DEPARTMENT OF HEALTH AND HUMAN SERVICES

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Food and Drug Administration

21 CFR Part 184

[Docket No. 1999P–5332]

Substances Affirmed as Generally Recognized as Safe: Menhaden Oil

AGENCY: Food and Drug Administration, HHS.

ACTION: Tentative final rule.

SUMMARY: The Food and Drug Administration (FDA) is issuing a tentative final rule to amend its regulations by reallocating the uses of menhaden oil in food that currently are established in § 184.1472 (21 CFR 184.1472). FDA has tentatively concluded that these uses of menhaden oil are generally recognized as safe (GRAS), but only when the menhaden oil is not used in combination with other added oils that are significant sources of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). Because FDA's proposed rule of February 26, 2002, did not include a condition of use for other added oils, FDA is issuing this tentative final rule to give interested persons an opportunity to comment on this use limitation.

DATES: Submit written or electronic comments by [*insert date 75 days after date of publication in the* **Federal Register**].

ADDRESSES: Submit written comments to the Division of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to *http://www.fda.gov/dockets/ecomments.*

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FOR FURTHER INFORMATION CONTACT: Andrew J. Zajac, Center for Food Safety and Applied Nutrition (HFS–265), Food and Drug Administration, 5100 Paint Branch Pkwy., College Park, MD 20740–3835, 202–418–3095.

SUPPLEMENTARY INFORMATION:

I. Background

Menhaden oil is a refined marine oil that is derived from menhaden fish (*Brevoortia* species). Menhaden oil differs from edible vegetable oils and animal fats in its high proportion of polyunsaturated fatty acids, including omega-3 fatty acids. EPA and DHA are the major source of omega-3 fatty acids from fish oil and together comprise approximately 20 percent by weight of menhaden oil. In response to a petition (GRASP 6G0316) from the National Fish Meal and Oil Association, FDA issued a final rule on June 5, 1997 (62 FR 30751) (the June 1997 final rule), affirming menhaden oil as GRAS for use as a direct human food ingredient with limitations on the maximum use levels of menhaden oil in specific food categories. FDA concluded that these limitations are necessary to ensure that daily intakes of EPA and DHA from menhaden oil do not exceed 3.0 grams per person per day (g/p/d). As discussed in the following paragraphs, the maximum limit of 3.0 g/p/d on the total daily intake of EPA and DHA is a safeguard against the possible effects of these fatty acids on increased bleeding time (the time taken for bleeding from a standardized skin wound to cease), glycemic control in non-insulin-dependent diabetics, and increased levels of low-density lipoprotein (LDL) cholesterol. The concerns over possible adverse effects of fish oil consumption on bleeding time, glycemic control, and LDL cholesterol were discussed in the June 1997 final rule.

As part of FDA's evaluation of GRASP 6G0316, FDA examined the scientific literature for evidence that consumption of fish oils may contribute to excessive bleeding. In the June 1997 final rule, FDA concluded based on this examination of the scientific literature, including more than 50 reports on fish oils with data on bleeding time, that when consumption of fish oils is limited to 3.0 g/p/d or less of EPA and DHA, there is no significant risk for increased bleeding time beyond the normal range (62 FR 30751 at 30752 to 30753). FDA also concluded that amounts of fish oils providing more than 3.0 g/p/d of EPA and DHA have generally been found to produce increases in bleeding time that are statistically significant, but that there are insufficient data to evaluate the clinical significance of this finding. Therefore, because of the lack of data on clinical significance and because of the potential risk of excessive bleeding in some individuals with intakes at higher levels, FDA concluded that the safety of menhaden oil was generally recognized only at levels that limit intake of EPA and DHA to 3.0 g/p/d.

FDA also concluded in the June 1997 final rule that 3.0 g/p/d of EPA and DHA is a safe level with respect to glycemic control (62 FR 30751 at 30753). This conclusion was based on FDA's review of a series of studies on non-insulin-dependent diabetics. Studies on type-II diabetics that reported increased glucose used higher amounts (4.5 to 8 g/p/d) of omega-3 fatty acids. One study found no change in fasting blood glucose levels among type-II (non-insulin-dependent) diabetics treated with 3.0 g/p/d EPA plus DHA for 2 weeks. Two other studies that used 3.0 g/p/d EPA plus DHA for 6 weeks and 2.7 g/p/d EPA plus DHA for 8 weeks found only transient increases in blood glucose halfway through their respective supplementation periods. Another study that used 3.0 g/p/d EPA plus DHA for 3 weeks found comparable increases in

fasting blood glucose when either fish oil or safflower oil was fed, so the increase cannot be attributed specifically to omega-3 fatty acids. A study that compared the effects of fish oil and olive oil fed 3.0 g/p/d of EPA plus DHA did not find a difference in fasting glucose or glycosylated hemoglobin after fish oil supplementation compared to baseline; they did find a significant difference compared to the olive oil treatment, which produced changes in the opposite direction from fish oil. Based on its evaluation of the available information, FDA concluded in the June 1997 final rule that consumption of EPA and DHA in fish oils at 3.0 g/p/d by diabetics has no clinically significant effect on glycemic control, although higher amounts of EPA and DHA (4.5 g/p/d and above) remain of concern.

The June 1997 final rule also considered the reported effects of fish oil on LDL cholesterol levels in healthy persons with normal cholesterol levels, as well as in persons with diabetes mellitus, hypertension, abnormal blood lipid levels, and cardiovascular disease (62 FR 30751 at 30753 to 30754). As a result of its evaluation, FDA found that although reported study reports are variable, there appears to be a trend toward increased LDL cholesterol values with increased fish oil consumption in all population subgroups, with the magnitude of the increase appearing greater and more consistent in populations with abnormal blood lipid levels, hypertension, diabetes, and cardiovascular disease. Based on its evaluation, FDA concluded that 3.0 g/p/d of EPA and DHA is a safe level with respect to LDL cholesterol.

In the **Federal Register** of February 26, 2002 (67 FR 8744), FDA published a proposed rule to amend § 184.1472 by reallocating the uses of menhaden oil in food, while maintaining the total daily intake of EPA and DHA from menhaden oil at a level not exceeding 3.0 g/p/d. The proposal was based on

a citizen petition from the National Fish Meal and Oil Association. The maximum limit of 3.0 g/p/d on the total daily intake of EPA and DHA is a safeguard against the possible adverse effects discussed in the June 1997 final rule and the February 2002 proposed rule. The reallocation is performed by the following three actions: (1) Reducing the maximum levels of use of menhaden oil in some of the currently listed food categories; (2) adding additional food categories along with assigning maximum levels of use in these new categories; and (3) eliminating the listing of subcategories, e.g., cookies and crackers, breads and rolls, fruit pies and custard pies, and cakes, and including them under broader food categories, e.g., baked goods and baking mixes.

per. A. Zajac 12/23/03 rtg

The purpose of the maximum use levels of menhaden oil in the food categories is to ensure that the total daily intake of EPA and DHA does not exceed 3.0 g/p/d (67 FR 8744 to 8745). When the June 1997 final rule published affirming that menhaden oil is GRAS for use as a direct human food ingredient with specific limitations, FDA considered food sources of EPA and DHA likely to be in the diet at that time, but the agency did not take into account that other sources of EPA and DHA might be developed in the future. The implicit basis for the restrictions in the menhaden oil regulation was that while menhaden oil might be blended with other oils to make a particular food product, the sum of DHA and EPA would not exceed 3.0 g/p/d because other oils were not significant sources of DHA and EPA. However, since publication of the proposed rule, FDA has received notices from three companies that have concluded that fish oils, other than menhaden oil, are GRAS for use in the same food categories as those currently listed in § 184.1472(a)(3) at maximum use levels that are designed to assure that the combined daily intake of EPA and DHA would not exceed 3.0 g/p/d. These oils included small planktivorous

pelagic fish body oil (oil derived primarily from sardine and anchovy fish) (Ref. 1), a fish oil concentrate (manufactured from oil extracted from edible marine fish species that normally include anchovy, sardine, jack mackerel, and mackerel) (Ref. 2), and tuna oil (Ref. 3). In each case, the company acknowledged the concerns raised by FDA in the June 1997 final rule and the proposed rule, about consumption of high levels of EPA and DHA. Furthermore, in each case the company stated that its determination of GRAS status related only to the circumstance where its fish oil product is used as the sole added source of EPA and DHA in any given food category and is not combined or augmented with any other EPA/DHA-rich oil.

Because of developing interest in food ingredients that are sources of EPA and DHA, FDA now believes that it is necessary to state explicitly in the regulation that when menhaden oil is added as an ingredient in foods, it may not be used in combination with any other added oil that is a significant source of EPA and DHA. Without this restriction, the intake of DHA and EPA could exceed 3.0 g/p/d. Because this use restriction was not contained in the proposed rule, FDA is issuing this regulation as a tentative final rule under 21 CFR 10.40(f)(6). FDA will review any comments that are relevant to this condition of use and that are received within the 75-day comment period and will respond accordingly to these comments in the **Federal Register.**

FDA is also making an editorial update to § 184.1472(a)(2)(iii) to reflect that the name for the Office of Premarket Approval has been changed to the Office of Food Additive Safety.

II. Comments on the Proposed Rule

The agency provided 75 days for comments on the proposed rule. At the close of the comment period, the agency had received two comments that

expressed concern regarding the environmental impact of the proposed rule. These two comments are addressed separately in section III of this document. The agency also received comments that were submitted from a fish oil company and a trade association that represents the fish oil industry that merely expressed general support for the agency's proposed rule. The other comments were from individual consumers who were opposed to the proposed rule.

Most of the comments FDA received expressing opposition to the proposed rule objected to declaring menhaden oil on food labels by the name "omega-3 fatty acids" or a variation of this name. Many of these comments asserted that "omega-3 fatty acids" is a misleading name for menhaden oil. Some comments were from vegetarians and vegans who stated that listing menhaden oil by the name "omega-3 fatty acids" will make it difficult for them to avoid this animal product in foods. There were also comments that stated that listing menhaden oil by the name "omega-3 fatty acids" will make it difficult for those with fish allergies to avoid this fish oil in foods.

The proposed rule did not address how menhaden oil is to be listed as an ingredient on food labels. Generally, under section 403(i)(2) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 343(i)(2)), a food is misbranded unless its label bears the common or usual name of each ingredient. Although menhaden oil is a significant source of omega-3 fatty acids, FDA knows of no basis for considering omega-3 fatty acids to be its common or usual name. Any consideration of an alternative name for menhaden oil, such as "omega-3 fatty acids," is outside the scope of the proposed rule.

FDA also received comments from consumers asking the agency to consider the use of omega-3 fatty acids from sources other than menhaden fish,

such as flax seed. FDA notes that although menhaden oil does contain omega-3 fatty acids (primarily EPA and DHA), omega-3 fatty acids are not the subject of the proposed rule. Therefore, the use of other oils is outside the scope of the proposed rule.

A few comments stated that the menhaden fish is unsuitable for human consumption and, therefore, oil from this fish should not be used as a food ingredient. As stated in the proposed rule, menhaden oil is already affirmed as generally recognized as safe as a direct human food ingredient (§ 184.1472). FDA has not received any new information or comments that would alter its previous determination that menhaden oil that meets the specifications in § 184.1472 is generally recognized as safe for use in food under the conditions specified.

Some of the comments FDA received expressing opposition to the proposed rule were against the addition of menhaden oil to foods because of a concern about the possibility of high levels of contaminants in the menhaden oil due to bioaccumulation of these contaminants in the menhaden fish. Bioaccumulation describes the process that results in an increase in the concentration of a chemical in a biological organism over time, compared to the chemical's concentration in the environment. FDA has evaluated data on levels of various chemical contaminants, such as pesticides, polychlorinated biphenyls and dioxins in menhaden oil. Based on these data, FDA finds no basis for a safety concern from food uses of menhaden oil due to possible bioaccumulation of lipophilic chemical contaminants in the source fish.

III. Environmental Impact

The agency received two comments expressing concern about the impact that the proposed rule will have on the menhaden fish population. One

comment asked whether this action will result in the "near extinction" of menhaden, mackerel, and sardines, and further asked how near extinction, if it results, would effect ocean ecosystems. The other comment asserted that menhaden are being overfished to extinction, and that because of their population decline, larger game fish populations off the Atlantic coast are dropping proportionately. Neither comment cited supporting data or information.

To ensure that the maximum sustainable yield of menhaden is not exceeded and to provide long-term production, the menhaden fisheries are monitored by the Atlantic and Gulf States Marine Fisheries Commissions (which are under the jurisdiction of the National Marine Fisheries Service (NMFS)), as well as by State authorities. If there is a threat to the long-term yield of a fishery, generally, limits will be imposed by these organizations. At present, the Atlantic and Gulf menhaden fisheries are considered to be healthy and not overfished. With regard to the impact that the proposed rule will have on mackerel and sardines, the United Nation's Foreign Agricultural Organization reports that the primary practice used to catch menhaden has one of the lowest discard ratios of any method for general commercial fishing. (Less than 3 percent by weight of the total menhaden catch are other species of fish.) In addition, NMFS reports a numerical bycatch incidence (i.e., fish that are unintentionally caught) of less than 0.1 percent for the menhaden fishing industry. For these reasons, the agency does not believe that the proposed rule would result in overfishing of menhaden or have a significant impact on other species of fish. In summary, the comments do not provide a basis on which to change the conclusions of the environmental analysis that was prepared for the proposed rule, as discussed in the following paragraph.

The agency has previously considered the environmental effects of affirming menhaden oil as GRAS as a direct human food ingredient, provided that the combined daily intake of EPA and DHA from menhaden oil does not exceed 3.0 g/p/d (62 FR 30751 at 30754). The analysis assumed that the maximum use levels would be completely used for each food category and concluded that this action will not have a significant impact on the menhaden population. This rule will reallocate the maximum levels among food categories but will not increase the total maximum allowable level. Therefore, our previous analysis is applicable. No new information or comments have been received that would affect the agency's previous determination that there is no significant impact on the human environment, and that an environmental impact statement is not required.

IV. Analysis of Economic Impacts

A. Final Regulatory Impact Analysis

FDA has examined the economic implications of this tentative final rule as required by Executive Order 12866. Executive Order 12866 directs agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). Executive Order 12866 classifies a rule as significant if it meets any one of a number of specified conditions, including: having an annual effect on the economy of $100 million, adversely affecting a sector of the economy in a material way, adversely affecting competition, or adversely affecting jobs. A regulation is also considered a significant regulatory action if it raises novel legal or policy

issues. FDA has determined that this tentative final rule is not a significant regulatory action as defined by Executive Order 12866.

In the economic analysis of the proposed rule, we stated that the main benefit of this rule would be the expansion of the potential uses of menhaden oil made possible by the new maximum levels. Firms choosing to use menhaden oil will bear labeling and other costs. Because these costs are voluntary, they will be borne only if doing so is anticipated to be advantageous to the firm. Although firms making products that now use menhaden oil at levels below the current maximum but above the new maximum could bear potential compliance costs, we noted in the proposed rule that FDA did not know of any products in that category. We received no comments on this conclusion, or on any other part of the preliminary regulatory impact analysis.

B. Final Regulatory Flexibility Analysis

FDA has examined the economic implications of this tentative final rule as required by the Regulatory Flexibility Act (5 U.S.C. 601–612). If a rule has a significant economic impact on a substantial number of small entities, the Regulatory Flexibility Act requires agencies to analyze regulatory options that would lessen the economic effect of the rule on small entities. FDA finds that this tentative final rule would not have a significant economic impact on a substantial number of small entities.

The use of the menhaden oil by any small business is voluntary and will be undertaken only if doing so is anticipated to be advantageous to the small business. Small businesses would only bear a compliance cost if, as stated previously, they make products that are below the current maximum but above the new maximum.

The agency specifically requested comments from small businesses on its assumption that no small businesses make products that will be affected by reducing the maximum levels of menhaden oil in pies, cakes, fats, oils, fish products, and meat products. We received no comments on that assumption or any other part of the initial regulatory flexibility analysis.

C. Unfunded Mandates

Title II of the Unfunded Mandates Reform Act of 1995 (Public Law 104–4) requires cost-benefit and other analyses before any rulemaking if the rule would include a "Federal mandate that may result in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of $100,000,000 or more (adjusted annually for inflation) in any 1 year." The current inflation-adjusted statutory threshold is $112 million. FDA has determined that this tentative final rule does not constitute a significant rule under the Unfunded Mandates Reform Act.

V. Paperwork Reduction Act

This tentative final rule contains no collections of information. Therefore, clearance by the Office of Management and Budget under the Paperwork Reduction Act of 1995 is not required.

VI. Federalism

FDA has analyzed this tentative final rule in accordance with the principles set forth in Executive Order 13132. FDA has determined that the tentative final rule does not contain policies that have substantial direct effects on the States, on the relationship between the National Government and the States, or on the distribution of power and responsibilities among the various levels of government. Because the agency concludes that this tentative final

rule does not contain policies that have federalism implications as defined in the order, a federalism summary impact statement is not required.

VII. Comments

Interested person may submit to the Division of Dockets Management (see **ADDRESSES**) written or electronic comments regarding this document. Submit a single copy of electronic comments or two paper copies of any mailed comments, except that individuals may submit one paper copy. Comments are to be identified with the docket number found in the brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

VIII. References

The following references have been placed on display in the Division of Dockets Management (see **ADDRESSES**) and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday.

1. GRAS notice GRN 000102, including the response letter to GRN 000102 dated September 3, 2002, from Alan M. Rulis of FDA to Edward Iorio of Jedwards International, available at *http://www.cfsan.fda.gov/~rdb/opa-gras.html.*

2. GRAS notice GRN 000105, including the response letter to GRN 000105 dated October 15, 2002, from Alan M. Rulis of FDA to Nancy L. Schnell of Unilever United States, Inc., available at *http://www.cfsan.fda.gov/~rdb/opa-gras.html.*

3. GRAS notice GRN 000109, including the response letter to GRN 000109 dated December 4, 2002, from Alan M. Rulis of FDA to Anthony Young of Piper Rudnick, LLP, available at *http://www.cfsan.fda.gov/~rdb/opa-gras.html.*

List of Subjects in 21 CFR PART 184

✓ RN King Bonb OFR 12-07

Food additives.

■ Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, and redelegated to the Director, Center for Food Safety and Applied Nutrition, it is proposed that 21 CFR part 184 be amended as follows:

PART 184—DIRECT FOOD SUBSTANCES AFFIRMED AS GENERALLY RECOGNIZED AS SAFE

■ 1. The authority citation for 21 CFR part 184 continues to read as follows:

Authority: 21 U.S.C. 321, 342, 348, 371.

■ 2. Section 184.1472 is amended by revising paragraph (a)(2)(iii) and (a)(3) and adding paragraph (a)(4) to read as follows:

§ 184.1472 Menhaden oil.

(a) * * *

(2)(iii) *Saponification value.* Between 180 and 200 as determined by the American Oil Chemists' Society Official Method Cd 3–25—"Saponification Value" (reapproved 1989), which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies of this publication are available from the Office of Food Additive Safety, Center for Food Safety and Applied Nutrition (HFS–200), Food and Drug Administration, 5100 Paint Branch Pkwy., College Park, MD 20740, or available for inspection at the Center for Food Safety and Applied Nutrition's Library, Food and Drug Administration, 5100 Paint Branch Pkwy., College Park, MD 20740, or at the Office of the Federal Register, 800 North Capitol St. NW., suite 700, Washington, DC.

* * * * *

(3) In accordance with § 184.1(b)(2), the ingredient may be used in food only within the following specific limitations to ensure that total intake of

eicosapentaenoic acid or docosahexaenoic acid does not exceed 3.0 grams/ person/day:

Category of food	Maximum level of use in food (as served)
Baked goods, baking mixes, § 170.3(n)(1) of this chapter.	5 0 percent
Cereals, § 170.3(n)(4) of this chapter.	4 0 percent
Cheese products, § 170.3(n)(5) of this chapter.	5 0 percent
Chewing gum, § 170.3(n)(6) of this chapter.	3.0 percent
Condiments, § 170.3(n)(8) of this chapter.	5.0 percent
Confections, frostings, § 170.3(n)(9) of this chapter.	5.0 percent
Dairy product analogs, § 170.3(n)(10) of this chapter.	5.0 percent
Egg products, § 170.3(n)(11) of this chapter.	5.0 percent
Fats, oils, § 170 3(n)(12) of this chapter, but not in infant formula.	12.0 percent
Fish products, § 170.3(n)(13) of this chapter.	5.0 percent
Frozen dairy desserts, § 170.3(n)(20) of this chapter.	5.0 percent
Gelatins, puddings, § 170.3(n)(22) of this chapter.	1.0 percent
Gravies, sauces, § 170.3(n)(24) of this chapter.	5.0 percent
Hard candy, § 170.3(n)(25) of this chapter.	10.0 percent
Jams, jellies, § 170 3(n)(28) of this chapter.	7.0 percent
Meat products, § 170.3(n)(29) of this chapter.	5.0 percent
Milk products, § 170.3(n)(31) of this chapter.	5.0 percent
Nonalcoholic beverages, § 170.3(n)(3) of this chapter.	0.5 percent
Nut products, § 170.3(n)(32) of this chapter.	5.0 percent
Pastas, § 170.3(n)(23) of this chapter.	2.0 percent
Plant protein products, § 170.3(n)(33) of this chapter.	5.0 percent
Poultry products, § 170.3(n)(34) of this chapter.	3.0 percent
Processed fruit juices, § 170.3(n)(35) of this chapter.	1.0 percent
Processed vegetable juices, § 170.3(n)(36) of this chapter.	1.0 percent
Snack foods, § 170.3(n)(37) of this chapter.	5.0 percent
Soft candy, § 170.3(n)(38) of this chapter.	4.0 percent
Soup mixes, § 170.3(n)(40) of this chapter.	3.0 percent
Sugar substitutes, § 170.3(n)(42) of this chapter.	10.0 percent
Sweet sauces, toppings, syrups, § 170.3(n)(43) of this chapter.	5.0 percent
White granulated sugar, § 170.3(n)(41) of this chapter.	4.0 percent

(4) To ensure safe use of the substance, menhaden oil shall not be used in combination with any other added oil that is a significant source of eicosapentaenoic acid or docosahexaenoic acid.

* * * * *

Dated: 1/6/04

January 6, 2004.

L. Robert Lake,
Director,
Office of Regulations and Policy,
Center for Food Safety and Applied Nutrition.

[FR Doc. 03-????? Filed ??-??-03; 8:45 am]

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