



Sherwin Chen
Super Beta Glucan
5 Holland, Unit 109
Irvine, CA 92618

Re: GRAS Notice No. GRN 000995

Dear Mr. Chen:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 000995. We received Super Beta Glucan's (SBG) notice on August 18, 2020 and filed it on July 21, 2021. SBG submitted amendments to the notice on November 16, 2021, December 23, 2021, and April 14, 2022, providing information about the production organism, the composition of the ingredient, clarifying information regarding the manufacturing process, specifications, the dietary exposure estimate, and an updated literature search.

The subject of the notice is β -glucans from *Antrodia cinnamomea* strain ATCC 200183 (*A. cinnamomea* ATCC 200183) for use as an ingredient in various foods at the maximum use levels specified in Table 1.^{1,2} The notice informs us of SBG's view that this use of β -glucans from *A. cinnamomea* ATCC 200183 is GRAS through scientific procedures.

Table 1. Food categories and corresponding maximum use levels of β -glucans from *A. cinnamomea* ATCC 200183

Food category	Foods	Maximum use level (%)
Baked goods and baking mixes	Cookies	0.5 to 0.375
Beverages and beverage bases	Non-milk meal replacement beverages	0.0625
Cereals and cereal products	Nutritional bars (breakfast, granola, and protein)	0.375
Dairy product analogs	Soy milk	0.0625

¹ SBG states that β -glucans are not intended for use in infant formula or foods formulated for infants, or in any products under the jurisdiction of the United States Department of Agriculture (USDA).

² In the amendment dated November 16, 2021, SBG provides the intended food categories and corresponding use levels expressed on a percent basis calculated using the maximum use level and serving amounts for the specific food categories according to 21 CFR 101.12.

Food category	Foods	Maximum use level (%)
Milk and milk products	Meal replacement beverages	0.0625
	Beverages containing live microorganisms	0.0625
	Yogurt	0.0882
	Yogurt beverages	0.0625
Plant protein products	Soy protein bars	0.375
Processed fruits and fruit juices	Fruit beverages (drinks, juices, and smoothies)	0.0625
Soft candy	Chocolate confections	0.375

SBG provides information on the identity and composition of β -glucans from *A. cinnamomea* ATCC 200183 and describes it as a light beige powder. SBG states that the typical composition of β -glucans from *A. cinnamomea* ATCC 200183 consists of $\geq 65\%$ β -D-Glucan, (1-3), (1-4)- β -D-Glucan, and/or β -glucosylglucan. SBG states that the molecular weight of β -glucans from *A. cinnamomea* ATCC 200183 ranges from 9.6 kDa to 298 kDa.

SBG describes the method of manufacture of β -glucans from *A. cinnamomea* ATCC 200183, a non-pathogenic and non-toxigenic fungal strain that lives in the inner cavity of the tree, *Cinnamomum kanehirai*, originally isolated in Hsinchu, Taiwan. SBG states that *A. cinnamomea* ATCC 200183 is deposited in the culture collection of the American Type Culture Collection (ATCC) in Manassas, Virginia. SBG states that β -glucans from *A. cinnamomea* ATCC 200183 is produced by inoculating *A. cinnamomea* ATCC 200183 mycelium into a sterile carbohydrate medium, followed by incubation for 6-8 weeks at 24-27 °C. The resulting culture is then extracted using a high-speed homogenizer and ultrasonic vibration, filtered to remove residual carbohydrates (<3 kDa), and concentrated. The concentrate is then pooled, dried, and ground into a powder. SBG states that β -glucans from *A. cinnamomea* ATCC 200183 is manufactured under current good manufacturing practices using food-grade starting materials, processing aids and food-contact materials, which are used in accordance with U.S. regulations. SBG states that no components of the culture medium are allergens or are derived from allergenic sources.

SBG provides specifications for β -glucans from *A. cinnamomea* ATCC 200183 that include total carbohydrates (>90%), β -glucans (minimum 65%), fat (<1.0%), saturated fat (<1.0%), protein (<1.0%), moisture (<5.0%), ash (<3.0%); limits for heavy metals, including lead (<0.1 mg/kg); and limits for microorganisms, including *Salmonella* serovars (<limit of detection of 10 colony forming units (CFU)/g). SBG provides validated analytical methods used to analyze the specification parameters and results from 5 non-consecutive batches to demonstrate that β -glucans from *A. cinnamomea* ATCC 200183 meet set specifications. SBG notes that β -glucans from *A. cinnamomea* ATCC 200183 has a shelf-life of 3 years when stored in ambient, dry conditions.

SBG provides the estimated dietary exposure to β -glucans from *A. cinnamomea* ATCC

200183 based on the intended uses. SBG states that the intended use and use levels of β -glucans from *A. cinnamomea* ATCC 200183 are the same as in GRN 000413.^{3,4} SBG also states that the notified uses would be substitutional, and that it will not increase the current dietary exposure to β -glucan. SBG estimates the eaters-only mean and 90th percentile to β -glucans from *A. cinnamomea* ATCC 200183 to be 291.3 mg/person (p)/d (6.3 mg/kg body weight (bw)/d) and 583.4 mg/p/d (14.5 mg/kg bw/d), respectively.

SBG discusses the metabolism of β -glucans and notes that humans are unable to digest carbohydrate polymers with β -glycosidic linkages and, therefore, absorption by the intestinal epithelium and significant systemic exposure to particulate mushroom β -glucans is unlikely. SBG discusses a published pivotal subchronic study on β -glucans from *A. cinnamomea* ATCC 200183 conducted in CD (SD) IGS rats. SBG states that the findings from the study, performed in accordance with Organization for Economic Cooperation and Development guidelines, suggest that oral administration of their product at levels up to 2000 mg/kg bw/d the highest dose tested, for 90 days did not cause adverse effects in male or female rats. SBG further states this study supports the safety of estimated dietary exposure at the 90th percentile of 14.5 mg/kg bw/d from the proposed uses of β -glucans from *A. cinnamomea* ATCC 200183. SBG also discusses the results of their published genotoxicity studies (Ames assay, *in vitro* chromosomal aberration assay and *in vivo* micronucleus assay). SBG states that β -glucans from *A. cinnamomea* ATCC 200183 was neither genotoxic nor mutagenic in any of these assays. SBG references *in vivo* and *in vitro* studies conducted on *A. cinnamomea* ATCC 200183 and states that the results of these studies support the safety of their source material. SBG discusses human studies on β -glucans as corroborative support for their GRAS conclusion and states that the results from these studies demonstrate that β -glucans are safe and well-tolerated. SBG addresses the potential for allergenicity of β -glucans from *A. cinnamomea* ATCC 200183 by stating that allergy to *A. cinnamomea* has not been reported. SBG also notes that the residual amount of protein in β -glucans from *A. cinnamomea* ATCC 200183 is very low (<1 %). Finally, SBG conducted a comprehensive review of the literature through October 2021 and found no publications that would raise questions regarding the safety of β -glucans from *A. cinnamomea* ATCC 200183 for its intended use.

SBG includes the report of a panel of individuals (SBG's GRAS panel). Based on its review, SBG's GRAS panel concluded that β -glucan from the *A. cinnamomea* ATCC 200183 is safe under the conditions of its intended use.

³ The subject of GRN 000413 is β -glucans derived from *Ganoderma lucidum* strain ATCC 32472. FDA evaluated this notice and responded in a letter dated August 10, 2012, stating that we had no questions at the time regarding the notifier's GRAS conclusion.

⁴ In GRN 000413 the eaters-only mean and 90th percentile dietary exposures were estimated to be 291.3 mg/p/d (6.3 mg/kg bw/d) and 583.4 mg/p/d (14.5 mg/kg bw/d), respectively. GRN 000413 used the dietary exposure presented in GRN 000309, which was estimated using data from the USDA 1994-1996 Continuing Survey of Food Intakes by Individuals (CSFII 1994-1996). The subject of GRN 000309 is β -glucan derived from *Aureobasidium pullulans* strain KCCM 10307. FDA evaluated this notice and responded in a letter dated June 14, 2010, stating that we had no questions at that time regarding the notifier's GRAS conclusion.

Based on the totality of data and information included in their notice, SBG concludes that β -glucans from *A. cinnamomea* ATCC 200183 is GRAS for its intended use.

Standards of Identity

In the notice, SBG states its intention to use β -glucans from *A. cinnamomea* ATCC 200183 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 & Cosmetic Act (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). If products containing β -glucans from *A. cinnamomea* ATCC 200183 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 the Office of Nutrition and Food Labeling (ONFL) in the Center for Food Safety and Applied Nutrition. The Office of Food Additive Safety did not consult with ONFL on this issue or evaluate any information in terms of labeling claims. Questions related to food labeling should be directed to ONFL.

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 SBG's notice concluding that β -glucans from *A. cinnamomea* ATCC 200183 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 β -glucans from *A. cinnamomea* ATCC 200183. Accordingly, our response should not be construed to be a statement that foods containing β -glucans from *A. cinnamomea* ATCC 200183, if introduced or delivered for introduction into interstate commerce, would not violate section 301(II).

Conclusions

Based on the information that SBG provided, as well as other information available to FDA, we have no questions at this time regarding SBG's conclusion that β -glucans from *A. cinnamomea* ATCC 200183 is GRAS under its intended conditions of use. This letter is not an affirmation that β -glucans from *A. cinnamomea* ATCC 200183 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 000995 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

Susan J.
Carlson -S

Digitally signed by Susan J.
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Director
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