DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Washington, DC 20204

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VIA FACSIMILE AND U.S. MAIL

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Re: Health Claim: Omega-3 Fatty Acids and Coronary Heart Disease (Docket No. 91N-0103)

Dear Mr. Emord:

This letter corrects an oversight in our letter to you dated October 31, 2000 (the October 31 letter). This letter makes clear the applicability of certain provisions under 21 C.F.R. §101.14 to the condition for the exercise of our enforcement discretion that the qualified claim meet the general requirements for health claims in 21 C.F.R. §101.14 (see the October 31 letter at 24).

In the October 31 letter, we reconsidered, in response to the court decision, *Pearson v. Shalala*, 164 F.3d 650 (D.C. Cir. 1999), the health claim "Consumption of omega-3 fatty acids may reduce the risk of coronary heart disease" in dietary supplement labeling. The agency found that, considering the totality of publicly available scientific evidence, there is not significant scientific agreement as to the validity of the relationship between omega-3 fatty acids and reduced risk of coronary heart disease (CHD). The agency also found, however, that the scientific evidence in support of a qualified claim about this relationship outweighs the evidence against the claim. Further, the agency found that it may appropriately exercise enforcement discretion with respect to the use of the qualified claim about the strength of the scientific evidence in the general population, provided that certain conditions are met.

The general requirements for health claims in 21 C.F.R. §101.14 include § 101.14(d)(2)(v), which requires that a claim enable "the public to comprehend the information provided and to understand the relative significance of such information in the context of a total daily diet." Further, § 101.14(e)(3) prohibits a health claim unless "[n]one of the disqualifying levels identified in paragraph [(a)(4)] of this section is

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exceeded..."[1] We clarify, below, how the provisions in § 101.14 (a)(4), (d)(2)(v) and (e)(3) relate to the exercise of our enforcement discretion for the qualified claim discussed in the October 31 letter.

*Disqualifying levels*

We note that, in the October 31 letter, we did not address the fact that dietary supplements of EPA and DHA omega-3 fatty acids might not meet the fat content requirement of § 101.14(a)(4) and (e)(3) because they may contain greater than 13 grams of fat per 50 grams (for foods with reference amounts customarily consumed of 30 grams or less). We are advising you that FDA intends to exercise its enforcement discretion for dietary supplements of EPA and DHA omega-3 fatty acids that bear the qualified health claim provided below and that do not meet the fat content requirement of 21 C.F.R. §101.14(a)(4). In addition, we intend to exercise enforcement discretion for such dietary supplements that do not meet the requirement in § 101.14(e)(3) that the fat content disqualification levels in § 101.14(a)(4) not be exceeded. However, as a condition of our enforcement discretion, such supplements must meet the requirement in § 101.14(e)(3), with respect to bearing a disclosure statement, when such supplements contain a disqualifying level of fat. Section 101.14(e)(3) requires a disclosure statement, in compliance with § 101.13(h), that highlights the nutrient (fat) that exceeds the disqualifying level. Hence, a condition of our enforcement discretion is that this disclosure statement (i.e., "See nutrition information for fat content.") be included on the supplement label immediately adjacent to the qualified health claim. We remind you that the nutrition labeling requirements of 21 C.F.R. §101.36(b)(2) must be followed with respect to declaration of fat-related characteristics when dietary supplements contain an amount of fat that exceeds the amount that can be declared as zero.

*Context of the total daily diet*

FDA has an obligation to ensure that food labeling is truthful and not misleading. Under the Federal Food, Drug, and Cosmetic Act, a claim can be misleading, and thereby misbrand the food, based on information that it does not include, as well as information that it does include. See U.S.C. 343(a)(1) (a food is misbranded if its labeling is false or misleading in any particular); 21 U.S.C. 321(n) ("[I]n determining whether the labeling or advertising is misleading there shall be taken into account . . . not only representations made or suggested by statement, word, design, device, or any combination thereof, but also the extent to which the labeling or advertising fails to reveal facts material in the light of such representations or material with respect to consequences which may result from the use of the article to which the labeling or advertising relates under the conditions of use prescribed in the labeling or advertising thereof or under such conditions of use as are customary or usual.").

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[1] We note that the regulation contains a typographic error referring to paragraph (a)(5) instead of paragraph (a)(4).

A health claim is a claim that "expressly or by implication . . . characterizes the relationship of any substance to a disease or health-related condition" (21 C.F.R. §101.14(a)(1)). The general health claim requirements state that a health claim must be complete, truthful, and not misleading (21 C.F.R. §101.14(d)(2)(iii)), and that the claim must enable the public to comprehend the information provided and to understand the relative significance of such information in the context of a total daily diet (21 C.F.R. §101.14(d)(2)(v)).

These requirements ensure that consumers will be able to comprehend the significance of the health benefit described in a health claim within the context of the total daily diet so that they may modify their diets to improve their health. As FDA stated in the preamble to the final rule on general requirements for health claims on conventional foods (58 FR 2478 at 2513; January 6, 1993), a wide variety of factors may need to be addressed in a health claim in order to allow consumers to understand the substance-disease relationship in the context of the total daily diet.

In all of its authorized health claim regulations relating food substances (e.g., lipids, soluble fiber, soy protein, stanol esters) to reduced risk of heart disease, FDA has concluded that information about the total diet must be included as part of the claim. The agency requires all such claims to inform consumers that diets low in saturated fat and cholesterol may reduce the risk of heart disease, or that the substance that is the subject of the health claim should be consumed as part of a diet low in saturated fat and cholesterol.[2] *See* 21 C.F.R. §§ 101.75(c)(2)(i)(A), 101.77(c)(2)(i)(A) , 101.81(c)(2)(i)(A), 101.82(c)(2)(i)(A), and 101.83(c)(2)(i)(A). The agency determined that such language was necessary for the public to understand fully, in the context of the total daily diet, the significance of consumption of the substance in question on the risk of heart disease.

Thus, the agency has consistently emphasized the need for inclusion of the context of the total daily diet in its authorized health claims. In the case of all claims relating specific substances to reduced risk of heart disease, this "context of the total daily diet" has taken the form of inclusion of the statement that "diets low in saturated fat and cholesterol may reduce the risk of heart disease." A substance/heart disease claim lacking this context fails to enable the consumer to comprehend the information provided and to understand the relative significance of the information in the context of the total daily diet.

In recent rulemakings authorizing health claims to reduce the risk of heart disease, FDA has continued to emphasize the importance of consuming a low saturated fat, low cholesterol diet. In the preamble to the final rule authorizing a health claim for soy protein, the agency noted that such a diet is "the dietary pattern associated most strongly with reduction of risk from heart disease" (64 FR 57700 at 57719). In the preamble to the final rule authorizing a health claim for oats, FDA expressed concern that consumers would be misled if information about dietary context were omitted, in that the claim

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[2] This requirement applies regardless of whether the food bearing the health claim contains saturated fat or cholesterol.

would then imply that a diet containing oats could substitute for a diet low in saturated fat and cholesterol (62 FR 3584 at 3594).

FDA's conclusions about the importance of a low saturated fat, low cholesterol diet in reducing the risk of heart disease are supported by the recommendations of other government agencies and respected scientific and medical bodies. For example, the recently distributed Dietary Guidelines for Americans, 2000, a joint publication of the Department of Agriculture and the Department of Health and Human Services, state "Choose a diet that is low in saturated fat and cholesterol and moderate in total fat."[3] The report of the Dietary Guidelines Advisory Committee notes that this recommendation is based on strong scientific evidence of the role of diet in CHD.[4] Likewise, the Dietary Guidelines of the American Heart Association recommend limiting foods high in saturated fat and cholesterol, again based on "continuing evidence that high total and LDL cholesterol are strongly related to coronary artery disease risk and that reductions in LDL cholesterol levels are associated with reduced coronary disease risk."[5]

Diets low in saturated fat and cholesterol are considered by expert groups–including the National Academy of Sciences, the National Heart, Lung and Blood Institute, and the Expert Panel of the National Cholesterol Education Program[6]–to be the most effective

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[3] U.S. Department of Agriculture and U.S. Department of Human Services. Nutrition and Your Health: Dietary Guidelines for Americans, 2000, 5th ed. Home and Garden Bulletin No. 232, 2000, p. 28 (http://www.health.gov/dietaryguidelines).

[4] Report of the Dietary Guidelines Advisory Committee on the Dietary Guidelines for Americans, 2000, p. 34 (http://www.ars.usda.gov/dgac/dgac_ful.pdf).

[5] Krauss, R.M., et al. AHA Dietary Guidelines, Revision 2000: A Statement for Healthcare Professionals from the Nutrition Committee of the American Heart Association. *Circulation* 2000; 102:2284. (http://circ.ahajournals.org/cgi/content/full/102/18/2284).

[6] The Coordinating Committee of the National Cholesterol Education Program (NCEP) includes representatives from numerous federal agencies and expert professional groups. The health care and professional organizations represented include (among others) the American Heart Association, the American Medical Association, the American Academy of Family Physicians, the American Academy of Pediatrics, the American College of Cardiology, the American College of Occupational Medicine, the American Diabetes Association, , the American Nurses Association, the American Pharmaceutical Association, the American Red Cross, the Association of State and Territorial Health Officials, and the Society for Nutrition Education. Federal agencies that are represented on the NCEP coordinating committee include the CDC, the National Heart, Lung and Blood Institute, the National Cancer Institute, the Department of Agriculture, FDA, the Public Health Services' Office of Disease Prevention and Health Promotion, the National Center for Health Statistics, and the Department of Defense.

dietary means of reducing heart disease.[7,8,9] Although other dietary factors may contribute to reducing the risk of heart disease, their roles are generally recognized as being of smaller magnitude.[10] In addition, the evidence for the role of a low saturated fat, low cholesterol diet in reducing the risk of heart disease is strong, in that it has been found to meet the significant scientific agreement standard in 21 U.S.C. §343(r)(3) and 21 C.F.R. §101.14(c). By contrast, the evidence for a relationship between EPA and DHA omega-3 fatty acids and reduced risk of CHD has been found not to meet the significant scientific agreement standard.

For all these reasons, consumers need to be informed about the relationship between low saturated fat, low cholesterol diets and reduced risk of heart disease in order to understand the information provided in the qualified claim about omega-3 fatty acids and CHD, and to understand its relative significance in the context of their total daily diets. This information is a vital piece of health-related information supported by the consensus of scientists in the field.

We sent you letters on November 28, 2000, (the November 28 letter) and February 9, 2001 (the February 9 letter) in further response to your petition of May 25, 1999, regarding a health claim about the relationship between folic acid, vitamin $B_6$, and vitamin $B_{12}$ dietary supplements and vascular disease. In those letters, the agency identified a qualified claim about that relationship. FDA advised that it intends to exercise enforcement discretion with respect to that qualified claim, provided the claim, in compliance with § 101.14(d)(2)(v), includes a statement that diets low in saturated fat and cholesterol may reduce the risk of heart disease. We further explained that without this language the claim is misleading because it fails to reveal the most effective dietary means of reducing the risk of heart disease. Therefore, we identified an appropriately qualified claim that begins with the sentence: "It is known that diets low in saturated fat and cholesterol may reduce the risk of heart disease."

We believe that this introductory sentence is necessary to appropriately qualify the claim identified in the October 31 letter about the quality of the scientific evidence about the relationship between omega-3 fatty acids and CHD. The strong relationship between low saturated fat, low cholesterol diets and reduced risk of heart disease is a material fact.

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[7] National Research Council, National Academy of Sciences. Diet and Health: Implications for Reducing Chronic Disease Risk. National Academy Press, Washington, DC, 1989, pp. 537 and 540-541.

[8] U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health, National Heart, Lung and Blood Institute, National Cholesterol Education Program. Report of the Expert Panel on Population Strategies for Blood Cholesterol Reduction. NIH Publication No. 93-3046, 1993.

[9] U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health, National Heart, Lung and Blood Institute, National Cholesterol Education Program. Second Report of the Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel II). NIH Publication No. 93-3095, 1993.

[10] National Research Council, *supra* note 9, at 541.

Without this sentence, not only is the claim misleading, within the meaning of sections 403(a) and 201(n) of the act, but the claim fails to enable the public to understand the relative significance of the information in the context of the total daily diet.[11] Such a claim should therefore include this element to comply with § 101.14(d)(2)(v). Accordingly, the agency would consider the following claim to be appropriately qualified:

> It is known that diets low in saturated fat and cholesterol may reduce the risk of heart disease. The scientific evidence about whether omega-3 fatty acids may reduce the risk of coronary heart disease (CHD) is suggestive, but not conclusive. Studies in the general population have looked at diets containing fish and it is not known whether diets or omega-3 fatty acids in fish may have a possible effect on reduced risk of CHD. It is not known what effect omega-3 fatty acids may or may not have on risk of CHD in the general population.

We recognize that there may be dietary supplements currently in interstate commerce, containing EPA and DHA omega-3 fatty acids that bear the qualified claim addressed in the October 31 letter, and that do not bear on their labels either the introductory sentence, as indicated above, or the disclosure statement discussed earlier in this letter. Manufacturers may also have an inventory of label stock that does not include these additional statements. Therefore, we intend, as part of our enforcement discretion, to allow a period of three months from the date of this letter to elapse before we will consider taking or recommending enforcement action against dietary supplements of EPA and DHA omega-3 fatty acids that do not bear the additional introductory and disclosure statements. We believe, based on industry labeling practices, that this would allow adequate time for industry to change its labels.

A dietary supplement bearing a claim that is not properly qualified, as described above, or consistent with the weight of the evidence is subject to regulatory action as a misbranded food under section 403(a)(1) and 403(r)(1)(B) of the Federal Food, Drug, and Cosmetic Act, a misbranded drug under section 502(f)(1), and as an unapproved new drug under section 505(a).

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[11] Even if the claim were not misleading without a statement about low saturated fat, low cholesterol diets and reduced risk of heart disease, FDA still has authority to require such a statement. The agency has an interest in promoting the health of American citizens, and that interest is not limited to preventing misleading statements in labeling. *See Rubin v. Coors Brewing Co.*, 514 U.S. 476, 482 (1995) (the prevention of misleading statements "need not be the exclusive government interest " served by [a statutory provision]; promoting and protecting public health also qualify as substantial government interests under First Amendment commercial speech doctrine); *see also 44 Liquormart v. Rhode Island,* 517 U.S. 484, 501 (1996) (the regulation of commercial messages to require the disclosure of beneficial consumer information is a purpose that is consistent with the reasons for according constitutional protection to commercial speech).

We hope that this letter clarifies the conditions under which we intend to exercise our enforcement discretion in this matter.

Sincerely yours,

/s/

for Christine J. Lewis, Ph.D.
Director
Office of Nutritional Products, Labeling
and Dietary Supplements
Center for Food Safety
and Applied Nutrition