GR

Orginial Submission

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3/21/2002

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OFFICE OF
FOOD ADDITIVE SAFETY

Office of Premarket Approval (HFS-200)
Center for Food Safety and Applied Nutrition
Food and Drug Administration
200 C St, SW
Washington DC, 20204

GRAS Notice

Notifier:

Dr. Edward Iorio representing Jedwards International
10 Furnace Brook Parkway
Quincy, MA 02169

Location of supporting documentation:

10 Furnace Brook Parkway
Quincy, MA 02169

Small planktivorous pelagic fish body oil (SPPFBO), as a direct human food ingredient, is exempt from the premarket approval requirements of the Food, Drug, and Cosmetic Act because Jedwards International has determined that such use is GRAS. This determination is based upon a scientific procedure.

The data and information that are the basis for Jedwards International's GRAS determination are available for the Food and Drug Administration's review and copying at reasonable times at the above address or will be sent to FDA upon request.

SPPFBO is made up of the body oil of small planktivorous pelagic fish, primarily sea-harvested Sardine (*Sardina pilchardus*) and Anchovy (*Cetengraulis mysticetus*). Menhaden, Sardine and Anchovy are all plankton eating fish closely related to Herring differing essentially only in size. SPPFBO is manufactured in the same manner as Menhaden oil and is virtually chemically identical in composition, with the notable exception that it contains a higher level of the omega-3 fatty acids EPA and DHA. Therefore, we submit that SPPFBO could be safely used as a natural source of omega-3 fatty acids at reduced levels to those currently approved for Menhaden oil.

Upon examining the fatty acid profiles of Menhaden and SPPFBO the similarity is immediately apparent. (Data on Menhaden and Soybean oil obtained from the Menhaden oil GRAS petition; 21 CFR part 184 Docket No. 86G-0289 hereby incorporated by reference in its entirety).

Fatty acid profile (% weight):

Fatty acid	Menhaden	SPPFBO	Soybean
14:0	9.0	6.5	0.2
16:0	19.0	15.5	10.7
18:0	3.8	2.9	3.9
16:1	13.3	8.3	0.3
18:1	15.5	10.1	22.8
22:1	0.7	1.3	-
18:2	2.0	1.2	50.8
18:3	1.0	0.7	6.8
20:5	12.5	18.0	-
22:6	7.9	12.0	-

SPPFBO is desirable as a direct human food ingredient because of the high level of unsaturated fatty acids it contains naturally. There has been no formal determination of the health benefits of these substances nor is any health claim being made here. However, the FDA did conduct a study to evaluate the claim that consumption of omega-3 fatty acids is associated with a decreased risk of coronary heat disease. In the Federal Register of January 6, 1993 (58 FR 2682), the FDA published a final rule not to allow a direct claim due to

conflicting evidence in the scientific literature but did acknowledge there was a large body of evidence that seemed to support the claim.

SPPFBO would be used at levels 1/3 lower than those established by the accepted levels for Menhaden oil in CFR Title 21 sec. 184.1472 in order to ensure conformity with the approved 3 g/p/d limit for omega-3 fatty acids. The general population would be expected to consume these foods. Therefore, if there were any alterations to the approved method for use of Menhaden oil the same would apply to SPPFBO. The proposed uses for Menhaden oil and therefore SPPFBO as well are listed below:

Category of food	Maximum level of use in food
Cookies, crackers,	3.3%
Breads, rolls (white & dark)	0.7%
Fruit pies, custard pies	4.7%
Cakes	6.7%
Cereals	2.7%
Fats, oils (but not in infant formulas)	13.3%
Yogurt	2.7%
Cheese products	3.3%
Frozen dairy products	3.3%
Meat products	6.7%
Egg products	3.3%
Fish products	13.3%
Condiments	3.3%
Soup mixes	2.0%
Snack foods	3.3%
Nut products	3.3%
Gravies, sauces	3.3%

This product has no single chemical name since, like other edible vegetable oils, it consists of a complex mixtures of glycerides, fatty acids, unsaponifiables and phospholipids. The CAS registry number for fish oils is 8016-13-5.

As in the case of other food lipids, SPPFBO consists mainly of a mixture of triglycerides of various long chain fatty acids with small amounts of mono and diglycerides. Triglycerides are

esters of glycerol and fatty acids with chains of 14 to 22 carbon atoms. The fatty acids that characterize SPPFBO and other fish oil are similar to those in the various edible vegetable oils and animals fats differing principally in their relatively higher proportions of polyunsaturated fatty acids with five and six double bonds.

General Specifications for SPPFBO:
SPPFBO is a clear brilliant yellow oil. Odor and taste are fishy, but not rancid.

Specification	**Value**
Saponification value	Min 180 KOH/g
Iodine number	Min 150 g I/100g
Unsaponifiable matter	Max 1.3%
Free fatty acid	Max 0.5%
Peroxide value	Max 5 meq/Kg
Lead	Max 0.1 ppm
Mercury	Max 0.5 ppm

Specific method references are listed in CFR title 21 184.1472 Menhaden oil.

The processing of fish oils regardless of the species is standardized. The fish are cooked and pressed, the oil being separated from the expressed liquor and processed further in accordance with current good manufacturing practice using standard methods and equipment employed in the processing of other edible oils and fats. Refining involves winterization, neutralization, bleaching and deodorization.

Based on the findings of the Food and Drug Administrations report 21 CFR Part 184 [Docket No. 86G-0289] incorporated here by reference in its entirety consumption of fish oil is limited to 3 g/p/d of the omega-3 fatty acids EPA and DHA (EPA: Eicosapentaenoic Acid, DHA: Docosahexanoic Acid).

Jedwards International's GRAS determination is based upon a scientific procedure and supported by the following: (1) the precedent that the FDA has affirmed the oil produced from Menhaden, a type of planktivorous pelagic fish (Sec. 184.1472 of Title 21) GRAS as a direct food substance with specific limitations; (2) the scientific documentation and literature review, included in the Menhaden oil petition (Food additive petition for Menhaden oil under 21 CFR part 184 Docket No. 86G-0289 hereby incorporated by reference in its entirety) which discusses the oils of these types of fish. An exhaustive chemical analysis of fish oils

can be found in the formal petition for GRAS status of Menhaden oil. Additionally, chemical techniques for the analysis of fish oils as well as copies of a very large body of scientific literature from around the world are included in the petition and are available both at the FDA's archives as well as on record at Jedwards International. Supporting material was obtained by Jedwards International from the FDA freedom of information staff (HFI- 35, 5600 Fishers lane, Rockville, MD 20857).

Sardines and Anchovy are widely consumed as food products in the United States. Therefore, the fish oil derived from this type of fish is already consumed indirectly. Isolated fish body oils of planktivrous pelagic fish have been consumed in the United States as an encapsulated dietary supplement for at least two decades. Cod Liver oil has been widely consumed for a long time in sizeable daily doses and is identified as safe for human consumption by its inclusion in the U.S. Pharmacopeia.

Health concerns for fish oil are limited. However in the Food and Drug administrations report 21 CFR Part 184 [Docket No. 86G-0289] incorporated here by reference, a few health concerns are examined. The health concern for fish oils that were examined include: (1) the possibility that omega-3 fatty acids may cause increased bleeding times; (2) the possibility that non-insulin-dependent diabetics may experience increased glucose levels; (3) the possibility of increased LDL levels following fish oil consumption. The FDA examined the scientific documentation for these health concerns and found conflicting results. However, the body of evidence supported the conclusion that there appeared to be no statistically relevant risks as long as the consumption of fish oil is limited to 3 g/p/d of EPA and DHA.

Regards,

Dr. Edward James Iorio, Ph.D.
Special Projects Director
3/21/2002

End Submission

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Edward James Iorio
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7/15/2002

Division of Biotechnology and
GRAS Notice Review
5100 Paint Branch Parkway
HFS-255
College Park, MD 20740-3835
Att: Karin Ricker, Ph.D.
Consumer Safety Officer

RECEIVED
JUL 18 2002
OFFICE OF
FOOD ADDITIVE SAFETY

Dear Karin:

Please allow me to clarify certain points about which the FDA has expressed concern. Regarding GRAS submission 102 [Small planktivorous pelagic fish body oil (SPPFBO)], this substance is to be used as the only supplemental source of EPA and DHA in any given food category and is not to be combined or augmented with any other food ingredient containing EPA and DHA. This is to maintain the integrity of the 3 g/p/d limit which the FDA recommends.

Furthermore, if the proposed rules in Docket No. 99P-5332, 21 CFR Part 184 are adopted then the new levels for use of Small planktivorous pelagic fish body oil will effectively be the following:

Baked goods and baking mixes	3.3%
Cereals	2.7
Cheese Products	3.3
Condiments	3.3
Egg Products	3.3
Fats and Oils, but not in infant formula	8.0
Fish products	3.3
Frozen dairy desserts	3.3
Gravies and sauces	3.3
Meat Products	3.3
Milk Products	3.3
Nut Products	3.3

Snack Foods	3.3
Soup mixes	2.0
Nonalcoholic beverages	0.3
Chewing gum	2.0
Confections and frostings	3.3
Diary product analogs	3.3
Gelatins and puddings	0.7
Pastas	1.3
Hard Candy	6.7
Jams and jellies	4.7
Plant protein products	3.3
Poultry products	2.0
Processed fruit juices	0.7
Processed vegetable juices	0.7
Soft Candy	2.7
White granulated sugar	2.7
Sugar substitutes	6.7
Sweet sauces, toppings, and syrups	3.3

Regards,

Edward James Iorio, Ph.D.
Special Projects Director
7/15/02