Human Foods Program

Amy Mozingo
GRAS Associates, LLC
11810 Grand Park Ave, Suite 500 North
Bethesda, MD 20852

Re: GRAS Notice No. GRN 001213

Dear Ms. Mozingo:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 001213. We received the notice that you submitted on behalf of Crossway Foods Limited (Crossway) on October 24, 2024, and filed it on November 25, 2024. Crossway submitted amendments on January 30, 2025, and February 14, 2025, that clarified the specifications, dietary exposure, and aspects of the safety narrative.

The subject of the notice is goat milk lactose for use as an ingredient in goat milk-based, non-exempt infant formula for term infants at levels up to 15 g/100 g of powdered infant formula or up to 1.9 g/100 mL of ready-to-feed infant formula.[1] The notice informs us of Crossway's view that this use of goat milk lactose is GRAS through scientific procedures.

Our use of the term, "goat milk lactose," 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 "goat milk lactose."

Crossway describes the identity and composition of goat milk lactose, which is composed of ≥99% (dry matter) lactose. D-lactose monohydrate (CAS Registry number 64044-51-5) is a disaccharide of glucose and galactose. Lactose is the primary carbohydrate found in the milk of most mammals. Crossways states that lactose obtained from goat milk is chemically identical to lactose found in cow and human milk.

[1] Crossway states that goat milk lactose is not intended for use in hypoallergenic infant formula or formula labeled for infants with lactose intolerance.

Crossway describes the manufacture of goat milk lactose, which is produced from liquid goat whey. The goat whey is pasteurized and then ultra-filtered, which results in a protein fraction (retentate) and lactose fraction (permeate). The permeate is dried by evaporation and then cooled to promote crystallization. After crystallization, the concentrate is decanted and washed with water. The washed product is dried in a fluidized bed dryer and then passed through fluidization silos to remove residual moisture. The dried lactose is milled, sieved, and stored until packaged. Crossway states that goat milk lactose is produced according to current good manufacturing practices and that all raw materials, processing aids, and food contact substances used are food-grade and permitted by U.S. regulations or have previously been determined to be GRAS for their respective uses.

Crossway provides specifications for goat milk lactose that include content of lactose (≥ 99%, dry matter basis), and limits for protein (≤ 0.5%), ash (≤ 0.3%), moisture (≤ 1%), scorched particles (≤ Disc A), pH (4 to 7), and microorganisms, including *Cronobacter* spp. (absent in 10 g), *Salmonella* serovars (absent in 25 g), and *Listeria monocytogenes* (absent in 25 g). Crossway provides additional specifications that are used for the periodic monitoring of goat milk lactose that include limits for nitrates (≤ 50 mg/kg), nitrites (≤ 2 mg/kg), arsenic (≤ 0.01 mg/kg), cadmium (≤ 0.005 mg/kg), lead (≤ 0.02 mg/kg), and mercury (≤ 0.005 mg/kg).[2] Crossway provides the results from three non- consecutive batch analyses to demonstrate that goat milk lactose can be manufactured to meet these specifications.

Crossway estimates the dietary exposure to goat milk lactose based on the intended use and infant formula consumption data from the 2017-2020 National Health and Nutrition Examination Survey. Crossway reports the mean and 90$^{th}$ percentile estimates of infant formula consumption for male and female infants 0-6 and 7-12 months of age and estimates dietary exposure to goat milk lactose based on the maximum intended use level of 15 g/100 g formula powder and a recommended reconstitution rate of ~12.9 g/100 mL of formula as consumed. Crossway estimates the mean and 90$^{th}$ percentile eaters-only dietary exposure to goat milk lactose for infants 0-6 months of age to be 15.2 g/person (p)/d (2.4 g/kg body weight (bw)/d) and 23.2 g/p/d (3.7 g/kg bw/d), respectively, and for 7-12 months of age to be 12.6 g/p/d (1.4 g/kg bw/d) and 21.2 g/p/d (2.3 g/kg bw/d), respectively.

Goat milk lactose is intended for use in goat milk-based, non-exempt infant formula for term infants, and Crossway notes that the infant formula will also contain lactose that is a constituent of the goat milk and goat whey that are also components of the formula.
Based on the typical concentrations of lactose in goat milk and goat whey and their intended infant formula composition, Crossway estimates the total concentration of lactose to be 53.9 g/100 g in powdered infant formula. Based on this concentration of lactose, Crossway estimates the highest (i.e., boys in the 0-6 months age group) cumulative mean and 90$^{th}$ percentile dietary exposure to goat milk lactose to be 70.3 g/p/d (9.6 g/kg bw/d) and 105.4 g/p/d (14.4 g/kg bw/d), respectively.

[2] Crossway notes that each lot of infant formula containing goat milk lactose is tested for compliance with the specifications described, including chemical and microbiological impurities and heavy metals.

Crossway discusses publicly available data and information to support the safety of goat milk lactose. They state that lactose, a disaccharide, is the primary carbohydrate found in several mammalian milks, including milk from cows, goats, and humans, and is digested by the lactase enzyme into glucose and galactose, which are normally absorbed in the small intestine by the sodium/glucose cotransporter 1. Crossway notes that infant formula is typically supplemented with lactose to match the carbohydrate profile of human milk, and that lactose serves several important functions, including maintaining the osmotic pressure in human milk and infant formula, and facilitating the absorption of minerals like calcium. Thus, the use of lactose in infant formula has a robust history of safe consumption by infants.

Crossway discusses clinical studies considered pivotal to their GRAS conclusion, including a randomized, double-blind study of lactose-free and lactose-containing cow- milk-based formula in 137 healthy term infants (Heubi et al, 2000); a randomized blinded controlled study of lactose-free and lactose-containing cow-milk-based formula in 128 healthy term infants (Laskekan et al., 2011); and a randomized double-blinded controlled study of 79 infants fed goat milk or cow-milk-based formula up to 6 months (Xu et al., 2015). Crossway states that these studies show that dietary exposure to lactose at levels comparable to that from the intended use in healthy infants is safe and tolerable. Crossway further discusses six other infant clinical studies, as well as one systematic review supporting the safety of goat milk-based infant formulas.

Crossway notes that given that lactose itself is a distinct molecule, regardless of source, and that the allergenicity of goat milk and cow milk is similar, the allergenicity of goat milk lactose is expected to be similar to lactose derived from other sources, including cow milk.

Based on the totality of the data and information, Crossway concludes that goat milk lactose is GRAS for its intended use.

**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 goat milk lactose 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. 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.

**Intended Use in Infant Formulas**

Under section 412 of the FD&C Act, a manufacturer of a new infant formula must make a submission to FDA providing required assurances about the formula at least 90 days before the formula is marketed. Our response to Crossway's GRAS notice does not alleviate the responsibility of any infant formula manufacturer that intends to market an infant formula containing goat milk lactose to make the submission required by section 412. Infant formulas are the purview of the Office of Critical Foods in NCE.

**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 Crossway's notice concluding that goat milk lactose 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 goat milk lactose. Accordingly, our response should not be construed to be a statement that foods containing goat milk lactose, if introduced or delivered for introduction into interstate commerce, would not violate section 301(ll).

**Conclusions**

Based on the information that Crossway provided, as well as other information available to FDA, we have no questions at this time regarding Crossway's conclusion that goat milk lactose is GRAS under its intended conditions of use. This letter is not an affirmation that goat milk lactose 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 001213 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

Susan J. Carlson -S

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Date: 2025.02.21 15:25:23 -05'00'

Susan J. Carlson, Ph.D. Director
Division of Food Ingredients
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