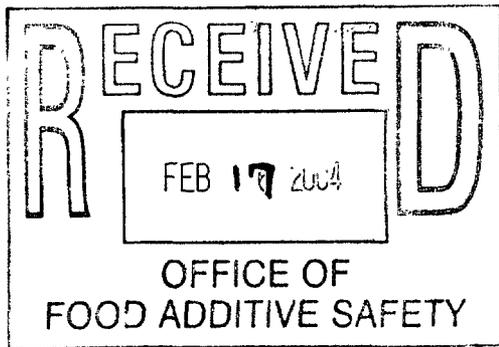


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ORIGINAL SUBMISSION

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04-02-17P03902-ARNV

87305

Dr. Edward Iorio
10 Furnace Brook Parkway
Quincy, MA 02169
(617)-472-9300
Fax: (617)-472-9359
jedwardsinc@mindspring.com
2/11/2004

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

Salmon Oil 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.

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Salmon oil is made up of the body oil of salmon, primarily *Salmo Salar*. Salmon oil is manufactured in the same manner as Menhaden oil and is virtually chemically identical in composition. Both Salmon oil and Menhaden oil both have omega-3 levels of approximately 20%. Where Menhaden oil is 12% EPA and 8% DHA, Salmon oil is 8% EPA and 12% DHA. Therefore, we submit that Salmon oil could be safely used as a natural source of omega-3 fatty acids at the same levels to those currently approved for Menhaden oil.

Salmon Oil 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 heart 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.

Salmon oil would be used at the same levels as those established by the accepted levels for Menhaden oil in CFR Title 21 sec. 184.1472 and subsequently updated in Docket No. 99P-5332, 21 CFR Part 184, both of which are hereby incorporated by reference their entirety, 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 Salmon oil. The proposed uses for Menhaden oil and therefore Salmon oil as well are listed below:

Baked goods and baking mixes	5.0%
Cereals	4.0
Cheese Products	5.0
Condiments	5.0
Egg Products	5.0
Fats and Oils, but not in infant formula	12.0
Fish products	5.0
Frozen dairy desserts	5.0

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Gravies and sauces	5.0
Meat Products	5.0
Milk Products	5.0
Nut Products	5.0
Snack Foods	5.0
Soup mixes	3.0
Nonalcoholic beverages	0.5
Chewing gum	3.0
Confections and frostings	5.0
Diary product analogs	5.0
Gelatins and puddings	1.0
Pastas	2.0
Hard Candy	10.0
Jams and jellies	7.0
Plant protein products	5.0
Poultry products	3.0
Processed fruit juices	1.0
Processed vegetable juices	1.0
Soft Candy	4.0
White granulated sugar	4.0
Sugar substitutes	10.0
Sweet sauces, toppings, and syrups	5.0

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, Salmon oil 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 Salmon oil 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	
Iodine number	Min 140 g I/100g

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Unsaponifiable matter	
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).

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Salmon is widely consumed as food in the United States. Therefore, the fish oil derived from this type of fish is already consumed indirectly. Isolated fish body oils of salmon 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.

Salmon oil 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.

Regards,



Dr. Edward James Iorio, Ph.D.
Special Projects Director
2/11/2004

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SUBMISSION END

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Dr. Edward Iorio
10 Furnace Brook Parkway
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(617)-472-9300
Fax: (617)-472-9359
6/16/04

Richard E. Bonnette
Consumer Safety Officer
Division of Biotechnology and GRAS Notice Review
Office of Food Additive Safety
Center for Food Safety and Applied Nutrition
Food and Drug Administration
5100 Paint Branch Pkwy., HFS-255
College Park, MD 20740

Dear Richard:

Please allow me to clarify certain points about which the FDA has expressed concern. Regarding GRAS submission 146 (Salmon Oil).

1.0 Usage Levels

Salmon oil would be used at the same levels as those established for Menhaden oil in CFR Title 21 sec. 184.1472. The levels listed in GRAS submission 146 as suggested by Docket No. 99P-5332, 21 CFR Part 184 would be adopted for Salmon oil once approved for Menhaden oil.

Current approved levels:

<u>Category of food</u>	<u>Maximum level of use in food</u>
Cookies, crackers,	5.0%
Breads, rolls (white & dark)	1.0%
Fruit pies, custard pies	7.0%
Cakes	10.0%
Cereals	4.0%
Fats, oils (but not in infant formulas)	20.0%
Yogurt	4.0%
Cheese products	5.0%
Frozen dairy products	5.0%
Meat products	10.0%
Egg products	5.0%
Fish products	20.0%
Condiments	5.0%
Soup mixes	3.0%
Snack foods	5.0%
Nut products	5.0%
Gravies, sauces	5.0%

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2.0 Specifications for Salmon oil.

General Specifications for Salmon Oil:

Salmon oil is a light orange colored oil. Odor and taste are fishy, but not rancid.

Specification	Value
Saponification value	Min 180 KOH/g
Iodine number	Min 140 g I/100g
Unsaponifiable matter	Max 1.4%
Free fatty acid	Max 0.5%
Peroxide value	Max 5 meq/Kg
Lead	Max 0.1 ppm
Mercury	Max 0.5 ppm
Dioxin	Max 2 ppt
Dioxin like PCBs	Max 12 ppt

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

The FDA has expressed some concern in PAH which is a toxin produced when organic material is burned without sufficient oxygen present. PAH contamination is generally not considered to be an issue for standard fish oils although it might be a problem in smoked fish products.

Regards,

Edward James Iorio, Ph.D.

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7/6/04

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Food and Drug Administration
5100 Paint Branch Pkwy., HFS-255
College Park, MD 20740
Fax: (202)-418-3034

Dear Richard:

Please allow me to clarify on the issues presented by the FDA in a 6/23/04 email. Regarding GRAS submission 146 (Salmon Oil).

1.0 EPA and DHA level

Crude salmon oil received by the refinery are tested for EPA and DHA levels. Certain lots of salmon are higher in one fatty acid than the other. These lots are then blended to achieve the standardized amount 8/12 which could be viewed as an average.

2.0 Purification methods.

There are two primary methods of purification for salmon oil. Oil is filtered through both clay as well as activated charcoal. The clays tend to remove heavy metal contaminates. The activated charcoal has been show to be effective in removing certain organic contaminants such as dioxin.

3.0 Organochlorine pesticides

Organochlorine pesticides are lower than detection limits in our salmon oil.

Please also find on a separate page a typical certificate of analysis for our salmon oil. (sent by fax)

Regards,

Edward James Iorio, Ph.D.

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CERTIFICATE OF ANALYSIS

PURE SALMON OIL

LOT: 94/04

Date of production: March 8, 2004

Date of Expiration: March 8, 2007

Source: The oil is produced from Atlantic Salmon (Salmon Salar).

Description: Salmon oil is a triglyceride oil. The appearance is a clear brilliant orange / pink. Odor and taste are fishy but not rancid.

	UNITS	LIMITS		RESULT	METHODS
		Min	Max		
C20:5 n3 (EPA)	mg/g	7.2		8.2	AOCS Ce 1b-89 m
C22:6 n3 (DHA)	mg/g	10.8		11.3	AOCS Ce 1b-89 m
Saturated Fatty Acids	Area%			21.8	AOCS Ce 1b-89 m
Monounsaturated Fatty Acids	Area%			39.0	AOCS Ce 1b-89 m
Poly-unsaturated Fatty Acids	Area%			34.6	AOCS Ce 1b-89 m
ACID VALUE	mg KOH/g		1.0	0.2	AOCS Ca 5a-40
PEROXIDE VALUE	mEq/Kg		5.0	1.6	AOCS Cd 8-53
COLD TEST	5.5h/0°C		Pass	Pass	AOCS Cc 11-53
COLOR	Visual	Yellowish	Orange		
VITAMIN E	ppm	1000	2000	1100	
Environmental Analysis					
Dioxin and Furans	ng/kg WHOTEQ		2.0	1.5	Dr Wiertz

Shelf life is guaranteed for three years from the date of production if the product is stored in unopened original container at or below 30°C and protected from light.

Because Salmon Oil is sensitive to oxidation, it is saturated with nitrogen and drummed with nitrogen atmosphere for protection. If drums are opened for sampling, be sure to refill drum atmosphere with nitrogen. Drums that have been opened should be tested at least yearly to ensure potency.

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Bonnette, Richard

From: Edward J Iorio [jedwardsinc@mindspring.com]
Sent: Wednesday, August 04, 2004 2:16 PM
To: 'Bonnette, Richard'
Subject: RE: Question regarding salmon oil GRAS notice GRN 142

Hello Richard:

I received the following information on the pesticides which were tested. The detection limit which is next to each pesticide is in mg/Kg. The salmon oil tests below these limits.

Aldrin < 0,01
Dieldrin < 0,01
Endrine < 0,01
Total chloradane < 0,03
Chlorothalonil < 0,01
Total DDT (DDE, DDE, DDT) < 0,05
Total Endosulfane < 0,03
Alpha -HCH < 0,01
Beta -HCH < 0,01
Delta -HCH < 0,01
Total HCH isomeres < 0,05
Lindane < 0,01
Heptachlor < 0,01
cis-Heptachlor < 0,01
trans- Heptachlor < 0,01
Hexachlorobenzene < 0,01
Mirex < 0,01
Iprodione < 0,05
Procymidone < 0,05
Vinclozolin < 0,01
Sum of Toxaphene- congeners 26, 50 ,62 < 0,06.

Regards,

Ed Iorio

From: Bonnette, Richard [mailto:Richard.Bonnette@cfsan.fda.gov]
Sent: Wednesday, July 21, 2004 12:41 PM
To: 'Edward J Iorio'
Subject: Question regarding salmon oil GRAS notice GRN 142

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Ed,

We do have one more point of clarification regarding the notice and your last addendum (July 6, 2004). I'm hoping that it will be fairly easy to address quickly. Your July 6, 2004, letter stated that organochlorine pesticides are lower than the limits of detection. Can you tell us which pesticides were analyzed, the method(s) used, and the limits of detection?

8/24/2004

Thanks,
Richard

Richard E. Bonnette
Consumer Safety Officer
Division of Biotechnology and GRAS Notice Review
Office of Food Additive Safety
Center for Food Safety and Applied Nutrition
Food and Drug Administration

Mailing Address

5100 Paint Branch Pkwy., HFS-255
College Park, MD 20740

Telephone (202) 418-3034
FAX (202) 418-3179
rbonnett@cfsan.fda.gov

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8/24/2004

SU


Bonnette, Richard

From: Edward J Iorio [jedwardsinc@mindspring.com]
Sent: Friday, August 20, 2004 2:41 PM
To: 'Bonnette, Richard'
Subject: RE: Question regarding salmon oil GRAS notice GRN 142

Richard:

I have some more exact information for you:

PCDD/PCDF- and WHO-PCB-analysis for food and feeding stuff is in consideration of Method 1613 "Tetra- through Octa-chlorinated Dioxins and Furans by Isotope Dilution HRGC/HRMS" from the U.S. Environmental Protection Agency (October 1994).

-Hope this is sufficient.

Ed

From: Bonnette, Richard [mailto:Richard.Bonnette@cfsan.fda.gov]
Sent: Friday, August 20, 2004 7:26 AM
To: 'Edward J Iorio'
Subject: RE: Question regarding salmon oil GRAS notice GRN 142

Ed,
 Thank you for this response. I think we do still need a more specific reference for (or description of) the analytical method used to determine the original concentration prior to calculating the TEQ.
 Thanks,
 Richard

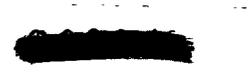
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 rbonnett@cfsan.fda.gov

-----Original Message-----

From: Edward J Iorio [mailto:jedwardsinc@mindspring.com]
Sent: Monday, August 16, 2004 11:48 AM
To: 'Bonnette, Richard'
Subject: RE: Question regarding salmon oil GRAS notice GRN 142

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8/24/2004

Richard:

I received back the following statement from the laboratory that does the analysis:

Regarding method of analyzing Dioxin and Dioxin like PCB (non-ortho and mono-ortho PCB): The method we use is described by WHO (world health organisation) and calculated according to their system.

Is this adequate?

Regards,

Ed Iorio

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8/24/2004

M



Jedwards International
10 Furnace Brook Parkway
Quincy, MA 02169
3/10/05

Consumer Safety Officer
Division of Biotechnology and
GRAS Notice Review
Office of Food Additive Safety
Center for Food Safety and Applied Nutrition
Food and Drug Administration

To whom it may concern:

To the best of our knowledge Salmon oil would not act as an effective color additive with the levels of use described in GRN (146).

Regards,

Edward James Iorio, Ph.D.

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