Ocean Nutrition Canada
Omega-3 Fatty Acids
Request for Expansion of Enforcement Discretion

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Dr. Kathleen Ellwood
Director, Division of Nutrition Programs and Labeling (HFS-830)
Office of Nutritional Products, Labeling, and Dietary Supplements
Center for Food Safety and Applied Nutrition
Food and Drug Administration
5100 Paint Branch Parkway
College Park, MD 20740

Dear Dr. Ellwood:

As we stated in our meeting with you and other officials from the Center for Food Safety and Applied Nutrition ("CFSAN") on August 26, 2003, Ocean Nutrition Canada's ("ONC's") position is that conventional foods fortified with its omega-3 fatty acid products can make the qualified health claim regarding omega-3 fatty acids and coronary heart disease (CHD) currently permitted for dietary supplements without any further review by FDA. As CFSAN suggested in the meeting, however, we write to formally request this expansion of FDA's enforcement discretion.

Attached is a copy of our entire presentation from that meeting (Tab A). Also attached is a copy of our bioavailability study (Tab B), which is not publicly available. As detailed below, we regard that manuscript as confidential. We have also attached copies of recent articles supporting the public health benefit of omega-3s (Tab C) and ONC's GRAS Notification (Tab D).

Legal Basis for Request

There is no legal impediment to the granting of our request. It is well-recognized that the breadth of FDA's enforcement discretion is vast. The Supreme Court has held that the Food, Drug, and Cosmetic Act's enforcement provisions "commit complete discretion to the Secretary to decide how and when they should be exercised." Heckler v. Chaney, 470 U.S. 821, 835 (1985)(citing, inter alia, 21 U.S.C. § 372).

FDA already exercises this discretion to allow a qualified CHD claim for dietary supplements containing omega-3 fatty acids. The extension of its enforcement discretion to the same claim for conventional foods containing omega-3 fatty acids is perfectly permissible, and equally supported by the same legal principle. FDA has implicitly recognized as much in issuing the Guidance that formalizes its criteria for when it will invoke its enforcement discretion for qualified claims in conventional foods. Guidance for Industry and FDA, "Interim Procedures for Qualified Health

Claims in the Labeling of Conventional Human Food and Dietary Supplements," July 2003 ("the Guidance").

In its qualified health claims initiative for conventional foods, FDA noted that permitting qualified claims for supplements and not conventional foods "lead[s] to consumer confusion and biased consumption choices." Task Force Report, p. 5. Granting our request would eliminate that disparity for the qualified omega-3 fatty acid/CHD claim, and would further FDA's goal of stimulating the flow of meaningful and up-to-date information to consumers about the health consequences of their dietary choices. See, e.g., 67 Fed. Reg. 78002 (Dec. 20, 2002).

We recognize that the Guidance establishes a procedure for Agency review of qualified health claims for conventional foods. However, ONC believes that this procedure should be reserved for the review of *new* qualified claims, meaning claims that involve a new substance or that pose some other novel issue. ONC does not propose to use a new substance; indeed, the omega-3s that are the focus of the company's request derive from fish oil -- the same source as those mentioned in virtually all the references in the earlier health claims petition review process. Nor does the extension of the use of the qualified CHD claim to conventional foods with omega-3 fatty acids pose any novel questions that would be appropriate for resolution by the cumbersome petition process.

Our requested expansion of FDA's enforcement discretion is not only permissible; it is compelling. It is supported by the same First Amendment calculus that persuaded the Pearson court to compel FDA to allow the same qualified claim for dietary supplements with omega-3 fatty acids. Pearson v. Shalala, 164 F.3d 650 (D.C. Cir. 1999). Moreover, as demonstrated below, the supporting safety and efficacy data are sound, and the public health benefit that should result from allowing the claim would be profound. In the face of such compelling support, it would be inadvisable to force ONC through the time-consuming petition review process, which could delay the health benefits by roughly 1 year.

Efficacy

The expansion of FDA's enforcement discretion is supported by the large body of scientific evidence regarding the efficacy of omega-3 fatty acids, specifically eicosapentaenoic acid ("EPA") and docosahexaenoic acid ("DHA"), in preventing CHD. Since 1970, there have been more than 8,000 peer-reviewed scientific publications on fish oil, most of which deal with the health benefits of omega-3 fatty acids. In 2001, the effectiveness of long-chain omega-3s from fish oil in reducing triglycerides, favorably affecting platelet function, and decreasing blood pressure in people with hypertension was again confirmed by the American Heart Association.[1] FDA has already reviewed the vast majority of these data, and concluded that there was sufficient evidence to permit a qualified health claim regarding omega-3 fatty acids and CHD for dietary supplements. Since the determination on the qualified claim for omega-3 fatty acids and CHD,

additional studies have been published that add to the weight of the evidence in support of the claim.

The same evidence is equally supportive of the qualified claim in conventional foods, particularly because the EPA and DHA in ONC's microcaps are scientifically indistinguishable from the EPA and DHA used in dietary supplements. Indeed, ONC is the major oil supplier to the dietary supplement market. To verify the effectiveness of its omega-3 fatty acid powder, ONC carried out a bioequivalence study.* That study shows that the EPA/DHA in its microcaps powder and the EPA/DHA used in dietary supplements have equivalent incorporation into serum phospholipids and a resultant equivalent effect in triglyceride lowering. (A copy of the study is attached at Tab B. This is a pre-publication version that will be submitted to the Canadian Medical Association Journal. It is confidential commercial information that should be protected from public disclosure until its publication.) Thus, based on the bioequivalence study, the microcaps have been shown to be just as effective at preventing CHD as dietary supplements, and there is no reason why the same qualified claim should not be permitted for both dietary supplements and foods containing omega-3 fatty acids.

Safety

ONC has self-affirmed that its EPA/DHA products are generally recognized as safe ("GRAS") using expert panels. (A copy of the panel's conclusions regarding the microcaps is attached at Tab D.) Because ONC's product is toxicologically indistinguishable from the omega-3 fatty acids already recognized as GRAS, their safety is also supported by the no-objection letters for Unilever (GRN 000105), and Jedwards (GRN 000102), and the GRAS affirmation for menhaden oil (21 C.F.R. § 184.1472). The microcaps will be used as a fortificant in the same categories of food permitted for menhaden oil, and their use will be consistent with the 3g/day upper limit currently established by FDA.

ONC's manufacturing process is very rigorous, and as a result, the EPA/DHA in its products is extremely pure. Some of its omega-3 products are marketed in Canada as drugs. Thus, ONC manufactures its microcaps in accordance with Canadian drug GMPs. The company also follows the Council for Responsible Nutrition Voluntary Monograph on Long Chain Omega-3 EPA and DHA. Its purification process virtually eliminates contaminants -- mercury, for instance, cannot be detected even with a detection limit as low as 0.01 ppm. (A copy of the chemical analysis of the microcaps can be found on pages 16 and 21 of ONC's GRAS Notification at Tab D.)

* Holub BJ, et al. The comparison of bioequivalence of encapsulated and microencapsulated low-dose fish oil supplementation on selected blood lipid risk factors of CHD.

Public Health Benefit

As discussed at our meeting and summarized herein, the use of the qualified CHD claim on conventional foods fortified with ONC's microcaps should have a significant impact on the public health. Consequently, the use of the claim on these foods should be allowed and encouraged by FDA. CHD is the biggest killer in North America. The scientific literature demonstrates that by age 55, roughly half of Americans have CHD. Major clinical trials and epidemiological studies have shown that increasing the dietary intake of omega-3 fatty acids, in the form of fish or of fish oil supplements, can have a profound effect upon this disease,[2-8] and recent reviews and meta-analyses of these studies have reached the same conclusion.[9-13] A variety of mechanisms of action by which omega-3 fatty acids exert their various beneficial effects (prevention of arrhythmias, reduction in blood triglyceride levels, stabilization of atherosclerotic plaque, reduction in platelet aggregation, reduction in blood pressure) have been devised and described in the literature in the past 3 years.[10-15]

As omega-3 fatty acid intake increases, the relative risks of total mortality, cardiovascular death and sudden death decline significantly, by approximately 29%, 21%, and 53%, respectively, when dietary fish intake is increased from less than once per month to 1-2 times per week.[3] The GISSI-Prevenzione study has shown that the beneficial effect of EPA/DHA supplementation of about 1 gram/day is rapid, leading to reductions in sudden death (56%), coronary death (28%), cardiac death (38%), cardiovascular disease death (36%) and total mortality (41%) after only 3 months of treatment.[5] Even in those people with no evidence of prior cardiovascular disease, blood levels of omega-3 fatty acids are found to be inversely related to the risk of sudden death, according to a 2002 analysis of data from the Physicians' Health Study published in the New England Journal of Medicine: men in the upper third and fourth quartiles of omega-3 blood levels were found to have relative risk levels 72% and 81%, respectively, lower than those in the lowest quartile.[4] The Nurses' Health Study has shown that women can also significantly reduce their risk of coronary heart disease by increasing dietary intake of omega-3 fatty acids.[7,8]

Unfortunately, there is a huge gap between the intake of EPA/DHA recommended by the American Heart Association (and others), and the amount that North Americans actually consume.[10,11,16,17] Given the magnitude of the gap, and the unlikelihood that North Americans will dramatically increase their consumption of fatty fish, fortification of food with omega-3 fatty acids is a good way to increase consumption of omega-3 fatty acids, and thereby reduce CHD, especially CHD that results in sudden death. The American Heart Association has suggested the possibility of fortifying a wide variety of foods with stearidonic acid, the biochemical precursor to EPA and DHA, as a way to circumvent the taste and stability issues of liquid fish oil supplements.[1] Fortification of food with ONC's powdered, microencapsulated EPA/DHA products would address these issues without having to resort to synthesizing a biochemical precursor. Further, such supplementation will save both public and private money. It is estimated

that using omega-3 fatty acids would result in roughly $27 billion in health care cost savings per year.

Summary

There is no legal, scientific, or public health justification for FDA to decline to extend its enforcement discretion to permit the use of the qualified CHD claim to conventional foods fortified with ONC's EPA/DHA products. As discussed above, the expansion is supported by sound scientific evidence and would provide meaningful public health benefits. Finally, allowing the qualified CHD claim on these foods without further review will enable us to reap those benefits and the resulting cost savings quickly, without a large expenditure of Agency resources.

We appreciate the opportunity to present ONC's position on this matter. Please call me if you have any questions on this letter or on any other matter involving the use of the qualified claim for conventional foods. Thank you for your prompt consideration.

Very truly yours,

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Counsel to Ocean Nutrition Canada

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