



Donald F. Schmitt, M.P.H
Senior Managing Scientist
ToxStrategies, Inc.
931 W. 75th St., Suite 137, PMB 263
Naperville, IL 60565

Re: GRAS Notice No. GRN 000682

Dear Mr. Schmitt:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 000682. We received the notice on November 23, 2016, that you submitted on behalf of Cargill, Incorporated (Cargill) and filed it on January 10, 2017. We received amendments that clarified intended uses and exposure estimates and contained additional safety information on January 10, 2017, April 28, 2017, and May 17, 2017.

The subject of the notice is canola lecithin for use as an ingredient, an emulsifier, wetting or instantizing agent, viscosity modifier, releasing agent, extrusion aid, low-flavor binding material, and dietary fat source in food (including as an emulsifying agent in meat and poultry products) at levels not to exceed current good manufacturing practice (cGMP), and as a dietary source of choline in milk-based non-exempt infant formula for term infants at levels up to 3 g per 100 g. The notice informs us of Cargill's view that these uses of canola lecithin are GRAS, through scientific procedures.

Cargill describes the identity and composition of canola lecithin. Canola lecithin is a complex mixture of phosphatides (primarily phosphatidylcholine (PC), phosphatidylethanolamine, phosphatidylinositol, and phosphatidic acid), triglycerides, fatty acids and carbohydrates. Canola lecithin is produced as a viscous green-brown liquid and as a beige powder.

Cargill describes the manufacturing process for canola lecithin. Canola seeds are cleaned, dried and pressed prior to extraction with hexane. The resulting mixture of oil, lecithin, and hexane is filtered to remove any remaining solid impurities. The crude canola oil is heated to remove the hexane followed by a water degumming process. This crude lecithin is then dried under vacuum. A de-oiled fraction containing canola lecithin is produced using an acetone wash. The acetone is then evaporated to yield either a fluid containing 17% PC or a powder composed largely of phospholipids containing 28% PC. Cargill states that de-oiled canola lecithin powder and canola lecithin fluid are produced in accordance with cGMP. All raw materials and processing aids used in the manufacturing process are food grade.

Cargill provides specifications for canola lecithin. The specifications include total phospholipids ($\geq 60\%$ in fluid and $\geq 96\%$ in powder, w/w), and limits for peroxide

value (≤ 5 milliequivalents/kg), acid value (≤ 35 mg KOH/g), moisture (≤ 1.5 %), and lead (≤ 1 mg/kg). Cargill provides analytical data for three non-consecutive lots of both the fluid and powder forms of canola lecithin to demonstrate that these products meet all specifications.

Cargill references the estimated dietary exposures presented in GRN 000533¹ as representative of canola lecithin in the current notice. Cargill states that the intended uses of canola lecithin will replace other canola lecithin and therefore, total lecithin dietary exposure would not increase. Cargill states that based on the intended food categories and use levels of canola lecithin presented in GRN 000533, average dietary exposure to canola lecithin is 6.8-9.5 g per person per day (g/p/d). This is equivalent to a daily exposure of 113-160 mg/kg bw/d for a 60 kg adult, and 226-320 mg/kg bw/d for a 30 kg child. Cargill estimates the intake of lecithin at approximately 1.25-5.4 g/kg bw/d for a 2 to 3-month old infant weighing approximately 5-6.4 kg, based on the intended average and maximum incorporation of lecithin in infant formula of approximately 1 to 3 g/100 g of formula.

Cargill reviewed and discusses publicly available information and published studies up to November, 2016, supporting the safety of canola lecithin. Cargill notes the similarities of canola lecithin to other lecithins from vegetables whose uses have been affirmed as GRAS under 21 CFR 184.1400 with no limitations other than cGMP. Cargill states that the phospholipids and fatty acids in canola lecithin undergo digestion, absorption, distribution, metabolism, and elimination processes and pathways that are well established. Cargill cites GRN 000533 which addressed a similar canola lecithin that has the same intended uses with the exception of USDA regulated products. To further support the safety of canola lecithin, Cargill cites previous GRAS notices for lecithins from other sources for which FDA had no questions: GRN 000134 (soy protein hydrolysate with enzyme-modified lecithin), GRN 000186 (soy lecithin enzymatically modified to have increased phosphatidylserine), GRN 000226 (lecithin derived from krill), and GRN 000534 (hydrogenated lecithin from soy). Next, Cargill addresses the differences in the relative composition of phospholipids and fatty acids across lecithins from different sources and concludes that there is no effect on the safety profile of this substance. In addition, Cargill summarizes the results from multiple published studies that administered phospholipids or lecithin including acute and repeated dose oral toxicity studies, reproductive and developmental toxicity studies, and carcinogenicity studies in animals, and clinical studies in humans. Cargill concurs with the no adverse effect determinations reported in these studies. Citing published studies, Cargill further notes that lecithin or related phospholipids are not mutagenic or genotoxic. Cargill states that the safety of lecithins were reviewed by the European Commission Scientific Committee for Food, the European Food Safety Authority, the Cosmetic Ingredient Review, the Select Committee on GRAS Substances in 1979, and the Joint FAO/WHO Expert Committee on Food Additives in 1974. These reviews found no evidence of adverse effects.

¹ Canola-derived lecithin/lysolecithin (CDL) was the subject of GRN 000533, which informed FDA of the view of American Lecithin Company that CDL is GRAS. In a letter dated March 20, 2015, FDA stated that the agency had no questions at that time regarding American Lecithin Company's GRAS conclusion.

Cargill includes the statement of a panel of individuals (Cargill's GRAS panel). Based on its review, Cargill's GRAS panel concluded that canola lecithin is safe under the conditions of its intended uses.

Based on all the publicly available information discussed above, Cargill concludes that canola lecithin is GRAS for its intended uses.

Standards of Identity

In the notice, Cargill states its intention to use canola lecithin in several food categories, including foods for which standards of identity exist, located in Title 21 of the Code of Federal Regulations. 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

In discussing canola lecithin as a choline-enriching dietary ingredient, Cargill raises a potential issue under the labeling provisions of the Federal Food, Drug, and Cosmetic Act (FD&C Act). Section 403(r) of the FD&C Act lays out the statutory framework for the use of labeling claims that characterize the level of a nutrient in a food or that characterize the relationship of a nutrient to a disease or health-related condition. If products that contain canola lecithin bear any claims on the label or in labeling, such claims are the purview of the Office of Nutrition and Food Labeling (ONFL). The Office of Food Additive Safety (OFAS) neither consulted with ONFL on this labeling issue nor evaluated the information in your notice to determine whether it would support any claims made about canola lecithin on the label or in labeling.

Potential Requirement for a Color Additive Petition

There is no GRAS provision for color additives. In the notice, Cargill describes canola lecithin in fluid as green-brown. As such, the use of canola lecithin 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 000682 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 Petition Review in OFAS.

Intended Use in Infant Formula

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. Cargill should be aware that FDA's response to Cargill's GRAS notice does not alleviate the responsibility of any infant formula manufacturer who intends to market an infant formula that contains canola lecithin to make the submission required by section 412. Infant formulas are the purview of ONFL.

Use in Products under USDA Jurisdiction

As provided under 21 CFR 170.270, during our evaluation of GRN 000682, 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 advises that per 9 CFR 424.21, lecithin is approved for use as an emulsifying agent and antioxidant in oleomargarine, shortening, and various meat and poultry products. Thus, the intended use of Cargill's canola lecithin in meat and poultry is already approved by USDA.

Section 301(II) of the FD&C Act

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

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 canola lecithin is GRAS under its intended conditions of use. This letter is not an affirmation that canola lecithin 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 000682 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,
**Michael A.
Adams -S**



Digitally signed by Michael A. Adams -S
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