555 Eleventh Street, N.W., Suite 1000
Washington, D.C. 20004-1304
Tel: (202) 637-2200 Fax: (202) 637-2201
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December 9, 2005

VIA HAND DELIVERY

Kathleen C. Ellwood, Ph.D.
Director, Division of Nutrition Programs and Labeling
Office of Nutritional Products, Labeling and Dietary Supplements
FDA/CFSAN
HFS-830
5100 Paint Branch Parkway
College Park, MD 20740

Re: Ocean Nutrition Canada, Ltd.: August 26, 2005 Nutrient Content Claim Notification

Dear Dr. Ellwood:

Please find enclosed a courtesy copy of Ocean Nutrition Canada, Ltd.'s Nutrient Content Claim that was filed, and accepted by FDA on August 26, 2005. Prior to filing the Notification, we called FDA to confirm the procedures and address for hand delivery of the Notification. Based on information provided by FDA, a messenger service delivered two copies of the Notification to the Office of Nutritional Products, Labeling and Dietary Supplements at the address identified on the cover page of the attached Notification. The messenger service has provided us with a copy of its delivery manifest from August 26, 2005, which confirms that the Notification was delivered to FDA's office at 5100 Paint Branch Parkway, College Park, MD on August 26. The manifest documents that the Notification was accepted and signed-for by an FDA employee.

We understand that at the time of delivery, the messenger service contacted our office and asked whether the FDA employee could sign for the Notification, as the FDA employee told the messenger that a date stamp was unavailable. We advised the messenger service that a signature would be acceptable, provided that the employee also included the date time that the Notification was accepted. The first page of the attached Notification includes a signature, date and time evidencing acceptance of the Notification.

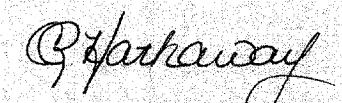
Based on these facts, we believe that the filing of the Notification was effective under the Food and Drug Modernization Act of 1997 ("FDAMA"). While we understand that the Notification, once accepted by the FDA, may have been internally misrouted, this fact does not affect the adequacy or sufficiency of our filing. Therefore, it is our position that the review period provided for in FDAMA began on August 26, 2005, and that the nutrient content claims

2006P-0137 CP 1

proposed in the Notification will therefore become effective on December 26, 2005, 120 days from the date of filing.

Please do not hesitate either Carolyne Hathaway or John Manthei at (202) 637-2200 if you would like to discuss this matter further.

Sincerely,



Carolyne R. Hathaway
John R. Manthei
of LATHAM & WATKINS LLP

Attachments

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Washington, D.C. 20004-1304
Tel: (202) 637-2200 Fax: (202) 637-2201
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August 26, 2005

VIA HAND DELIVERY

Division of Standards & Labeling Regulations
Office of Nutritional Products, Labeling & Dietary Supplements
Center for Food Safety & Applied Nutrition
Food & Drug Administration
HFS - 800
5100 Paint Branch Parkway
College Park, MD 20740-3835

3:50 8/26/05

NOTIFICATION FOR A NUTRIENT CONTENT CLAIM
BASED ON AN AUTHORITATIVE STATEMENT

Submitted by: **Ocean Nutrition Canada, Ltd.**

Dear Sir or Madam:

We submit this notification on behalf of Ocean Nutrition Canada, Ltd. ("ONC") pursuant to section 403(r)(2)(G) of the Federal Food, Drug and Cosmetic Act ("FDCA"),[1] as amended by the Food and Drug Administration Modernization Act of 1997 ("FDAMA"). The purpose of this submission is to notify the Food and Drug Administration ("FDA") of ONC's intent to use nutrient content claims for foods and dietary supplements containing a combination of the Omega-3 fatty acids docosahexaenoic acid ("DHA") and eicosapentaenoic acid ("EPA"). Specifically, this notification proposes a nutrient content claim for a food or dietary supplement that contains an aggregate of 32 mg or more of those nutrients in combination.

These proposed nutrient content claims are based upon authoritative statements made by the Institute of Medicine ("IOM"), a division of the National Academy of Sciences ("NAS"), in its 2002 report entitled *Dietary Reference Intakes: Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein and Amino Acids* (the "IOM Report"). This notification

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1 21 U.S.C. § 343(r)(2)(G).

Guidance for Industry: Notification of a Health Claim or Nutrient Content Claim Based on an Authoritative Statement of a Scientific Body (June 11, 1998) (hereinafter, the "FDA Guidance").[2]

I. INTRODUCTION

At least two nutrient content claim notifications have been filed by interested parties for EPA, DHA and alpha-linolenic acid ("ALA"), or a combination thereof, pursuant to Section 403(r)(2)(G) of the FDCA.[3] Both of these previous notifications rely upon the IOM Report. The first notification, filed by Olsson, Frank and Weeda, P.C. on January 16, 2004 (the "OF&W Notification") proposed nutrient content claims for foods and dietary supplements containing DHA, EPA, and/or ALA. The second notification, filed by Hogan & Hartson LLP on January 21, 2005 (the "Hogan Notification"), proposed the use of nutrient content claims for DHA and ALA, but not EPA. The FDA did not formally object to either of these nutrient content claim notifications, and thus both are effective under law.

Despite both notifications' reliance on the IOM Report, the OF&W Notification and the Hogan Notification proposed strikingly dissimilar nutrient content claims. In the OF&W Notification, a group of seafood producers proposed nutrient content claims based on an interpretation of the IOM Report and relevant FDA regulations that resulted in an artificially high Daily Value ("DV") for the proposed EPA, DHA and ALA claims. The nutrient content claims permissible under OF&W Notification therefore apply only to products containing very high levels of these nutrients – i.e., fatty fish and other seafood products. In contrast, the Hogan Notification applied a more straightforward interpretation of the IOM Report and proposed nutrient content claims that better reflect the relevant FDA regulatory scheme for such claims when promulgated through rulemaking; however, the notification excluded EPA from the scope of the proposed claims.

As discussed in greater detail below, the IOM Report establishes Adequate Intake ("AI") values for ALA for individuals 14 yrs of age or older of 1.1 g per day for females and 1.6 g per day for males.[4] The IOM Report explicitly states that up to 10% of the total AI value for ALA can be contributed by EPA and DHA.[5] Based on this value, the OF&W Notification sought nutrient content claims for DHA and EPA based on 100% of the population-weighted average AI for ALA of 1.3 g per day. Thus, pursuant to the OF&W Notification, a party may make an "excellent source" claim for a product containing 130 mg or more of DHA or EPA. However, under FDA regulations, "excellent source" claims may be made for products

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2 *Guidance for Industry: Notification of a Health Claim or Nutrient Content Claim Based on an Authoritative Statement of a Scientific Body* (June 11, 1998), FDA, Center for Food Safety and Applied Nutrition, Office of Food Labeling, http://www.cfsan.fda.gov/~dms/hclmguid.html.

3 *See* OF&W Notification, FDA Docket No. 2004N-0217; Hogan Notification, FDA Docket No. 2005P-0189.

4 IOM Report at 8-38.

5 *Id.*

containing 20% or more the calculated daily value for a nutrient.[6] Thus, the OF&W Notification proposed a claim inconsistent with the approach FDA has taken in promulgating nutrient content claims for other nutrients. This resulted in a qualifying level (130 mg of DHA or EPA) that is arbitrarily and unnecessarily high.

In contrast, the "excellent source" claims proposed in the Hogan Notification were based on 20% of the AI value for the population group with the highest need (here, adult males). Using these benchmarks, the Hogan Notification proposed "excellent source" claims for products containing 32 mg of DHA or 320 mg of ALA. The Hogan Notification did not, however, include EPA within the scope of its claims.

We believe that the claims proposed in the OF&W Notification are flawed. They are based on a percentage of AI inconsistent with FDA's traditional standard for "excellent source" claims, and they use an arbitrary average AI value rather than the typically-used highest AI measure to determine the appropriate AI value for ALA. Moreover, none of the claims currently permissible under the OF&W or Hogan Notification directly address the *combination of EPA and DHA*, which we believe to be the most appropriate basis for establishing nutrient content claims derived from the IOM Report.

We are therefore submitting this notification in order to establish nutrient content claims that are fully consistent with the IOM Report, which recognizes that both EPA and DHA may contribute to the AI for ALA. Further, this notification proposes claims based on the FDA's regulatory standard of 20% of the AI to establish the threshold amount for "excellent source" claims. We respectfully request that FDA permit "excellent source" claims for products containing 32 mg or more of EPA and DHA in combination, unless and until the agency promulgates a rule clarifying the nutrient content claims that can be made for these important nutrients.

II. THIS NOTIFICATION SUPPORTS THE USE OF A COMBINED EPA/DHA NUTRIENT CONTENT CLAIM PURSUANT TO FDAMA AND FDA GUIDANCE

Under FDAMA, manufacturers may use nutrient content claims based on published, authoritative statements from certain federal scientific bodies, including the National Academy of Sciences and its subdivisions, that are currently in effect and that identify the nutrient level to which the claim refers, provided that a number of elements are met.[7] In particular, as set forth in the statute and the FDA Guidance, in order to make a nutrient content claim, a notification must specify:

(1) The exact words of the nutrient content claim;

(2) The authoritative statement on which the notifier relies in making the nutrient content claim;

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6 *See* 21 C.F.R. § 101.54(b).

7 21 U.S.C. § 343(r)(2)(G)-(H).

(3) A concise description of the bases for determining that the requirements for an authoritative statement have been satisfied; and

(4) A balanced representation of the scientific literature relating to the nutrient level to which the claim refers.[8]

This notification will address each element in turn.

A. Exact Words of the Nutrient Content Claim

This notification proposes the following nutrient content claims:

"Excellent source of Omega-3 EPA and DHA." ("High in Omega-3 EPA and DHA;" "Rich in Omega-3 EPA and DHA"). Contains __ mg of EPA and DHA combined per serving, which is __% of the 160 mg Daily Value for a combination of EPA and DHA. [Products must contain a combined total of at least 32 mg of EPA and DHA to qualify for this claim.]

These claims adopt the terminology of the FDA regulations governing nutrient content claims. Specifically, the regulations provide that claims using the words "high in," "rich in" or "excellent source of" may be used on labels if a product contains at least 20% of the recommended dietary allowance ("RDA") of the nutrient per reference amount customarily consumed ("RACC").[9]

Further, these claims are based on the IOM Report's authoritative statement that up to 10% of the AI of ALA can be contributed by EPA and DHA. As discussed above, two prior notifications regarding these Omega-3 fatty acids have been submitted to FDA and are effective under law. However, neither reflects the IOM's identification of EPA and DHA *in combination*. Our claims therefore more accurately and completely reflect the IOM Report's conclusions.

B. Authoritative Statements on which the Notifier Relies in Making the Nutrient Content Claim regarding EPA and DHA

Our proposed nutrient content claims are consistent with the authoritative statements made regarding EPA and DHA in the IOM Report. The IOM Report establishes an AI for adult males of 1.6 g per day of ALA. The Report explicitly states that "EPA and DHA can contribute up to 10 percent of the total n-3 [Omega] fatty acid intake and therefore up to this

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8 21 U.S.C. § 343(r)(2)(G)-(H); *Guidance for Industry: Notification of a Health Claim or Nutrient Content Claim Based on an Authoritative Statement of a Scientific Body* (June 11, 1998), FDA, Center for Food Safety and Applied Nutrition, Office of Food Labeling, http://www.cfsan.fda.gov/~dms/hclmguid.html.

9 21 C.F.R. § 101.54(b).

percent can contribute towards the AI of [ALA]."[10] Thus, the daily value ("DV") of 160 mg for the combination of EPA and DHA may be derived from the AI for ALA. Applying FDA's 20% regulatory threshold for "excellent source" claims, an excellent source claim can be made for products containing a combined total of at least 32 mg (*i.e.*, 20% of 160 mg) of EPA and DHA.[11]

The IOM Report makes clear that the combination of EPA and DHA may contribute to the 10% of the AI for ALA. For instance, the IOM Report discusses acceptable macronutrient distribution ranges ("AMDRs") of various energy sources (*i.e.*, ranges of intakes for particular energy sources that are associated with reduced risk of chronic disease and that also provide adequate intakes of essential nutrients) and, states that the AMDR for ALA "is set at 0.6 to 1.2 percent of energy," and that up to 10 percent of this range can be consumed as EPA and DHA.[12]

Consistent with the IOM Report, our "excellent source" nutrient content claims may be made for any combination of EPA and DHA, so long as the aggregate amount of EPA and DHA combined is 32 mg. The claims proposed in this notification therefore provide flexibility regarding the levels at which each of these nutrients is present in the product (provided that the required minimum amount is met in the aggregate). This approach more appropriately tracks the language and intent of the IOM Report than do the currently permitted claims.

C. Bases For Determining that the Requirements for an Authoritative Statement Have Been Satisfied

FDAMA requires that nutrient content claims developed by manufacturers and others be based upon published, authoritative statements by certain federal scientific bodies, including the National Academy of Sciences and its subdivisions.[13] Such claims must be currently in effect and identify the nutrient levels to which the claims refer.[14] The FDA Guidance on this topic sets forth six factors to be used in determining whether a statement complies with the FDA requirements

As an initial matter, we note that both the OF&W and Hogan Notifications proposed claims based on the AI for ALA established in the IOM Report, and the Report's

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10 IOM Report at 8-38.

11 We agree with the Hogan Notification's position that it is inappropriate to limit the use of "excellent source" claims to products that contain 100% of the daily value of a nutrient (as required by the OF&W Notification). We believe that the regulatory benchmarks established by FDA (here, 20% of the RDA) should be used to determine when a product contains a sufficient amount of a nutrient to support inclusion of an "excellent source" claim on its labeling. *See* 21 C.F.R. § 101.54(b); *see also* 58 Fed. Reg. 2302, 2344 (Jan. 6, 1993) (FDA states that the 20% threshold is appropriate because it "will permit a sufficient number of food items to bear a high claim to allow consumers to use the claim in selecting a varied diet").

12 IOM Report at S-6 (emphasis added).

13 *See* 403(r)(2)(G).

14 *Id.*

explicit statement that up to 10% of this value can be supplied by a combination of EPA and DHA.. The FDA did not formally object to either of these previous notifications, and both are now legally effective. The claims proposed in this notification rely upon the same authoritative statements in the IOM report, and reflect a more accurate and complete interpretation of those statements. Thus, there is ample justification to conclude that the statements in the IOM Report satisfy the FDAMA statutory criteria and the FDA Guidance.

As FDA did not formally object to the previous nutrient content claim notifications for EPA, DHA and ALA, we believe that FDA should also not object to this notification, rendering it effective under the FDAMA procedures. As discussed in Section I, the currently permissible claims for EPA, DHA and ALA are based on differing interpretations of the operative sections of the IOM Report. The claims proposed in this notification address the inadequacies of the currently permissible claims and create a level playing field for all members of industry pending FDA rulemaking on this subject, should it occur.

Each of the FDA Guidance's six factors is discussed in turn.

(1) **The statement identifies "the nutrient level to which the claim refers":** The IOM Report identifies the adequate intake for ALA (1.6 g. per day) and explicitly provides that 10% of that AI that can come from EPA and DHA (160 mg total).

(2) **The statement is "published by a scientific body":** The statements are made in the published version of the 2002 IOM Report.

(3) **The statement is "currently in effect":** The 2002 IOM Report is the most recent edition of that publication. It is a "comprehensive effort" by the IOM on the subject of Dietary Reference Intakes and has not been superseded by a separate publication.[15]

(4) **The statement does "not include a statement of an employee of the scientific body made in the individual capacity of the employee":** The statements represent the findings, conclusions and recommendations of the Panel on Macronutrients, Panel on the Definition of Dietary Fiber, Subcommittee on Upper Reference Levels of Nutrients, Subcommittee on Interpretation and Uses of Dietary Reference Intakes, and the Standing Committee on the Scientific Evaluation of Dietary Reference Intakes. They are not opinions of individual members of such Panels or Committees.

(5) **The statement "reflect[s] a consensus within the identified scientific body...":** The Food and Nutrition Board ("FNB"), of which the Panels and Committees are a part, is tasked with pursuing the following mission on behalf of the IOM as a whole: "[t]he FNB addresses issues of safety, quality, and adequacy of the food supply; establishes principles and guidelines of

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[15] IOM Report at 1-1.

adequate dietary intake; and renders authoritative judgments on the relationships among food intake, nutrition, and health."[16] The Panels and Committees responsible for developing the IOM Report analyzed the evidence included in the Report and concurred with the Report's conclusions.[17]

(6) **The statement is "based on a deliberative review by the scientific body of the scientific evidence":** The Panel and Committee undertook a "comprehensive effort" in reaching the findings, conclusions and recommendations in the IOM Report. Moreover, the IOM Report underwent institutional review prior to publication.

D. Balanced Presentation of the Scientific Literature Relating to the Level of EPA and DHA to which the Claim Refers

According to FDA Guidance, a "balanced representation of the scientific literature" should include a summary of how available information supports (or detracts from) the authoritative statements made, as well as a bibliography of scientific literature on the subject of the nutrient content claim.[18] The IOM Report includes a balanced review of the scientific literature supporting the establishment of an AI for ALA at 1.6 g/day, and the conclusion that up to 10% of this amount may be contributed by DHA and EPA.[19] Further, the OF&W and Hogan Notifications provide reviews of the scientific literature supporting the nutrient content claims sought in those notifications.[20]

These recent reviews of the scientific literature equally support the claims sought pursuant to this notification, and we will not repeat the lengthy analysis included in those documents. Instead, ONC has reviewed the scientific literature to identify any additional reports that either support or detract from the proposed claims. All scientific reports reviewed in connection with this notification support the authoritative statements of the IOM Report and the

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16 *See Food and Nutrition Board Mission and Priorities*, IOM, at http://www.iom.edu/board.asp?id=3788.

17 *See generally,* IOM Report Preface, pp. xiii-xvi.

18 *See* FDA Guidance.

19 *See* IOM Report Chapter 8 ("Dietary Fats: Total Fat and Fatty Acids"). The bibliography to this Chapter is provided as Attachment A to this notification. The recent publication of the Dietary Guidelines for Americans 2005 by the Department of Health and Human Services and the Department of Agriculture also support the higher, non-weighted average of 1.6 g/day for EPA and DHA. *See* http://www.health.gov/dietaryguidelines/. The report concludes that consumption of approximately two servings of fish per week (approximately 8 ounces total) may reduce the risk of mortality from coronary heart disease. *See id.* at 31. Consumption of this amount would provide approximately 500 mg/day of these nutrients. While the report associates consumption of this amount with reduced risk of coronary heart disease, and does not establish a daily value, it underscores the importance of achieving a high daily intake of EPA and DHA.

20 The bibliography to the Hogan Notification, the more recent of the previous notifications, is provided as Attachment B. The OF&W Notification did not include a separate bibliography.

nutrient content claims currently permissible under it. In fact, the 2005 Report of the Dietary Guidelines Advisory Committee on the Dietary Guidelines for Americans included a thorough review of the scientific literature pertaining to the question: "What are the relationships between n-3 [Omega] fatty acid intake and health?"[21] The Advisory Committee concluded that "[o]verall the evidence from the primary and secondary prevention studies supports the hypothesis that the consumption of n-3 [Omega] fatty acids (EPA, DHA, alpha-linolenic acid), fish and fish oils reduces all-cause mortality and various CVD [cardiovascular disease] outcomes. These outcomes include sudden death and cardiac death (coronary or myocardial in farct (MI) death)."[22]

The health benefits of EPA and DHA in combination have been conclusively established in the scientific literature. We provide below a condensed overview of the current scientific literature pertaining to the health effects of these nutrients. In particular, the following sections summarize literature demonstrating that (1) EPA and DHA are essential structural components of the body, which support key physiological functions; (2) EPA and DHA must be obtained primarily through diet in order for a sufficient amount to be present in the body; and (3) American diets typically provide inadequate amounts of EPA and DHA, such that labeling claims alerting consumers to the percentage of such nutrients in their food and dietary supplement products could benefit the public health.

1. EPA and DHA are essential structural components of the body, which support key physiological functions

EPA and DHA are Omega-3 polyunsaturated fatty acids. EPA is the precursor to Omega-3 eicosanoids, which have been shown to have beneficial effects in preventing coronary heart disease ("CHD"), arrhythmias and thrombosis.[23] EPA-derived Omega-3 eicosanoids have also been found to affect platelet aggregation, vessel wall constriction, and immune cell function.[24] Indeed, as the IOM Report concludes, "[g]rowing evidence suggests that dietary [Omega-3 polyunsaturated fatty acids EPA and DHA] reduce the risk of coronary heart disease and stroke."[25] Much of the evidence supporting this statement is derived from epidemiological studies using natural food sources such as fish and fish oil, which are high in both DHA and

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21 *See* Letter from Janet C. King, Ph.D., Chair, 2005 Dietary Guidelines Advisory Committee to Secretary of Health and Human Services Tommy Thompson and Secretary of Agriculture Ann Veneman, *available at* http://www.health.gov/dietaryguidelines/dga2005/report/HTML/CoverLetter.htm.

22 *See* HHS and USDA, 2005 Dietary Guidelines Advisory Committee Report: Part D (Science Base), Section 4 (Fats), *available at* http://www.health.gov/dietaryguidelines/dga2005/report/HTML/D4_Fats.htm (2005 Advisory Committee Report Science Base).

23 IOM Report at 8-5 (citing Kinsella et al. (1990)).

24 IOM Report at 8-14.

25 IOM Report at 11-40.

EPA, or which otherwise studied EPA in combination with DHA.[26] Scientific evidence supporting this statement includes the following studies:

- A controlled intervention trial of 11,323 adult myocardial infarction patients, dosed with 850-882 mg of EPA and DHA per day, resulted in a significant reduction in mortality after three months and a significant reduction in sudden death after four months.[27]
- A study of subjects in the Los Angeles Atherosclerosis Study with a genotype that increases risk of atherosclerosis found that dietary Omega-3 fatty acids attenuated the atherogenic effect of this genotype.[28]
- A study which examined the serum concentrations of DHA and EPA in 207 male and female subjects found that such concentrations were lower in myocardial infarction patients than in healthy individuals and that the percentage of total Omega-3 polyunsaturated fatty acids was associated with decreased risk of myocardial infarction in the population studied.[29]
- A number of other studies have found a strong association between intake of Omega-3 fatty acids and reduced risk of CHD,[30] and several review papers and meta-analyses have come to similar conclusions that the intake of EPA and DHA reduces the risk of CHD and/or risk of death.[31]

In addition to these robust findings regarding the benefits of Omega-3 fatty acids in reducing the risks of CHD and stroke, EPA appears to have specific effects on fatty acid metabolism, which results in inhibition of triacylglycerol ("TG") synthesis and very low density lipoprotein ("VLDL") secretion in the liver. These effects may result in lower serum TG counts and decreased numbers of highly atherogenic small, dense LDL particles.[32] EPA and DHA also affect eicosanoid metabolism and eicosanoid-dependent mechanisms (*e.g.*, intracellular signaling pathways, transcription factor activity and gene expression) in ways that may modulate expression of autoimmune diseases.[33]

DHA is an integral component of structural membrane lipids and is present in high concentrations in certain phospholipids of the nervous system and the retina. DHA

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26 *Id.*

27 Marchioli, R. et al. (2002).

28 Dwyer, J.H. et al. (2004).

29 Yli-Jama, P. et al. (2002).

30 *See, e.g.*, Albert, C.M et al. (2002); Hu, F.B. et al. (2002); Nilsen, D.W.T. et al. (1999); Lemaitre, R.N. et al. (2003); Hu et al (2003).

31 Mori, T.A. and Beilin, L.J. (2001); Harris, W.S. et al. (2003); Lichtenstein, A.H. (2003); Bucher, H.C. et al. (2002).

32 IOM Report at 8-14 (citing Berge et al., 1999; Wong and Nestel, 1987).

33 Simopoulos, A.P. (2002).

constitutes up to 20% of total fatty acids and up to 50% of the fatty acids in the retina, and thus is essential to optimal performance of these tissues.[34] DHA may contribute to maintaining cognitive activity during aging, as well as normal mental function, including prevention of depression.[35]

2. EPA and DHA must be obtained primarily through diet in order for a sufficient amount to be present in the body

ALA is the precursor in the synthesis of EPA and DHA, which are formed in varying amounts in animal tissues (particularly in fatty fish). Indeed, EPA and DHA are found in combination in several natural dietary sources, including fatty fish, fish oils, shellfish, meat and eggs.[36] EPA and DHA can be synthesized by the human body, but this process is slow, inefficient, and varies based on a number of factors (including, for instance, diet, age, gender and the ratio of Omega-6 to Omega-3 fatty acids present).[37] A number of studies indicate that the human body cannot produce sufficient EPA and DHA through *in vivo* synthesis, indicating the need for dietary supplementation.

- Recent studies and articles address the limited, inefficient conversion of ALA to EPA and DHA.[38]
- Synthesis of EPA from ALA is estimated to be 8% in men.[39] EPA is a shorter long chain fatty acid than DHA, and evidence suggests that the metabolic complexity involved in synthesizing DHA significantly limits the continued processing necessary to create DHA from ALA. The conversion rate of ALA to DHA is unclear, with estimates ranging from 4% to insignificant amounts.[40] Estimated conversion rates for women of reproductive age are higher, with one study reporting a conversion rate of 21% for EPA and 9% for DHA.[41]
- A study using the mean flow rate at which DHA is removed from the plasma of human adult subjects (*i.e.,* either catabolized or taken up into other organ systems) found that, in a 24 hour period, there was a net loss of approximately 173 mg of

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34 Uauy, Hoffman et al. (2001); IOM Report at 8-18.

35 Youdim, K.A., et al. (2000); Adams, P.D. et al. (1996).

36 *See, e.g,* 2005 Advisory Committee Report Science Base, at Table D4-3 ("EPA and DHA Content of Selected Types of Fish).

37 IOM Report at 8-11; SACN (2004); Joshi, et al. (2003); El Hafidi, et al. (2001); Hirosue and Hosogai (1993).

38 Muskiet, F.A.J. et al. (2004); Emken, E. (2003); Salem, N. et al. (2003); De Deckere, et al. (1998).

39 Burdge, et al. (2002); Emken, et al. (1994).

40 Emken et al. (1994); Burdge, et al. (2002); Burdge, et al. (2003).

41 Burdge and Wooton (2002).

DHA from the plasma.[42] This number provides a rough estimate of the amount of DHA required on a daily basis to maintain DHA concentration levels in plasma (the required amounts for the entire body would likely be considerably higher).

- A high ALA diet appears to be insufficient to increase EPA and DHA amounts to the needed levels,[43] particularly for pregnant and nursing women. Studies have found that ALA supplementation during pregnancy and lactation does not significantly increase DHA and EPA levels, while dietary DHA and EPA has been found to increase DHA and EPA levels in the body.[44]

In order to maintain optimal EPA and DHA levels, it is therefore important that EPA and DHA be supplemented by dietary intake.

3. Alerting consumers to the percentage of EPA and DHA in their food and dietary supplement products would be beneficial, as American diets typically provide inadequate amounts of these nutrients

According to the current Continuing Survey of Food Intake by Individuals ("CSFII"), daily EPA intake averages approximately 28 mg for all individuals.[45] This provides less than one-fifth of the amount suggested by the IOM Report for adult males. Similarly, DHA intake in the United States averages approximately 57 mg for all individuals, less than one-half of the amount suggested by the IOM Report for adult males. Further, in certain subpopulations, dietary intake of EPA and DHA is particularly low. These vulnerable populations include pregnant and lactating women, who, according to CSFII data, take in a mean of 20 mg of EPA and 52 mg of DHA per day. These CSFII averages are one-half to one-third of the amounts suggested by the IOM Report for these particular population groups.

Significantly, the IOM Report also notes that the ratio of Omega-6 to Omega-3 polyunsaturated fatty acids (*i.e.*, linolenic acid ("LA") to ALA) appears to affect the levels of DHA and EPA maintained in the body.[46] The IOM Report refers to FAO/WHO recommendations for LA: ALA ratios in the range of 5:1 to 10:1 and to a study of rats which concluded that a ratio of 8:1 was optimal for maintaining normal fatty acid concentrations.[47] Because a high LA:ALA ratio can inhibit conversion of ALA to EPA and DHA, it is of some concern that CSFII data indicate that the majority of the U.S. population has a ratio well in excess of the 5:1 baseline and either at or above the 10:1 ceiling. The mean LA:ALA ratios for the entire U.S. population range from 9.8:1 to 10.9:1.

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42 Pawlowsky, et al. (2003).

43 Pawlosky, et al. (2003); Dyerberg (1980); Sanders, T.A. (1983); Singer (1986); Kestin, et al. (1990); Chan, et al. (1993); Kelly, D.S. (1993); Freese, R. et al. (1994); Allman, et al. (1995).

44 De Groot, et al. (2004); Francois, et al. (2003); Jensen, et al. (2000); Fidler, et al. (2001).

45 *See* IOM Report, E-13.

46 IOM Report at 8-25 and 8-26.

47 ESPGAN Committee on Nutrition, 1991; Bourre, et al., 1996.

Certain sub-populations are particularly at risk. CSFII data suggests that among pregnant and lactating women, the range of LA:ALA for the 50th through 99th percentile is 9.8:1 and 9.2:1, and the range for women of childbearing age is 9.8:1 to 10.3-1. NHANES data suggest that minority populations suffer from an increased risk of inadequate levels of EPA and DHA because they consume much greater amounts of LA as compared to ALA.[48] NHANES data indicate that Mexican Americans have a ratio of LA:ALA of 12.1:1 and non-Hispanic Blacks have a ratio of 11.2:1. For young children under six years of age, CSFII found that children under 6 years of age have ratios ranging from 9.4:1 to 10.4:1, and NHANES determined that this group has a ratio of 10:1. All of these values are well in excess of the 5:1 baseline, and, thus, strongly support the need for increased EPA and DHA consumption.

III. CONCLUSION

This notification proposes nutrient content claims for the combination of EPA and DHA. The claims are to be used in labeling foods and dietary supplements containing a qualifying level of EPA and DHA, and are consistent with previous nutrient content claim notifications for these nutrients which are currently effective under FDAMA. Like the previous notifications, this notification relies upon the authoritative statements in the IOM Report regarding the AI of ALA and the amount of this AI that may be provided by EPA and DHA. In accordance with FDA regulations, "excellent source" claims would be permitted for products containing 20% of the 160 mg AI value for the combination of EPA and DHA; i.e., an aggregate total of at least 32 mgs of EPA and DHA.

We respectfully request that FDA give due consideration to this notification and permit the use of the proposed nutrient content claims proposed herein. Please do not hesitate to contact the undersigned at (202) 637-2200 should you have any questions or require additional information regarding this matter.

Respectfully submitted,

Carolyne R. Hathaway
LATHAM & WATKINS LLP

cc: Ocean Nutrition Canada

Attachments

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48 *See* http://www.cdc.gov/nchs/nhanes.htm.

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