



Steven Steinborn
Hogan Lovells US LLP
555 Thirteenth Street, NW
Washington, DC 20004

Re: GRAS Notice No. GRN 000900

Dear Mr. Steinborn:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 000900. We received Hogan Lovells US LLP (Hogan Lovells)'s notice on November 12, 2019,¹ and filed it on February 21, 2020. Hogan Lovells submitted amendments to the notice on May 1, 2020, June 11, 2020, June 15, 2020,² August 4, 2020, and October 21, 2020, that clarified the intended use, specifications, manufacturing, dietary exposure, and some literature references.

The subject of the notice is corn oil for use as a source of fat in cow milk-based, calorically dense, ready-to-feed, and exempt infant formula for term infants³ at a maximum use level of 3.0% by weight of the fat blend in formulas containing up to 50% of kilocalories (kcal) as fat. The notice informs us of Hogan Lovells' view that this use of corn oil is GRAS through scientific procedures.

Hogan Lovells provides information about the identity and composition of corn oil. Corn oil is comprised of a mixture of triglycerides, where the predominant fatty acids are linoleic (C18:2 n-6), oleic (C18:1 n-9), and palmitic (C16:0) acids. Hogan Lovells states that the following five fatty acids typically account for more than 90% of corn oil by weight: C16:0 (9-13%), C18:0 (1-3%), C18:1 (24-42%), C18:2 (49-62%), and C18:3 (≤2%). Hogan Lovells notes that corn oil contains total phytosterols at levels up to ~1%, and that these levels are typical in other vegetable oils currently used in infant formula.

Hogan Lovells describes the method of refining corn oil and states that it is obtained

¹ Hogan Lovells submitted Appendices A-C with confidential markings. In an email dated January 9, 2020, Hogan Lovells provided unredacted versions of Appendices A-C showing that only supplier-contact information had been redacted and not information related to safety.

² Hogan Lovells submitted the June 15, 2020, amendment with confidential markings and redacted supplier contact information not related to safety.

³ In amendments dated May 1, 2020, and October 21, 2020, Hogan Lovells specified the infant populations intended to consume infant formula containing corn oil. Hogan Lovells stated that corn oil is intended for term infants (i.e., birth to 12 months of age) with increased energy requirements and/or fluid restrictions and will be used under medical supervision.

from hexane extraction of the germ of *Zea mays* (Fam. Gramineae) grain and from standard methods of degumming, neutralization, bleaching, and deodorization. The bleaching process uses bleaching earth and, optionally, activated carbon.⁴ The deodorization step in the refining process ensures removal of any residual hexane residues. Hogan Lovells states that corn oil is produced in accordance with current good manufacturing practices, and that the corn grain source material is grown in accordance with good agricultural practices and meets appropriate standards for food-grade corn. Hogan Lovells further states that corn oil meets the specifications of the Food Chemicals Codex (FCC 11, 2018).

Hogan Lovells provides specifications for corn oil, including peroxide value (≤ 0.5 meq/kg), iodine value (120-130), free fatty acids ($\leq 0.1\%$), water ($\leq 0.1\%$), arsenic (≤ 0.1 mg/kg), lead (≤ 0.015 mg/kg), unsaponifiable matter ($\leq 1.5\%$), residual hexane (≤ 1 mg/kg), and limits for microorganisms, including *Cronobacter sakazakii* (absent in 10 g) and *Salmonella* serovars (absent in 25 g). Hogan Lovells provides results from non-consecutive batch analyses to demonstrate that corn oil can be manufactured to meet these specifications. Hogan Lovells describes the stability of corn oil as similar to other vegetable oils, with a minimum shelf life of 6 months if stored below 15 °C under nitrogen and away from light.

Hogan Lovells provides an estimate of dietary exposure to corn oil based on the intended use level. Corn oil will be used as part of a blend of fat with other food-grade vegetable oils; the use of corn oil is based on its high level of linoleic acid (an essential fatty acid). Based on the assumptions that infants consume 120 kcal/kg body weight (bw)/day (d),⁵ and that 50% of the calories are fat, Hogan Lovells estimates that infants would typically consume ~6.7 g fat/kg bw/d. Hogan Lovells estimates the 90th percentile value to be 8.0 g fat/kg bw/d, equal to approximately 1.2 times the typical intake value. If corn oil is 3% of fat, then estimates of dietary exposure to corn oil would be 0.2 and 0.24 g/kg bw/d at the mean and 90th percentile, respectively. Hogan Lovells states that the calorically dense formula will be fed to infants weighing up to 9 kg. On a per person (p) basis, the estimates of dietary exposure to corn oil are 1.8 and 2.2 g/p/d for a 9 kg infant at the mean and 90th percentile, respectively. Hogan Lovells also cites a maximum intake level of formula to be 175 kcal/kg bw/d from reports in published studies; at this level, a 9 kg infant would consume 2.6 g corn oil.

Hogan Lovells discusses the safety of corn oil in infant formula and indicates that a literature search for safety information was conducted. The notice discusses the absorption, distribution, metabolism, and excretion (ADME) properties of the triglyceride and plant sterol constituents of corn oil. Hogan Lovells states that the corn oil-containing infant formula can be safely consumed by healthy term infants, as well as the intended infant population in this notice,⁶ because the triglycerides and plant sterols

⁴ Hogan Lovells monitors its corn oil for environmental and processing contaminants (e.g., monochloropropanediol esters and glycidyl esters) and includes treating with activated carbon as needed.

⁵ Hogan Lovells notes that this value is consistent with reference energy needs for catch-up growth outlined by the Institute of Medicine (2005) in Dietary Reference Intakes for Energy, Carbohydrate, Fat, Fatty acids, Cholesterol, Protein, and Amino acids. Washington, DC: The National Academies Press.

⁶ In the amendment dated June 11, 2020, Hogan Lovells discusses the infant populations intended to

in the corn oil are expected to undergo the same metabolic fates known for edible lipids, including triglycerides and plant sterols.

Hogan Lovells discusses the findings of published clinical studies in infants fed infant formula containing corn oil as a principal component of its fat blend to support safety. The subjects of the studies included healthy term infants and low birth-weight infants. The infant formulas were administered for time periods that ranged from 18 days to 27 weeks. No formula-related adverse effects were observed in these studies. In addition, the dietary exposure to corn oil expected from Hogan Lovells' intended use is well below that found in these published studies. Hogan Lovells also assesses the outcome of feeding corn oil-containing infant formula to infants orally versus enterally, and concludes that there is no substantial difference with respect to dietary intake levels and safety. Finally, Hogan Lovells states that based on the intended use of corn oil in infant formula, the exposure to plant sterol constituents is safe.

Based on the totality of the data and information, Hogan Lovells concludes that corn oil 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 corn oil 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. 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.

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 Hogan Lovells' GRAS notice does not alleviate the responsibility of any infant formula manufacturer that intends to market an infant formula containing corn oil to make the submission required by section 412. Infant formulas are the purview of the 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

consume corn oil, as well as data and information supporting the safety of this intended use.

have been instituted and their existence made public, unless one of the exemptions in section 301(ll)(1)-(4) applies. In our evaluation of Hogan Lovells' notice concluding that corn oil 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 oil. Accordingly, our response should not be construed to be a statement that foods containing corn oil, if introduced or delivered for introduction into interstate commerce, would not violate section 301(ll).

Conclusions

Based on the information that Hogan Lovells provided, as well as other information available to FDA, we have no questions at this time regarding Hogan Lovells' conclusion that corn oil is GRAS under its intended conditions of use. This letter is not an affirmation that corn oil 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 000900 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

Susan J.

Carlson -S

Susan Carlson, Ph.D.

Director

Division of Food Ingredients

Office of Food Additive Safety

Center for Food Safety

and Applied Nutrition

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