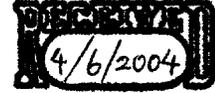


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April 5, 2004

BY OVERNIGHT and ELECTRONIC MAIL

Food and Drug Administration
Office of Nutritional Products, Labeling,
And Dietary Supplements (HFS-800)
5100 Paint Branch Parkway
College Park, MD 20740

**Re: Amendment to Qualified Health Claim Petition for
Conventional Foods and Dietary Supplements
Containing Omega-3 Fatty Acids Submitted by Martek
Biosciences on November 3, 2003; Docket Number 2003Q-
0401**

To Whom It May Concern:

This letter supplements and amends the qualified health claim petition submitted by our client, Martek Biosciences Corporation ("Martek"), on November 3, 2003 regarding the relationship between the omega-3 fatty acids, docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), and a reduced risk of coronary heart disease (CHD). We are submitting this amendment because there have been important proceedings and developments since filing the petition that should be considered by the Food and Drug Administration (FDA) as it evaluates the issues raised in Martek's qualified health claim petition.

Specifically we ask that FDA consider both the new methylmercury consumer advisory issued jointly by FDA and the Environmental Protection Agency last month and the deliberations of the December 10-11, 2003 Food Advisory Committee (FAC) regarding the consumer advisory about methylmercury in fish

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and shellfish. ^{1/} As will be discussed in more detail below, the data and information discussed during the FAC proceedings and the revised consumer advisory on methylmercury in fish and shellfish reinforce the importance of including an informational statement in the qualified health claim appearing on fish and shellfish that (1) advises pregnant and lactating women, women who may become pregnant and young children of the importance of limiting fish and shellfish intake due to methylmercury concerns and (2) discloses the potential adverse effects of methylmercury exposure on heart health.

The stated purpose of the FAC meeting on methylmercury was to (1) provide a report of how FDA has responded to FAC recommendations regarding development of a joint methylmercury advisory with the Environmental Protection Agency, and (2) seek the Committee's concurrence that FDA and the Agency should commence an outreach and educational program for methylmercury as soon as possible. Although the FAC did not, at the meeting, issue formal recommendations to the agency, the proceedings clearly illustrate the importance of providing consumers with adequate information regarding the dangers posed by methylmercury. Moreover, the Committee did appear to agree that agency outreach and education regarding methylmercury should be pursued as soon as possible. ^{2/}

Significantly, a major emphasis of the meeting was the need to balance the potential benefits of fish consumption with the potential risk of methylmercury

^{1/} *What You Need to Know About Mercury in Fish and Shellfish*, 2004 Environmental Protection Agency and FDA Advice For: Women Who Might Become Pregnant, Woman Who are Pregnant, Nursing Mothers, Young Children (March 2004) available at: <http://www.cfsan.fda.gov/~dms/admehg3.html> (accessed March 19, 2004); Center for Food Safety and Applied Nutrition (CFSAN) Food Advisory Committee Meeting, Methylmercury, Vol. 1-2 (Dec. 10-11, 2003), available at <http://www.fda.gov/ohrms/dockets/ac/cfsan03.html> (accessed March 5, 2004) (hereinafter "Transcript"). Page numbers cited below are approximate, and refer to the page numbers identified for each speaker or topic, as applicable, in the transcript table of contents. Specific page numbers are not provided in the public transcripts posted on the internet.

^{2/} See, e.g., Transcript, Vol. 2, at 209-end (statement of Dr. S. Miller).

exposure. ^{3/} In the context of the draft advisory, the emphasis was placed on the wisdom of balancing the “negative” advisory language with a positive message about the health benefits of fish. Although the emphasis is slightly different in the context of health claims, where the positive message is the initial consideration, the need for balance is no less important. Indeed, where a food is actively promoted for a specific health benefit, and therefore may be consumed in increasing amounts, the need for a balanced representation of benefits and risks is arguably most pressing. ^{4/}

The FAC proceedings also featured considerable discussion regarding the amount and types of fish that may be safely consumed. Significant questions were raised, during both the public comment period and FAC deliberations, regarding FDA’s recommendation that it is safe to consume a variety of 12 ounces of any fish, other than the four “do not eat” fish (*i.e.*, shark, swordfish, king mackerel, and tilefish). Similar issues of safety were further explored in a petition submitted by the Environmental Working Group on December 22, 2003, which sought, among other things, an expanded advisory. ^{5/} These safety concerns underscore the need for a cautious approach in any regulatory determination involving fish and shellfish, as well as careful dietary management to prevent excess exposure to methylmercury.

^{3/} See, *e.g.*, *id.* at 23-36 (statement of J. Pendergast, Environmental Protection Agency); *id.* at 36-83 (statement of Dr. D. Acheson, FDA), *id.* at 209-end (statement of Dr. M. Nelson).

^{4/} See *id.* (statement of Dr. J. Dwyer, FAC Member) (“I don’t think that FDA’s first mandate is to promote fish. I think the first mandate is to promote the public health, and in this specific case, to avoid a contaminant . . .”).

^{5/} Environmental Working Group Data Quality Act Challenge, Request for Correction of FDA’s “Advice for Women Who Are Pregnant, or Who Might Become Pregnant, and Nursing Mothers, about Avoiding Harm to Your Baby or Young child from Mercury in Fish and Shell Fish, Docket No. 2004P-0004, CP-1 (Dec. 22, 2003).

It is particularly noteworthy that several commenters at the meeting specifically identified potential concerns with methylmercury on cardiac health. ^{6/} Dr. David Wallinga, M.D., MPA, of the Institute for Agriculture and Trade Policy, even went so far as to suggest that a separate advisory dealing with cardiac endpoints would be of value to health professionals:

The literature about the cardioprotective effects of omega-3 fats is pretty good, but as the NAS also pointed out, there is much data from both animals and humans that exposure to methylmercury can have adverse effects on the developing and adult cardiovascular systems and that some research suggests that these adverse effects occur below levels associated with neurodevelopmental deficits. . . . [P]erhaps we need a separate advisory dealing with cardiac endpoints, so that, as a physician, we can give good advice to all our patients, and not just those expecting to get pregnant. ^{7/}

The recently issued consumer advisory on methylmercury attempts to provide a balanced message that identifies both the risks and benefits of fish and shellfish consumption. The advisory first discusses the many nutritional benefits of including seafood in the diet and specifically recognizes that a well-balanced diet with fish and shellfish can contribute to heart health and children's proper growth and development. The consumer advisory then discusses the health concerns with methylmercury in fish and shellfish by explaining that higher levels of mercury may harm an unborn baby or young child's developing nervous system. The advisory recommends restricted consumption for women who may become pregnant, pregnant women, nursing mothers and young children. Individuals in this targeted population are advised that they (1) should not eat shark, swordfish, king mackerel and tilefish because they contain high levels of mercury, (2) can eat up to 12 ounces

^{6/} *Id.* at 90-96 (statement of Dr. Wallinga); *id.* at 167-175 (statement of Dr. D. Zuckerman); *id.* at 175-203 (statement of Dr. J. Cohen) (noting both the risk posed by methyl mercury and the cardioprotective benefits of omega-3 fatty acids in fish).

^{7/} *Id.* at 90-96 (statement of Dr. Wallinga).

(2 average meals) per week of fish and shellfish that are low in mercury and provides examples of the five most commonly consumed low-mercury fish and shellfish (because canned albacore tuna contains higher mercury levels, the advisory recommends only six ounces of this product per week), and (3) should eat no more than six ounces of fish caught by family and friends in local waterways, unless information is available establishing that fish caught in those waterways contain lower levels of mercury.

As discussed in detail in its November 3, 2003 submission, Martek believes that a qualified health claim regarding the relationship between the omega-3 fatty acids DHA and EPA and a reduced risk of cardiovascular disease must disclose the potential health risks presented by methylmercury when the claim appears on fish and shellfish. Martek provided an example of an informational statement that tracked the language found in the earlier methylmercury consumer advisory. Now that the agency's consumer advisory has changed, Martek urges the Office of Nutritional Products, Labeling, and Dietary Supplements (ONPLDS) to develop an informational statement that adequately reflects the agency's current thinking on methylmercury. Martek believes that this would be accomplished by the following qualified health claim and informational statement:

A growing body of scientific literature suggests that higher intakes of the omega-3 fatty acids DHA and EPA may afford some degree of protection against coronary heart disease. [Name of seafood], like all seafood, may contain traces of mercury. For most people, the risk from mercury by eating fish and shellfish is not a health concern. Yet, some fish and shellfish contain higher levels of mercury that may harm an unborn baby or young child's developing nervous system. High levels of mercury also may diminish the protective effects of omega-3 fatty acids on heart health. To minimize the risk of mercury exposure, FDA recommends that pregnant and lactating women, women who may become pregnant and young children should eat no more than 12 ounces (2 average meals) per week of a variety of fish and shellfish that are low in mercury.

Martek has not included in the informational statement the recommendation to avoid shark, swordfish, king mackerel and tilefish because

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Martek believes that these and other high mercury fish that may be identified in the future should be ineligible for the qualified health claim given their high mercury content. Martek also does not believe that it is necessary to include in the informational statement recommendations on limiting consumption of fish caught in local waters by family and friends because those fish would not bear the qualified health claim.

Regardless of the precise language that ultimately is incorporated into the qualified health claim, it is imperative that fish and shellfish bearing the qualified health claim disclose the risks associated with methylmercury. The failure to include a message that balances the benefits and the risks of fish and shellfish consumption, could lead many consumers to increase seafood and shellfish intake to greater than 12 ounces per week, which would place unborn, nursing, and/or young children at an increased risk of neurological harm from mercury. The concerns raised by the FAC members also underscore the importance of disclosing the potential adverse effects of high methylmercury levels on cardiovascular health. The informational language used to accomplish these purposes must be sufficiently descriptive to allow consumers to make informed choices and wise dietary decisions based upon all pertinent considerations.

If you have any questions or comments regarding this information, please do not hesitate to contact us.

Sincerely,

A handwritten signature in black ink, appearing to read "Martin J. Hahn", written in a cursive style.

Martin J. Hahn