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*BY FEDERAL EXPRESS*

Kathleen Ellwood, Ph.D.  
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Office of Nutritional Products, Labeling, and Dietary Supplements  
Center for Food Safety and Applied Nutrition  
Food and Drug Administration  
5100 Paint Branch Parkway  
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Dear Dr. Ellwood:

On behalf of our client, Kraft Foods Global, Inc. (Kraft), attached is a notification for a health claim based on an authoritative statement of the National Heart, Lung, and Blood Institute (NHLBI). As described in the notification, Kraft intends to use the following health claim to educate consumers about NHLBI guidelines: "Diets low in saturated fat, trans fat, and cholesterol may reduce the risk of heart disease." Two hard copies and one electronic copy of the notification are attached.

Please let us know if there are any questions about this notification or if additional information would be helpful.

Respectfully submitted,



Ann Mileur Boeckman

Enclosures



Kraft Foods

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Richard M. Black, Ph.D.  
Vice President, Global Nutrition

**Notification for a Health Claim  
Based on an Authoritative Statement:**

**Diets Low in Saturated Fat, Trans Fat, and Cholesterol May  
Reduce the Risk of Heart Disease**

**DATE:** 07/05/2006

**SUBMITTED BY:** Richard Black, Ph.D.  
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**SUBMITTED TO:** Division of Nutrition Programs and Labeling  
Office of Nutritional Products, Labeling  
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Center for Food Safety and Applied Nutrition  
Food and Drug Administration  
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**Notification for a Health Claim  
Based on an Authoritative Statement:**

**Diets Low in Saturated Fat, Trans Fat, and Cholesterol May  
Reduce the Risk of Heart Disease**

**I. INTRODUCTION**

For nearly twenty years, the National Heart, Lung, and Blood Institute (NHLBI) has published clinical practice guidelines for the prevention and treatment of coronary heart disease (CHD). Through these guidelines, NHLBI and its parent agency, the National Institutes of Health (NIH), provide consensus recommendations on the protective role of diets low in saturated fat, trans fat, and cholesterol. Kraft is planning to use the following health claim to inform consumers of authoritative NHLBI guidelines:

“Diets low in saturated fat, trans fat, and cholesterol may  
reduce the risk of heart disease.”

As required by the Federal Food, Drug, and Cosmetic Act (FFDCA), Kraft is notifying the Food and Drug Administration (FDA) of plans to use this health claim. (FFDCA § 403(r)(3)(C); 21 U.S.C. 343(r)(3)(C)). Foods eligible to bear the claim meet the regulatory definitions for “low saturated fat” and “low cholesterol,” contain 0.5 g or less of trans fat per reference amount, contain less than 6.5 g of total fat per reference amount, and meet all general requirements for health claims.

**II. THE AUTHORITATIVE STATEMENTS**

**A. Overview of the National Cholesterol Education Program**

The National Cholesterol Education Program (NCEP) is a health education program administered by the NHLBI Office of Prevention, Education, and Control. The central mission of this office (and therefore NCEP) is to coordinate “the dissemination of research findings and scientific consensus to health professionals, patients, and the public so that information can be adapted for and integrated into health care practice and individual health behavior.” (NHLBI Office of Prevention, Education, and Control, Description and Background, available at <http://www.nhlbi.nih.gov/about/opec/index.htm> (accessed June 2006)). Patterned after a similar program for blood pressure management, NCEP aims to raise awareness about cholesterol reduction as a way to prevent or treat CHD. Another important NCEP role is translation of current research on cholesterol management into guidelines and recommendations for clinical practice.

NCEP functions are carried out by a Coordinating Committee of more than 40 public and private organizations, including several federal agencies. The Coordinating Committee sponsors expert panels, which develop consensus guidelines and recommendations for NCEP adoption. One NCEP panel has played an especially influential role in the development of dietary guidelines for reduction of CHD risk—the Expert Panel on the Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (also known as the “Adult Treatment Panel,” or ATP). Since 1988, the Adult Treatment Panel has issued three reports recommending clinical strategies for cholesterol management.

Although each ATP report reflects scientific consensus, the third report (ATP III) is noteworthy for the evidence-based approach taken by the panel. (NCEP, Third Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) (NIH Pub. No. 02-5215) (Sept. 2002)). In developing the guidelines, panel members critically and systematically reviewed the literature, drafted “evidence statements” to summarize current knowledge, and developed recommendations representing the available evidence and consensus judgments. The report was extensively peer reviewed and ultimately endorsed for publication by NCEP, NHLBI and NIH.

The ATP III report is also noteworthy for its emphasis on reducing CHD risk in the general population. The first two ATP reports focused almost exclusively on management of cholesterol in patients with existing CHD (i.e., “secondary prevention”); ATP III emphasized prevention in healthy persons, including those at elevated risk of CHD (i.e., “primary prevention”). The ATP III report is described as linking the public health or “population approach” to reducing CHD risk, which focuses on healthy life habits for the general population, and a clinical strategy addressing primary prevention of CHD over the long term (e.g., greater than 10 years). ATP III describes primary prevention efforts as relevant to both the public health and clinical arenas, concluding that “[l]ong-term prevention in the clinical setting . . . represents an extension of the public health approach.” (ATP III at II-31, II-33).

Clinical approaches to lifestyle changes are identified in ATP-III as “therapeutic lifestyle changes” (TLC). The TLC program calls for reduction of CHD risk through sound dietary habits, maintenance of a desirable body weight, and physical activity. Key dietary habits include reduced intake of saturated fat, trans fat, and cholesterol and adjustment of total calories as necessary to maintain a desirable body weight. The TLC guidelines suggest that saturated fat provide less than 7% of total calories, trans fat intake be kept low, and total fat contribute 25% to 35% of total calories.

## **B. Authoritative NIH and NHLBI Statements in the ATP III Report**

The ATP III report provides numerous authoritative statements addressing the relationship between diet and reduced CHD risk. These statements confirm that among the most important dietary factors affecting CHD risk are saturated fat, trans fat, and cholesterol intakes. Total fat intake, while important for other reasons (e.g., to help

avoid excessive energy intakes), is not directly related to CHD risk; moreover, a diet low in saturated fat, trans fat, and cholesterol will help to ensure that total fat consumption is moderate. The authoritative NCEP statements that form the basis for Kraft's proposed health claim are cited below.

## 1. Saturated and Trans Fat

Several authoritative NCEP statements affirm that diets low in saturated and trans fat reduce the risk of CHD:

**Evidence statements:** There is a dose response relationship between saturated fatty acids and LDL cholesterol levels. Diets high in saturated fatty acids raise serum LDL cholesterol levels (A1).<sup>1</sup> Reduction in intakes of saturated fatty acids lowers LDL cholesterol levels (A1, B1).

(ATP III at V-8).

**Evidence statements:** High intakes of saturated fatty acids are associated with high population rates of CHD (C2). Reduction in intake of saturated fatty acids will reduce risk for CHD (A1, B1).

(ATP III at V-9).

**Evidence statements:** *Trans* fatty acids raise serum LDL cholesterol levels (A2). Through this mechanism, higher intakes of *trans* fatty acids should increase risk for CHD. Prospective studies support an association between higher intake of *trans* fatty acids and CHD incidence (C2).

(ATP III at V-9).

**Recommendation:** Intakes of *trans* fatty acids should be kept low.

(ATP III at V-9).

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<sup>1</sup> Each evidence statement provided in ATP-III is ranked according to the category of evidence into which it falls and the overall strength of evidence. Categories of evidence include major randomized controlled clinical trials (RCTs) (A), smaller RCTs and meta-analyses of other clinical trials (B), observational and metabolic studies (C), and clinical experience (D). Strength of evidence rankings include very strong evidence (1), moderately strong evidence (2), and strong trend (3). (ATP III at I-1).

## 2. Cholesterol

NCEP evidence statements and recommendations for dietary cholesterol reflect expert judgment regarding the relationship between dietary cholesterol and risk of CHD:

**Evidence statements:** Higher intakes of dietary cholesterol raise serum LDL cholesterol levels in humans (A2, B1). Through this mechanism, higher intakes of dietary cholesterol should raise the risk for CHD. Reducing cholesterol intakes from high to low decreases serum cholesterol in most persons (A2, B1)

(ATP III at V-10).

## 3. Total Fat

The NCEP Panel concluded that a dietary approach to reduce CHD risk should focus on saturated fat, trans fat, and cholesterol, but not total fat intake, per se:

Among the fatty acids that make up the total fat in the diet, only saturated fatty acids and *trans* fatty acids raise LDL cholesterol levels. Thus, serum levels of LDL cholesterol are independent of intakes of total fat per se. ATP II advised limiting total fat in Step I and Step II (TLC) diet to ≤ 30 percent of calories primarily as a means of achieving lower intakes of saturated fatty acids. The focus of the dietary approach to reducing CHD risk then and now is on dietary fatty acids that raise LDL cholesterol concentrations.

(ATP III at V-11).

Based on this conclusion, the report offers the following consensus recommendation concerning total fat intake:

**Recommendation:** It is not necessary to restrict total fat intake for the express purpose of reducing LDL cholesterol levels, provided saturated fatty acids are reduced to goal levels.

(ATP III at V-11).

As a result of this decreased emphasis on total fat intake, NCEP recommendations now suggest that up to 35 percent of calories from total fat may be consumed as part of a healthy diet. This represents an increase from previous guidelines, which had recommended no more than 30 percent of calories from total fat.

### **III. NATURE OF THE CLAIM AND FOODS ELIGIBLE TO BEAR THE CLAIM**

Based on the ATP III report, Kraft intends to make an authoritative statement claim about the relationship between CHD risk and saturated fat, trans fat, and cholesterol on the label and/or labeling of qualifying food products. The exact wording of the claim is—

Diets low in saturated fat, trans fat, and cholesterol may reduce the risk of heart disease.

Foods eligible to bear the proposed claim meet the FDA definitions for low saturated fat and low cholesterol, contain 0.5 g or less of trans fat per reference amount, contain less than 6.5 g total fat per reference amount, and meet all general requirements for health claims in 21 C.F.R. § 101.14.

#### **A. Saturated fat and cholesterol content**

To qualify for the proposed claim, foods must meet the FDA criteria for “low saturated fat,” as defined in 21 C.F.R. § 101.62 (c)(2) and (3). Foods (other than meal products) marketed as “low” in saturated fat must contain 1 g or less of saturated fat per reference amount customarily consumed (RACC) and no more than 15% of calories from saturated fat.

Qualifying foods must also meet the FDA definitions for “low cholesterol,” as described in 21 C.F.R. § 101.62 (d)(2) and (3). For foods other than meal products, FDA has defined “low cholesterol” to mean 20 mg or less of cholesterol per RACC; food products with smaller RACCs (i.e., 30 g or less or 2 tablespoons or less) must not exceed 20 mg of cholesterol on a 50 g basis.

#### **B. Trans fat Content**

The ATP III report recommends that trans fat consumption be kept low. FDA has not identified a level of trans fat considered to be “low”; however, previous health claim notifications have reasonably allowed CHD health claims on products containing 0.5 g or less of trans fat, to help reduce trans fat consumption. (Health Claim Notification of Frito-Lay, Inc. (Docket No. 2005Q-0211) (effective June 2005); Health Claim Notification of Kraft Foods Global, Inc. (Docket No. 2003Q-0547) (effective Dec. 2003)). Based on this precedent, products bearing the planned health claim either must contain 0.5 g or less of trans fat per RACC or must meet any FDA definition of “low” trans fat, if a definition is established.

#### **C. Total Fat Content**

The ATP III report makes clear that restriction of total fat, per se, is not necessary to reduce CHD risk so long as saturated fat, trans fat, and cholesterol are

controlled. In our view, application of the health claim disqualifying level of 13 g total fat would be sufficient to prevent foods with excessive fat from bearing a CHD claim. Consistent with FDAMA notifications submitted for whole grain foods with a moderate fat content, however, foods bearing the proposed CHD health claim are required to contain less than 6.5 gram of total fat per RACC.

#### **D. Other Requirements**

The claim will be used only on foods that meet all applicable requirements of 21 C.F.R. § 101.14. Thus, for example, foods bearing the claim must not contain sodium at a level that exceeds the disqualifying amount set by FDA. (21 C.F.R. § 101.14(a)(4)).

Foods bearing the planned claim also must meet the minimum nutrient contribution requirement for health claims (i.e., the so-called “jelly bean” rule) (21 C.F.R. § 101.14(e)(6)).<sup>2</sup> Foods bearing the planned claim therefore must provide at least 10% of the daily value of vitamin A, vitamin C, iron, calcium, protein, or fiber per RACC.

### **IV. STATUTORY BASIS FOR THE CLAIM**

#### **A. Requirements for health claims based on authoritative statements**

The FFDCA, as amended by the Food and Drug Administration Modernization Act of 1997 (FDAMA) (21 U.S.C. § 343(r)(3)), authorizes the use of health claims based on consensus statements of authoritative scientific bodies. To provide “streamlined procedures” for conveying scientifically sound nutrition information to the public, FDAMA established a notification process to allow appropriate claims without prior FDA approval. (H.R. Rep. No. 105-399, at 98 (1997)). Health claims are authorized under the FDAMA process when the following criteria are met:

- The claim is based on an authoritative statement of a scientific body of the United States government about the relationship between a nutrient and a disease or health-related condition. The scientific body must have official responsibility for public health protection or research directly relating to human nutrition, such as the National Institutes of Health. The claim must be the statement of the scientific body and not of an employee.

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<sup>2</sup> As we have described in comments to FDA, a compelling case can be made to eliminate or substantially revise the jelly bean rule. Kraft Comments to Docket Nos. 1994P-0390, 1995P-0241 (Jan. 18, 2005). In our view, there has never been a defensible nexus between the 10% DV requirement and health claims. A restriction that broadly prevents many foods from bearing health claims is troubling in light of the ever-evolving nature of nutrition science as well as the complex relationship between diet and health. We also question whether continued use of the requirement is fully consistent with the demands of the First Amendment, which allows limitations on claims no more extensive than necessary to prevent deception.

- The authoritative statement is published and is currently in effect.
- The company planning to make the claim has submitted to FDA, at least 120 days before the first introduction into interstate commerce of the food with a label containing the claim, (1) a notice of the claim, including the exact words used in the claim and a concise description of the basis for determining that the applicable requirements have been satisfied, (2) a copy of the statement upon which the claim is based, and (3) a balanced representation of the scientific literature relating to the relationship between a nutrient and a disease or health-related condition to which the claim refers.
- The claim and the food for which the claim is made are in compliance with sections 403(a) and 201(n) of the FFDCFA. These sections prohibit labeling that is false and misleading in any particular, including labeling that is false or misleading because it omits material information.
- The claim is stated in a manner so that the claim is an accurate representation of the authoritative statement and so that the claim enables the public to comprehend the information provided in the claim and to understand the relative significance of such information in the context of a total daily diet.

In 1998, FDA issued guidance on the types of claims that qualify as FDAMA authoritative statements and the procedures that should be followed for submitting a health claim notification. (FDA/CFSAN Guidance for Industry: Notification of a Health Claim or Nutrient Content Claim Based on an Authoritative Statement of a Scientific Body (June 11, 1998)).<sup>3</sup> In addition to the statutory criteria described above, FDA advised that an authoritative statement should be based on a deliberative review of the scientific evidence and should reflect scientific consensus within the identified scientific body, if published by a subdivision of one of the federal scientific bodies.

The FDA guidance document further stated that the agency interprets FDAMA as requiring notified health claims to be supported by significant scientific agreement—the same standard that is required for health claim regulations. Although the FDAMA provisions do not specifically require the authoritative statement to be based on “significant scientific agreement,” FDA stated in its guidance document that such a

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<sup>3</sup> The 1998 guidance represented FDA’s current thinking, as of the date of its issuance, on the procedures to be followed for notifying the agency of a health claim or nutrient content claim based on an authoritative statement of a scientific body. As posted on the internet, the guidance contains a link that references more recent information on food labeling. (<http://www.cfsan.fda.gov/~dms/hclmguid.html>). Among the significant developments in recent years are judicial decisions concerning the role of the First Amendment in shaping government regulation of commercial speech, including health-related claims. *See, e.g., Pearson v. Shalala*, 164 F.3d 650 (D.C. Cir. 1999).

conclusion is based on the legislative history and on the language of the statute. FDA explained that the significant scientific agreement standard would not allow for a claim based, for example, on findings characterized as preliminary results, statements that indicate research is inconclusive, or statements intended to guide future research.

Separately, FDA has also taken the position that a health claim based on an authoritative statement must not address the same diet-disease relationship as an existing health claim regulation. (63 Fed. Reg. 34101, 34102 (June 22, 1998)). As explained more fully below, the proposed health claim addresses a different diet-disease relationship than existing health claims.

## **B. Authoritative Status of the ATP III Report Statements**

The ATP III statements upon which the proposed health claim is based qualify as “authoritative statements” under section 403(r)(3)(C) of the FFDCFA, as amended by FDAMA. The statements address the relationship between three nutrients (saturated fat, trans fat, and cholesterol) and CHD, a serious and chronic disease that is associated with dietary habits over a lifetime. The statements are based upon a deliberative review of the literature by an expert panel established by the NCEP under NHLBI oversight. The final report in which the statements appear is endorsed by NHLBI and printed as an official document of NIH, an agency that is identified in FDAMA as an authoritative body that may be the source of authoritative statements. Because the statements all appear in boxed-off text as “evidence statements” and recommendations, they are reasonably characterized as reflecting consensus within the authoritative body.

The statements also are “currently in effect” and based on significant scientific agreement. Since publication of the ATP III Report in 2002, important studies and dietary recommendations have confirmed the Report’s conclusions about the relationship between CHD and diets low in saturated fat, trans fat, and cholesterol. Scientific support for the statements was most recently confirmed in the 2005 *Dietary Guidelines for Americans*<sup>4</sup> and related consumer publications issued by the federal government.<sup>5</sup>

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<sup>4</sup> U.S. Department of Health and Human Services & U.S. Department of Agriculture, 2005 *Dietary Guidelines for Americans*, at 29-30. The *Dietary Guidelines* recommend that consumers restrict saturated fat, trans fat, and cholesterol. The *Guidelines* suggest that total fat intake be kept between 20% and 35% of calories, with most fats coming from sources of polyunsaturated and monounsaturated fatty acids, such as fish, nuts, and vegetable oils.

<sup>5</sup> U.S. Department of Health and Human Services, *A Healthier You: Based on the Dietary Guidelines for Americans* 51 (2005) (“Eat less saturated and trans fats, and cholesterol . . . Eating too many saturated and trans fats, or cholesterol, may raise the level of LDL (bad) cholesterol and increase the risk of heart disease.”). As a book published by the U.S. Department of Health and Human Services for the specific purpose of providing guidance to consumers, *A Healthier You* itself qualifies as an authoritative statement under FDAMA.

### **C. Form and Content of Claim**

The form and content of the proposed health claim satisfy FDAMA criteria for health claims based on authoritative statements. The form and content of the claim closely track the relevant authoritative statements and provide an accurate representation of the central ATP III messages on CHD risk and diet. The claim is also truthful and not misleading, consistent with sections 403(a) and 201(n) of the Act, because it relies on well-established nutrient content criteria for saturated fat and other nutrients. Compliance with general requirements for health claims, such as disqualifying levels for sodium, will further ensure that the claim is used in a truthful and not misleading way.

The proposed claim also allows the public to comprehend the information and to understand its significance in the context of the total daily diet. The claim directly relates to total diets low in three substances that should be limited to reduce CHD risk—saturated fat, trans fat, and cholesterol. As is the case with several other health claims, such as health claims for whole grains, no reference to total dietary fat is needed because the proper focus is saturated fat, trans fat, and cholesterol.

### **D. Relationship to Existing Claims**

The plain language of the statute provides that a health claim “which is not authorized by the Secretary in a regulation . . . shall be authorized and may be made with respect to a food” if the FDAMA notification process is followed (FFDCA § 403(r)(3)(C)). The proposed claim is distinct from any health claim the agency has authorized by regulation. An existing FDA regulation authorizes a health claim regarding the relationship between CHD and diets low in cholesterol and saturated fat, but this claim does not include information on trans fat (21 C.F.R. § 101.75). In addition, this regulation requires foods bearing the health claim to meet FDA’s definition of “low fat”; in contrast, foods that contain less than 6.5 g of total fat per RACC could bear the planned health claim. Thus, the claim described in this Notification “is not authorized by the Secretary in a regulation” and is appropriately addressed through FDAMA.

The similarity of the proposed claim to an existing health claim regulation raises a question concerning the relationship between existing health claim requirements and FDAMA. The interplay between health claim regulations and notified claims is most directly addressed in a Senate report accompanying an earlier version of the bill that was ultimately adopted by a Conference Committee and enacted into law. The Senate report affirms FDA’s authority to regulate notified claims by issuing regulations to prohibit or modify claims to which FDA objects:

Under this legislation, the agency retains the full range of enforcement powers it has possessed historically to remedy misleading claims, including the powers of product seizure, injunction, and criminal penalties. In addition, new section 403(r)(3)(D) assures that FDA retains full authority to regulate health claims based on the statements of authoritative bodies through rulemaking. Once FDA

regulations governing health claims concerning a particular diet/disease relationship (e.g., calcium and osteoporosis) have become effective, no claim concerning that diet/disease relationship based on the statement of an authoritative scientific body could be made unless it is consistent with the FDA regulation. The legislation specifically provides that FDA may prohibit or modify such health claims through rulemaking.

(S. Rept. 105-43, at 51 (1997)).

This paragraph is most reasonably understood to address the scope of FDA's authority after a FDAMA claim is submitted and the agency objects to the claim; read in context, it does not seem to address health claims issued under NLEA, as allowed under section 403(r)(3)(B) of the FFDCFA. Thus, Congress appears to have anticipated broad latitude for claims based on authoritative statements, with a two-step process for any FDAMA claims to which FDA objects: (1) FDA may issue a regulation (as described in section 403(r)(3)(D)) to prohibit the claim, to modify the claim, or finding that the basic FDAMA requirements were not met;" and (2) once such an FDA regulation takes effect, then it governs all FDAMA claims about that particular diet-disease relationship. This reading is consistent with the plain language and basic purpose of FDAMA, which is intended to speed messages about consensus science to consumers. It is not unreasonable to assume that Congress would allow claims based on authoritative statements to take precedence over outdated health claim regulations, especially where the agency has a clear remedy if a claim presents any concern.

We recognize that in at least one instance, FDA has interpreted the language quoted above to mean that the FDAMA process cannot be used to authorize a health claim that addresses the same diet-disease relationship as an existing health claim regulation. (63 Fed. Reg. 34101, 34103 (June 22, 1998)). Although we offer a different perspective, even under FDA's interpretation, the proposed claim is appropriate because it addresses a diet-disease relationship that differs from any health claim regulation. The relevant health claim regulation addresses diets low in saturated fat and cholesterol; the proposed FDAMA regulation addresses diets low in saturated fat, trans fat, and cholesterol.

We note that two health claims do not address the same diet-disease relationship simply because the claims share some elements. For example, a health claim concerning the relationship between hypertension and stroke and dietary potassium and sodium was authorized under FDAMA even though an FDA-approved health claim already addressed the relationship between sodium and hypertension. Similarly, FDA has not objected to FDAMA claims regarding CHD and diets rich in whole grains and low in saturated fat and cholesterol, even though several FDA-approved CHD health claims address saturated fat and cholesterol. In each case, the addition of a new disease

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" Section 403(r)(3)(D) states in relevant part that a FDAMA claim "may be made until . . . such time as the Secretary issues a regulation . . . prohibiting or modifying the claim and the regulation has become effective, or . . . finding that the requirements . . . have not been met." FFDCFA § 403(r)(3)(D).

and/or nutrient to the health claim took the claim outside of the regulation, making it appropriate for the FDAMA process.

In addition, to the extent that the Senate report addresses NLEA-authorized claims at all, it says only that a FDAMA claim must be “consistent with” an FDA regulation, suggesting that a flexible approach was intended. Thus, where a claim mischaracterized the mechanism by which calcium reduces osteoporosis risk, directly contradicting both an FDA regulation and consensus science, FDA promptly rejected the claim (63 Fed. Reg. 34101, 34103 (June 22, 1998)). In contrast, the proposed claim about CHD risk and diets low in saturated fat, trans fat, and cholesterol is consistent with the FDA health claim regulation about diets low in saturated fat and cholesterol. The claim and the criteria described in this notification simply add trans fat to the claim language and make more foods eligible to bear the claim, based on consensus science about the relevance of total fat intake.

Finally, we suspect that, had Congress intended to limit the scope of FDAMA in a significant way, that intent almost certainly would have been communicated more clearly. For example, the legislative history could have made this point explicitly by stating that “once any FDA health claim regulations concerning a particular diet/disease relationship (e.g., calcium and osteoporosis) have become effective, no claim based on an authoritative statement may be authorized for that diet/disease relationship.” Similarly, Congress could have said that “once FDA regulations governing health claims concerning a particular diet/disease relationship (e.g., calcium and osteoporosis) have become effective, no claim based on an authoritative statement may be authorized for that diet/disease relationship unless it complies with the FDA regulation.”

In summary, the claim that is the subject of this FDAMA notification is not currently authorized by regulation and addresses a different diet-disease relationship than any existing health claim. Even if that were not the case, based on the plain language of the statute and the legislative history, FDAMA is readily understood to allow authoritative statement claims that address the same diet-disease relationship as an existing health claim regulation. Congress anticipated potential conflict between FDAMA-authorized claims and other health claims, and provided FDA with a clear remedy—to issue a regulation prohibiting or modifying such claims. This interpretation is reasonable in light of the purpose of FDAMA to speed important health information to consumers; it is also consistent with First Amendment protections for speech. Significantly, the First Amendment caselaw pertinent to health claims has evolved considerably since FDA first considered the scope of the FDAMA process in June 1998.

## **VII. REPRESENTATION OF THE SCIENTIFIC LITERATURE REGARDING THE RELATIONSHIP BETWEEN CHD AND DIETS LOW IN SATURATED FAT, TRANS FAT, AND CHOLESTEROL**

A health claim regarding the relationship between CHD and diets low in saturated fat, trans fat, and cholesterol is well-supported by the scientific evidence. A

thorough review and assessment of the supportive literature may be found in several authoritative reports issued since publication of the ATP III report, including reports of the Institute of Medicine (IOM) and the 2005 *Dietary Guidelines* Advisory Committee. These reports provide a balanced representation of the literature pertinent to the proposed health claim and demonstrate that foods containing a moderate amount of total fat can contribute to a healthful diet.

The IOM report commonly known as the “Macronutrient Report” reflects a systematic and extensive review of scientific evidence addressing the health implications of total fat, saturated fat, trans fat, and cholesterol. (IOM, *Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids* Ch. 8 and 11 (2002/2005) (“Macronutrient Report”). In preparing the report, an expert panel convened by the IOM Food and Nutrition Board considered numerous studies of the relationship between LDL cholesterol and dietary saturated fat, trans fat, and cholesterol. Concerning total fat, the report examined data regarding the effects of total fat and carbohydrate intake on blood lipid concentrations, body weight, and metabolic parameters for glucose and insulin.

Based on the panel’s review of the evidence, the report ultimately recommended that consumption of saturated fat, trans fat, and cholesterol be as low as possible within the context of a nutritionally adequate diet. The report concluded that total fat, per se, is not associated with the incidence of CHD, but that total fat intake should be moderate because diets with more than 35% of energy from fat tend to provide excessive amounts of saturated fatty acids and may pose other risks:

**Conclusions.** A few case-control studies have shown an association between total fat intake and risk for CHD. However, a detailed evaluation of these studies shows that it is not possible to separate total fat intake from saturated fatty acid intake, which is known to raise LDL cholesterol concentrations. Unsaturated fatty acids, which do not raise LDL cholesterol concentrations compared to carbohydrate, have not been implicated in risk for CHD through adverse effects on lipids or other risk factors. Nonetheless, practical efforts to create “heart-healthy” menus reveal that intakes of total fat exceeding 35 percent of total energy result in unacceptably high intakes of saturated fatty acids. Moreover, there is the possibility that higher fat intakes may enhance a prothrombotic state, although the evidence to support this mechanism for enhancing CHD risk is not strong enough alone to make solid recommendations.

(Macronutrient Report at 801-02).

The report established recommendations, in the form of an “Acceptable Macronutrient Distribution Range” (AMDR), for total fat for adults of 20 to 35% of energy. The upper range of the AMDR was intended to accommodate diets low in saturated fat, but moderate in total fat. The report noted that consumption of total fat within the recommended range would help avoid “the apparent risk for CHD that may

occur on low fat diets and the risk for increased energy intake and therefore obesity with the consumption of high fat diets.” (Macronutrient Report at 809). An AMDR for carbohydrate was set in conjunction with fat at 45 to 65% of energy.

The relationship between total fat intake and CHD was also examined in an April 2004 meeting of the Nutrition Subcommittee of the FDA Food Advisory Committee. Following a thorough discussion of the state of the science, the Subcommittee voted to advise FDA that current scientific evidence does not suggest a relationship between total fat, per se, and CHD risk. (Summary Minutes, Meeting of the Nutrition Subcommittee of the Food Advisory Committee (Apr. 27-28, 2004), available at <http://www.fda.gov/ohrms/dockets/ac/cfsan04.html> (accessed June 2006)). The need to control saturated fat and trans fat intake to lower CHD risk was emphasized, as was the importance of achieving energy balance.

In August 2004, the 2005 *Dietary Guidelines* Advisory Committee published an evidence-based review of the latest findings concerning total fat, saturated fat, trans fat, and cholesterol. (Report of the Dietary Guidelines Committee, Part D, Sec. 4 (Aug. 2005)). The Committee relied heavily on the data and conclusions presented in the IOM Macronutrient Report, while also reviewing more recent studies. The Committee endorsed the IOM AMDR of 20-35% of calories from fat, reasoning that intakes lower than 20% of calories from total fat may adversely affect blood lipids (e.g., by decreasing serum HDL concentrations) and make it difficult to achieve recommended intakes of important nutrients, while total fat intakes contributing greater than 35% of calories are associated with increased saturated fat intakes. The Committee also noted that high fat intakes (i.e., greater than 35%) may provide excessive calories and contribute to obesity. The 2005 *Dietary Guidelines for Americans*, released in January 2005, are in agreement with the Advisory Committee’s findings and recommendations.

Literature published after January 2005 does not call into question the well-established conclusions, set out in the *Dietary Guidelines* and elsewhere, about the healthfulness of moderate fat diets with appropriate intake of calories, saturated fat, and trans fat. For example, a major dietary intervention study in postmenopausal women recently addressed the health significance of reduced fat dietary patterns (specifically, an 8.2% reduction from a baseline mean of 37.8% of energy from total fat). (B.V. Howard, PhD, et al., *Low-Fat Dietary Pattern and Risk of Cardiovascular Disease*, 295 J. Am. Med. Assn 655 (2006); R.L. Prentice, PhD, et al. *Low-Fat Dietary Pattern and Risk of Invasive Breast Cancer* 295 J. Am. Med. Assn 629 (2006); S.A.A. Beresford, PhD, et al. *Low-Fat Dietary Pattern and Risk of Colorectal Cancer*, 295 J. Am. Med. Assn 643 (2006)). The investigators found a lower fat dietary pattern to have no significant effects on risk of CHD, among other diseases. The findings from this important trial,<sup>7</sup> although controversial in some respects, support the generally accepted principle that total fat intake, per se, is not associated with the risk of CHD.

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<sup>7</sup> The investigators described the trial as the “largest long-term randomized trial of a dietary intervention ever conducted to our knowledge.” *Low-Fat Dietary Pattern and Risk of Cardiovascular Disease*, at 662.

## VIII. ADDITIONAL EVIDENCE IN SUPPORT OF THE CLAIM

As discussed previously, the proposed claim and eligibility criteria are based upon, and consistent with, the major findings presented in the ATP III Report. Since publication of the report, comparable recommendations and other evidence concerning saturated fat, trans fat, cholesterol, and total fat have emerged. These recommendations and related evidence confirm that continued emphasis should be placed on diets low in saturated fat, trans fat, and cholesterol. Control of saturated fat, trans fat, and cholesterol is important to reduce CHD risk and help ensure that total fat intakes are moderate, as recommended by current dietary guidelines.

### A. Nutrition Public Policy: The 2000-2005 *Dietary Guidelines for Americans*

For many years, public health authorities recommended a low-fat, high carbohydrate diet to reduce CHD risk. Such recommendations were made explicitly in the fourth edition of the *Dietary Guidelines for Americans* (U.S. Department of Agriculture, U.S. Department of Health and Human Services, 1995), which stated, “Choose a diet low in fat, saturated fat, and cholesterol.” Similar recommendations were a cornerstone of the second NCEP report, published in 1994 and the predecessor to ATP-III.

Evolving science regarding the role of saturated fat versus total fat on the risk of CHD has caused these (and other) public health recommendations to be updated. Current policy statements from governmental and other authorities now universally recognize the appropriateness of low saturated fat, trans fat, and cholesterol diets with moderate amounts of total fat (i.e., up to 35% of total energy) as alternatives to low-fat, high-carbohydrate diets. Nutrition policy concerning the role of saturated fat versus total fat has also been reflected in FDA’s regulatory precedent for many years.

The *Dietary Guidelines for Americans* represent official nutrition policy of the U.S. government, and guide all federal activities relating to human nutrition. A significant shift in policy regarding total fat occurred in the 2000 edition of the *Guidelines* (U.S. Department of Agriculture and the U.S. Department of Health and Human Services, 2000). Specifically, in 2000, Americans were advised to “Choose a diet that is low in saturated fat and cholesterol and *moderate* (emphasis added) in total fat,” rather than the low-fat diet that was previously recommended. Support for this approach continued in the 2005 *Guidelines*, which advised that—

Fats and oils are part of a healthful diet, but the type of fat makes a difference to heart health, and the total amount of fat consumed is also important. High intake of saturated fats, *trans* fats, and cholesterol increases the risk of unhealthy blood lipid levels, which, in turn, may increase the risk of coronary heart disease. A high intake of fat (greater than 35 percent of calories) generally increases

saturated fat intake and makes it more difficult to avoid consuming excess calories. A low intake of fats and oils (less than 20 percent of calories) increases the risk of inadequate intakes of vitamin E and of essential fatty acids and may contribute to unfavorable changes in high-density lipoprotein (HDL) blood cholesterol and triglycerides.

(2005 *Dietary Guidelines* at 29).

Based on these findings, the 2005 *Dietary Guidelines* provided the following key recommendations concerning fats and oils, among others:

- Consume less than 10 percent of calories from saturated fatty acids and less than 300 mg/day of cholesterol, and keep *trans* fatty acid consumption as low as possible.
- Keep total fat intake between 20 to 35 percent of calories, with most fats coming from sources of polyunsaturated and monounsaturated fatty acids, such as fish, nuts, and vegetable oils.
- When selecting and preparing meat, poultry, dry beans, and milk or milk products, make choices that are lean, low-fat, or fat-free.
- Limit intake of fats and oils high in saturated and/or *trans* fatty acids, and choose products low in such fats and oils.

(2005 *Dietary Guidelines* at 30).

## **B. Regulatory Precedent**

The shift in U.S. nutrition policy toward moderate fat diets is reflected in several rulemakings and other actions involving CHD-related health claims. In 1999, in identifying the foods that qualify for a health claim concerning soy protein and CHD, FDA recognized the health benefits of foods made from whole soybeans and that contain no added fat. (64 Fed. Reg. 67700, 67717 (Oct. 26, 1999)). The agency allowed such foods to bear the CHD health claim even though they may not meet the technical regulatory definition for “low fat” foods. FDA reasoned that the amount by which these foods would exceed the “low fat” criterion was small. The agency also characterized such foods as useful sources of soy protein that could appropriately be included in a low fat diet.

In 2000, FDA concluded that spreads and dressings for salad should not be required to comply with the total fat disqualifier level on a 50 g basis in order to qualify for a health claim about sterol/stanol esters and CHD. (65 Fed. Reg. 54686, 54709-10 (Sept. 8, 2000)). Thus, foods containing more than 13 g of fat per 50 g could bear the health claim if an appropriate disclosure statement for total fat was provided (e.g., “See nutrition information for fat content”). In reaching this decision, FDA observed:

Although diets high in saturated fat and cholesterol are implicated in CHD, current scientific evidence does not indicate that diets high in unsaturated fat are associated with CHD. Furthermore, the 2000 Dietary Guidelines Advisory Committee concluded that the scientific evidence on dietary fat and health supports assigning first priority to reducing saturated fat and cholesterol intake, not total fat intake. In fact, the new guideline for fat intake in the Dietary Guidelines for Americans, 2000 states, “Choose a diet that is low in saturated fat and cholesterol and moderate in total fat.”

(65 Fed. Reg. at 54710). FDA later extended this approach to a decision to expand the interim health claim concerning sterol and stanol esters and CHD to cover vegetable oils for home use. In a February 14, 2003 letter, FDA expressed its intent to allow, pending publication of a final rule, the stanol/sterol health claim to appear on vegetable oils for home use, even though such oils exceed the total fat disqualifier level. (FDA Letter Regarding Enforcement Discretion With Respect to Expanded Use of an Interim Health Claim Rule About Plant Sterol/Stanol Esters and Reduced Risk of Coronary Heart Disease (Feb. 14, 2003)). To qualify for enforcement discretion, vegetable oils that bear the health claim also must contain a disclosure statement about total fat content.

Since allowing the sterol and stanol esters health claim, FDA has not objected to two FDAMA notifications for whole grain foods with a moderate fat content (less than 6.5 g of total fat per RACC). (Health Claim Notification of Frito-Lay, Inc. (Docket No. 2005Q-0211) (effective June 2005); Health Claim Notification of Kraft Foods Global, Inc. (Docket No. 2003Q-0547) (effective Dec. 2003)). In addition, FDA has decided to exercise enforcement discretion and allow several health claims for foods that are, or that contain, considerable amounts of healthful fats, including nuts, foods containing omega-3 fatty acids, and olive oil. (*See, e.g.*, Qualified Health Claim Letter of Enforcement Discretion - Nuts and Coronary Heart Disease (July 14, 2003); Letter Responding to Health Claim Petition dated November 3, 2003 (Martek Petition): Omega-3 Fatty Acids and Reduced Risk of Coronary Heart Disease (Sept. 8, 2004); Letter Responding to Health Claim Petition dated August 28, 2003: Monounsaturated Fatty Acids from Olive Oil and Coronary Heart Disease (Nov. 1, 2004)).

In all of these cases, FDA decided to permit an appropriate CHD health claim on foods that do not meet the regulatory definition of “low fat.” As the agency explained in allowing a claim concerning CHD risk and monounsaturated fatty acids from olive oil:

FDA concurs with current dietary guidelines that consuming diets low in saturated fat and cholesterol is more important in reducing CHD risk than consuming diets low in total fat. Therefore, FDA has decided not to consider, in the exercise of its enforcement discretion, that olive oil, vegetable oil spreads, dressings for salads, shortenings, and olive oil-containing foods that bear a

MUFAs from olive oil and CHD qualified health claim meet the "low fat" criterion.

These regulatory decisions provide a clear precedent for this proposal to use an appropriate health claim for foods that are low in saturated fat, trans fat, and cholesterol, but not necessarily "low" in total fat as that term has been defined by FDA.

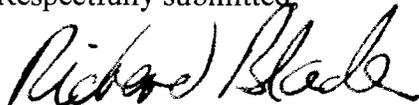
## **IX. SUMMARY AND CONCLUSIONS**

This notification describes the factual, legal, and scientific basis for Kraft's decision to use the following health claim to inform consumers of authoritative NHLBI guidelines:

"Diets low in saturated fat, trans fat, and cholesterol may reduce the risk of heart disease."

This claim reflects consensus science concerning dietary fats and health. For over five years, there has been significant scientific agreement that healthful diets include a moderate amount of total fat and are low in saturated fat, trans fat, and cholesterol. This agreement is reflected in FDA's regulatory precedent, which increasingly permits appropriate flexibility in total fat criteria for health claims. The criteria included in this notification are consistent with those in other FDAMA notifications accepted by FDA, as well as the general requirements of FDAMA, the FFDCFA, and the First Amendment. Significantly, use of the above claim will help to underscore important messages about diet and health, helping consumers to make healthful and informed dietary choices.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "Richard Black". The signature is fluid and cursive, written over a white background.

Richard Black, Ph.D.  
Vice President, Global Nutrition  
Kraft Foods Global, Inc.

**APPENDIX A**

**Authoritative Statement**

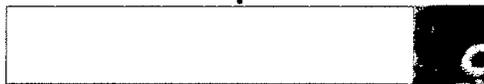
Third Report of the  
National Cholesterol  
Education Program (NCEP)  
Expert Panel on



Detection,  
Evaluation,  
and Treatment  
of High Blood  
Cholesterol  
in Adults  
(Adult Treatment  
Panel III)



Final Report



*National Cholesterol Education Program  
National Heart, Lung, and Blood Institute  
National Institutes of Health  
NIH Publication No. 02-5215  
September 2002*

## V. Adopting Healthful Lifestyle Habits to Lower LDL Cholesterol and Reduce CHD Risk

### 1. Population approach: promoting a base of healthy life habits

NCEP advocates a two-pronged approach for reducing CHD risk: the population approach and the clinical strategy. The two are closely linked. The population approach, which is outlined in the 1990 report of the Population Panel,<sup>5,6</sup> is designed to lower risk in the whole population through adoption of healthy life habits including a healthy diet, weight control, and increased physical activity. The clinical strategy is described in the ATP reports. This section summarizes the population approach and connects it to the clinical strategy. The clinical management team must recognize that they are an integral part of the population approach and contribute to it by providing education and guidance to the patient with high serum cholesterol and the patient's family.

The health community has provided the American public with consistent messages on cardiovascular risk reduction for the past four decades. These messages have encouraged avoidance or cessation of cigarette smoking, reduction of intakes of saturated fats and cholesterol, achieving and maintaining a healthy body weight, regular physical activity, and routine medical check-ups for blood pressure and cholesterol. Table V.1-1 (derived from the Healthy People 2010 publication)<sup>620</sup> reports the current status of the U.S. population on various healthy lifestyle habits and compares it with the goals for 2010.

Although progress has been made, it is clear that much more is needed to bring about the changes required to achieve the goals for 2010. The physician has an important role to play in this effort to help attain these goals.

The NHLBI, American Heart Association, and other organizations have mounted a major effort to reduce risk factors for CHD in the United States. Not only is there continuing research on improved methods for risk reduction, but national educational programs have also been put into effect. Table V.1-2 lists some of the Web sites of the programs sponsored by the U.S. Government.

Table V.1-1. Status Report on Healthy Lifestyle Habits: Healthy People 2010

Lifestyle Habit	Status in the 1990s	Goal for 2010
Healthy weight (BMI <25 kg/m <sup>2</sup> )	42%	60%
Saturated fat intake <10% calories	36%	75%
Vegetable intake of at least 3 servings/day with at least 1/3 dark green or orange	3%	50%
Fruit intake of at least 2 servings/day	28%	75%
Grain intake of at least 6 servings/day with at least 1/3 whole grain	7%	50%
Smoking cessation by adult smokers	41%	75%
Regular physical activity of moderate intensity	15%	30%

Table V.1-2. Government-Sponsored Web Sites for Public Information: An Effective Way to Implement the Public Health Approach

<b>Diet</b>	<a href="http://www.nhlbi.nih.gov/chd">www.nhlbi.nih.gov/chd</a> <a href="http://www.nhlbi.nih.gov/subsites/index.htm">www.nhlbi.nih.gov/subsites/index.htm</a> — then click Healthy Weight <a href="http://www.nhlbi.nih.gov/hbp">www.nhlbi.nih.gov/hbp</a> <a href="http://www.nutrition.gov">www.nutrition.gov</a>
<b>Physical activity</b>	<a href="http://www.fitness.gov">www.fitness.gov</a>
<b>Body weight</b>	<a href="http://www.nhlbi.nih.gov/subsites/index.htm">www.nhlbi.nih.gov/subsites/index.htm</a> — then click Healthy Weight
<b>Cholesterol</b>	<a href="http://www.nhlbi.nih.gov/chd">www.nhlbi.nih.gov/chd</a>
<b>Blood pressure</b>	<a href="http://www.nhlbi.nih.gov/hbp">www.nhlbi.nih.gov/hbp</a>
<b>Smoking cessation</b>	<a href="http://www.cdc.gov/tobacco/sgr_tobacco_use.htm">www.cdc.gov/tobacco/sgr_tobacco_use.htm</a>

After another 6 weeks, the response to dietary therapy should be evaluated. If the LDL cholesterol goal is achieved, the current intensity of dietary therapy should be maintained indefinitely. If the patient is approaching the LDL goal, consideration should be given to continuing dietary therapy before adding LDL-lowering drugs. If it appears unlikely that the LDL goal will be achieved with dietary therapy alone, drug therapy should be considered (see Section IV).

Thereafter, the metabolic syndrome, if present, becomes the target of therapy (see Section II). First-line therapy for the metabolic syndrome is weight control and increased physical activity. Again, referral to a nutrition professional for medical nutrition therapy to assist in weight reduction is recommended.

Finally, long-term monitoring for adherence to TLC is required. Revisits are indicated every 4–6 months during the first year of therapy and every 6–12 months in the long term. If a person is started on drug therapy, more frequent visits are advised.

The information shown in Table V.2–6 may be helpful for the physician both for dietary and lifestyle assessment and for guidance of the patient adopting TLC recommendations. The table is compiled from current ATP III dietary recommendations, Dietary Guidelines for Americans (2000),<sup>241</sup> Obesity Education Initiative (OEI) guidelines for weight reduction,<sup>78,79</sup> and the Surgeon General’s Report on Physical Activity.<sup>238</sup>

### 3. Components of the TLC Diet

#### a. Major nutrient components

The major LDL-raising dietary constituents are saturated fat and cholesterol. A reduction in intakes of these components is the core of the TLC Diet. The scientific foundation for the relationship between high intakes of saturated fat and increased LDL levels dates back several decades and consists of several lines of evidence: observational studies, metabolic and controlled feeding studies, and clinical studies, including randomized clinical trials. These data have been reviewed in detail in previous reports of the NCEP,<sup>1,2,5,6</sup> the U.S. Dietary Guidelines Committees,<sup>241</sup> and the American Heart Association.<sup>393</sup> The other major nutrients—unsaturated fats, protein, and carbohydrates—do not raise LDL cholesterol levels. In developing an LDL-lowering diet

**Table V.2–5. Food Sources of Viscous (Soluble) Fiber**

Food Source	Soluble Fiber (g)	Total Fiber (g)
<b>Cereal Grains (½ cup cooked)</b>		
■ Barley	1	4
■ Oatmeal	1	2
■ Oatbran	1	3
■ Seeds		
– Psyllium Seeds, Ground (1 Tbsp)	5	6
<b>Fruit (1 medium fruit)</b>		
■ Apples	1	4
■ Bananas	1	3
■ Blackberries (½ cup)	1	4
■ Citrus Fruit (orange, grapefruit)	2	2–3
■ Nectarines	1	2
■ Peaches	1	2
■ Pears	2	4
■ Plums	1	1.5
■ Prunes (¼ cup)	1.5	3
<b>Legumes (½ cup cooked)</b>		
■ Beans		
– Black Beans	2	5.5
– Kidney Beans	3	6
– Lima Beans	3.5	6.5
– Navy Beans	2	6
– Northern Beans	1.5	5.5
– Pinto Beans	2	7
■ Lentils (yellow, green, orange)	1	8
■ Peas		
– Chick Peas	1	6
– Black Eyed Peas	1	5.5
<b>Vegetables (½ cup cooked)</b>		
■ Broccoli	1	1.5
■ Brussels Sprouts	3	4.5
■ Carrots	1	2.5

Table V.2-6. Guide to Therapeutic Lifestyle Changes (TLC)

**Healthy Lifestyle Recommendations for a Healthy Heart**

Food Items to Choose More Often	Food Items to Choose Less Often	Recommendations for Weight Reduction	Recommendations for Increased Physical Activity
<p><b>Breads and Cereals</b></p> <p>≥6 servings per day, adjusted to caloric needs</p> <p>Breads, cereals, especially whole grain; pasta; rice; potatoes; dry beans and peas; low fat crackers and cookies</p> <p><b>Vegetables</b></p> <p>3-5 servings per day fresh, frozen, or canned, without added fat, sauce, or salt</p> <p><b>Fruits</b></p> <p>2-4 servings per day fresh, frozen, canned, dried</p> <p><b>Dairy Products</b></p> <p>2-3 servings per day</p> <p>Fat-free, 1/2%, 1% milk, buttermilk, yogurt, cottage cheese; fat-free &amp; low-fat cheese</p> <p><b>Eggs</b></p> <p>≤2 egg yolks per week</p> <p>Egg whites or egg substitute</p> <p><b>Meat, Poultry, Fish</b></p> <p>≤5 oz per day</p> <p>Lean cuts loin, leg, round; extra lean hamburger; cold cuts made with lean meat or soy protein; skinless poultry; fish</p> <p><b>Fats and Oils</b></p> <p>Amount adjusted to caloric level: Unsaturated oils; soft or liquid margarines and vegetable oil spreads, salad dressings, seeds, and nuts</p> <p><b>TLC Diet Options</b></p> <p>Stanol/sterol-containing margarines; viscous fiber food sources: barley, oats, psyllium, apples, bananas, berries, citrus fruits, nectarines, peaches, pears, plums, prunes, broccoli, brussels sprouts, carrots, dry beans, peas, soy products (tofu, miso)</p>	<p><b>Breads and Cereals</b></p> <p>Many bakery products, including doughnuts, biscuits, butter rolls, muffins, croissants, sweet rolls, Danish, cakes, pies, coffee cakes, cookies</p> <p>Many grain-based snacks, including chips, cheese puffs, snack mix, regular crackers, buttered popcorn</p> <p><b>Vegetables</b></p> <p>Vegetables fried or prepared with butter, cheese, or cream sauce</p> <p><b>Fruits</b></p> <p>Fruits fried or served with butter or cream</p> <p><b>Dairy Products</b></p> <p>Whole milk/2% milk, whole-milk yogurt, ice cream, cream, cheese</p> <p><b>Eggs</b></p> <p>Egg yolks, whole eggs</p> <p><b>Meat, Poultry, Fish</b></p> <p>Higher fat meat cuts: ribs, t-bone steak, regular hamburger, bacon, sausage; cold cuts: salami, bologna, hot dogs; organ meats: liver, brains, sweetbreads; poultry with skin; fried meat; fried poultry; fried fish</p> <p><b>Fats and Oils</b></p> <p>Butter, shortening, stick margarine, chocolate, coconut</p>	<p><b>Weigh Regularly</b></p> <p>Record weight, BMI, &amp; waist circumference</p> <p><b>Lose Weight Gradually</b></p> <p>Goal: lose 10% of body weight in 6 months. Lose 1/2 to 1 lb per week</p> <p><b>Develop Healthy Eating Patterns</b></p> <ul style="list-style-type: none"> <li>■ Choose healthy foods (see Column 1)</li> <li>■ Reduce intake of foods in Column 2</li> <li>■ Limit number of eating occasions</li> <li>■ Select sensible portion sizes</li> <li>■ Avoid second helpings</li> <li>■ Identify and reduce hidden fat by reading food labels to choose products lower in saturated fat and calories, and ask about ingredients in ready-to-eat foods prepared away from home</li> <li>■ Identify and reduce sources of excess carbohydrates such as fat-free and regular crackers; cookies and other desserts; snacks; and sugar-containing beverages</li> </ul>	<p><b>Make Physical Activity Part of Daily Routines</b></p> <ul style="list-style-type: none"> <li>■ Reduce sedentary time</li> <li>■ Walk, wheel, or bike-ride more, drive less; Take the stairs instead of an elevator; Get off the bus a few stops early and walk the remaining distance; Mow the lawn with a push mower; Rake leaves; Garden; Push a stroller; Clean the house; Do exercises or pedal a stationary bike while watching television; Play actively with children; Take a brisk 10-minute walk or wheel before work, during your work break, and after dinner</li> </ul> <p><b>Make Physical Activity Part of Exercise or Recreational Activities</b></p> <ul style="list-style-type: none"> <li>■ Walk, wheel, or jog; Bicycle or use an arm pedal bicycle; Swim or do water aerobics; Play basketball; Join a sports team; Play wheelchair sports; Golf (pull cart or carry clubs); Canoe; Cross-country ski; Dance; Take part in an exercise program at work, home, school, or gym</li> </ul>

for ATP III, consideration was given not only to these long-established factors but also to new and emerging data that support the importance of the appropriate distribution of other nutrients that are related to cardiovascular health as well as general health. Therefore, the rationale for the recommendations for each component of the TLC diet will be described briefly.

### 1) Saturated fatty acids

Saturated fatty acids are a major dietary determinant of LDL cholesterol level.<sup>241</sup> The effects of saturated fatty acids on serum total cholesterol (and LDL cholesterol) levels have been studied extensively.<sup>622</sup> Several meta-analyses and reviews have been carried out to estimate the impact of saturated fatty acids on cholesterol levels.<sup>623,624</sup> These analyses indicate that for every 1 percent increase in calories from saturated fatty acids as a percent of total energy, the serum LDL cholesterol rises about 2 percent. Conversely, a 1 percent reduction in saturated fatty acids will reduce serum cholesterol by about 2 percent. Recent trials confirm the efficacy of diets low in saturated fatty acids for lowering LDL levels. For example, the DELTA Study<sup>625</sup> investigated the effects of reducing dietary saturated fatty acids from 15 percent of total calories to 6.1 percent of total calories. On the diet low in saturated fatty acids, LDL cholesterol was reduced by 11 percent. Another study, beFIT,<sup>626,627</sup> tested effects of an NCEP therapeutic diet in individuals with hypercholesterolemia with and without hypertriglyceridemia. Compared to the participants' baseline diet, LDL cholesterol levels were reduced on the therapeutic diet by approximately 8 percent. Large-scale randomized controlled trials have been carried out to assess the safety of reduced intakes of saturated fatty acids and cholesterol in children and have found no evidence for compromised growth or development.<sup>628,629</sup>

**Evidence statements:** There is a dose response relationship between saturated fatty acids and LDL cholesterol levels. Diets high in saturated fatty acids raise serum LDL cholesterol levels (A1). Reduction in intakes of saturated fatty acids lowers LDL cholesterol levels (A1, B1).

The beneficial effects of reducing saturated fatty acids and cholesterol in the diet can be enhanced by weight reduction in overweight persons. Several studies have shown that LDL cholesterol levels can be lowered through weight reduction in overweight persons.<sup>78,79</sup> And most important, as shown in the MRFIT study, weight reduction will enhance serum cholesterol lowering brought about by a reduction in intakes of saturated fatty acids and cholesterol.<sup>630,631</sup>

**Evidence statements:** Weight reduction of even a few pounds will reduce LDL levels regardless of the nutrient composition of the weight loss diet (A2), but weight reduction achieved through a calorie-controlled diet low in saturated fatty acids and cholesterol will enhance and sustain LDL cholesterol lowering (A2).

**Recommendation:** Weight loss through reduced caloric intake and increased levels of physical activity should be encouraged in all overweight persons. Prevention of weight gain also should be emphasized for all persons.

Epidemiological studies show that populations that consume high amounts of saturated fatty acids and cholesterol have a high risk for CHD.<sup>19,632</sup> The evidence that lowering serum cholesterol levels by decreasing intakes of saturated fatty acids reduces the risk for CHD has been demonstrated in the meta-analysis by Gordon.<sup>409,410</sup> This analysis included six robust dietary trials, in aggregate including 6,356 person-years of follow up. It showed that lowering serum cholesterol levels by reducing the intake of saturated fatty acids significantly decreased the incidence of CHD by 24 percent. There was also a trend toward a decrease in coronary mortality (21 percent) and total mortality (6 percent). No increase in non-CVD mortality was found.

The data from dietary trials, in combination with the results of controlled clinical trials with cholesterol-lowering medications,<sup>455,633</sup> document that reducing serum cholesterol and LDL cholesterol by diet alone or with pharmacological means will reduce CHD endpoints. The current American diet contains an average of about 11 percent of total calories as saturated fatty acids. The major sources of saturated fatty acids in the diet are high-fat dairy products (whole milk, cheese,

butter, ice cream, and cream); high-fat meats; tropical oils such as palm oil, coconut oil, and palm kernel oil; and baked products and mixed dishes containing dairy fats, shortening, and tropical oils. To maximize LDL cholesterol lowering by reducing saturated fatty acid intake in the therapeutic diet, it will be necessary to lower intakes from the population mean intake of approximately 11 percent to <7 percent of total energy.

**Evidence statements:** High intakes of saturated fatty acids are associated with high population rates of CHD (C2). Reduction in intake of saturated fatty acids will reduce risk for CHD (A1, B1).

**Recommendation:** The therapeutic diet to maximize LDL cholesterol lowering should contain less than 7 percent of total calories as saturated fatty acids.

## 2) *Trans fatty acids*

*Trans* fatty acids are those in which double bonds are in the *trans* configuration. They are generally produced by hydrogenation of vegetable oils but some are found naturally in animal fats. Substantial evidence from randomized clinical trials indicates that *trans* fatty acids raise LDL cholesterol levels, compared with unsaturated fatty acids.<sup>634-646</sup> These studies also show that when *trans* fatty acids are substituted for saturated fatty acids, HDL cholesterol levels are lower,<sup>647</sup> with a dose response effect observed. Recent United States data show that the use of liquid vegetable oil or semiliquid margarine results in the most favorable total and LDL cholesterol levels and ratios of total cholesterol to HDL cholesterol, whereas the use of butter or stick margarine results in the worst lipid levels.<sup>634</sup> In addition, evidence from some epidemiological cohort studies suggests that high intakes of *trans* fatty acids are associated with higher risk for CHD.<sup>648-651</sup> Whether this association is due to adverse effects of *trans* fatty acids on lipoproteins, to other adverse actions, or to confounding variables is uncertain.

The mean U.S. level of *trans* fatty acids intake is about 2.6 percent of total energy (compared with saturated fatty acids intake of ~11 percent of energy). Major sources of *trans* fatty acids in the diet include products made from partially hydrogenated oils such as baked

products including crackers, cookies, doughnuts, breads, and products like french fries or chicken fried in hydrogenated shortening. Animal sources including dairy products provide smaller amounts of *trans* fatty acids. Soft margarines, tub and liquid, and vegetable oil spreads have low amounts of *trans* fatty acids. Some margarines and spreads are now *trans*-fatty acid free. Some hydrogenation of vegetable oils is the primary technology currently used to provide form to food products, so that they can be eaten out of the hand, rather than with a spoon.

**Evidence statements:** *Trans* fatty acids raise serum LDL cholesterol levels (A2). Through this mechanism, higher intakes of *trans* fatty acids should increase risk for CHD. Prospective studies support an association between higher intakes of *trans* fatty acids and CHD incidence (C2). However, *trans* fatty acids are not classified as saturated fatty acids, nor are they included in the quantitative recommendations for saturated fatty acid intake of <7 percent of calories in the TLC Diet.

**Recommendation:** Intakes of *trans* fatty acids should be kept low. The use of liquid vegetable oil, soft margarine, and *trans* fatty acid-free margarine are encouraged instead of butter, stick margarine, and shortening.

## 3) *Dietary cholesterol*

Dietary cholesterol causes marked hypercholesterolemia in many laboratory animals, including nonhuman primates. High intakes of cholesterol in humans, however, do not cause such a marked increase in serum cholesterol. Nonetheless, controlled metabolic studies in humans indicate that high cholesterol intakes raise LDL cholesterol levels. The degree of rise varies from person to person, as is true for all nutrients. Meta-analyses of studies done in controlled settings confirm the LDL-raising action of dietary cholesterol.<sup>652,653</sup> A recent meta-analysis showed that dietary cholesterol raises the ratio of total to HDL cholesterol, adversely affecting the serum cholesterol profile.<sup>654</sup> A lesser effect of dietary cholesterol has been found in studies carried out in the outpatient setting;<sup>655</sup> in this circumstance, failure to detect the full effect of dietary cholesterol is likely related to lack of tight metabolic

control. On average, the response of serum cholesterol to dietary cholesterol as revealed in tightly controlled studies is approximately 10 mg/dL per 100 mg dietary cholesterol per 1000 kcal.<sup>656,657</sup>

In the past 40 years, there has been a progressive decline in intakes of dietary cholesterol. This has been the result of decreased intakes of eggs, high-fat meat, and high-fat dairy products. This reduction in cholesterol intake, along with a substantial reduction in the proportion of calories from saturated fatty acids, corresponds with the decline in serum cholesterol levels that has occurred in the U.S. population over four decades.<sup>658</sup> At present, the average U.S. daily consumption of cholesterol is 256 mg, higher for men (331 mg) than for women (213 mg).<sup>659</sup> Eggs contribute about one-third of the cholesterol in the food supply and this fraction has increased somewhat in recent years.<sup>660</sup> Other sources of dietary cholesterol include animal products, dairy, meats, poultry, and shellfish.

Some epidemiological data, namely the Western Electric Study, suggest dietary cholesterol increases heart disease risk independently of its effect on serum LDL cholesterol levels.<sup>661</sup> In contrast, data from two prospective cohort studies, the Nurses Health Study and the Health Professionals Study, found no significant association between frequency of reported egg consumption and CHD, except among diabetic women.<sup>662</sup>

**Evidence statements:** Higher intakes of dietary cholesterol raise serum LDL cholesterol levels in humans (A2, B1). Through this mechanism, higher intakes of dietary cholesterol should raise the risk for CHD. Reducing cholesterol intakes from high to low decreases serum LDL cholesterol in most persons (A2, B1).

**Recommendation:** Less than 200 mg per day of cholesterol should be consumed in the TLC Diet to maximize the amount of LDL cholesterol lowering that can be achieved through reduction in dietary cholesterol.

#### 4) *Monounsaturated fatty acids*

The most common form of monounsaturated fatty acids is oleic acid, which occurs in the *cis* form. Substitution of *cis*-monounsaturated fatty acids for saturated fatty acids results in a fall in LDL cholesterol levels.<sup>624</sup> Moreover, substitution of monounsaturated fatty acids for saturated fatty acids results in little or no decrease in HDL cholesterol and does not increase triglycerides as occurs with very high intakes of carbohydrates (>60 percent of total energy).<sup>624,663-665</sup>

Monounsaturated fatty acids—as part of a diet that is low in saturated fatty acids and cholesterol and rich in vegetables, fruits, and grain products—have received increased attention as being potentially beneficial for risk reduction because of their association with low rates of CHD in olive-oil consuming populations of the Mediterranean basin.<sup>19,20,632</sup> Despite epidemiological support for higher intakes of monounsaturated fatty acids, there are no controlled clinical trials that are designed to compare effects of monounsaturated and saturated fatty acids on CHD endpoints. This lack of data contrasts with several trials that replaced saturated fat with polyunsaturated fat.

**Evidence statements:** Monounsaturated fatty acids lower LDL cholesterol relative to saturated fatty acids (A2, B2). Monounsaturated fatty acids do not lower HDL cholesterol nor raise triglycerides (A2, B2).

**Evidence statement:** Dietary patterns that are rich in monounsaturated fatty acids provided by plant sources and rich in fruits, vegetables, and whole grains and low in saturated fatty acids are associated with decreased CHD risk (C1). However, the benefits of replacement of saturated fatty acids with monounsaturated fatty acids has not been adequately tested in controlled clinical trials.

**Recommendations:** Monounsaturated fatty acids are one form of unsaturated fatty acid that can replace saturated fatty acids. Intake of monounsaturated fatty acids can range up to 20 percent of total calories. Most monounsaturated fatty acids should be derived from vegetable sources, including plant oils and nuts.

### 5) Polyunsaturated fatty acids

Polyunsaturated fatty acids, consisting mainly of n-6 linoleic acid, reduce LDL cholesterol levels when substituted for saturated fatty acids. At high intakes, linoleic acid also can produce small reductions in HDL cholesterol and triglycerides, although these responses are variable. Compared to cis-monounsaturated fatty acids, polyunsaturated fatty acids often cause a slightly greater reduction in LDL cholesterol levels.<sup>624</sup>

Several controlled clinical trials have compared the effects of polyunsaturated fatty acids, as a replacement for saturated fatty acids, on coronary endpoints.<sup>657</sup> Meta-analysis of trial results indicates that substitution of polyunsaturated fatty acids for saturated fatty acids reduces risk for CHD.<sup>409,410,624</sup> This positive result is supported by research in primates that indicates that polyunsaturated fatty acids are antiatherogenic when substituted for saturated fatty acids.<sup>666</sup>

Despite evidence of CHD risk reduction from polyunsaturated fatty acids, there are no large populations that have consumed large quantities of polyunsaturated fatty acids for long periods. Thus, high intakes have not been proven safe in large populations; this introduces a note of caution for recommending high intakes.

**Evidence statements:** Linoleic acid, a polyunsaturated fatty acid, reduces LDL cholesterol levels when substituted for saturated fatty acids in the diet (A1, B1). Polyunsaturated fatty acids can also cause small reductions in HDL cholesterol when compared with monounsaturated fatty acids (B2). Controlled clinical trials indicate that substitution of polyunsaturated fatty acids for saturated fatty acids reduces risk for CHD (A2, B2).

**Recommendations:** Polyunsaturated fatty acids are one form of unsaturated fatty acids that can replace saturated fat. Most polyunsaturated fatty acids should be derived from liquid vegetable oils, semi-liquid margarines, and other margarines low in *trans* fatty acids. Intakes of polyunsaturated fat can range up to 10 percent of total calories.

### 6) Total fat

Among the fatty acids that make up the total fat in the diet, only saturated fatty acids and *trans* fatty acids raise LDL cholesterol levels.<sup>657</sup> Thus, serum levels of LDL cholesterol are independent of intakes of total fat per se. ATP II<sup>1,2</sup> advised limiting total fat in Step I and Step II diets to  $\leq 30$  percent of calories primarily as a means of achieving lower intakes of saturated fatty acids. The focus of the dietary approach to reducing CHD risk then and now is on dietary fatty acids that raise LDL cholesterol concentrations.

**Evidence statement:** Unsaturated fatty acids do not raise LDL cholesterol concentrations when substituted for carbohydrates in the diet (A2, B2).

**Recommendation:** It is not necessary to restrict total fat intake for the express purpose of reducing LDL cholesterol levels, provided saturated fatty acids are reduced to goal levels.

For many years, other public health groups have recommended low intakes of total fat in an effort to curtail obesity and to reduce the risk for some forms of cancer. These recommendations were based largely on experiments in laboratory animals and cross-cultural studies. Several short-term studies also suggest that higher fat intakes (>35 percent of calories) modify the body's metabolism in ways that favor fat accumulation.<sup>667-672</sup> However, isocaloric exchange of fat for carbohydrate does not produce weight gain over a period of many months.<sup>673,674</sup> Further, although some prospective studies have suggested a relationship between the percentage of dietary fat and obesity,<sup>675,676</sup> recent prospective studies (or meta-analysis of studies) have failed to detect a causative link between them.<sup>677,678</sup> Evidence related to these areas is reviewed in detail in the recent rationale report of the Dietary Guidelines for Americans (2000).<sup>241</sup>

Studies in laboratory animals and cross-cultural studies have suggested a relationship between fat intake and risk for certain cancers.<sup>679-682</sup> Moreover, a major clinical trial is presently underway to determine whether low-fat diets will reduce risk for breast cancer in women; this trial is a component of the Women's Health Initiative<sup>683</sup> and is scheduled to end in 2005.

Even so, recent prospective studies have not confirmed an association between fat intake and cancer.<sup>684-687</sup> Thus, a strong recommendation to reduce fat intake for the purpose of preventing cancer does not seem warranted at this time.<sup>241</sup>

The Dietary Guidelines for Americans (2000)<sup>241</sup> noted that some investigators are concerned that recommendations that emphasize lower total fat intakes (<30 percent of energy) may have led to an overconsumption of carbohydrates, contributing to an increased prevalence of obesity. Moreover, very high intakes of carbohydrates (>60 percent of calories) in overweight/obese persons can aggravate some of the risk factors of the metabolic syndrome.<sup>663,664,688-691</sup> These latter responses have led some investigators to propose that populations with a high prevalence of insulin resistance and the metabolic syndrome should avoid very high-carbohydrate diets and should consume relatively more unsaturated fatty acids.<sup>692</sup>

**Evidence statement:** The percentage of total fat in the diet, independent of caloric intake, has not been documented to be related to body weight or risk for cancer in the general population.<sup>241</sup> Short-term studies suggest that very high fat intakes (>35 percent of calories) modify metabolism in ways that could promote obesity (C2). On the other hand, very high carbohydrate intakes (>60 percent of calories) aggravate some of the lipid and non-lipid risk factors common in the metabolic syndrome (A2, B2, C2).

**Recommendations:** Dietary fat recommendations should emphasize reduction in saturated fatty acids. Further, for persons with lipid disorders or the metabolic syndrome, extremes of total fat intake—either high or low—should be avoided. In such persons, total fat intakes should range from 25–35 percent of calories. For some persons with the metabolic syndrome, a total fat intake of 30–35 percent may reduce lipid and nonlipid risk factors.

## 7) Carbohydrate

When carbohydrates are substituted for saturated fatty acids, the fall in LDL cholesterol levels equals that with monounsaturated fatty acids. However, compared with monounsaturated fatty acids, substitution of carbohydrate for saturated fatty acids frequently causes a fall in HDL cholesterol and a rise in triglyceride.<sup>624,663,689,693</sup> This effect apparently persists in the long term, as suggested by differences in population lipid levels in the presence of different habitual diets.<sup>694,695</sup> When carbohydrate is consumed along with high-fiber diets, however, the rise in triglycerides or fall in HDL cholesterol has been reported to be reduced.<sup>693,696,697</sup>

Digestible carbohydrates include starches (complex carbohydrates) and sugar. Some foods, such as whole grains, vegetables, and some fruits, contain viscous fiber that helps to lower LDL cholesterol as well (see Table V.2–5). Sugars and starches occur naturally in many foods that also supply other important nutrients. Examples of these foods include fat-free and low-fat dairy products, fruits, some vegetables, breads, cereals, and grains. Inclusion of these foods helps provide daily recommended intakes of essential nutrients.<sup>241</sup>

An old concept receiving recent attention is the “glycemic” potential of different foods. Glycemic index refers to the value obtained by feeding a carbohydrate load and measuring the level of blood glucose. Study of this factor is complicated because there is a wide range in the glycemic index for each group of foods, attributed to factors such as its form when eaten, the way it is processed, how it is chewed, how it is emptied from the stomach, and an individual’s physiologic and metabolic responses.<sup>698</sup> To date the glycemic index has not been widely accepted as a practical means by which to select specific carbohydrate-containing foods for dietary therapy.<sup>241</sup>

## **APPENDIX B**

### **Analytical Methodology**

## Analytical Methodology

In agency guidance (“Guidance for Industry: Notification of a Health Claim or Nutrient Content Claim Based on an Authoritative Statement of a Scientific Body”), FDA has advised that it “believes that information on analytical methodology for the nutrient that is the subject of the claim should be submitted as part of the notification, consistent with 21 C.F.R. 101.69 and 21 C.F.R. 101.70.” The cited regulations describe petition requirements for traditional nutrient content and health claims and require the availability of appropriate analytical methods for assessing regulatory compliance.

This notification contains criteria for saturated fat, trans fat, cholesterol, and total fat. These nutrients are mandatory nutrients that must be declared in nutrition labeling, if present in a food, as required by 21 C.F.R. § 101.9. Rules for acceptable analytical methods for these nutrients are described in 21 C.F.R. § 101.9(g). That section states that the “Official Methods of the AOAC International,” 15<sup>th</sup> Ed. (1990) should be used, and if no AOAC method is available or appropriate, other appropriate reliable analytical procedures may be used. *Id.* § 101.9(g)(2). Appropriate methods for analyzing saturated fat, trans fat, cholesterol, and total fat are available and routinely used in developing nutrition labeling.

The foods eligible to bear the proposed health claim are similar to those described in Kraft’s 2003 FDAMA notification for whole grain foods with a moderate fat content, which established identical quantitative criteria for saturated fat, trans fat, cholesterol, and total fat (in addition to whole grain content, which is not addressed in this notification).<sup>1</sup> Kraft would be happy to provide a specific list of examples of foods eligible to bear the proposed claim if helpful to the agency.

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<sup>1</sup> Notification for a Health Claim Based on an Authoritative Statement: Whole Grains and Coronary Heart Disease (Docket 2003Q-0547)(posted Dec. 2003).

## **APPENDIX C**

### **References**

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