U.S. FOOD & DRUG ADMINISTRATION

Human Foods Program

Jo Anne Shatkin, Ph.D.
Vireo Advisors, LLC
111 Perkins Street
Apartment 216
Boston, MA 02130

Re: GRAS Notice No. GRN 001284

Dear Dr. Shatkin:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 001284. We received the notice that you submitted on behalf of All G Co Holdings Pty Limited (All G) on May 29, 2025, and filed it on September 17, 2025. All G submitted amendments to the notice on January 15, 2026, and March 9, 2026, that clarified the intended uses, specifications, dietary exposure, and aspects of the safety narrative.

The subject of the notice is recombinant bovine lactoferrin isolate produced by *Komagataella phaffii* "Ppas_337" expressing the gene encoding bovine lactoferrin (rbLf isolate) for use as an ingredient in foods at the maximum levels shown in Table 1. All G states that rbLf isolate is not intended for use in infant formula. The notice informs us of All G's view that these uses of rbLf isolate are GRAS through scientific procedures.

Table 1: Intended food categories and use levels for rbLf isolate

Food Categories	Food Uses	Maximum Use Levels[a]
Dairy and plant-based yogurt products	Dairy, plant-based, and frozen yogurts; yogurt-based dips, yogurt drinks	100 mg/100 g
Plant-based milk	Soy, oat, almond, coconut, flavored plant-based milks	135 mg/serving
Powdered milk	Dry milk (not reconstituted), powdered coffee creamer	400 mg/100 g
Fermented milk drinks	Buttermilk, kefir	495 mg/serving
Sports drinks	Sports drink powder, fluid replacement, low calorie sports drink	360 mg/serving
Nutritional bars	Granola, cereal, nutrition, protein, breakfast, meal replacement	375 mg/100 g
Nutritional beverages	Nutritional shake, nutritional drink powder mix, protein drink, meal replacement drink, fortified beverages	210 mg/serving
Non-alcoholic beverages	Smoothies, powdered drink mixes, flavored drinks, flavored water, energy drink, coconut water	120 mg/serving

[a] The Reference Amount Customarily Consumed is 240 mL for plant-based milk, fermented milk drinks, nutritional beverages, and non-alcoholic beverages and 360 mL for sports drinks.

All G provides information on the identity and composition of rbLf isolate, describing it as a light brown to light pink powder containing >90% protein (of which >95% is rbLf), ash, and moisture. The native bovine lactoferrin (bLf) is an iron-binding glycoprotein of 689 amino acids, has a molecular weight of approximately 80 kilodaltons, and is designated by CAS Registry Number 146897-68-9. All G states that rbLf is highly similar in structure and function to bLf.

All G describes the production organism used in the manufacturing process for rbLf isolate. The production organism, *K. phaffi* "Ppas_337," is constructed through genetic modification of the parent strain, *K. phaffi* "BG11", including introduction of expression cassettes to enable expression and secretion of rbLf. All G states that all genetic modifications are confirmed by whole genome sequencing and that the strain is non-pathogenic, non-toxigenic, and does not contain antibiotic resistance genes.

All G states that rbLf isolate is manufactured through precision fermentation of the production organism, *K. phaffi* "Ppas_337," under controlled conditions. After fermentation, the biomass is removed from the fermentation media via filtration. The expressed rbLf remains soluble in the fermentation media and is separated and purified from the media by chromatography. The eluate containing rbLf undergoes concentration and dialysis using ultrafiltration/diafiltration to remove salts and further purify the rbLf. The resulting rbLf solution is then microfiltered using sterile membrane filters to remove any contaminants or microorganisms before drying to obtain the final rbLf isolate. All G states that rbLf isolate is manufactured in accordance with current good manufacturing practices and that all raw materials and processing aids are food grade and are used in accordance with applicable U.S. regulations, are GRAS for their intended uses, or are the subject of an effective food contact notification. All G states that the raw materials used in the manufacturing process for rbLf isolate are not considered allergens.

All G provides specifications for rbLf isolate that include total protein (>90% protein, of which >95% is rbLf), moisture (<4.5%), ash (<3.5%), pH (5.2-7.2 for 2% solution), iron (<200 mg/kg), and limits for heavy metals, including lead (<0.1 mg/kg), cereulide (<0.1 µg/kg), and microorganisms, including *Escherichia coli* (<10 colony forming units/g), *Salmonella* serovars (absent in 25 g), *Listeria* spp. (absent in 25 g), and *Cronobacter* spp. (absent in 25 g). All G provides the results from three non-consecutive batch analyses to demonstrate that rbLf isolate can be manufactured to meet these specifications.

Using food consumption data from the the 2021-2023 National Health and Nutrition Examination Survey, All G estimates the eaters-only dietary exposure to rbLf from the intended uses to be 220 mg/person (p)/d (3.4 mg/kg body weight (bw)/d) at the mean, and 480 mg/p/d (7.5 mg/kg bw/d) at the 90th percentile for the U.S. population aged 2 years and older. All G states that the intended uses of rbLf isolate are not completely substitutional for those in other GRAS notices but are similar to the current uses of bLf. All G estimates the eaters-only cumulative dietary exposure to Lf that includes background sources, current uses of Lf, and the intended uses of rbLf isolate to be 246 mg/p/d (3.8 mg/kg bw/d) at the mean, and 540 mg/p/d (8.7 mg/kg bw/d) at the 90th

percentile for the U.S. population aged 2 years and older.

All G discusses publicly available data and information supporting the safety of rbLf isolate. In support of safety, All G describes data and information supporting the physiochemical equivalence of rbLf isolate to bLf that has been widely and safely consumed as a component of cow milk. All G notes that rbLf isolate undergoes substantial gastrointestinal digestibility via breakdown in simulated gastric and intestinal conditions, resulting in low molecular weight peptides rather than intact protein, which limits systemic exposure and further supports the safety of its intended use in food.

All G summarizes the results of an updated comprehensive literature search through January 2026, to identify available safety information relevant to rbLf isolate. All G did not identify any safety concerns or information that would contradict its GRAS conclusion. All G provides a summary of the literature, including published acute, short-term, subchronic, and chronic oral toxicity studies of bLf to support the safety of the intended use of rbLf isolate. Additionally, All G summarizes the results of published clinical studies in adult subjects administered bLf and notes that under the conditions of the studies, bLf was well tolerated and no adverse effects were reported.

Based on the weight of evidence, All G concludes that rbLf isolate does not pose an increased allergenic or toxigenic risk to consumers. All G further characterizes residual proteins from the production strain and concludes that there is reasonable certainty that these peptides do not pose an allergenic or toxigenic risk to consumers.

Based on the totality of the data and information, All G concludes that rbLf isolate is GRAS for its intended use.

Standards of Identity

In the notice, All G states its intention to use rbLf isolate 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 (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 rbLf isolate 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 Nutrition Center of Excellence. The Office of Pre-Market Additive Safety (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. rbLf isolate requires labeling under the FD&C Act because it is a milk protein.

Potential Requirement for a Color Additive Petition

There is no GRAS provision for color additives. In the notice, All G describes rbLf isolate as a light brown to light pink powder. As such, the use of rbLf isolate in food products may constitute a color additive use under section 201(t)(1) of the FD&C Act and FDA's implementing regulations in 21 CFR Part 70. Under section 201(t)(1) and 21 CFR 70.3(f), a color additive is a material that is a dye, pigment, or other substance made by a synthetic process or similar artifice, or is extracted, isolated, or otherwise derived from a vegetable, animal, mineral, or other source. Under 21 CFR 70.3(g), a material that otherwise meets the definition of a color additive can be exempt from that definition if it is used (or is intended to be used) solely for a purpose or purposes other than coloring. Our response to GRN 001284 is not an approval for use as a color additive nor is it a finding of the Secretary of the Department of Health and Human Services within the meaning of section 721(b)(4) of the FD&C Act. Questions about color additives should be directed to the Division of Food Ingredients in OPMAS.

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 All G's notice concluding that rbLf isolate 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 rbLf isolate. Accordingly, our response should not be construed to be a statement that foods containing rbLf isolate, if introduced or delivered for introduction into interstate commerce, would not violate section 301(ll).

Conclusions

Based on the information that All G provided, as well as other information available to FDA, we have no questions at this time regarding All G's conclusion that rbLf isolate is GRAS under its intended conditions of use. This letter is not an affirmation that rbLf isolate 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 001284 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

Susan J. Carlson -S

Digitally signed by Susan J. Carlson -S
Date: 2026.03.25 15:56:11 -04'00'

Susan J. Carlson, Ph.D.
Director
Division of Food Ingredients
Office of Pre-Market Additive Safety
Office of Food Chemical Safety, Dietary Supplements, and Innovation
Human Foods Program