Witty Brathwaite
Cargill, Inc.
Scientific & Regulatory Affairs NA
15407 McGinty Road
Wayzata, MN 55391

Re: GRAS Notice No. GRN 001069

Dear Ms. Brathwaite:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 001069. We received Cargill, Inc. (Cargill)'s notice on March 16,2022, and filed it on September 14, 2022.[1] Cargill submitted amendments to the notice on June 2, 2023, July 21, 2023, August 11, 2023, and October 18, 2023 that revised the specifications and intended uses and clarified the method of manufacture, estimates of dietary exposure, protein composition, safety narrative, and the suitability of corn protein in products under the jurisdiction of the USDA.

The subject of the notice is ethanol-extracted corn gluten meal containing ≥65% protein (corn protein) for use as a binder in comminuted meat and poultry products at a maximum level of 3.5% and for use as a source of protein, stabilizer and thickener, formulation aid (binder, filler), and emulsifier in other food categories at the maximum levels specified in Table 1.[2] The notice informs us of Cargill's view that these uses of corn protein are GRAS through scientific procedures.

Our use of the terms, "ethanol-extracted corn gluten meal containing ≥65% protein" or "corn protein" 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 Code of Federal Regulations (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 non-standardized 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 "ethanol-extracted corn gluten meal containing ≥65% protein" or "corn protein."

[1] The contact person for GRN 001069 was updated in correspondence dated April 7, 2023.
[2] Cargill states that corn protein is not intended for use in infant formula or in foods for which standards of identity do not permit its addition.

Table 1: Intended food categories and use levels of corn protein

Food category	**Maximum use level (g/100g)**
Flatbread and pizza crust[3]	8
Biscuits, English muffins, muffins[3]	8
Gluten-free breads/rolls	8
Gluten-free pancakes and waffles	8
Batter, breading and coating mixes for frying (includes use in meat and poultry products)	2
Ready-to-eat (RTE) breakfast cereal, all types	30
Dairy alternatives (imitation cheese and sour cream, cream substitute, non-dairy topping)	10
Margarine-type spreads	10
Non-dairy frozen desserts and ices	10
Meat alternatives and vegetarian mixed dishes (e.g., chili, pot pie) made with meat alternatives	40
Prepackaged mixed dishes with sauce including frozen and canned products	0.08
Mixed dishes (rice, pasta, potato-based) prepared from box mixes	0.08
Imitation milks	5
Peanut butter (excluding full-fat) and nut butters	10
Nutrition bars, including meal replacement and protein bars	25
Cooked pasta	5
Comminuted meat and poultry products	3.5
Powder mixes (not reconstituted) for nutritional drinks/shakes including meal replacements	35.3
Ready-to-drink nutritional drinks/shakes including meal replacements	5
Milk- and cream-based sauces, cheese sauce, other sauces (lemon-butter, horseradish)	1.5
Cereal and granola bars	15
Snack foods including crackers, chips, pretzels, and puffs	15

Cargill describes corn protein as a pale yellow to light tan powder, with a minimum of 65% protein (dry weight (DW) basis), with the remainder being starch (up to approximately 24%) and fiber (3-6%), with low levels of residual ash (1-2%) and fat (<0.2%). Corn protein is obtained from the ethanol treatment and (optional) enzymatic removal of starch from corn gluten meal (CGM), a byproduct of standard corn milling procedures. The level of starch in the corn protein ingredient is reduced from

[3] The July 21, 2023, amendment clarified that the proposed uses include gluten-free and non-gluten free versions of these foods.

approximately 22-24% to 2-3% with the use of the amylase treatment. With reduction of starch, there is a concomitant increase in the percent of protein, from approximately 68-70% protein in corn protein produced without amylase treatment to 89-92% protein in corn protein produced with amylase treatment.

Cargill states that the corn or maize (*Zea mays*) grain, the raw material used to produce CGM, is produced in compliance with current good agricultural practices. CGM is produced as a direct byproduct from the wet milling of corn, wherein the corn kernels are steeped in water containing sulfur dioxide, degermed, dehulled and the remainder separated into starch and CGM fractions. CGM is affirmed as GRAS (21 CFR 184.1321) for use as a nutrient supplement and texturizer in food, at levels not to exceed current good manufacturing practices (cGMPs).

Cargill describes the production of corn protein from the CGM starting material. The CGM (slurry) is pH adjusted using food-grade buffers, jet cooked, mixed (optionally) with a heat-resistant alpha-amylase, and incubated at 75-85 °C. The insoluble protein is pH adjusted and recovered by filtration using water and up to 2% oxidizing agent (hydrogen peroxide). Alternatively, CGM may be cooked and recovered by filtration without the enzyme treatment to remove starch. After filtration, the CGM (with or without amylase treatment) is present as a wet cake (40-55% solids) that is dried and washed with food-grade ethanol to remove ethanol-soluble non-protein components (e.g., carotenoids and other lipids). The ethanol is removed by evaporation and an oxidizing agent is added at no more than 2% to reduce the levels of sulfur dioxide. The corn protein is then placed in a desolventizer, and the resulting powder (minimum 88% solids) is subjected to milling (or other physical processes) or may be spray dried with food-grade oil, lecithin, or other safe and suitable ingredients. Cargill states that corn protein is produced in accordance with cGMPs and all raw materials and processing aids are safe and appropriate for food use.

Cargill provides specifications for corn protein that include minimum content of protein (≥65% DM basis) and limits for residual ethanol (<1%), loss on drying (≤12%), sulfur dioxide (<100 mg/kg), lead (≤0.1 mg/kg), arsenic (<0.1 mg/kg), cadmium (<0.1 mg/kg), mercury (<0.1 mg/kg) and microorganisms, including *Salmonella* serovars (negative in 25 g) and *Enterobacteriaceae* (<10 colony forming units (CFU)/g). Cargill provides the results from the analyses of five non-consecutive batches each of corn protein produced with and without enzyme treatment to demonstrate that the ingredient can be manufactured to meet these specifications. Cargill states that corn protein is stable for 24 months when stored at 20-30 °C, 20-40% relative humidity, and away from light.

Cargill estimates the dietary exposure to corn protein using food consumption data from the 2015-16 and 2017-18 National Health and Nutrition Examination Survey (NHANES), recipes from the USDA's corresponding Food and Nutrient Database for Dietary Studies (FNDDS), and assuming the maximum proposed use level for corn protein in each food category. Cargill estimates the eaters-only dietary exposure to corn protein to be 14.7 g/p/d (0.25 g/kg bw/d) at the mean and 29.0 g/p/d (0.57 g/kg bw/d) at the 90th percentile for the total US population. On a body weight basis, the highest eaters-only estimates of dietary exposure to corn protein are for children 1-6 years of

age, where the mean and 90th percentiles are 12.3 g/p/d (0.73 g/kg bw/d) and 23.0 g/p/d (1.31 g/kg bw/d), respectively. On a per person basis, the highest eaters-only estimates of dietary exposure are for teenagers 13-19 years of age of 16.5 g/p/d (0.26 g/kg bw/d) at the mean and 32.5 g/p/d (0.51 g/kg bw/d) at the 90th percentile. Cargill notes that corn protein is intended to be an alternative source of plant-based protein in food and is not expected to result in an increase in the overall consumption of protein in the US diet.

Cargill discusses all relevant publicly available safety data and information provided in the notice. Cargill states that corn is one of the most widely consumed grains worldwide, and therefore, its proteins have been historically safely consumed as part of the normal human diet. Cargill notes that the starting material for corn protein, CGMl, contains two predominant protein types: zein[4] and glutelin. Cargill performed a search of the published scientific literature and notes that no data or information that would contradict a GRAS conclusion for the proposed uses of corn protein were identified. Additionally, Cargill states that of the publications on zein or glutelin, none demonstrated safety concerns with respect to human consumption of these proteins. Cargill discusses the potential for anti-nutritional factors associated with native corn (maize) to be present in corn protein and concludes that these factors are likely reduced during processing, as demonstrated in the published literature. Cargill addresses the allergenicity of corn protein and states that a food allergy to native corn (maize) is rare. Cargill notes that the primary corn allergen is a non-specific lipid transfer protein (LTP). Cargill states that the level of LTP found in corn protein is expected to be similar to the starting material, CGM. Cargill concludes that the nominal increase in protein content between the starting material and the article of commerce will not result in an increased risk of allergenic potential.

Based on the available data and information, Cargill concludes that corn protein is GRAS for its intended uses.

Standards of Identity

In the notice, Cargill states its intention to use corn protein 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 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 corn

[4] Cargill notes that zein is GRAS-affirmed for use as a surface-finishing agent in food at levels not to exceed current good manufacturing practice per 21 CFR § 184.1984.

protein 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.

Use in Products under USDA Jurisdiction

As provided under 21 CFR 170.270, during our evaluation of GRN 001069, we coordinated with the Food Safety and Inspection Service (FSIS) of the United States Department of Agriculture. Under the Federal Meat Inspection Act, the Poultry Products Inspection Act, and the Egg Products Inspection Act, FSIS determines the efficacy and suitability of ingredients used in meat, poultry, and egg products, and prescribes safe conditions of use. Suitability relates to the ingredient's effectiveness in performing its intended technical effect and the assurance that the ingredient's use will not result in products that are adulterated or misleading for consumers.

FSIS has completed its review and has no objection to the use of corn protein used at up to 2% as a stabilizer, thickener, formulation aid (binder, filler) and emulsifier in batter, breading, and coating mixes for frying, and at up to 3.5% as a binder in comminuted meat and poultry products. Regarding labeling, meat or poultry products containing corn protein are required to be labeled in the ingredients statement with the common or usual name.

FSIS requested that we advise you to seek regulatory guidance from its Risk Management and Innovations Staff (RMIS) about the use of corn protein in meat, poultry, and egg products. You should direct such an inquiry to Stephanie Hretz, Director, RMIS, Office of Policy and Program Development, FSIS by email at Stephanie.Hretz@usda.gov.

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

Conclusions

Based on the information that Cargill provided, as well as other information available to FDA, we have no questions at this time regarding Cargill's conclusion that corn protein is GRAS under its intended conditions of use. This letter is not an affirmation that corn protein 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 001069 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

Susan J. Carlson -S

Digitally signed by Susan J. Carlson -S
Date: 2024.02.05 18:07:38 -05'00'

Susan J. Carlson, Ph.D.
Director
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cc: Stephanie Hretz, M.P.H.
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