U.S. FOOD & DRUG ADMINISTRATION
Human Foods Program

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Re: GRAS Notice No. GRN 001241

Dear Dr. Lester:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 001241. We received the notice you submitted on behalf of Verley Food (Verley; previously known as Bon Vivant SAS) on December 20, 2024, and filed it on April 15, 2025. Verley submitted amendments to the notice on June 23, 2025, July 3, 2025, and July 29, 2025, providing clarifications on the microorganism, manufacturing method, and specifications, as well as the change in the company name of the notifier.

The subject of the notice is β-lactoglobulin produced by *Aspergillus oryzae* expressing a gene encoding bovine β-lactoglobulin (β-lactoglobulin) for use as a source of protein at levels up to 35% in various foods as shown in Table 1 (excluding uses in infant formula and products under the jurisdiction of the United States Department of Agriculture). The notice informs us of Verley's view that these uses of β-lactoglobulin are GRAS through scientific procedures.

Table 1. Intended food uses and use levels for β-lactoglobulin

Food Category	Food Uses	Maximum Use Level (%)
Nutritional products	Meal replacements and supplements	15
	Powdered nutritional beverages	25
	Electrolyte-type sports drinks	6
	Performance nutritional beverages, high protein	25
	Nutritional bars	35
Dairy and dairy-based products	Milk, powdered milk, flavored milk, milk-based drinks and drink mixes, milk substitutes	6
	Cream, half and half, cream cheese, cheese spread, whipped cream	15
	Spreads, dips	10
	Cream substitutes	15
	Yogurt and fermented milk products	8

Food Category	Food Uses	Maximum Use Level (%)
	Frozen dairy desserts and mixes	10
	Cheese used as ingredient	15
	Semi-hard cheese	25
	Mousses and desserts	5
Sugar-based products	Confections (including chocolate)	10
	Coatings and fillings	10
Baked goods	Cookies, brownies	5
	Doughnuts, toaster pastries, muffins	10
	French toast, crepes, pancakes, bagels, scones, biscuits, croissants	10
	Bread, rolls, English muffins, pizza crust	10
	Crackers, popcorn, tortilla chips, potato chips, hard pretzels, snack mix	5
Dressings	Salad dressings	5
	Minor entrée sauces (e.g., Alfredo sauce)	6
Egg products	Egg substitutes	10

Our use of the term "β-lactoglobulin" 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 Nutrition Center of Excellence (NCE). The Office of Pre-Market Additive Safety (OPMAS) did not consult with ONFL regarding the appropriate common or usual name for "β-lactoglobulin."

Verley provides information about the identity and composition of β-lactoglobulin and describes it as a white to off-white or yellowish powder containing at least 80% protein, with β-lactoglobulin comprising more than 90% of the total protein. β-lactoglobulin is a whey protein present in bovine milk at a concentration of 2-3 g/L, representing 7-9% of total milk protein. Verley states that β-lactoglobulin has a molecular weight of 18.3 kDa and that the amino acid sequence is identical to native bovine β-lactoglobulin variant B, except for two amino acids, which are substituted to the amino acid that occurs in the same position in one of the other β-lactoglobulin variants.

Verley states that the *A. oryzae* "TFB-CLEO75TA" production organism is non-pathogenic and non-toxigenic. Verley states that the production organism was constructed through genetic modification of host strain *A. oryzae* "TFB-A00010" through chromosomal integration of an expression cassette carrying a gene encoding the modified β-lactoglobulin. Verley states that the inserted DNA is stably integrated into the genome of the production organism and is confirmed by DNA sequencing.

Verley states that the β-lactoglobulin is manufactured by controlled fermentation of a pure culture of *A. oryzae* "TFB-CLEO75TA." β-lactoglobulin is secreted into the fermentation medium, separated from the biomass by filtration, and concentrated by a second filtration step. Verley states that β-lactoglobulin concentrate may be subjected to an optional heat-treatment step at 90°C to improve the heat stability and technological properties. The concentrate is then spray-dried and packaged. Verley states that none of the materials used during the manufacturing process are derived from major food allergens. Verley states that β-lactoglobulin is manufactured in accordance with current good manufacturing practices and that all raw materials and processing aids are food grade and approved for their respective uses in accordance with an applicable U.S. regulation, are GRAS for their intended use, or are the subject of an effective food contact notification.

Verley provides specifications for β-lactoglobulin that include protein content (≥ 80 % w/w), β-lactoglobulin as % of the total protein content (≥ 90 % w/w), moisture (≤ 7 % w/w), ash (≤ 6 % w/w), fat (≤ 2 % w/w), total carbohydrates (≤ 15 % w/w), pH (5.0 – 8.0), arsenic (≤ 0.1 mg/kg), cadmium (≤ 0.01 mg/kg), mercury (≤ 0.01 mg/kg), lead (≤ 0.1 mg/kg), and limits for microorganisms. Verley provides the results from the analyses of three non-consecutive batches to demonstrate that β-lactoglobulin can be manufactured to meet the specifications.

Verley states that the food uses and use levels for β-lactoglobulin are the same as the prior notified uses of β-lactoglobulin produced by microbial fermentation (GRN 001056 and GRN 001145).[1] Using food consumption data from the 2017-2020 National Health and Examination Survey (NHANES), Verley estimates the updated eaters-only dietary exposures β-lactoglobulin from the intended uses to be 29 g/person (p)/d at the mean and 55 g/p/d at the 90th percentile for the U.S. population aged 2 years and older. Verley states that the uses of β-lactoglobulin are substitutional for other added protein ingredients, and therefore, the cumulative dietary exposure to protein is not expected to increase.

Verley discusses publicly available data and information supporting the safety of β-lactoglobulin. Verley states that the β-lactoglobulin that is the subject of this notice is equivalent to various isoforms of β-lactoglobulin that are widely and safely consumed as a component of cow's milk. Verley summarizes the results of a comprehensive literature search through June 2025, to identify available safety information relevant to β-lactoglobulin. Verley does not identify any safety concerns or information that would contradict its GRAS conclusion. Verley states that the safety of β-lactoglobulin is further supported by the GRAS status of bovine milk derived protein substances and recombinant β-lactoglobulin produced by microbial fermentation that have been evaluated by FDA.[2]

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[1] The subjects of GRNs 001056 and 001145 are β-lactoglobulin produced by *Komagataella phaffii* and β-lactoglobulin produced by *A. oryzae*, respectively. We evaluated these notices and responded in letters dated February 15, 2023 and December 18, 2023, respectively, stating that we had no questions at that time regarding the notifiers' GRAS conclusions.

[2] The subjects of GRNs 000037, 000633, 000504, 000863, and 001056 are whey protein isolate and

Based on the weight-of-evidence, including results of *in silico* sequence alignment-based approaches, Verley concludes that β-lactoglobulin that is the subject of this notice does not pose an increased allergenic or toxigenic risk to consumers relative to β-lactoglobulin present in bovine milk. Verley states that bovine milk β-lactoglobulin is a known allergenic protein and states that the β-lactoglobulin preparation will likely elicit an allergic response in milk-allergic consumers. Therefore, adequate, and informative food allergen labeling will be applicable to all products containing β-lactoglobulin.

Based on the totality of the data and information, Verley concludes that β-lactoglobulin is GRAS for its intended use.

Standards of Identity

In the notice, Verley states its intention to use β-lactoglobulin 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). If products containing β-lactoglobulin 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 in the NCE. OPMAS 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.

Allergen Labeling

The FD&C Act requires that the label of a food that is or contains an ingredient that contains a "major food allergen" declare the allergen's presence (section 403(w)). The FD&C Act defines a "major food allergen" as one of nine foods or food groups (i.e., milk, eggs, fish, Crustacean shellfish, tree nuts, peanuts, wheat, soybeans, and sesame) or a food ingredient that contains protein derived from one of those foods. β-lactoglobulin labeling under the FD&C Act because it contains protein derived from milk.

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dairy product solids, concentrated milk protein with a ≥ 60:40 whey:casein ratio, milk protein concentrate and milk protein isolate, β-lactoglobulin produced by *Trichoderma reesei*, and β-lactoglobulin produced by *Komagataella phaffii*, respectively. We evaluated these notices and responded in letters dated April 21, 2000, September 21, 2016, November 21, 2014, March 25, 2020, and February 15, 2023, respectively, stating that we had no questions at that time regarding the notifier's GRAS conclusion.

Section 301(ll) of the FD&C Act

Section 301(ll) 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(ll)(1)-(4) applies. In our evaluation of Verley's notice concluding that β-lactoglobulin is GRAS under its intended conditions of use, we did not consider whether section 301(ll) or any of its exemptions apply to foods containing β-lactoglobulin. Accordingly, our response should not be construed to be a statement that foods containing β-lactoglobulin, if introduced or delivered for introduction into interstate commerce, would not violate section 301(ll).

Conclusions

Based on the information that Verley provided, as well as other information available to FDA, we have no questions at this time regarding Verley's conclusion that β-lactoglobulin is GRAS under its intended conditions of use. This letter is not an affirmation that β-lactoglobulin 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 001241 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

Susan J. Carlson -S

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