Mary M. Murphy, M.S., R.D.
Exponent
1150 Connecticut Ave., NW
Suite 1100
Washington, DC 20036

Re: GRAS Notice No. GRN 001172

Dear Ms. Murphy:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 001172. We received Synlait Milk Limited (Synlait)'s notice on February 22, 2024, and filed it on March 1, 2024. Synlait submitted an amendment to the notice on April 23, 2024, that clarified the specifications and aspects of the safety narrative.

The subject of the notice is liquid milk, both whole and nonfat, combined with lactose and water (liquid milk blend) for use as an ingredient in cow milk-based, non-exempt infant formula for term infants at a maximum level of 25 g solids/100 g infant formula powder. The notice informs us of Synlait's view that this use of liquid milk blend is GRAS through scientific procedures.

Our use of the term, "liquid milk blend," 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 "liquid milk blend."

Synlait describes liquid milk blend as a liquid preparation that is a combination of whole cow milk, nonfat cow milk, lactose, and water in approximately 4:1:1:4 proportions by weight, respectively. Synlait states that liquid milk blend is produced to provide a standardized composition of solids and macronutrients for its intended use in infant formula. Synlait provides data and information on the composition of liquid milk blend and notes that it has a lower solids content relative to liquid whole milk or liquid nonfat milk. Synlait states that the solids fraction of liquid milk blend is approximately 64% whole milk solids, 24% lactose, and 12% nonfat milk solids.

Synlait describes the manufacture of liquid milk blend and states that the starting materials are raw milk, lactose, and water. Synlait notes that the raw materials meet applicable regulations and are food grade. Synlait states that liquid milk blend is manufactured using current good manufacturing practices and uses standard dairy processing steps to produce whole milk and nonfat milk from raw milk. The resulting whole milk and nonfat milk are combined with an aqueous lactose solution and water, and the mixture is subjected to a heat treatment step that is consistent with the pasteurization conditions of the 2019 Pasteurized Milk Ordinance. Synlait notes that the manufacture of liquid milk blend is part of a continuous process in the manufacture of infant formula powder. Immediately after the liquid milk blend is produced, the other ingredients of the infant formula are added, and the subsequent formulation is dried to produce the final infant formula base powder.

Synlait provides specifications for liquid milk blend that include the content of solids (7.3 to 8.2%, as is basis), protein (21.3 to 23.3% on a dry matter basis (DM)), fat (19.6 to 21.8%, DM), carbohydrates (48.8 to 58.2%, DM), ash (2.4 to 5.1 %, DM), lead (<0.005 mg/kg), arsenic (<0.003 mg/kg), cadmium (<0.002 mg/kg), mercury (<0.005 mg/kg), and microorganisms, including *Salmonella* serovars (absent in 25 g), *Bacillus cereus* (<10 colony forming units/mL), *Listeria monocytogenes* (absent in 25 g), and *Cronobacter* sp. (absent in 100 g). Synlait provides the results from four non-consecutive batch analyses to demonstrate that liquid milk blend can be manufactured to meet these specifications.

Synlait estimates the dietary exposure to the solids fraction of liquid milk blend based on the intended use and infant formula consumption data from the combined 2011-2018 National Health and Nutrition Examination Survey. Using the maximum intended use level of 25 g liquid milk blend solids/100 g infant formula powder, Synlait states that the use level is equivalent to 5 g solids/100 kcal or 3.4 g solids/100 mL of formula as consumed based on a reconstitution rate of 20 g formula powder/100 kcal and a caloric content of 67 kcal/100 mL for formula as consumed. Synlait estimates the dietary exposure to the solids fraction of liquid milk blend for infants up to one year of age (i.e., 0-2 months, 3-5 months, 6-8 months, and 9-11 months). The reported mean and 90th percentile eaters-only dietary exposures range from 23 to 28 g/person (p)/day (d) and 35 to 43 g/p/d, respectively, across the first year of life. Synlait determined that infants aged 3 to 5 months have the highest dietary exposures with mean and 90th percentile estimates of 28 and 43 g/p/d, respectively, and infants aged 0 to 2 months have the highest dietary exposures on a body weight (bw) basis with mean and 90th percentile estimates of 4.8 and 7.3 g/kg bw/d, respectively.

Synlait discusses published data and information to support the safety of liquid milk blend. Synlait states that milk and milk products, including infant formula ingredients from cow milk, have a long history of use in the U.S. food supply. Synlait discusses key physico-chemical similarities and differences among unmodified milk, dry whole milk, dry nonfat milk, and the liquid milk blend, stating that any differences have no effect on the safety profile of the various forms of milk. Synlait discusses safety information on dry whole milk and anhydrous milk fat provided in GRNs 000898, 000980, and

001041.[1] Synlait states that the findings from various clinical studies provide support that milk fat used as a component of up to 50% of the fat blend in infant formula is safe and well tolerated. Synlait states that as liquid milk blend provides only a portion of the nutrients needed as part of an infant formula formulation, any potential adverse effects reported in the literature from consuming fluid whole milk as a sole source of infant nutrition is not a safety concern.

Synlait states that the use of liquid milk blend will provide a source of constituents typically present in lower concentrations in infant formula, such as phospholipids and other lipids present in cow milk fat but not in vegetable oils. Based on analytical data, Synlait states that the levels of these components provided by liquid milk blend will result in levels similar to or well below the mean concentrations reported in human milk. Synlait also states that the safe consumption of commercially available infant formulas containing liquid milk blend in Australia and the United Kingdom provides supportive evidence of safety for the intended use.

Based on the totality of the data and information, Synlait concludes that liquid milk blend 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 liquid milk blend 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 ONFL. OFAS 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. Liquid milk blend requires labeling under the FD&C Act because it contains milk.

Intended Use in Infant Formulas

Under section 412 of the FD&C Act, a manufacturer of a new infant formula must make

[1] Anhydrous milk fat was the subject of GRN 000898; dry whole milk was the subject of GRNs 000980 and 001041. We evaluated these notices and responded in letters dated October 28, 2020, July 13, 2021, and May 10, 2022, respectively, stating that we had no questions at that time regarding the notifiers' GRAS conclusions.

a submission to FDA providing required assurances about the formula at least 90 days before the formula is marketed. Our response to Synlait's GRAS notice does not alleviate the responsibility of any infant formula manufacturer that intends to market an infant formula containing liquid milk blend to make the submission required by section 412. Infant formulas are the purview of ONFL.

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

Conclusions

Based on the information that Synlait provided, as well as other information available to FDA, we have no questions at this time regarding Synlait's conclusion that liquid milk blend is GRAS under its intended conditions of use. This letter is not an affirmation that liquid milk blend 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 001172 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

Susan J. Carlson -S

Digitally signed by Susan J. Carlson -S
Date: 2024.05.20 09:30:37 -04'00'

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