Agency Response Letter GRAS Notice No. GRN 000226

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CFSAN/Office of Food Additive Safety

January 03, 2008

Edward A. Steele
EAS Consulting Group, LLC
1940 Duke Street, Suite 200
Alexandria, Virginia 22314

Re: GRAS Notice No. GRN 000226

Dear Mr. Steele:

The Food and Drug Administration (FDA) is responding to the notice, dated May 26, 2007, that you submitted on behalf of Enzymotec, Ltd. (Enzymotec) in accordance with the agency's proposed regulation, proposed 21 CFR 170.36 (62 FR 18938; April 17, 1997; Substances Generally Recognized as Safe (GRAS); the GRAS proposal). FDA received the notice on May 29, 2007, filed it on May 31, 2007, and designated it as GRAS Notice No. GRN 000226.

The subject of this notice is lecithin derived from krill (krill-derived lecithin). The notice informs FDA of the view of Enzymotec that krill-derived lecithin is GRAS, through scientific procedures, for use in various products as described below (Table 1).

Table 1
Enzymotec's intended conditions of use

Food	Level of Use
Breakfast bars	3.8 percent
Dairy product analogs (soy products)	0.6 percent
Fat spreads	10.0 percent
Milk-based beverages	0.6 percent
Yogurt	0.7 percent
Soft candy	3.3 percent

Enzymotec's krill-derived lecithin is a complex mixture of primarily neutral and polar phospholipids, with phosphatidylcholine as the principle phospholipid present. Enzymotec defines phosphatidylcholine as 1,2-diacyl-*sn*-glycero-3-phosphocholine. Enzymotec notes that the fatty acid substituents of phosphatidylserine from plant and marine sources are different. In the case of krill-derived lecithin, Enzymotec notes that these fatty acids are primarily the long-chain polyunsaturated fatty acids docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA). Enzymotec notes that plant-derived lecithin is GRAS for use in foods generally, in accordance with good manufacturing practices (21 CFR 184.1400).

Enzymotec describes the method of manufacture of its krill-derived lecithin. Krill are shrimp-like crustaceans of the family Euphausiidae. The starting material is a composite biomass of krill known as krill meal. The protein and sugar content of the krill meal is removed using a solvent extraction process, leaving the lecithin-containing lipid fraction. Enzymotec notes that the solvents used in this process are of food-grade quality and are used in accordance with the current good manufacturing practice.

Enzymotec states that krill-derived lecithin is produced in two grades, A and B that differ in the purification level of phospholipids and the combined DHA and EPA content. For Grade A, total phospholipids are specified to be between 40 and 50% w/w, and for Grade B total phospholipids are to be between 70 and 95% w/w. The combined DHA and EPA content is approximately 14-18% for Grade A, and 20-25% for Grade B. Enzymotec provides batch analysis data indicating that phosphatidylcholine represents up to approximately 80% of the total phospholipids present in both Grade A and Grade B. Batch analysis data also indicate that Grade A contains approximately 50% neutral lipids (mono, di-, triglycerides and free fatty acids), whereas, in Grade B, these are not detected. Enzymotec provides additional specifications for both Grade A and Grade B krill-based lecithin, including peroxide value, moisture, lead, cadmium and mercury.

Enzymotec states that phosphatidylcholine is a common constituent of plant and animal cells and, as such, is a normal constituent of the human diet. Enzymotec describes several commonly consumed phosphatidylcholine-rich foods, such as egg yolk, soybean oil, sunflower oil, rapeseed oil, various grains, wheat germ, fish, legumes, yeast, and peanuts.

Enzymotec indicates that the metabolism of phosphatidylcholine is well described in the scientific literature and notes that there is no difference in the metabolism of phosphatidylcholine derived from plant or animal sources. Enzymotec reviews published information regarding the normal absorption, distribution, metabolism and excretion of phosphatidylcholine consumed in the diet indicating that phosphatidylcholine is metabolized through well-described processes to safe and endogenous products.

Enzymotec discusses FDA's recommendations regarding the levels of menhaden oil used in various foods that are consistent with safe levels of exposure to DHA and EPA.(1) Enzymotec emphasizes that in all applications where either krill-based lecithin or menhaden oil can be used, the levels of lecithin (hence the combined levels of DHA and EPA) from krill-based lecithin are lower than what is allowed from menhaden oil. The notifier also assures that krill-based lecithin will not be used in foods that contain other significant sources of DHA and EPA as ingredients. The notifier also states that the menhaden oil rule permits several additional applications where krill-based lecithin would not be used.

With regard to potential environmental contaminants associated with krill that could pose a health risk, Enzymotec notes that krill are unlikely to bioaccumulate lipid-soluble environmental contaminants since they are very low in the marine food chain. Further, Enzymotec presents analytical data for both Grade A and Grade B lipid fractions for contaminants, such as PCBs, pesticides, dioxins, arsenic, lead, mercury and cadmium, and state that the levels are consistent with levels found in other food ingredients.

Allergen Labeling

The Food Allergen Labeling and Consumer Protection Act of 2004 (FALCPA) amends the Federal Food, Drug, and Cosmetic Act to require that the label of a food that is or contains an ingredient that bears or contains a "major food allergen" declare the presence of the allergen (section 403 (w)). FALCPA defines a "major food allergen" as one of eight foods or food groups (i.e., milk, eggs, fish, Crustacean shellfish, tree nuts, peanuts, wheat, and soybeans) or a food ingredient that contains protein derived from one of those foods. Issues associated with labeling food are the responsibility of the Center for Food Safety and Applied Nutrition's Office of Nutritional Products, Labeling, and Dietary Supplements.

Standards of Identity

In the notice, Enzymotec states its intention to use krill-derived 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.

Conclusion

Based on the information provided by Enzymotec, as well as other information available to FDA, the agency has no questions at this time regarding Enzymotec's conclusion that krill-derived lecithin is GRAS under the intended conditions of use. The agency has not, however, made its own determination regarding the GRAS status of the subject use of krill-derived lecithin. As always, it is the continuing responsibility of Enzymotec to ensure that food ingredients that the firm markets are safe, and are otherwise in compliance with all applicable legal and regulatory requirements.

In accordance with proposed 21 CFR 170.36(f), a copy of the text of this letter responding to GRN 000226, as well as a copy of the information in this notice that conforms to the information in the proposed GRAS exemption claim (proposed 21 CFR 170.36(c)(1)), is available for public review and copying on the homepage of the Office of Food Additive Safety (on the Internet at http://www.cfsan.fda.gov/~lrd/foodadd.html).

Sincerely,

Laura M. Tarantino, Ph.D.
Director
Office of Food Additive Safety
Center for Food Safety and Applied Nutrition

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(1)FDA has affirmed the GRAS status of menhaden oil for use as a direct food ingredient (21 CFR 184.1472) provided that the combined intake of EPA and DHA from consumption of menhaden oil does not exceed 3 grams per person per day (g/p/d). FDA had raised concerns about the consumption of high levels of EPA and DHA and possible adverse effects of consumption on bleeding time, glycemic control, and low-density lipoprotein cholesterol levels (62 FR 30751 at 30757; June 5, 1997). FDA subsequently revised the menhaden oil rule to reallocate the uses of menhaden oil in conventional food, while maintaining the 3 g/p/d limit on EPA and DHA, and to require that menhaden oil not be used as an ingredient in foods in combination with another added oil that is a significant source of EPA and DHA (70 FR 14530; March 23, 2005).

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