



Donald F. Schmitt, MPH
ToxStrategies, Inc.
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Re: GRAS Notice No. GRN 000939

Dear Mr. Schmitt:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 000939. We received the notice that you submitted on behalf of Sternchemie GmbH & Co. KG (Sternchemie) on May 18, 2020 and filed it on August 26, 2020. Sternchemie submitted amendments to the notice on November 5, 2020, November 17, 2020, November 19, 2020,¹ and December 21, 2020, providing additional information and clarifications regarding the intended use, specifications, and safety studies.

The subject of the notice is sunflower lecithin for use as an emulsifier,² dispersing agent, wetting agent, and release agent in food, at levels not to exceed current good manufacturing practice (cGMP). Sternchemie also intends to use sunflower lecithin as a dietary source of choline, in addition to the aforementioned technical effects, in milk-based non-exempt infant formula for term infants at levels up to 3 g per 100 g of formula powder. The notice informs us of Sternchemie's view that these uses of sunflower lecithin are GRAS through scientific procedures.

Sternchemie describes the identity and composition of sunflower lecithin. Sunflower lecithin is a complex mixture of primarily phospholipids (phosphatidylcholine, phosphatidylethanolamine, phosphatidylinositol, and phosphatidic acid) and varying amounts of triglycerides, fatty acids, and carbohydrates. Sternchemie states that sunflower lecithin may be optionally produced in hydrolyzed or de-oiled forms. Sternchemie describes sunflower lecithin and hydrolyzed sunflower lecithin as viscous

¹In the November 19, 2020 amendment, Sternchemie includes analytical results that are designated confidential. Sternchemie acknowledges that the information is outside the scope of FDA's request for the results from analyses of three non-consecutive batches for *Cronobacter sakazakii*. FDA notes that this information is not relevant to our safety evaluation.

² Sternchemie intends to use sunflower lecithin as an emulsifying agent in meat and poultry products. Sunflower lecithin is not intended for use as a dispersing agent, wetting agent, release agent or a dietary source of choline in products that are under the jurisdiction of the United States Department of Agriculture.

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brown fluids, and de-oiled sunflower lecithin as a greyish-yellow to greyish-brown powder.

Sternchemie describes the manufacturing process for sunflower lecithin and states that all materials used are food grade. Sunflower seeds are cleaned, dried, tempered, conditioned, dehulled, and pressed to remove the oil. Any remaining oil in the press cake is removed by extraction with food-grade hexane. The resulting mixture of oil and hexane is filtered to remove solid impurities; the hexane is then removed by steam stripping to obtain a crude oil. The crude oil is subjected to a degumming process during which water-hydratable phosphatides (gums) precipitate and are separated by centrifugation. Sternchemie states that water, phospholipids and glycolipids, triglycerides, carbohydrates, traces of sterols, free fatty acids, and carotenoids are present in the gum fraction. The crude sunflower lecithin product is then obtained by drying under vacuum.

Sternchemie describes three forms of sunflower lecithin made from the crude product; they are standardized, de-oiled, and hydrolyzed sunflower lecithins. Standardized sunflower lecithin is produced by the addition of sunflower oil and/or sunflower-based oleic fatty acids to the crude product. De-oiled sunflower lecithin is produced from the crude product by extraction with acetone. The acetone fraction is then separated by centrifugation followed by drying to remove acetone. The dried extract is in a powder or granulated form, and Sternchemie states that silicon dioxide may be added as necessary as a free-flow agent. Hydrolyzed sunflower lecithin is produced by treatment of the crude product with phospholipase A2³ that catalyzes hydrolysis of fatty acids at the sn-2 position and results in lysophospholipids. Sternchemie notes that hydrolyzed sunflower lecithin is a mixture of phospholipids and lysophospholipids and the mixture is dried under vacuum and heat which inactivates the enzyme and yields the final hydrolyzed sunflower lecithin product.

Sternchemie provides specifications for sunflower lecithin. The specifications include total acetone insoluble matter (i.e., total phospholipids) ($\geq 60\%$ in standardized sunflower lecithin, $\geq 56\%$ in hydrolyzed sunflower lecithin, and $\geq 96\%$ in de-oiled sunflower lecithin), total toluene insoluble matter ($\leq 0.3\%$), peroxide value (≤ 5 milliequivalents peroxide/kg), acid value (≤ 30 mg KOH/g for standardized sunflower lecithin, ≤ 45 mg KOH/g for hydrolyzed sunflower lecithin, and ≤ 35 mg KOH/g for de-oiled sunflower lecithin), moisture ($\leq 0.8\%$ in standardized sunflower lecithin, $\leq 1\%$ in hydrolyzed sunflower lecithin, and $\leq 1.5\%$ in de-oiled sunflower lecithin), lead (≤ 1 mg/kg), as well as limits on microorganisms, including *Salmonella* serovars (absent in 25 g) and *C. sakazakii* (absent in 10 g). Sternchemie provides the results from three

³ Sternchemie provides information for the phospholipase A2 used in the manufacture of hydrolyzed sunflower lecithin and states that it is a food-grade enzyme obtained by submerged culture of a non-pathogenic and non-toxicogenic strain of *Aspergillus niger*. Sternchemie notes that phospholipase A2 enzyme preparation from *Aspergillus niger* expressing a gene encoding porcine phospholipase A2 was the subject of GRN 000183. FDA evaluated this notice and responded in a letter dated May 11, 2006, stating that we had no questions at that time regarding the notifier's GRAS conclusion.

non-consecutive batches for each form⁴ of sunflower lecithin to demonstrate that each product can be made to meet the specifications.

Sternchemie discusses the estimated dietary exposure to sunflower lecithin and incorporates information presented in GRN 000533.⁵ Sternchemie notes that under 21 CFR 184.1400, lecithin derived from soy, safflower, or corn oils is used in food without limitation other than cGMP. Sternchemie states that the intended uses of sunflower lecithin will be substitutional for other lecithins and, therefore, does not expect dietary exposure to lecithin to increase. In GRN 000533, the notifier estimated average dietary exposures to different forms of canola lecithin based on their intended use levels to be 6.8-9.5 g/person/d, which is equivalent to 113-160 mg/kg body weight (bw)/d for a 60 kg adult and 226-320 mg/kg bw/d for a 30 kg child. Sternchemie also discusses estimated dietary exposure to sunflower lecithin from the intended uses in infant formula. Based on published recommendations for infant formula consumption, Sternchemie states that an infant of 2 to 3 months of age would consume approximately 700 g of liquid formula/d (equivalent to 108 g of formula powder). Based on the maximum intended use level of sunflower lecithin, Sternchemie estimates dietary exposure to sunflower lecithin to be 3.2 g/d and equivalent to 0.7 g/kg bw/d for a 2- to 3-month old infant weighing 4.5 kg, which the notifier considers to be the group with the highest dietary exposure on a body weight basis.

Sternchemie states that the identity and composition of their sunflower lecithin, including the phospholipid and fatty acid profiles, are similar to approved lecithin and lecithin-derived products from other sources and consistent with specifications listed in the Food Chemicals Codex (11th edition). Sternchemie states that lecithins are naturally occurring components in human cells and body and are formed in the gastrointestinal tract as part of normal digestion of food. Sternchemie further states that dietary lecithin is generally well-absorbed in humans, with the majority being hydrolyzed by pancreatic phospholipase A2 to lysolecithins, which are taken up by mucosal cells and undergo: 1) re-esterification with fatty acids; 2) complete lipolysis (into fatty acids and triglycerides); and 3) absorption into portal circulation.

Sternchemie states that a literature search was conducted since the evaluation of GRN 000682⁶ and through September 2020; they found no additional data relevant to the safety of the intended use of sunflower lecithin. Sternchemie incorporates data and information discussed in GRNs 000226, 000533 and 000534,⁷ and summarizes and

⁴ Sternchemie provided the results of the analysis of three batches of standardized sunflower lecithin for *C. sakazakii*. This analyte was not included in batch analyses of hydrolyzed or de-oiled sunflower lecithin.

⁵ The subject of GRN 000533 is canola-derived lecithin/lysolecithin (CDL). We evaluated this notice and responded in a letter dated March 20, 2015, stating that we had no questions at the time regarding the notifier's GRAS conclusion.

⁶ The subject of GRN 000682 is canola lecithin. We evaluated this notice and responded in a letter dated July 7, 2017, stating that we had no questions at the time regarding the notifier's GRAS conclusion.

⁷ The subjects of GRNs 000226 and 000534 are lecithin derived from krill and hydrogenated soybean-derived lecithin, respectively. We evaluated these notices and responded in letters dated January 3, 2008, and December 22, 2014, respectively, stating that we had no questions at the time regarding the notifiers' GRAS conclusions.

discusses published studies, as well as unpublished data supporting the safety of their sunflower lecithin. Sternchemie states that they also rely on available data and information for lecithin metabolites or derivatives of lecithin.

Sternchemie discusses the safety evaluation of lecithins by other regulatory agencies and organizations to corroborate safety of their sunflower lecithin. Sternchemie further states that potential dietary choline intake resulting from the intended use is well below the tolerable upper limit established by the Food and Nutrition Board of the National Institute of Medicine.

Sternchemie includes the report of a panel of individuals (Sternchemie's GRAS panel). Based on its review, Sternchemie's GRAS panel concluded that sunflower lecithin is safe under the conditions of its intended use.

Based on the totality of data and information discussed in the notice, Sternchemie concludes that sunflower lecithin is GRAS for its intended uses.

Standards of Identity

In the notice, Sternchemie states its intention to use sunflower lecithin 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 sunflower lecithin 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 (CFSAN). The Office of Food Additive Safety (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.

Potential Requirement for a Color Additive Petition

There is no GRAS provision for color additives. In the notice, Sternchemie describes sunflower lecithin and hydrolyzed sunflower lecithin as viscous brown fluids and de-oiled sunflower lecithin as a greyish-yellow to greyish-brown powder. As such, the use of sunflower 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 000939 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 OFAS.

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 Sternchemie's GRAS notice does not alleviate the responsibility of any infant formula manufacturer that intends to market an infant formula containing sunflower lecithin to make the submission required by section 412. Infant formulas are the purview of ONFL in CFSAN.

Use in Products under USDA Jurisdiction

As provided under 21 CFR 170.270, during our evaluation of GRN 000939, 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.

Lecithin from any source is approved for use as an emulsifying agent and antioxidant in oleomargarine, shortening, and various meat and poultry products at levels described in 9 CFR 424.21. Thus, the intended use of Sternchemie's sunflower lecithin as an emulsifying agent in meat and poultry is already approved by USDA.

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

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(ll)(1)-(4) applies. In our evaluation of Sternchemie’s notice concluding that sunflower lecithin 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 sunflower lecithin. Accordingly, our response should not be construed to be a statement that foods containing sunflower lecithin, if introduced or delivered for introduction into interstate commerce, would not violate section 301(ll).

Conclusions

Based on the information that Sternchemie provided, as well as other information available to FDA, we have no questions at this time regarding Sternchemie’s conclusion that sunflower lecithin is GRAS under its intended conditions of use. This letter is not an affirmation that sunflower 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 000939 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

Susan J.
Carlson -S

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