The amendment contained additional information about the toxicological data and the intended use of the substance.

The subject of the notice is resistant glucan for use as an ingredient at levels from 1.9% to 22.3% in baked goods and baking mixes, beverages and beverage bases, breakfast cereals, chewing gum, fats and oils, frozen dairy desserts and mixes, gelatins, puddings and fillings, hard candy, jams and jellies, milk products, nuts and nut products, snack foods, soft candy, soups and soup mixes, and sugar substitutes;¹ and, for use as a formulation aid in dietary supplements. The notice informs us of NSK's view that this use of resistant glucan is GRAS through scientific procedures.

Our use of the term "resistant glucan" in this letter is not our recommendation of that term as an appropriate common or usual name for declaring the substance in accordance with FDA's labeling requirements. Under 21 CFR 101.4, each ingredient must be declared by its common or usual name. In addition, 21 CFR 102.5 outlines general principles to use when establishing common or usual names for nonstandardized foods. Issues associated with labeling and the common or usual name of a food ingredient are under the purview of the Office of Nutrition and Food Labeling (ONFL) in the Center for Food Safety and Applied Nutrition. The Office of Food Additive Safety (OFAS) did not consult with ONFL regarding the appropriate common or usual name for "resistant glucan."

¹ NSK states that resistant glucan is not intended for use in infant formula, or any meat or poultry products that are under the jurisdiction of the United States Department of Agriculture.

NSK describes the identity and composition of resistant glucan. NSK states that the substance is a type of glucan that is resistant to hydrolysis by digestive enzymes. It consists of a mixture of glucose polymers containing various glycosidic linkages (α - and β -1,2-, 1,3-, 1,4- and 1,6- linkages). Resistant glucan has an average molecular weight of 2,100.

NSK describes the manufacture of resistant glucan. Resistant glucan is manufactured from glucose syrup by way of a polymerization reaction under high heat in the presence of an activated carbon catalyst. At the completion of the reaction, the solution is filtered to remove the activated carbon, decolorized using fresh activated carbon, and deionized with the use of a mixed bed ion-exchange resin. The solution is then concentrated by evaporation to produce the liquid concentrate formulation of resistant glucan, which is subsequently spray-dried to produce the powder formulation.

NSK states that the manufacturing process for resistant glucan is consistent with current good manufacturing practice and that all raw materials and processing aids used in the manufacture of resistant glucan are certified to be food grade and are suitable for use in the U.S. for such purposes.

NSK provides specifications for the two formulations. The liquid concentrate contains a maximum of 28% water, while the powder contains a maximum of 7% water. On a dry weight basis, the rest of the specifications for both formulations are identical. These include specifications for total glucan ($\geq 90\%$), total dietary fiber ($\geq 75\%$),² free glucose ($\leq 6\%$), levoglucosan ($\leq 4\%$), 5-hydroxymethylfurfural ($\leq 0.1\%$), which is a byproduct of the polymerization process, and lead (≤ 0.5 mg/kg). NSK also provides limits on microbial contaminants, which include a maximum 300 CFU/g using the standard plate count method; 100 CFU/g each of yeast and mold and negative for coliforms. NSK provides the results of three non-consecutive batch analyses to demonstrate compliance with these specifications.

NSK estimates the dietary exposure to resistant glucan. NSK intends to use resistant glucan in baked goods and baking mixes, beverages and beverage bases, breakfast cereals, chewing gum, fats and oils, frozen dairy desserts and mixes, gelatins, puddings and fillings, hard candy, jams and jellies, milk products, nuts and nut products, snack foods, soft candy, soups and soup mixes, and sugar substitutes at levels from 1.9% to 22.3% on a dry weight basis. Using the data from NHANES 2011-2012, NSK estimates a conservative dietary exposure to resistant glucan for the U.S. population will be 21.1 g/d at the mean and 36.7 g/d at the 90th percentile. On a body weight basis, these estimates are 0.35 g/kg bw/d at the mean and 0.66 g/kg bw/d at the 90th percentile. NSK states that dietary exposure to resistant glucan when used as a formulation aid in dietary supplements will be minimal.

² AOAC official method 2001.03 Total Dietary Fiber in Foods Containing Resistant Maltodextrin. FDA understands that NSK's use of the term "dietary fiber" is for the purpose of the specifications for resistant glucan.

NSK discusses published and unpublished studies to support the safety of resistant glucan. The following studies utilized the resistant glucan that is the subject of the notice. NSK discusses a published 90-day rat feeding study in which no significant effects were observed at 3.3 g/kg bw/d and 3.9 g/kg bw/d in males and females, respectively. The published acute study in rats reported the LD₅₀ value to be greater than 10 g/kg bw. The results of the published Ames assay showed that resistant glucan is not mutagenic. NSK discusses a published human study that reports no effects at 0.3 or 0.5 g/kg bw/d. Mild gastro-intestinal gurgling and flatulence were reported at 0.7 and 0.9 g/kg bw/d. These findings, as noted by NSK, using the published literature, are comparable to other poorly digested carbohydrates.

NSK includes the report of a panel of individuals (NSK's GRAS panel). Based on its review, NSK's GRAS panel concluded resistant glucan is safe under the conditions of its intended use.

Based on the totality of information discussed above, NSK concludes that resistant glucan is GRAS for its intended use.

Standards of Identity

In the notice, NSK states its intention to use resistant glucan in several food categories, including foods for which standards of identity exist, located in Title 21 of the CFR. We note that an ingredient that is lawfully added to food products may be used in a standardized food only if it is permitted by the applicable standard of identity.

Potential Labeling Issues

Under section 403(a) of the Federal Food, Drug, and Cosmetic (FD&C) Act, a food is misbranded if its labeling is false or misleading in any way. Section 403(r) of the FD&C Act lays out the statutory framework for labeling claims characterizing a nutrient level in a food or the relationship of a nutrient to a disease or health-related condition (also referred to as nutrient content claims and health claims). The notice raises a potential issue under these labeling provisions. In the notice, NSK cites studies that describe resistant glucan as having certain health benefits and considers that apart from its technical effect when added to conventional food, resistant glucan can be a source of dietary fiber.³ If products containing resistant glucan bear any nutrient content or health claims on the label or in labeling, such claims are subject to the applicable requirements and are under the purview of ONFL. OFAS did not evaluate any information in terms of labeling claims. Questions related to food labeling should be directed to ONFL.

³ The definition of "dietary fiber" in 21 CFR 101.9(c)(6)(i) was added by FDA's final rule revising the nutrition and supplement facts labels (81 FR 33742, May 27, 2016). This final rule, among other things, defines dietary fiber as non-digestible soluble and insoluble carbohydrates (with three or more monomeric units), and lignin that are intrinsic and intact in plants; isolated or synthetic non-digestible carbohydrates (with three or more monomeric units) determined by FDA to have physiological effects that are beneficial to human health.

Section 301(II) of the FD&C Act

Section 301(II) of the FD&C Act prohibits the introduction or delivery for introduction into interstate commerce of any food that contains a drug approved under section 505 of the FD&C Act, a biological product licensed under section 351 of the Public Health Service Act, or a drug or a biological product for which substantial clinical investigations have been instituted and their existence made public, unless one of the exemptions in section 301(II)(1)-(4) applies. In our evaluation of NSK's notice concluding that resistant glucan is GRAS under its intended conditions of use, we did not consider whether section 301(II) or any of its exemptions apply to foods containing resistant glucan. Accordingly, our response should not be construed to be a statement that foods containing resistant glucan if introduced or delivered for introduction into interstate commerce, would not violate section 301(II).

Conclusions

Based on the information that NSK provided, as well as other information available to FDA, we have no questions at this time regarding NSK's conclusion that resistant glucan is GRAS under its intended conditions of use. This letter is not an affirmation that resistant glucan is GRAS under 21 CFR 170.35. Unless noted above, our review did not address other provisions of the FD&C Act. Food ingredient manufacturers and food producers are responsible for ensuring that marketed products are safe and compliant with all applicable legal and regulatory requirements.

In accordance with 21 CFR 170.275(b)(2), the text of this letter responding to GRN 000711 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,
Michael A. Adams

-S

Dennis M. Keefe, Ph.D.
Director
Office of Food Additive Safety
Center for Food Safety
and Applied Nutrition

Digitally signed by Michael A. Adams -S
DN: c=US, o=U.S. Government, ou=HHS, ou=FDA,
ou=People, 0.9.2342.19200300.100.1.1=1300042713,
cn=Michael A. Adams -S
Date: 2017.12.26 15:19:10 -05'00'