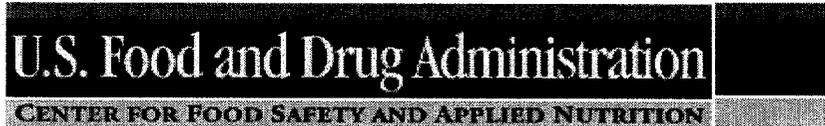


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CFSAN/Office of Food Additive Safety
April 20, 2004

Agency Response Letter GRAS Notice No. GRN 000138

Dr. James T. Heimbach
JHeimbach LLC
4530 Broad Branch Road, N.W.
Washington, DC 20008

Re: GRAS Notice No. GRN 000138

Dear Dr. Heimbach:

The Food and Drug Administration (FDA) is responding to the notice, dated September 26, 2003, that you submitted on behalf of Ocean Nutrition Canada, Ltd. (ONC), 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 October 1, 2003, filed it on October 3, 2003, and designated it as GRAS Notice No. GRN 000138.

ONC describes the subject of the notice as 18/12 TG, which is a fish oil derived predominantly from anchovy. For the purpose of this letter, FDA refers to this ingredient as "fish oil (predominantly anchovy)" and, for simplicity, "fish oil." The notice informs FDA of the view of ONC that its fish oil is GRAS, through scientific procedures, for use as a direct food ingredient at the levels listed in Table 1. ONC describes two formulations of its fish oil: an oil and a microencapsulated oil product. At this time, ONC intends for the oil to be used in the same food categories as those currently listed in 21 CFR 184.1472(a)(3) (menhaden oil) at levels that are 67 percent of the levels specified in that regulation. In the microencapsulated form of its product, fish oil constitutes approximately 55-60 percent (by weight) of the dry powder. ONC, therefore, intends for the microencapsulated oil product to

be used in the same food categories as those currently listed in the menhaden oil regulation at levels that are 120 percent of the levels specified in that regulation. These use levels are listed in Table 1 as 'Initial Intended Use Levels.' ONC notes that the FDA issued a proposed rule (menhaden oil proposal; 67 FR 8744, February 26, 2002) that would amend 21 CFR 184.1472(a)(3) by changing the maximum use levels and food categories in which menhaden oil may be used. ONC asked that the agency apply any such amendments to its fish oil. These values are incorporated in the column labeled 'Future Intended Use Levels' in Table 1. Subsequent to receiving ONC's notice, FDA issued a tentative final rule that would amend 21 CFR 184.1472 (69 FR 2313; January 15, 2004).

As with the use of menhaden oil, the maximum levels of use of ONC's fish oil are designed to assure that the combined daily intake of two fatty acids that are components of its fish oil and microencapsulated fish oil product (i.e., eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA)) would not exceed 3 grams per person per day (g/p/d). In its notice dated September 26, 2003, ONC notes that its fish oil would be used as the sole added source of EPA and DHA in any given food category and that its fish oil would not be combined or augmented with any other EPA/DHA-rich oil in making a food product.

In GRN 000138, ONC includes a summary of conclusions of a panel of individuals (ONC's GRAS panel) who evaluated the data and information that are the basis for ONC's GRAS determination. ONC considers the members of its GRAS panel to be qualified by scientific training and experience to evaluate the safety of substances added to food. ONC's GRAS panel evaluated dietary exposure, source of the substance, method of manufacture, specifications, contaminant levels, and information from recent published toxicological and human studies. ONC's GRAS panel concluded that fish oil and microencapsulated fish oil product, meeting food grade specifications, are GRAS under the intended conditions of use.

ONC describes the intended use of fish oil in foods and provides a table that lists the food categories and intended use level in each food category (Table 1). ONC's fish oil is intended to be used as a direct food ingredient in food categories listed in 21 CFR 184.1472(a)(3) at maximum use levels that are 67 percent of the levels specified in that regulation. ONC intends for the microencapsulated fish oil product to be used in the same food categories as those currently listed in the menhaden oil regulation at levels that are 120 percent of the levels specified in that regulation. ONC estimates that the mean intake of EPA and DHA combined from the proposed uses of ONC's fish oil would not exceed 3 g/p/d.

Table 1
Maximum Intended Use Levels of Free and Microencapsulated Fish Oil Product*

Food Category	Initial Intended Use Levels (percent by Weight)		Future Intended Use Levels (Percent by Weight)	
	Fish Oil	Micro-encapsulated Fish Oil Product	Fish Oil	Micro-encapsulated Fish Oil Product

Cookies, crackers (1)**	3.3	6.0	-	-
Breads, rolls (white and dark) (1)**	0.7	1.2	-	-
Fruit pies, custard pies (1)**	4.7	8.4	-	-
Cakes (1)**	6.7	12.0	-	-
Cereals (4)	2.7	4.8	2.7	4.8
Baked goods and baking mixes (1)	-	-	3.3	6.0
Fats and oils (12) (not including infant formula)	13.4	24.0	8.0	14.4
Yogurt (31)***	2.7	4.8	-	-
Milk products (31)	-	-	3.3	6.0
Cheese products (5)	3.3	6.0	3.3	6.0
Frozen dairy products (20)	3.3	6.0	3.3	6.0
Meat products (29)	6.7	12.0	3.3	6.0
Egg products (11)	3.3	6.0	3.3	6.0
Fish products (13)	13.4	24.0	3.3	6.0
Condiments (8)	3.3	6.0	3.3	6.0
Soup mixes (40)	2.0	3.6	2.0	3.6
Snack foods (37)	3.3	6.0	3.3	6.0
Nut products (32)	3.3	6.0	3.3	6.0
Gravies and sauces (24)	3.3	6.0	3.3	6.0
Plant protein products (33)	-	-	3.3	6.0
Processed vegetable juices (36)	-	-	0.7	1.2
Hard candy (25)	-	-	6.7	12.0
Soft candy (38)	-	-	2.7	4.8
Jams and jellies (28)	-	-	4.7	8.4
Dairy product analogs (10)	-	-	3.3	6.0
Nonalcoholic beverages (3)	-	-	0.3	0.6
Pastas (23)	-	-	1.3	2.4
Poultry products (34)	-	-	2.0	3.6
Processed fruit juices (35)	-	-	0.7	1.2
White granulated sugar (41)	-	-	2.7	4.8
Sugar substitutes (42)	-	-	6.7	12.0

Chewing gum (6)	-	-	2.0	3.6
Gelatins and puddings (22)	-	-	0.7	1.2
Confections and frosting (9)	-	-	3.3	6.0
Sweet sauces, toppings, and syrups (43)	-	-	3.3	6.0
<p>* The food categories correspond to those listed in 21 CFR 170.3(n). The number in parenthesis following each food category is the paragraph listing of that food category in 21 CFR 170.3(n). ** Subsumed by "baked goods and baking mixes." *** Subsumed by "milk products."</p>				

ONC describes generally available information about the identity and composition of fish oil (predominantly anchovy). ONC's fish oil is a mixture of fatty acids, primarily in the form of triglycerides. ONC presents the fatty acid profiles for fish oil, herring oil, sardine oil, and salmon oil to show that its fish oil is similar to other edible fish oils. ONC's fish oil contains EPA at a level of approximately 18.5 percent (by weight) of total fatty acids and DHA at a level of approximately 11.8 percent (by weight) of total fatty acids, for a combined level of EPA and DHA of approximately 30 percent (by weight) of total fatty acids. By comparison, menhaden oil contains a combined level of EPA and DHA of approximately 21 to 22 percent of total fatty acids.

ONC also describes the manufacture of its fish oil (predominantly anchovy). ONC's fish oil is extracted from multiple edible marine fish species caught off the coast of Peru, including anchovy (95-99 percent), sardine (1-5 percent), jack mackerel, Pacific mackerel, and other occasional species. Processing of the crude fish oil extract includes: 1) winterization; 2) deodorization; 3) treating with activated carbon (discussed in more detail below); 4) bleaching; and 5) blending with mixed tocopherols and other appropriate antioxidants. Optional steps include alkali refining (also called neutralization), and treatment with citric acid. Microencapsulated fish oil product is manufactured by encapsulating it in a crosslinked gelatin/polyphosphate shell. ONC provides specifications for the crude oil, the food-grade oil, and the food-grade, microencapsulated oil product.

In a series of meetings between FDA and ONC on February 13, 2004, and March 31, 2004, FDA and ONC discussed the potential for contamination of ONC's product with polycyclic aromatic hydrocarbons (PAHs). At the latter meeting, and reiterated in an amendment from ONC dated April 2, 2004, ONC provided data to demonstrate that an activated carbon treatment, described in the original notice as 'optional,' successfully reduces the levels of PAH in oils, including its fish oil. ONC stated that it is revising its standard procedure by removing the word 'optional' and requiring that activated carbon be used as a standard part of the production of the fish oil product that is the subject of GRN 138.

ONC acknowledges that FDA has previously raised concerns about the consumption of high levels of two fatty acids (i.e., DHA and EPA), which may increase bleeding time, increase levels of low-density lipoprotein cholesterol, and have an effect on glycemic control in non-insulin dependent diabetics (menhaden oil final rule; 62 FR 30571; June 5, 1997). In affirming the GRAS status of menhaden oil, FDA concluded that the use of

menhaden oil as a direct food ingredient is GRAS, provided that the combined daily intake of EPA and DHA from consumption of menhaden oil does not exceed 3 grams per person per day (g/p/d). To assure that the combined exposure to EPA and DHA would not exceed 3 g/p/d, FDA established maximum levels of use of menhaden oil that would be permitted in specified food categories (21 CFR 184.1472(a)(3)). In ONC's view, a review of the scientific literature published since FDA issued the menhaden oil final rule confirms FDA's conclusion that consumption of EPA and DHA is safe as long as the combined daily intake does not exceed 3 g/p/d.

Based on the information provided by ONC, as well as other information available to FDA, the agency has no questions at this time regarding ONC's conclusion that fish oil (predominantly anchovy) 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 fish oil. As always, it is the continuing responsibility of ONC to ensure that food ingredients that the firm markets are safe, and are otherwise in compliance with all applicable legal and regulatory requirements.

During its evaluation of GRN 000138, FDA consulted with the Labeling and Consumer Protection Staff of the Food Safety and Inspection Service (FSIS) of the United States Department of Agriculture (USDA). Under the Federal Meat Inspection Act and the Poultry Products Inspection Act, FSIS is responsible for determining the efficacy and suitability of food ingredients in meat and poultry products as well as prescribing safe conditions of use. Suitability relates to the effectiveness of the ingredient in performing the intended purpose of use and the assurance that the conditions of use will not result in an adulterated product, or one that misleads consumers. FSIS advised that ONC seek regulatory guidance about the use of these ingredients in meat and poultry products from Dr. Robert Post, Director of Labeling and Consumer Protection Staff, Office of Policy, Program Development and Evaluation, Food Safety and Inspection Service, 1400 Independence Ave., S.W., Suite 602, Annex, Washington, DC 20250-3700. The telephone number for his office is (202)205-0279 and the telefax number is (202)205-3625.

In accordance with proposed 21 CFR 170.36(f), a copy of the text of this letter, as well as a copy of the information in your notice that conforms to the information in 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,

/s/

George H. Pauli, Ph.D.

Acting Director

Office of Food Additive Safety

Center for Food Safety

and Applied Nutrition

cc: Dr. Robert Post, Director
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