



FEB 25 2003

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Washington, DC 20004-2401

RE: Health Claim Petition/California Walnut Commission

Dear Ms. Taylor:

This letter responds to the health claim petition you submitted on March 15, 2002, on behalf of the California Walnut Commission. This petition requests that the Food and Drug Administration (FDA) authorize a health claim about the relationship between the consumption of walnuts and the risk of coronary heart disease (CHD) on the label or in the labeling of whole or chopped walnuts. Specifically, you request that FDA authorize the following model health claim: "Diets including walnuts can reduce the risk of heart disease."

FDA filed the petition for comprehensive review on June 21, 2002, in accordance with section 403 (r)(4)(A)(i) of the Federal Food, Drug, and Cosmetic Act (the Act). The initial deadline for FDA's response was September 19, 2002. After mutual agreement, the deadline for the agency's response was extended 90 days to December 18, 2002, and then to February 28, 2003.

Before making our decision on the petition, we are providing this letter that outlines our tentative conclusions. We invite your client to schedule a meeting with our scientific staff to discuss them. Specifically, this letter briefly addresses the following with regard to a health claim about CHD on the label or in the labeling of whole or chopped walnuts:

- Our tentative conclusions about whether FDA should 1) authorize a health claim based on significant scientific agreement or 2) exercise enforcement discretion for a qualified health claim about the relationship between consumption of walnuts *per se* and reduced risk of CHD;
- Our tentative conclusions about whether FDA should exercise enforcement discretion for a qualified health claim about the relationship between consumption of nuts as a category of food and reduced risk of CHD; and
- Our tentative conclusions about other requirements pertaining to health claims and about possible wording for a qualified health claim.

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A. Evaluation of a Health Claim for Walnuts *per se* Based on Significant Scientific Agreement

Two groups of experts, one convened by the Life Sciences Research Office (LSRO) and another retained by FDA, concluded that there is not significant scientific agreement about the science underlying the statement that walnuts *per se* may reduce the risk of CHD. The LSRO group prepared a report for the California Walnut Commission, which you provided in your petition. The group of experts retained by FDA consisted of three outside experts in the field of nutrition and CHD. They independently reviewed the scientific evidence pertaining to a relationship of walnut consumption and CHD risk. In coming to the tentative conclusion that there is not significant scientific agreement FDA considered the following:

- In the six intervention studies submitted with the petition, there are limited data showing a lowering of LDL- and total-cholesterol when the intervention diet containing walnuts results in modification of the fatty acid composition of the overall diet so that the ratio of unsaturated fatty acids to saturated fatty acids is higher in the intervention (walnut) diet compared to the other diets being tested. There are also limited data to suggest there may be an effect of walnut-containing diets above that of simple displacement of one type of fat with another. However, all of the studies have relatively low numbers of individuals and they are of short duration. It is unclear whether the observed cholesterol-lowering benefits will be sustained over time. In addition, the studies used a large amount of walnuts (43 – 84 g/day) to achieve the lowering of cholesterol. Apparently, data from trials in which the intervention was a large amount of walnuts were used alone to extrapolate to the effects on serum cholesterol at low doses of walnuts. No studies were done with moderate to low doses of walnuts (< 43 g/day), as may be more typical of human consumption patterns.
- Observational data submitted with the petition described the intake of nuts and incidence/mortality pertaining to CHD. FDA believes that these data suggest an association between the reduced incidence and mortality from CHD and nut consumption, but these studies were not specific to walnuts.
- The outside experts (LSRO and those retained by FDA) concluded that the strength of the evidence did not demonstrate a specific health claim for walnuts with respect to CHD. The data were instead called “suggestive,” “promising,” or “a strong trend” by each group of outside experts. Each recommended additional studies with more subjects, of longer duration, and with lower amounts of walnuts. Specifically, the LSRO report concluded: “The supporting human clinical walnut intervention studies

- suggest reduced relative risk of coronary heart disease, yet they are inconclusive because there have been only five controlled, peer-reviewed published trials with few subjects. There are few trials of extended duration essential for critical evaluation of the sustainability of the health-beneficial outcomes and evidence of adverse effects (e.g., body weight gain and gastrointestinal intolerance).” The outside experts retained by FDA also noted the short duration of the trials, the high amount of walnuts consumed in order to show a positive benefit, and the commonality of the mechanism of lowering serum cholesterol when the ratio of unsaturated fat to saturated fat is increased. They pointed out that when unsaturated fats are increased at the expense of saturated fats numerous studies have shown a beneficial effect on serum cholesterol values, but noted, however, this effect is not unique to walnuts.

B. Evaluation of a Qualified Health Claim for Walnuts *per se*.

For claims that do not meet the significant scientific agreement standard, FDA may consider whether to exercise enforcement discretion for qualified claims about the substance and disease relationship. Based on this review, FDA has tentatively concluded that walnuts *per se* are not a substance that could be the subject of a qualified health claim about CHD. In coming to this tentative conclusion, FDA considered the following:

- The effect of walnuts is not unique but appears to be characteristic of nuts in general. The mechanism by which walnuts appear to lower LDL- and total-cholesterol is not known and is probably multifactorial. The intervention studies appear to support a “marker” of a good ratio of unsaturated to saturated fatty acid. In each instance in which the intervention studies showed a beneficial effect of lowering LDL- and/or total-cholesterol, the lipid profiles of the diets had a better ratio of unsaturated fatty acids to saturated fatty acids in the “walnut” diet as compared to the other diets. However, walnuts are not the only food that may work by this mechanism, so the effect is not specific to walnuts, nor would the marker be specific to walnuts. It is well documented that altering the ratio of unsaturated:saturated fat in the diet lowers LDL- and total-cholesterol, which in turn are considered important biomarkers for protection against CHD. This marker may also indicate other potentially protective substances in the food in addition to the fatty acid profile (e.g., phytochemicals, fiber, and amino acid profiles).
- There is strong precedent for providing for claims that accurately reflect the true subject of the claim rather than for claims that misleadingly attribute the benefit to a single food source of the substance or to a single food which is in fact part of a larger category of foods that produce a

- positive benefit to health through the same or similar mechanism. For example, it is unreasonable to expect consumers to eat two ounces of walnuts daily, 365 days of the year, which is the amount of walnuts necessary to produce a significant public health benefit of lowering LDL- and total-cholesterol. It is reasonable that consumers would be able to use nuts interchangeably on a regular basis rather than only one type of nut on a daily basis.

C. Evaluation of a Qualified Health Claim about Consumption of Nuts and Reduced Risk of Coronary Heart Disease.

FDA is considering whether there is a basis for a qualified health claim about the relationship between consumption of nuts, including walnuts and reduced risk of CHD that could be used on the label or in the labeling of whole or chopped walnuts.

FDA reviewed the scientific evidence in your petition that would be relevant to a qualified health claim about consumption of nuts and reduced risk of CHD. Based on this review, FDA has tentatively concluded that there is a basis for a qualified health claim for nuts. In coming to this tentative conclusion, FDA has considered the following:

- The effect seen with walnuts is similar to the reported effects seen with nuts in general;
- There is a basis for highlighting the general category of nuts as part of a heart-healthy diet;
- There is a strong precedent for providing for claims that accurately reflect the true subject of the claim rather than for claims that misleadingly attribute the benefit to a single food source of the substance or to a single food which is in fact part of a larger category of foods that produces a positive benefit to health through the same or similar mechanism.
- A qualified health claim for nuts in general would be consistent with the reasonable expectation that the substance that is the subject of the claim would be consumed on a regular/daily basis so as to have an effect.

D. Other Requirements Pertaining to Health Claims and Possible Wording for a Qualified Health Claim

A qualified health claim on the label or in the labeling of whole or chopped walnuts would need to comply with the health claim general requirements in

§101.14 and be consistent with other applicable health claim regulations, except where FDA finds a justification for enforcement discretion as discussed below.

Disqualifying nutrient levels (§101.14(a)(4)). With regard to total fat, walnuts do not meet the limit for total fat per reference amount customarily consumed (RACC), per label serving size, or per 50 g. However, FDA believes that an appropriately qualified claim about consumption of nuts might assist consumers in maintaining healthy dietary practices, provided that the label bears a disclosure statement that complies with §101.13(h), (i.e., See “nutrition information for fat content”). (See Sec. 403(r)(3)(A)(ii) of the Act.)

10% nutrient contribution requirement (§101.14(e)(6)). Walnuts do not meet the requirement that a food contain 10 percent or more of the Reference Daily Intake or the Daily Reference Value for vitamin A, vitamin C, iron, calcium, iron, calcium protein, or fiber per RACC. A primary aim of this provision is to prevent health claims on foods of minimal nutritional value. However, a review of recent food composition data suggests that walnuts come close to meeting the 10% nutrient contribution requirement because they contain about 9% of the Daily Value for protein and about 8% of the Daily Value for dietary fiber per RACC. Consequently, FDA might not object to a qualified health claim of the type described herein on labels and in labeling for walnuts.

Context of a Total Daily Diet. FDA notes that implementing regulations for health claims require that a health 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. (See §101.14(d)(2)(iv) and Sec 403 (r)(3)(B)(iii) of the Act.) With regard to health claims that pertain to CHD, FDA requires information relative to a total diet low in saturated fat and cholesterol because this is an essential part of dietary guidance for reducing risk of heart disease.

Other general requirements for health claims. A qualified health claim on the label of whole or chopped walnuts would need to meet all other general requirements for a health claim.

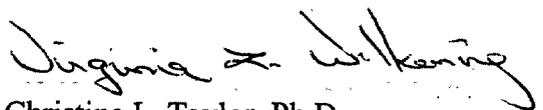
Criteria that the food shall meet all the nutrient content requirements of §101.62 for a “low saturated fat,” “low cholesterol,” and “low fat” food. Whole and chopped walnuts do not meet the definition of a “low saturated fat” food, although walnuts do not exceed the saturated fat disqualifying levels in §101.14(a)(4). Because walnuts and other nuts that have a high ratio of unsaturated fat to saturated fat may be useful in maintaining healthy dietary practices, FDA might not object to whole or chopped walnuts bearing the qualified health claim, provided that disclosure about saturated fat in addition to total fat is made as part of the claim statement.

In summary, we have considered the scientific evidence submitted with your petition and, as appropriate, have also considered other pertinent scientific evidence. Our tentative conclusion is that there is neither significant scientific agreement about the science underlying the statement that walnuts may reduce the risk of CHD nor justification to provide for a qualified health claim specifically and solely about walnuts. Rather, our tentative conclusion is that the science provides evidence that a qualified health claim is supported for a broad category of nuts, and that when appropriately worded so as not to mislead consumers, walnuts (chopped and whole) may make the following qualified claim on labels and in labeling:

"Nuts, including walnuts, as part of a diet low in saturated fat and cholesterol, may reduce the risk of heart disease. FDA evaluated the data and determined that, although there is scientific evidence supporting the claim, the evidence is not conclusive. See nutrition information for total fat and saturated fat content."

We look forward to your response when we meet with you. Please contact Ms. Brenda Adams at 301-436-2373 to schedule the meeting.

Sincerely,


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