



Kraft Foods



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3787 '03 DEC -4 10:51

August 8, 2003

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Office of Nutritional Products, Labeling and Dietary Supplements (HFS-800)
Center for Food Safety and Applied Nutrition
Food and Drug Administration
Harvey W. Wiley Federal Building
5100 Paint Branch Parkway
College Park, MD 20740-3835

**Re: Notification for a Health Claim Based on an Authoritative Statement:
Whole Grain Foods and Heart Disease**

Dear Sir or Madam:

Kraft Foods North America, Inc. (Kraft) is planning to use the food label to educate consumers about the well-established relationship between the consumption of whole grain foods and reduced risk of coronary heart disease (CHD). As required by section 403(r)(3)(C) of the Federal Food, Drug, and Cosmetic Act (FFDCA), 21 U.S.C. § 343(r)(3)(C), Kraft is notifying the Food and Drug Administration (FDA) that the company intends to make a health claim based upon an authoritative statement of the Food and Nutrition Board (FNB) of the National Research Council (NRC), the working arm of the National Academy of Sciences (NAS). The exact wording of the proposed claim is as follows: "Diets rich in whole grain foods and other plant foods, and low in saturated fat and cholesterol, may help reduce the risk of heart disease."

We have enclosed two copies of the complete notification document, including the required detailed review of the scientific literature supporting the claim. For your convenience we also have enclosed a compact disc with adobe (.pdf) files of the notification and appendices.

We look forward to your favorable reply. If you have questions, please do not hesitate to contact me at (847) 646-6125.

Sincerely,

Jean E. Spence
Senior Vice President
Research and Development

2003Q-0547

HCN¹

**Notification for a Health Claim
Based on an Authoritative Statement:
Whole Grain Foods and Heart Disease**

DATE: 08/6/2003

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

Whole Grain Foods and Heart Disease

I. INTRODUCTION

Kraft Foods North America, Inc. (Kraft) is planning to use the food label to educate consumers about the well-established relationship between the consumption of whole grain foods and reduced risk of coronary heart disease (CHD). As required by section 403(r)(3)(C) of the Federal Food, Drug, and Cosmetic Act (FFDCA), 21 U.S.C. § 343(r)(3)(C), Kraft is notifying the Food and Drug Administration (FDA) that the company intends to make a health claim based upon an authoritative statement of the Food and Nutrition Board (FNB) of the National Research Council (NRC), the working arm of the National Academy of Sciences (NAS). The exact wording of the proposed claim is as follows: "Diets rich in whole grain foods and other plant foods, and low in saturated fat and cholesterol, may help reduce the risk of heart disease."

The claim will be used on foods that contain a minimum of 51% whole grains (using dietary fiber as a marker), meet the regulatory definitions for "low saturated fat" and "low cholesterol," bear quantitative trans fat labeling in the Nutrition Facts box, and meet all general requirements for health claims in 21 C.F.R. § 101.14. In particular, the claim will appear on foods such as whole grain cereals, crackers, breads, and whole grain based snack mixes and bars.

The proposed claim is based upon the following authoritative statement made in the classic report *Diet and Health: Implications for Reducing Chronic Disease Risk*¹ (“*Diet and Health*”):

Diets high in plant foods – i.e., fruits, vegetables, legumes, and whole-grain cereals – are associated with a lower occurrence of coronary heart disease and cancers of the lung, colon, esophagus, and stomach.

(*Diet and Health*, at 8). Although this statement was published in 1989, the relationship between whole grain foods and reduced risk of CHD, in the context of a diet low in saturated fat and cholesterol, remains substantiated by a balanced review of the current scientific literature.

II. BACKGROUND—THE *DIET AND HEALTH* REPORT

The *Diet and Health* report reflects a comprehensive review and analysis of scientific literature addressing diet and the spectrum of major chronic diseases. The report presents the findings of the Committee on *Diet and Health* (the “Committee”), a 19-member interdisciplinary committee established by the FNB to explore the relationship between chronic disease risk and foods, food groups, food components, and dietary patterns. Widely considered a major work in the field of nutrition, the report remains respected and relevant today. It has been used as a basis for two authoritative statement health claims authorized pursuant to FDAMA notifications: in 1999, it was cited as a basis for a health claim concerning whole grain foods and reduced risk of CHD; in 2000, it provided a basis for a health claim addressing the relationship between potassium, blood pressure, and reduced risk of stroke.

¹ National Research Council, *Diet and Health: Implications for Reducing Chronic Disease Risk*, at 8 (National Academy Press 1989).

Kraft has carefully reviewed the conclusions set forth in the *Diet and Health* report concerning the beneficial relationship between whole grain foods and reduced risk of CHD. In addition to the information and findings set forth in the text of *Diet and Health*, our review considered the studies evaluated by the Committee on *Diet and Health* and cited in the report, more recent studies addressing whole grain foods and CHD, current recommendations concerning whole grain consumption, current recommendations and science concerning total fat intake, regulatory precedent including the currently authorized whole grain claim,² and other information relevant to the development of an authoritative statement health claim addressing whole grain foods and CHD.

On the basis of this review, Kraft concluded that *Diet and Health* supports the use of a health claim communicating the relationship between whole grains and CHD on a wide variety of whole grain foods. In particular, a review of the report and supporting literature demonstrates that consistency with *Diet and Health* does not require that the proposed claim be restricted to whole grain foods that meet the definition of “low fat” in 21 C.F.R. § 101.62. The “low fat” constraint was incorporated into the 1999 notification, but is not required by the report or underlying scientific evidence. Moreover, consumption of the whole grain foods that are the subject of this notification is entirely compatible with a healthful diet consistent with the recommendations of public health experts. Additionally, the whole grain and saturated fat criteria specified in this notification will operate as practical restrictions on total fat content, ensuring that products bearing the proposed claim will contain moderate levels of total fat considerably lower than the disqualifying level for total fat. When framed as proposed, the claim gives appropriate emphasis to the benefit of consuming whole grain foods that are low in saturated fat and cholesterol without unduly limiting communication focused on whole grains based upon total fat content.

² Whole Grain Foods Authoritative Statement Claim Notification, docket no. 99P-2209 (Mar. 10, 1999); Letter from S. Pape to C. Lewis (July 6, 1999).

III. AUTHORITATIVE STATEMENT

A. *Diet and Health*

The authoritative statement upon which the proposed whole grain health claim is based appears in the executive summary of the *Diet and Health* report. The executive summary, which reflects the Committee's major conclusions and their bases, contains the Committee's finding that—

Diets high in plant foods – i.e., fruits, vegetables, legumes, and whole-grain cereals – are associated with a lower occurrence of coronary heart disease and cancers of the lung, colon, esophagus, and stomach.

(*Diet and Health*, at 8). Immediately following this statement, the FNB offered possible explanations for the anticipated health benefits of plant-based foods, including whole grains:

Although the mechanisms underlying these effects are not fully understood, the inverse association with coronary heart disease may be largely explained by the usually low saturated fatty acid and cholesterol content of such diets. Such diets are also low in total fat, which is directly associated with the risk of certain cancers, but rich in complex carbohydrates (starches and fiber) and certain vitamins, minerals, trace elements, and nonnutritive constituents, and these factors probably also confer protection against certain cancers and coronary heart disease.

(*Diet and Health*, at 8). On the subject of total fat, the FNB stated (*Diet and Health*, at 7) that “[t]here is clear evidence that the total amounts and types of fats and other lipids in the diet influence the risk of atherosclerotic cardiovascular disease and, to a less well-established extent, certain forms of cancer and possibly obesity.” The FNB explained that a reduction in total fat consumption would be expected to promote health by facilitating concomitant reductions in intake of saturated fatty acids:

Intake of total fat *per se*, independent of the relative content of the different types of fatty acids, is not associated with high blood cholesterol levels and coronary heart disease. A reduction in total fat consumption, however, facilitates reduction of saturated fatty acid intake; hence, in addition to reducing the risk of certain

cancers, and possibly obesity, it is a rational part of a program aimed at reducing the risk of coronary heart disease.

(*Diet and Health*, at 7). The Committee on Diet and Health recommended that total fat intake be reduced to 30% or less of calories, with less than 10% of total calories derived from saturated fat. (*Diet and Health*, at 13). In offering this recommendation, the Committee again emphasized the need to limit saturated fat and cholesterol (*Diet and Health*, at 13):

A large and convincing body of evidence from studies in human and laboratory animals shows that diets low in saturated fatty acids and cholesterol are associated with low risks and rates of atherosclerotic cardiovascular diseases. High-fat diets are also linked to a high incidence of some types of cancer and, probably, obesity. Thus, reducing total fat and saturated fatty acid intake is likely to lower the rates of these chronic diseases. Fat intake should be reduced by curtailing the major sources of dietary fats rather than by eliminating whole categories of food. For example, by substituting fish, poultry without skin, lean meats, and low- or nonfat dairy products for high-fat foods, one can lower total fat and saturated fatty acid intake while ensuring an adequate intake of iron and calcium—two nutrients of special importance to women. Dietary fat can also be reduced by limiting intake of fried foods, baked goods containing high levels of fat, and spreads and dressings containing fats and oils.

B. Health Claims Based on *Diet and Health*

In 1999, the FNB's authoritative statement concerning whole grains was used to support the following health claim:

Diets rich in whole grain foods and other plant foods and low in total fat, saturated fat, and cholesterol, may help reduce the risk of heart disease and certain cancers.

The notification proposing this health claim (the "1999 whole grains notification") presented evidence that the proposed authoritative statement continued to be supported by the evolving body of science. The notification characterized the available science as reflecting significant scientific agreement regarding the ability of a low fat diet rich in whole grain foods to reduce the risk of CHD and certain cancers. The notification has been interpreted to require that foods

eligible to bear the notified claim must be “low” in fat, saturated fat, and cholesterol, as defined by FDA.

The 1999 whole grain notification also included a specification for whole grain content, defining “whole grain foods” for purposes of the proposed health claim as foods with 51% or more whole grain ingredient(s) by weight per Reference Amount Customarily Consumed (RACC). Such foods provide a minimum of 16 grams of whole grain, which is the equivalent whole grain food serving under the Food Guide Pyramid.

It was proposed that dietary fiber be used as a marker to identify whole grain foods for the purpose of assessing compliance with the claim. A formula³ based on the fiber content of whole wheat (the most prevalent grain in the U.S. diet) was proposed to calculate the minimum amount of fiber necessary for foods with different RACCs to qualify for the claim. The result of this calculation for different RACCs is provided in Table 1.

Table 1
Minimum Fiber Content to Qualify for the Whole Grain Health Claim
for Different Reference Amounts Customarily Consumed

RACC (g)	Minimum fiber content (g)
30	1.7
45	2.5
50	2.8
55	3.0

³Dietary fiber necessary to qualify for the claim = (11 grams dietary fiber per 100 grams whole wheat x 51% x RACC)/100.

C. Total fat intake as addressed in *Diet and Health*

Although the claim proposed in the 1999 notification expressly referenced low fat diets, and the notification required foods bearing the claim to be “low fat” as defined by FDA, neither the *Diet and Health* report nor more recent science mandates such an approach. The *Diet and Health* report reflects significant scientific agreement that diets low in saturated fat and cholesterol are associated with a reduced risk of CHD. The Committee on Diet and Health did suggest that diets high in total fat may increase CHD risk, primarily because such diets may also be high in saturated fat. The emphasis placed in *Diet and Health* on saturated fat and cholesterol supports a similar emphasis and approach in claims pertaining to CHD risk. The continued relevance of this approach is confirmed by recent literature and dietary recommendations, which are discussed in detail in Parts VII and VIII below.

Although saturated fat and cholesterol are predominant concerns identified in *Diet and Health*, it is appropriate to consider total fat intake in fashioning a claim addressing CHD risk. There should be some assurance that foods bearing such claims do not promote excessive or otherwise unreasonable consumption of fat. There is, however, no basis for concluding that a food that does not meet the technical definition of “low fat” in 21 C.F.R. 101.62(b)(2) cannot be part of a diet that contains an appropriate amount of total fat. The Committee on Diet and Health suggested that high fat foods should be limited, but did not recommend the elimination of foods that may contain moderate levels of fat.

A flexible approach to total fat content is particularly warranted in the case of whole grains, for which a beneficial effect has been demonstrated. The beneficial effect of whole grains independent of fat intake was evident in studies considered in the preparation of *Diet and Health* and is corroborated by more recent science. The available literature supports a conclusion that the total fat content, *per se*, of

diets rich in fiber or whole grain foods is unrelated to CHD, and provides no persuasive evidence that whole grain foods that are low in saturated fat and cholesterol, but not necessarily low in total fat, are any less effective in reducing the risk of CHD than their low-fat counterparts. A balanced review of 40 studies with original data on the effect of whole grain foods or dietary fiber (a marker for whole grains) on the risk or incidence of CHD is provided below in Part VII.

IV. EXACT WORDING OF THE PROPOSED CLAIM

Kraft intends to make the following authoritative statement claim on the label and/or labeling of certain whole grain food products:

Diets rich in whole grain foods and other plant foods, and low in saturated fat and cholesterol, may help reduce the risk of heart disease.

This claim is similar to the currently authorized whole grains health claim except that the claim is succinctly worded to focus upon the relationship between heart disease and diets rich in whole grains and low in saturated fat and cholesterol. As noted previously, this focus is fully consistent with *Diet and Health* and is further supported by substantial amounts of additional data and recommendations that have become available since *Diet and Health* was published. The supportive data and other information are discussed in detail in Parts VII and VIII of this notification.

V. STATUTORY BASIS FOR THE CLAIM

Section 303 of the Food and Drug Administration Modernization Act of 1997 (FDAMA) (21 U.S.C. § 343(r)(3)) authorizes food manufacturers to make health claims without prior FDA approval provided certain conditions are met. In

enacting the FDAMA notification scheme for health and nutrient content claims, Congress intended to provide "streamlined procedures" for the dissemination of scientifically sound nutrition information to the public (H.R. Rep. No. 105-399, at 98 (1997)). The ultimate legislative goal, well-served by the present notification, was to ensure a flexible regulatory mechanism by which well-established diet and health information reaches consumers. This objective is in line with FDA's recently announced Consumer Health Information for Better Nutrition initiative.

A. Requirements for health claims based on authoritative statements

The FFDCA, as amended by FDAMA, specifically authorizes the use of health claims based on authoritative statements when the following criteria are met:

(i) a scientific body of the United States Government with official responsibility for public health protection or research directly relating to human nutrition (such as the National Institutes of Health or the Centers for Disease Control and Prevention) or the National Academy of Sciences or any of its subdivisions, has published an authoritative statement, which is currently in effect, about the relationship between a nutrient and a disease or health-related condition to which the claim refers;

(ii) a person has submitted to the Secretary, at least 120 days (during which the Secretary may notify any person who is making a claim as authorized by clause (C) that such person has not submitted all the information required by such clause) before the first introduction into interstate commerce of the food with a label containing the claim, (I) a notice of the claim, which shall include the exact words used in the claim and shall include a concise description of the basis upon which such person relied for determining that the requirements of subclause (i) have been satisfied, (II) a copy of the statement referred to in subclause (i) upon which such person relied in making the claim, and (III) 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;

(iii) the claim and the food for which the claim is made are in compliance with clause (A)(ii) and are otherwise in compliance with paragraph (a) and section 201(n); and

(iv) the claim is stated in a manner so that the claim is an accurate representation of the authoritative statement referred to in subclause (i) 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.

(FFDCA § 403(r)(3)(C)). The FFDCA further provides that the statement "shall not include a statement of an employee of the scientific body made in the individual capacity of the employee."

In 1998, FDA issued a document providing 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 (Guidance for Industry (June 11, 1998)). In this guidance document, FDA identified six criteria for FDAMA claims, four of which are based on the plain language of the statute and the last two of which are based on FDA's interpretation of the statute and its legislative history. According to the FDA guidance document, an authoritative statement:

- 1) is about the relationship between a nutrient and a disease or health-related condition;
- 2) is "published by the scientific body";
- 3) is "currently in effect";
- 4) "shall not include a statement of an employee of the scientific body made in the individual capacity of the employee";
- 5) should reflect a consensus within the identified scientific body if published by a subdivision of one of the federal scientific bodies; and

- 6) should be based on a deliberative review by the scientific body of the scientific evidence.

The FDA guidance document further stated that the agency interprets FDAMA as requiring health claims to be supported by significant scientific agreement—the same standard that is required for health claim regulations.⁴ Separately, FDA has also advised that a health claim based on an authoritative statement must not be equivalent to a health claim that is the subject of an authorizing regulation issued by the agency pursuant to section 403(r)(3)(B) of the FFDCFA. (63 Fed. Reg. 34101, 34102 (June 22, 1998)).

B. Authoritative status of the *Diet and Health* statement

The *Diet and Health* statement upon which the proposed whole grains health claim is based qualifies as an “authoritative statement” under section 403(r)(3)(C) of the FFDCFA, as amended by FDAMA. The statement concerns the relationship between whole grain foods and CHD, a serious and chronic disease that is associated with dietary habits over a lifetime. It is based upon a deliberative review of the literature by an expert Committee established by the FNB and the NRC, which in turn are affiliated with the NAS, an agency that is identified in FDAMA as an authoritative body that may be the source of authoritative statements. Because the statement appears in the executive summary of a major report of the NRC (the working arm of the NAS), it is reasonably characterized as reflecting consensus within an authoritative body. Indeed, in its review of the 1999 whole grains notification, FDA determined this precise

⁴ 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 (<http://www.cfsan.fda.gov/~dms/hclmguid.html#foot1>), the guidance contains a link that references more recent information on food labeling. 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, and completion of the report of the agency’s Task Force on Consumer Health Information for Better Nutrition, along with the associated guidance documents. See, e.g., *Pearson v. Shalala*, 164 F.3d 650 (D.C. Cir. 1999); 68 Fed. Reg. 41387 (July 11, 2003).

statement to be an authoritative statement upon which a health claim may be based.

The statement also is "currently in effect," as required by FDAMA. Since the 1999 whole grains notification, multiple papers, studies, and dietary recommendations have corroborated the conclusions set forth in *Diet and Health* concerning the relationship between CHD and diets rich in whole grains and low in saturated fat and cholesterol. These papers, studies, and recommendations are discussed fully in Parts VII and VIII of this notification.

C. Form and Content of Claim

In addition to establishing criteria for authoritative statements, FDAMA also sets forth criteria that proposed claims based on authoritative statements must meet. The form and content of the proposed whole grain health claim satisfy these criteria. In particular, the form and content of the proposed claim (1) provide an accurate representation of the authoritative statement; (2) are truthful and not misleading, consistent with sections 403(a) and 201(n) of the Act; (3) enable the public to comprehend the information and to understand its significance in the context of the total daily diet; and (4) are supported by significant scientific agreement concerning diets rich in whole grains and low in saturated fat and cholesterol.

Additionally, the proposed claim is distinct from, and not equivalent to, any health claim the agency has authorized by regulation, including FDA-approved health claims addressing the relationship between CHD risk and soy protein, plant sterol and stanol esters, or certain types of fiber-containing foods. Significantly, the proposed health claim is distinct from approved claims concerning fiber-containing foods because whole grain foods as such have been shown to confer beneficial health effects. The anticipated benefits of whole grains are not attributed to fiber, *per se*, or any other isolated component of whole grains.

VI. NATURE OF THE FOOD ELIGIBLE TO BEAR THE CLAIM

Foods bearing the claim would meet the following criteria: first, as specified in the 1999 whole grain notification, "whole grain foods" would contain 51% or more whole grain ingredient(s) by weight per RACC using dietary fiber as a compliance marker; second, foods would meet the FDA definitions for low saturated fat (21 CFR § 101.62 (c)(2)) and low cholesterol (21 CFR § 101.62 (d)(2)); third, the Nutrition Facts on the label would include trans fat labeling consistent with the final rule published in the July 11, 2003 *Federal Register* (68 Fed. Reg. 41434). The claim would be used on appropriate whole grain products, including whole grain cereals, crackers, breads and whole grain based snack mixes and bars. Label examples that illustrate the application of these criteria for a whole grain cereal and a whole grain cracker product are provided in Appendix D. The basis for selecting these criteria is discussed in detail below.

A. Whole grain content

Kraft intends to use the eligibility criterion for whole grain content as specified in the 1999 whole grain notification. This criterion was described in detail in the 1999 submission (see p. 11-12 of Appendix B) and is summarized in Part III of this document. Specifically, weight of fiber per RACC is used as a marker for foods that contain at least 51% whole grain ingredients according to the following formula: grams of minimum fiber per RACC = (11 grams fiber x 51% x RACC)/100.

B. Fat and Cholesterol Content

To qualify for the proposed claim, whole grain foods would be required to meet the FDA definitions for low saturated fat and low cholesterol, as set forth in 21 C.F.R. §§ 101.62 (c)(2) and 101.62 (d)(2), respectively. Use of the claim for such

foods is justified based on the *Diet and Health* report and the studies underlying this report. The concern expressed by FNB regarding total fat was based on indirect effects that may result from high fat diets, primarily, high intakes of saturated fat. The FNB characterized saturated fat intake as “the major dietary determinant of the serum total cholesterol and LDL cholesterol levels in populations and thereby of coronary heart disease risk in populations.” (*Diet and Health*, at 7-8).

With respect to total fat, the eligibility criteria discussed in this notification will limit the amount of total fat that can be present in foods bearing the proposed health claim, thereby facilitating a total fat intake that is consistent with dietary guidelines. The proposed criteria stipulate that products must be low in saturated fat, low in cholesterol, and contain at least 51% whole grain ingredient(s) by weight per RACC. In addition, such products would be required to meet all other conditions specified in 21 CFR § 101.14, including the disqualifier level for total fat. Thus, whole grain snacks, crackers and cereals with a RACC of 30 g could contain no more than 8 g total fat per RACC, because these foods must contain no more than 13 grams of total fat per 50 grams.

Application of the total fat disqualifier level *alone* is sufficient to ensure that increased consumption of whole grain foods prompted by the health claim will not result in excessive intakes of total fat. In setting the disqualifier levels at 20% of the daily reference value (DRV), FDA concluded that foods containing fat at levels up to the disqualifier level could be consumed as part of a diet consistent with dietary guidelines (58 Fed. Reg. 2478, 2494 (Jan. 6, 1993)):

With levels set at 20 percent of the DRV's for fat, saturated fat, cholesterol, and sodium, the question arises as to whether there are foods included among those containing 20 percent or less of a DRV that may lead to a diet inconsistent with dietary guidelines for maintaining good health. On reconsideration, the agency believes that the answer is no.

FDA noted that the disqualifier levels were being increased from 15 percent of the DRV (as originally proposed) to 20 percent of the DRV to allow foods that are specifically recommended by dietary recommendations (e.g., the Dietary Guidelines for Americans) to bear health claims (58 Fed Reg. at 2494):

Based on considerations of foods highlighted by the comments as well as on a review of the food composition data available to the agency, FDA agrees that the use of a 20 percent DRV criterion will permit foods that are appropriately included in an overall healthy diet, for example a greater variety of bran and oat breakfast cereals or legume and vegetable products, to bear a health claim, even though they would not have been permitted to do so under the 15 percent DRV criterion.

Whole grain foods are excellent examples of products that are “recommended for increased consumption”. Such foods are recommended by the Dietary Guidelines for Americans, the Food Guide Pyramid, the Food Guide Pyramid for Young Children, “Healthy People 2010,” the American Cancer Society, the American Diabetes Association, the American Dietetic Association and the American Heart Association, as discussed more fully in Part VIII of this notification.

Although the total fat disqualifier level is sufficient to prevent excessive consumption of fat, in practice, most foods bearing the proposed claim will contain fat at considerably lower levels. In most cases, limitations on fat content due to the physical nature of whole grain products, in conjunction with the proposed saturated fat limitation, are expected to be considerably more constraining than the disqualifier level.

1. Physical nature of whole grain foods

The physical characteristics of whole grain foods tend to limit fat content. In Table 2, we have compiled the average fat content of a broad sample of existing grain based products.

Table 2
Average Fat Content of Grain Based Foods: Breads, Cereals, Crackers and Certain Snacks

Product Category ^a	RACC	Fat Content of Other Grain Based Foods (g per RACC)		Fat Content of Whole Grain Foods ^b (g per RACC)	
		Average	Range	Average	Range
Breads	50 g	2.0	1.4 – 2.9	1.8	1.1 – 2.7
Cereals	30 g	1.0	0 – 3.5	1.1	0.5 – 2.0
Cereals	55 g	2.2	0.6 – 4.0	2.2	0.6 – 6.2
Crackers	30 g	3.4	0 – 6.2	2.6	0 – 4.8
Snack Mixes	30 g	5.3	2.0 – 9.0	None found	

^aProducts included are listed in Appendix C.

^bIncludes whole-grain products that meet the proposed health claim eligibility criteria but are *not* necessarily low in fat.

The data in Table 2 show that the fat content of whole grain products is similar to (or slightly lower than) that of other grain based foods and typically well below the disqualifier level. The fat content of new products developed to take advantage of the proposed claim would be comparable to those of whole grain products already in the marketplace.

2. Low saturated fat criterion—effect on total fat

The low saturated fat criterion also will influence the amount of fat that can be added to products that qualify for the whole grain health claim. This criterion would disqualify any product that contains more than one gram of saturated fat per RACC or more than 15% of calories from saturated fat. The maximum amount of common fats and oils that could be used per RACC as determined by simultaneous application of the low saturated fat criterion and the total fat disqualifier level is presented in Table 3.

Table 3
Maximum Weight of Fats and Oils that could be Used Per RACC
of Products Eligible for the Whole Grain Health Claim

Type of fat	Weight of fat that contains 1 g saturated fat (g)	Maximum amount of fat that could be used per RACC (g)	
		≤ 30 g RACC	>30 g RACC
Canola oil	14.0	8.0	13.0
Safflower oil	13.5	8.0	13.0
Flaxseed oil	10.7	8.0	10.7
Sunflower oil	10.3	8.0	10.3
Corn oil	8.0	8.0	8.0
Olive oil	7.5	7.5	7.5
Sesame oil	7.1	7.1	7.1
Soybean oil	6.8	6.8	8.8
Peanut oil	5.9	5.9	5.9
Cottonseed oil	3.9	3.9	3.9
Palm oil	2.0	2.0	2.0
Butter oil	1.6	1.6	1.6
Palm kernel oil	1.2	1.2	1.2
Coconut oil	1.2	1.2	1.2

Source: USDA Nutrient Database for Standard Reference (Release 15).

The data in Table 3 show that the proposed saturated fat eligibility criterion would be more restrictive than the total fat disqualifier level for fats with higher concentrations of saturated fat. For example, fats with a saturated fat content greater than corn oil would be permitted only at levels below the total fat disqualifier level for products with a 30 g RACC (e.g., crackers, most cereals, snacks). The practical significance of this constraint is to encourage the use of fats with a desirable fatty acid profile in whole grain products that are formulated to bear the claim. It is important to note that the most widely used commercial fat in the United States is soybean oil.

C. Trans fat labeling

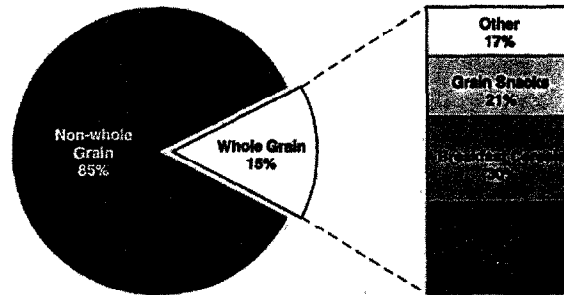
The label of foods that bear the claim also would provide quantitative trans fat labeling in the manner required by the final rule published in the July 11, 2003 *Federal Register* (68 Fed. Reg. 41434 (amending 21 C.F.R. § 101.9)). The required information concerning trans fat content would be provided in the Nutrition Facts box regardless of the January 1, 2006 effective date imposed by FDA in the final rule. This criterion has the effect of mandating early compliance with the final trans fat labeling rule for foods that bear the proposed claim and will ensure that consumers have adequate information regarding trans fat content at the point of purchase.

D. Product categories

Use of the proposed claim is permitted on appropriate whole grain foods, including, but not limited to, products in the following categories: cereals, crackers, breads, whole grain based snack mixes and bars. The product categories identified in this notification are the major contributors of whole grains in the U.S. diet (Cleveland, 2000). The data in Figure 1 show that breads, cereals and snacks comprise 83% of all whole grain servings. These categories present an excellent opportunity to increase whole grain consumption.

Figure 1

Proportion of Total Grain Servings from Whole Grains and Non-Whole Grains and Major Food Source of Whole-Grain Servings



Source: Cleveland, L.E. *et.al.* J. Am. Col. Nutr. 19:331S (2000).

VII. REVIEW OF SCIENTIFIC LITERATURE REGARDING THE RELATIONSHIP BETWEEN WHOLE GRAINS AND CHD

The appropriateness of a health claim concerning CHD and diets rich in whole grains and low in saturated fat and cholesterol is corroborated by the studies published before the *Diet and Health* report as well as more recent literature concerning the health benefits of whole grains.

A. Literature Review

1. Literature published before *Diet and Health*

Nineteen studies that examined the effect of whole grain foods or dietary fiber on the risk of CHD were cited in the *Diet and Health* report or the 1999 whole grains notification. The relevance of these studies to the current notification is discussed below.

a. Literature cited in *Diet and Health*

As expected, the studies cited in *Diet and Health* provide strong support for the conclusion that whole grain foods reduce the risk of CHD. Seven observational

studies (Morris *et.al.*, 1977; Burr and Sweetnam, 1982; Kromhout *et.al.*, 1982; Liu *et.al.*, 1982; Kromhout and de Lezenne Coulander, 1984; Kushi *et.al.*, 1985; Khaw and Barrett-Connor, 1987) and seven dietary intervention studies (Keys *et.al.*, 1960; Grande *et.al.*, 1965; Schweizer *et.al.*, 1983; Challen *et.al.*, 1983, Karlstrom *et.al.* 1984; Anderson *et.al.*, 1984; Kay *et.al.*, 1985) were discussed in this report. The *Diet and Health* report did not specifically address whether whole grain foods that are low in saturated fat and cholesterol, but not necessarily low in total fat, have a protective effect on CHD. As discussed below, although the studies cited in this report were not designed to assess the effects of total fat intake on the cardioprotective effects of whole grains or fiber, they do provide some evidence that cardioprotective effects are independent of total dietary fat content.

Observational Studies

Of the 7 observational studies, two failed to provide evidence for a protective effect of dietary fiber or whole grain foods on a risk factor or incidence of CHD. Kromhout *et.al.* (1982) initially found a 4-fold increase in mortality from CHD in men in the lowest quartile of dietary fiber intake, but this inverse relationship was lost during multivariate analyses. Similarly, Kushi et al (1985) had a fairly strong ($p=0.05$) inverse relationship between dietary fiber intake and risk of death from CVD, but the significance was lost when other factors were controlled.

Two prospective cohort studies found that intake of dietary fiber or whole grain foods was associated with reduced risk of CHD, but found no apparent association with total fat. The populations studied included 859 men and women aged 50-79 living in California (Khaw and Barret-Connor, 1987), and 327 middle-aged men from the United Kingdom (Morris *et.al.*, 1977). In Khaw and Barrett-Connor (1987), a 6 gm increment in daily fiber was associated with a 25% reduction in Ischemic Heart Disease (IHD) mortality ($p<0.01$) independent of other dietary variables including total fat. In this study, the fat intakes averaged between 36% to 38% of total kcal. In Morris et al (1977), men with a high energy

intake had a lower rate of CHD than the rest and independently of this, so did men with a high intake of dietary fiber from cereals. Though not included in the statistical analyses, the high energy group had the highest intake of total dietary fat ranging from 41% to 56% of total energy.

Three additional observational studies did not provide information on dietary fat (Burr and Sweetnam, 1982; Liu *et.al.*, 1982; Kromhout and de Lezenne Coulander, 1984).

In summary, of the two out of 7 studies reporting dietary fat intakes and cardioprotective effects of whole grains or dietary fiber, fat intakes ranged from 36% to 56% of total energy intake. Importantly, one of these studies showed total fat intake not to be associated with CHD risk (Khaw and Barrett-Connor 1987)

Intervention Studies

Of the 7 intervention studies discussed, 3 had study designs that did not allow for isolation of fat and fiber interactions since multiple dietary variables relevant to CVD biomarkers were changing at the same time (Keys et al 1965, Kay et al 1985, Schweizer et al 1985).

It is important to note that Kay *et. al.* (1985) fed diets of varying fat and fiber contents for five weeks to 12 moderately hypercholesterolemic subjects in a randomized, crossover study. Increasing dietary fat from 27% to 40% of energy did not diminish the ability of a diet containing 53-55 g fiber per 2,500 kcal to lower TC (175 mg/dl and 186 mg/dl, respectively) or LDLC (117 mg/dl and 122 mg/dl, respectively) compared to a control diet with 40% fat and 19 g fiber per 2,500 kcal. However, the control diet had 617 mg of cholesterol per 2500 kcal while the experimental diets had 252 and 245 mg of cholesterol per 2500 kcal as well as higher linoleic acid and PUFA contents of the diets – making interpretation of these findings difficult.

In 3 studies where total fat levels were controlled, higher dietary whole grain or legume intakes still significantly decreased CVD biomarkers of total and LDL cholesterol (Grande et al 1965, Anderson et al 1984, Karlstrom et al 1984). Grande et al (1965) compared the isocaloric substitution of carbohydrates from leguminous seeds for sucrose in diets containing 40% of total energy from fat and was still able to demonstrate a significant decrease in serum cholesterol concentration with the leguminous seeds. In this study both the level and type of fats [saturated, polyunsaturated, monounsaturated] were controlled. In Anderson et al (1984) the control and test diets provided equivalent energy, fat (37% of total kcal) and cholesterol but the test diets had twice more total and 3-fold more soluble fiber than the control resulting in significantly reduced total and LDL cholesterol in subjects consuming the oat-bran or bean containing diets. Karlstrom et al (1984) compared a diabetic diet, containing 18.9 g dietary fiber per 1600 kcal to a similar higher fiber diet containing 42.4 g dietary fiber per 1600 kcal in a 3 week cross-over study in 14 Type 2 diabetic subjects. The fat content in both diets was 34% of total energy. In addition to the high fiber diet significantly lowering the blood glucose level and urinary glucose excretion, there were significant reductions in LDL triglyceride and cholesterol concentrations. These lipoprotein differences, however, were small.

Finally, one study (Challen *et.al.*, 1983), did not provide information on the fat content of the experimental diets.

In summary, in the 3 out of 7 studies where dietary fat intakes were controlled, there were no indications of attenuating effects on the cardioprotective effects of whole grains or dietary fiber from moderate levels of total dietary fat. In these studies fat intakes ranged between 34 % and 40% of total energy.

b. Literature not cited in *Diet and Health*

Five intervention studies published before 1989 were cited in the 1999 whole grains notification but not in the *Diet and Health* report (de Groot *et.al.*, 1963; Judd and Truswell, 1981; Fraser *et.al.*, 1981; Van Horn *et.al.*, 1986; Van Horn *et. al.* 1988). Four of these studies provide direct evidence that whole grains or vegetables have favorable effects on cardiovascular risk factors. One study (Judd and Truswell, 1981) showed that a diet containing 125 g rolled oats per day reduced T-C in seven of 10 subjects, but the results were only of borderline statistical significance.

Two studies demonstrating beneficial effects of whole grains or vegetables controlled for fat intake with intakes ranging from 30% to 42% of total energy (Van Horn et al 1986, Fraser et al 1981). Van Horn et al (1986) provided 60 gm per day of oatbran or oatmeal to study subjects receiving an AHA fat modified diet containing no more than 30% total energy as fat resulting in significant reductions in total cholesterol by 12 weeks of study. Fraser et al (1981) provided 42% of total kcal as fat while providing 400 kcal/day of whole grains noting significant reductions in total and LDL cholesterol as compared to the control.

The studies conducted by de Groot *et.al.* (1963) and Van Horn *et.al.* (1988) did not provide information on the fat content of the experimental diets.

Of these 5 studies not reported in the original *Diet & Health*, 2 provided sufficient information to evaluate the effects of dietary total fat intake on the cardioprotective effects of dietary whole grains or fiber intakes. The fat intakes ranged from 30 – 42% of total energy.

In summary, the studies discussed in this section provide consistent evidence that whole grain foods can reduce the risk of CHD. In addition, these studies provide no evidence that whole grain containing diets with moderate amounts of

total fat would be less effective in reducing CHD risk than their low-fat counterparts.

2. New scientific evidence corroborating conclusions set forth in *Diet and Health*

The findings published in *Diet and Health* are also corroborated by newer scientific evidence that confirms the cardioprotective properties of whole grain products that are low in saturated fat and cholesterol but not necessarily low in total fat. This body of literature includes 11 review papers as well as 15 observational and six intervention studies published since 1989. A brief discussion of these papers is provided below.

a. Observational studies

A case-control study with 287 females who had experienced acute myocardial infarction (MI) and 659 hospital-based controls with acute disorders unrelated to ischaemic heart disease (IHD) was reported by Gramenzi *et.al.* (1990). CHD incidence was associated with frequency of consumption of meat (1.5 odds ratio (OR) for the upper vs. lower thirds of consumption), ham and salami (1.4), butter (2.3), total fat added to food (1.6) and coffee (2.8). Inverse associations were seen for fish (0.6), carrots (0.4) and moderate alcohol intake (0.7). The only source of whole grain examined in this study (wholemeal bread) was not related to incidence of MI (OR = 1.1), but there was a very narrow range of consumption (1 to 3 servings per week). This study does not provide evidence for a cardioprotective role of whole grains, but the dietary data are very limited and the range of whole grain consumption may have been too narrow to see an effect. In addition, case-control studies are less persuasive than cohort studies due to a variety of methodological limitations.

Unlike the previous study, Fraser *et.al.* (1992) found that the Relative Risk (RR) of nonfatal MI was significantly lower among subjects who usually consumed whole wheat bread compared to those who usually ate white bread (RR = 0.56; 95% Confidence Interval (CI) 0.35, 0.89). The study was conducted among 26,473 Seventh-Day Adventists living in California who were followed for up to six years. These results were adjusted for age, gender, smoking, physical activity, body weight, hypertension and intake of nuts and beef which were the only other foods found to be related to CHD risk. This study did not provide data on total fat intake or use it to adjust the results. The authors conclude, "A reduction in the incidence of nonfatal myocardial infarction was...demonstrated for those who consumed only whole wheat bread."

A cross-sectional cohort study among 850 members of an ethnic minority in China (He *et.al.*, 1995) found that consumption of oats and buckwheat was associated with lower serum lipids. Values for the lowest vs. highest quartile of oat consumption for T-C were 4.03 and 3.59 mmol/L, respectively. Corresponding values for other lipids were LDL-C (1.85 vs. 1.76mmol/L), HDL-C (1.49 vs. 1.23mmol/L) and TGs (1.59 vs. 1.32mmol/L). The effect of oat consumption on T-C and LDL-C was no longer statistically significant after the data were corrected for age, BMI and dietary intakes of energy, cholesterol, alcohol, fat and the ratio of polyunsaturated (PUFA) to saturated (SFA) fatty acids whereas the effect of buckwheat on T-C and LDL-C remained significant with fat intakes ranging from 14% to 25% of total energy. However, the applicability of these data to the U.S. population is limited because the subjects were consuming diets low in fat (14 to 25% of energy), had low T-C levels (average = 150 mg/dL) and were very lean (average BMI = 20.8).

Rimm *et.al.* (1996) reported a significant inverse association of dietary fiber intake and CHD (age adjusted RR = 0.59; 95% CI 0.46, 0.76) among 43,757 male health professionals age 40 – 75 years. These prospective cohort data were based on 734 cases of MI during a six-year follow-up period. The inverse

association remained statistically significant after the data were corrected for saturated fat, vitamin E, age, BMI, physical activity, smoking, alcohol, hypertension, hypercholesterolemia, family history of MI and profession. Multivariate analysis of these data by source of fiber showed that the inverse association of cereal fiber and MI (RR = 0.71; 95% CI = 0.54, 0.92) was stronger than fiber from fruit (RR = 0.81; 95% CI = 0.62, 1.06) or from vegetables (RR = 0.83; 95% CI = 0.64, 1.08) after adjusting for the variables listed above. Total fat was not used to adjust the data in this study; presumably because it was not shown to be a risk factor for CHD in this population. The authors observed:

Most of the available epidemiological evidence strongly supports an inverse association between fiber and coronary heart disease. Some have argued that the inverse association between fiber and coronary heart disease can partially be explained by a displacement of fat in the diet. Our results suggest the contrary; among participants in the Health Professionals Follow-up Study, the positive association between saturated fat intake and coronary heart disease is almost entirely explained by lower fiber intake among the men who consumed more fat.

Pietinen *et al.* (1996) also reported an inverse association between dietary fiber and CHD mortality in a prospective cohort study of 21,930 Finnish subjects followed for 6.1 years. The RR of fatal CHD among the upper quintile of dietary fiber intake compared to the lowest was 0.73 (95% CI = 0.56, 0.95) after adjustment for age, smoking, BMI, blood pressure, education, physical activity and dietary intakes of energy, alcohol, saturated fatty acids, beta-carotene, vitamin C and vitamin E. Intake of rye products (a source of whole grain) was also inversely associated with CHD fatality after adjustment for these variables (RR = 0.75; 95% CI = 0.58, 0.98) as was cereal fiber (RR = 0.74; 95% CI = 0.57, 0.96), but not fiber from vegetables (RR = 0.88; 95% CI = 0.66, 1.10) or fruits (RR = 1.16; 95% CI = 0.08, 1.68). Total fat intakes were available but not reported nor used to adjust the data in this study. The authors conclude, "These findings suggest that independent of other risk factors, greater intake of foods

rich in fiber can substantially reduce the risk of coronary heart disease, and particularly coronary death, in middle-aged, smoking men.”

Intake of whole grain products was found to be inversely associated with CHD mortality independent of dietary fiber in a cohort of 34,492 postmenopausal women aged 55 – 69 followed for up to 9 years (Jacobs *et.al.*, 1998). The RR of death due to IHD was 0.6 (95% CI = 0.45, 0.81) for the highest quintile of total whole grain servings per week compared to the lowest after adjustment for age and energy intake. This inverse association remained significant (RR = 0.7; 95% CI = 0.5, 0.98) after additional adjustment for education, marital status, hypertension, diabetes, BMI, waist-to-hip ratio, physical activity smoking, alcohol intake, vitamin supplement use, oral contraceptive use, estrogen replacement therapy, Keys score, and dietary intake of fruit and vegetables (except juice), red meat, fish and seafood as well as sucrose. Total fat intake was not provided, nor was it used to adjust the data. The authors concluded that there is a clear inverse association between whole-grain intake and risk of IHD death.

Liu *et.al.* (1999) reported that consumption of whole grain foods was inversely associated with the incidence of fatal and non-fatal CHD in a cohort of 75,521 women aged 38-63 years. Participants were members of the Nurses' Health Study cohort and were followed prospectively for a period of 10 years. After adjustment for age and smoking, whole grain intake was inversely associated with risk of CHD. RRs from lowest to highest quintile of intake were 1.0, 0.92, 0.93, 0.83, 0.75 (95% CI for the upper quintile compared to the lowest was 0.54, 0.84). Further adjustment for BMI, post-menopausal hormone use, alcohol intake, multivitamin use, vitamin E supplement use, aspirin use, physical activity and types of fat intake did not appreciably change the results: RRs for quintiles of whole grain consumption were 1.0, 0.92, 0.93, 0.83, 0.75 (95% CI 0.59, 0.95). The RRs remained virtually unchanged when types of fat (i.e. SFA, PUFA, MUFA and TFA) were added to the multivariate model as a group. Fat intakes as % of

total energy were not available. This result strongly suggests that the type of fat intake does not attenuate the beneficial effect of whole grains on CHD mortality. These researchers concluded, "Increased consumption of whole grains may protect against CHD."

Following two years of additional data collection, the Nurses' Health Study cohort was examined again for a relationship between whole grain consumption and CVD (Liu *et.al.*, 2000). A sample of 75,521 women 38-63 years of age was followed for of 12 years. Whole grain consumption was significantly associated with reduced incidence of stroke after adjustment for age: RRs for quintiles of consumption were 1.0, 0.68, 0.69, 0.49, 0.57 (the 95% CI did not include unity for quintiles 2 through 5). This association remained significant after adjustment for smoking: RR for the upper quintile = 0.64; (95% CI = 0.47, 0.89) and numerous CVD risk factors (RR = 0.69; 95% CI = 0.50, 0.98) including SFA, TFA and total energy intake, but total fat was not adjusted for. The authors concluded, "In this cohort, higher intake of whole grain foods was associated with a lower risk of ischemic stroke among women, independent of known CVD risk factors. These prospective data support the notion that higher intake of whole grains may reduce the risk of ischemic stroke."

Whole grain consumption was inversely associated with all-cause mortality in a cohort of 38,740 Iowa women aged 55-69 years during a 9-year follow up period (Jacobs *et.al.*, 1999). Median whole grain consumption ranged from 1.5 servings per week in the lowest quintile to 22.5 servings per week in the highest. RRs for total mortality after adjustment for age and energy intake were 1.0, 0.76, 0.65, 0.66, 0.64 (the 95% CI did not include unity for any of the second through fifth quintiles). Analogous results after adjustment for age, energy intake, educational attainment, marital status, hypertension, diabetes, CHD, cancer, BMI, waist-to-hip ratio, age at first childbirth, physical activity, cigarette smoking, alcohol intake, vitamin supplement use, estrogen replacement therapy, total fat and saturated fat intake [values not reported], and intake of fruits, vegetables, red meat, fish and

seafood were: RR= 1.0, 0.95, 0.87, 0.81, 0.86 (the 95% CI did not include unity for quintiles 3 through 5). Whole grain consumption was significantly associated with reduced incidence of cancer and total cardiovascular disease (CVD), but not to CHD itself. The associations were not explained by dietary fiber the authors concluded, "Substitution of whole for refined grain may reduce chronic disease risk in the United States."

An analysis of the Iowa Women's Health Study cohort (Jacobs *et.al.*, 2000) reported that fiber from whole grains, but not from refined grains, was associated with reduced all-cause mortality. A population of 11,040 postmenopausal women was followed for 11 years. Women who consumed predominantly whole grain fiber (an average of 1.9 g and 4.7 g refined and whole grain fiber per 2,000 calories, respectively) had a 17% lower all-cause mortality rate than women who consumed diets predominant in refined grain fiber (RR = 0.83; 95% CI = 0.73, 0.94) after adjustment for age and a wide range of dietary, anthropometric, life-style and medical risk factors including total fat. The mean intakes of total fat as % of energy intake for the predominately whole grain group were 33.4%. As noted in a previous study with this cohort (Jacobs *et.al.*, 1999), whole grain consumption was not specifically associated with mortality due to CHD itself. The authors conclude that public health policy should recommend increased consumption of whole grain foods.

A study of 51,529 U.S. health professionals (Hu *et.al.*, 2000) reported that individuals who consistently followed a "prudent" dietary pattern characterized by whole grains, vegetables, fruits, fish and poultry experienced significantly lower incidence of CHD than subjects who followed a "Western" pattern characterized by higher intakes of refined grains, meats, sweets, french fries, and high-fat dairy products. After adjustment for age and CHD risk factors (excluding saturated fatty acids), the RRs for CHD from the lowest to highest scores of the "prudent" pattern were 1.0, 0.87, 0.79, 0.75, 0.90 (95% CI = 0.56, 0.86). Total fat intakes as a % of energy were not provided. There was an analogous increase in CHD

risk for increasing scores for the “Western” dietary pattern. Although the effect of whole grains on CHD could not be isolated from other dietary components in this analysis, it is consistent with the hypothesis that whole grains reduce the risk of CHD.

Liu *et al.* (2002) examined the relationship between dietary fiber and incidence of CVD and CHD using the Nurses’ Health Study cohort of 39,876 female health professionals. During a six-year follow-up period, age-adjusted incidence of CVD was inversely associated with dietary fiber intake (RR for lowest to highest quintile = 1.0, 0.71, 0.72, 0.64, 0.65; 95% CIs did not contain unity for quartiles 2 through 5). Analogous results for MI were RR = 1.0, 0.54, 0.54, 0.43, 0.46; 95% CIs did not contain unity for quartiles 2 through 5. However, adjustment for age, randomized treatment assignment, smoking, exercise, alcohol intake, hormone replacement therapy, BMI, use of multivitamin supplements, hypertension, hypercholesterolemia, diabetes, parental history of MI before age 60 and dietary folate, total fat, protein and energy attenuated both of these associations so that they were no longer statistically significant. The authors speculate that other characteristics of fiber-containing foods, rather than the fiber itself, may be responsible for the unadjusted inverse association of dietary fiber. It was concluded, “...these prospective data generally support current dietary recommendations to increase the consumption of fiber-rich whole grains, and fruits and vegetables as a primary preventive measure against CVD. This conclusion is particularly relevant in light of a previous analysis of this cohort (Liu *et al.*, 1999) that found a significant inverse association between whole grain consumption and CHD incidence.

Another study of the effect of a “prudent” dietary pattern including whole grain foods was reported by Michels and Wolk (2002) using a Swedish cohort of 59,038 women born between 1914 and 1948. The frequency of consumption of “recommend foods” (RF) including whole grain breads, cereals, fruits, vegetables, fish and low-fat dairy products was inversely associated with age-adjusted all-

cause mortality. RRs for the lowest to highest quintile were 1.0, 0.78, 0.72, 0.68, 0.71; 95% CIs did not include unity for quintiles 2 through 5. Adjustment for age, height, BMI, number of children, age at first birth, education, marital status, alcohol consumption, energy intake and consumption of “not recommended foods” (e.g. red meats, refined carbohydrates including sugars and foods high in saturated or *trans* fats) but not total fat intakes did not significantly alter this association. The intake of “not recommended foods” was not associated with all-cause mortality in this cohort. It is not possible to isolate the effect of whole grain foods from this study because multiple dietary factors were considered simultaneously. Nevertheless, the study provides suggestive evidence that whole grain foods promote health. The authors concluded, “A healthy diet can affect longevity. It appears more important to increase the number of healthy foods regularly consumed than to reduce the number of less healthy foods regularly consumed.”

Whole grain consumption was found to be favorably associated with risk factors for CVD and type 2 diabetes in the Framingham Offspring Study cohort (McKeown *et.al.*, 2002). This cross-sectional study of 2,941 subjects found that whole grain intake was inversely associated with BMI, waist-to-hip ratio, diastolic blood pressure, T-C, LDL-C, TG, fasting glucose and fasting insulin after adjustment for age, sex, energy intake, treatment of hypertension, smoking, alcohol use, multivitamin use, estrogen use, physical activity, BMI, percent energy from SFA and PUFA as well as intake of meat, fish, fruit and vegetables. Dietary intakes of total fat as % of total energy were not provided nor were used to adjust the data. The authors concluded that increased intake of whole grains may reduce disease risk by exerting favorable effects on metabolic risk factors.

Liu *et.al.* (2003) reported an inverse association between consumption of whole grain breakfast cereals and deaths due to CVD and CHD among 86,190 members of the Physicians' Health Study cohort during a 5.5-year follow-up period. Whole-grain breakfast cereal intake was inversely associated with total

and CVD-specific mortality, independent of age; body mass index; smoking; alcohol intake; physical activity; history of diabetes, hypertension, or high cholesterol; and use of multivitamins. The multivariate RR for CVD mortality for subjects who consumed ≥ 1 serving per day of these foods was 0.8 (95% CI = 0.66, 0.97) compared to participants who rarely consumed these foods. Analogous results for MI were RR = 0.71 (95% CI = 0.51, 0.98). The data were not adjusted for total fat or other dietary factors and total fat intakes were not reported. Cereals from refined grains were not associated with mortality from CVD or MI. The authors concluded, "These prospective data highlight the importance of distinguishing whole-grain from refined grain cereals in the prevention of chronic diseases."

In summary, the observational studies published since *Diet and Health* confirm the validity of the authoritative statement that is the basis for this notification. Eight studies provide direct evidence that whole grain foods (or dietary fiber) reduce the risk of CHD or CVD (Fraser *et.al.*, 1992; Rimm *et.al.*, 1996; Pietinen *et.al.*, 1996; Jacobs *et.al.*, 1998; Liu *et.al.*, 1999; Liu *et.al.*, 2000; McKeown *et.al.*, 2002 and Liu *et.al.*, 2003

Five studies provided suggestive evidence that whole grains are cardioprotective. He *et.al.* (1995), Jacobs *et.al.* (1999) and Liu *et.al.* (2002) reported that whole grains or dietary fiber were associated with reduced incidence of CHD, but the results were no longer statistically significant after adjustment for multiple potentially confounding variables. Hu *et.al.* (2000) and Michels and Wolk. (2002) reported that diets with "healthy" foods (including whole grains) were associated with reduced risk of CHD.

Only two studies failed to provide support for the cardioprotective properties of whole grain foods. No association was seen in a case-control study by Gramenzi *et.al.* (1990) and Jacobs *et.al.* (2000) reported a significant association between

whole grains and all-cause mortality, but not for CHD after adjustment for potentially confounding variables.

As with the studies cited in *Diet and Health*, none of these observational studies provide evidence that the fat content of whole grain diets influences their cardioprotective effect. It appears the majority of these investigators did not consider total fat as a significant factor impacting the effectiveness of whole grains or fiber on protection from CHD or CVD (*Diet and Health* at 7; National Cholesterol Education Program, 2001; Food and Nutrition Board, 2002) (see Part VIII below.)

Two studies (Hu *et.al.*, 2000; Michels *et.al.*, 2002) examined the effect of dietary patterns (i.e. whole grains in conjunction with other foods) on CHD risk, which does not allow for assessment of the effect of total fat content on the cardioprotective properties of whole grains *per se*.

Of the more recent 13 observational studies demonstrating the cardioprotective effects of whole grains or fiber, only four included fat intake data. Liu et al (1999) found that the inverse association between whole grain foods and CHD remained after the data were adjusted for type of fat. The remaining three studies found that adjustment of the data for multiple factors including total fat intake eliminated an inverse association between whole grains or dietary fiber and CHD seen in the uncorrected data. One of these studies (Liu *et.al.*, 2002) examined dietary fiber (not whole grains), and the authors hypothesized that the unadjusted protective effect they observed may be have been due to non-fiber constituents of whole grain foods. The other two studies (He *et.al.*, 1995; Jacobs *et.al.* 1999) found that the inverse association between whole grain foods and risk of CHD was eliminated by a correction for total fat, but numerous factors including age, total energy intake, educational attainment, marital status, high blood pressure, diabetes, CHD, cancer, BMI, waist-to-hip ratio, age at first childbirth, physical activity, cigarette smoking, alcohol intake, use of vitamin supplements, estrogen

replacement therapy, and the intake of saturated fat, fruits and vegetables, red meat as well as fish and seafood were adjusted simultaneously. Therefore, it is not possible to determine the relative importance of total fat intake, compared to other potentially confounding variables, in eliminating the statistical significance seen in the uncorrected data.

In conclusion, as with the studies published prior to *Diet and Health*, the newer observational studies discussed in this section provide consistent evidence that whole grains can reduce the risk of CHD, but fail to reveal evidence that diets with moderate amounts of total fat, but low in saturated fat and cholesterol, are any less effective than their low fat counterparts.

b. Intervention studies

A secondary prevention trial of CHD was conducted by Burr *et.al.* (1989) among 2,033 men (average age 56 years) who had recovered from MI. The subjects were randomized into one of four dietary treatments including a group who were instructed to increase intake of cereal fiber. Subjects in this group were successful in approximately doubling cereal fiber intake at six months (19 vs. 9 g per day in the control group) and at two years (17 vs. 9 g per day). There were no differences in the reoccurrence of IHD events or all-cause mortality between the fiber group and controls during a two-year follow-up period. No information on dietary fat or other constituents was provided for the fiber vs. control groups. This study does not provide evidence that dietary fiber can reduce the risk of CHD, but several factors limit its applicability. All subjects in this study had established heart disease (many were taking medications) and therefore do not reflect the healthy U.S. population. The intake of whole grain foods was not reported, and it is possible that dietary fiber acts to reduce the risk of CHD in healthy individuals, but is ineffective after CHD is already established.

Van Horn *et.al.* (1991) studied the effect of instant oats on serum lipids when added to the diet of 80 male and female, moderately hypercholesterolemic volunteers (average age 42 years). This study used a randomized parallel design and the intervention period was eight weeks. The participants were stratified on the basis of gender and baseline serum cholesterol (above or below 6.34 mmol/L). The experimental group was asked to isocalorically substitute 56.7 g of instant oats per day for other sources of dietary carbohydrate. Subjects in the oat group experienced significant decreases in T-C (0.32 mmol/L; 95% CI = 0.09, 0.54) and LDL-C (0.25 mmol/L; 95% CI = 0.02, 0.48) compared to controls at the end of the intervention period. Subjects with baseline cholesterol concentrations greater than 6.34 mmol/L experienced a greater decline in serum lipids (data not provided). There were no changes in HDL-C or body weight during the study. Interpretation of this study is complicated by the fact that the self-selected diets between the experimental and control groups differed not only in the components of oats (e.g. total fiber, soluble fiber), but also in total fat, SFA, MUFA and several other nutrients. These differences (which were small, but statistically significant) may have partially explained the observed changes in serum lipids. The mean total fat intakes reported as % of total energy were 36.2% for the experimental group and 39.8% for the control group. Nevertheless, results of the study are impressive because oats were shown to be hypocholesterolemic when fed as part of a typical American diet (approximately 37% of energy from fat). The authors conclude, "Daily inclusion of two ounces of oats appeared to facilitate reduction of serum total cholesterol and LDL-C in these hyperlipidemic individuals."

Davidson *et.al.* (1991) conducted a dose-response feeding study using oatmeal, oat bran or farina among 156 adults with LDL-C levels above 160 mg/dL or between 130 and 160 mg/dL. The study used a randomized, placebo-controlled, parallel design with farina serving as the placebo. After six weeks of treatment, subjects who consumed 84 g/d of oatmeal, 56 g/d of oat bran or 84 g/d of oat bran experienced significant reductions in both T-C and LDL-C compared to the

farina control. LDL-C decreased in these groups by 10.1, 15.9 and 11.5%, respectively. There were no significant changes in HDL-C or serum TGs. The fat content of the diets (approximately 26% of total energy) did not change during the experiment, and there was no significant difference in BMI. The authors conclude, "A dose-dependent reduction in LDL-C levels with oat cereals supports the independent hypocholesterolemic effects of β -glucan."

Johnston *et.al.* (1998) studied the effect of feeding a whole grain cereal (Cheerios[®]) compared to a non-whole grain control (corn flakes) on the serum lipids of 135 mildly hypercholesterolemic volunteers. The study used a randomized, parallel design and provided the test cereals for six weeks as part of a Step 1 diet. Subjects who consumed the whole grain cereal achieved a 3.8% reduction in T-C ($p = 0.0008$) and a 4.5% decrease in LDL-C ($p = 0.0065$). HDL-C and body weight were not different between the two groups. There were no significant differences in total fat between the control and experimental groups at the end of the treatment period with post-treatment mean intakes of 22.5% of total energy for the control group and 26.5% for the experimental group. The authors conclude, "...individuals can adhere to a cholesterol-lowering diet that includes a whole grain oat cereal that is readily available, convenient to consume, and easy to incorporate into a daily eating plan."

The effect of replacing refined rice with a mixture of whole-grains and legumes on various CVD risk factors among coronary artery disease patients was reported by Jang *et.al.* (2001). Seventy-six male patients were randomly assigned to consume the whole grain/legume mixture or continue their usual diet for 16 weeks. The use of anti-hypertensive and lipid-lowering drugs was continued throughout the experiment. Subjects in the whole grain/legume group had higher serum HDL-C concentrations, and experienced significant beneficial effects on fasting glucose, insulin, homocysteine concentrations and lipid peroxidation values compared to the controls. There were no differences in T-C or LDL-C between the two groups. The dietary fat content of all diets did not differ between groups with estimates of daily mean intakes of 16.1 % for the

control group and 19.5% for the experimental group This study provides suggestive evidence that whole grains exert a beneficial affect on serum lipids, but interpretation is limited due to the fact that whole grains were provided in combination with legumes, seeds and vegetables. In addition, the study does not reflect the healthy U.S. population because the subjects were CHD patients continuing to receive medications for hypertension or hyperlipidemia.

Jacobs *et.al.* (2002) used a randomized, crossover protocol to study the effect of whole grain consumption on enterolactone concentrations in 12 overweight, hyperinsulinemic, non-diabetic men and women aged 26-54 years. Subjects were randomized to diets containing whole grain foods (wheat, oats and rice) or refined grain foods for six weeks and then switched to the opposite diet after a 6-9 week washout period. Enterolactone is a lignan that may protect against CHD and breast cancer. Results of the study showed that whole grain feeding resulted in a significant increase in the serum concentrations of this compound. The total fat content of the diets was not provided. It was concluded that diets rich in whole grains could increase the concentration of serum enterolactone.

In summary, five of the six intervention studies conducted since *Diet and Health* provide direct or suggestive evidence that whole grain foods can reduce the risk of CHD (Van Horn *et.al.*, 1991; Davidson *et.al.*, 1991; Johnston *et.al.*, 1998; Jang *et.al.*, 2001; Jacobs *et.al.*, 2002).

Only one study (Burr *et.al.*, 1989) failed to support the notion that whole grain foods are cardioprotective, but this study utilized dietary fiber rather than whole grain foods and is not applicable to the healthy U.S. population because it was conducted with MI patients.

As with the studies cited in *Diet and Health*, none of these intervention trials provide evidence that the fat content of whole grain diets influences their

cardioprotective effect. Mean total dietary fat intakes were reported in 4 of the 6 studies and ranged from 26.5% to 36.2% of energy in the experimental groups.

In conclusion, as with the studies published prior to *Diet and Health*, the newer intervention studies discussed in this section provide consistent evidence that whole grains can reduce the risk of CHD, and fail to provide evidence that diets with moderate amounts of total fat, but low in saturated fat and cholesterol, are less effective than their low-fat counterparts.

c. Review papers

Kushi *et.al.* (1999) reviewed the observational data on cereals, legumes and chronic disease reduction. The paper concluded, "Overall, there is substantial epidemiologic evidence that dietary fiber and whole grains are associated with decreased risk of coronary artery disease and some cancers, whereas the role of legumes in these diseases appears promising but as yet inconclusive."

A review of the plausible mechanisms for the protective effect of whole grains (Slavin *et.al.*, 1999) concluded, "Clearly, the range of protective substances in whole grains is impressive and advice to consume additional whole grains is justified. Further study is needed regarding the mechanisms behind this protection so that the most potent protective components of whole grains will be maintained when developing whole grains into acceptable food products for the public."

Anderson *et.al.* (2000) considered the data linking whole grains with CHD risk and concluded, "...this meta-analysis of 12 population-based cohort studies indicated that those individuals with the highest intake of whole grains had an adjusted risk for CHD of 0.74 (95% CI, 0.67 to 0.80) compared to individuals with the lowest intake of whole grains. Whole grain intake has a stronger association with protection from CHD than intake of cereal fiber, vegetables or fruits. These

studies suggest that the intake of three servings of whole grains per day may have an important cardioprotective effect.”

Slavin *et.al.* (2001) summarized the data on whole grain intake and disease prevention as well as factors related to the low intake of whole grains in the U.S. The authors concluded that whole grains are a valuable source of nutrients lacking in the U.S. diet (e.g. dietary fiber, B vitamins, vitamin E, selenium, zinc, copper, magnesium) as well as phytochemicals, which may reduce the risk of chronic disease. The authors suggest that the 2000 revision of the Dietary Guidelines for Americans and the FDA-authorized health claim for whole grains may help increase consumption.

Three papers (Liu and Manson, 2001; Liu, 2002; Liu and Willett, 2002) reviewed the association between whole grain foods and type 2 diabetes and CHD from a glycemic index perspective. These papers hypothesize that high glycemic index foods contribute to the “metabolic syndrome” characterized by insulin resistance, hyperinsulinemia, dyslipidemia, hypertension and impaired fibrinolysis. The authors note that additional information is needed to understand this possible relationship, but conclude, “Until more definitive data are available, replacing refined grain products and potatoes with minimally processed plant-based foods such as whole grains, fruits, and vegetables, and reducing the intake of high glycemic load beverages may offer a simple strategy for reducing the incidence of coronary heart disease.”

The relationship between cereal grains and CHD was the subject of a comprehensive review of the literature by Truswell (2002). This review drew the following conclusions:

- Total cereal consumption is not clearly linked to CHD in studies conducted throughout the world
- Oatmeal and oat bran have been convincingly shown to cause modest reductions in total- and LDL-C, but studies with purified fibers have been inconsistent

- Observational data associating the consumption of whole grain products with reduced incidence of CHD is consistent and suggests other factors besides cholesterol-lowering are involved
- Fortification of cereal foods with folic acid may be contributing to their cardio-protective affects

Kris-Etherton *et.al.* (2002) published a review of food-based approaches and dietary patterns designed to reduce the risk of CHD. This paper discussed how the Dietary Approaches to Stop Hypertension Study, the Lyon Diet Heart Study and other intervention studies have prompted recommendations for the inclusion (rather than exclusion) of foods in the diet. Examples of cardioprotective foods include whole grains, fish, fruits and vegetables and low-fat dairy products and nuts. The authors conclude, "We are transiting an era in which recommendations are being shaped by an inclusionary philosophy (i.e. what foods should be featured in a heart healthy diet). Advances in nutrition research have identified a growing list of foods that confer beneficial effects on heart health. It is evident that an emerging issue that must be resolved is how these foods may be included in a diet that confers the optimal dietary pattern for CHD risk reduction, and does so in a way that promotes a healthy body weight (i.e. does not exceed energy requirements)."

Jones *et.al.* (2002) concluded that the weight of scientific evidence demonstrates that whole grains have beneficial effects on heart disease, diabetes and cancer. Nevertheless, consumption of fiber and whole grain foods in the U.S. is well below recommended amounts, and the author suggests a "call to action" to help Americans increase consumption. The following strategies were suggested to help promote the health benefits of whole grains:

- Maintain whole grains at the base of the Food Guide Pyramid
- Encourage and support whole grain research
- Pursue policy support and funding for whole grains research
- Reach consumers through health professionals and other vehicles
- Develop child-targeted education campaigns

- Encourage the whole grain industry to take action

Hu and Willett (2002) reviewed 147 scientific publications pertaining to diet and CHD including original investigations and reviews of metabolic studies, epidemiologic studies and dietary intervention trials. A synthesis of these data led to the following conclusion, “Substantial evidence indicates that diets using nonhydrogenated unsaturated fats as the predominant form of dietary fat, whole grains as the main form of carbohydrates, an abundance of fruits and vegetables, and adequate omega-3 fatty acids can offer significant protection against CHD.”

B. Summary of Literature

Forty studies with original data on the effect of whole grain foods or dietary fiber (a marker for whole grains) on the risk or incidence of CHD have been identified. These studies include those cited in *Diet and Health* as well as more recent publications. Thirty-four of these studies provide direct or suggestive support for the notion that whole grain foods are cardioprotective. Only six studies failed to provide direct evidence of this effect – primarily due to design limitations or use of non-healthy populations. Taken together, these studies continue to provide compelling evidence that whole grain foods can reduce the risk of CHD. Furthermore, this comprehensive body of literature provides evidence that the total fat content of fiber or whole-grain containing diets is unrelated to CHD, and provides no persuasive evidence that whole grain diets that are low in saturated fat and cholesterol, but not necessarily low in total fat, are any less effective in reducing the risk of CHD than their low-fat counterparts.

Slightly more than half of these studies are observational in nature. Observational studies are capable of identifying *associations* between dietary components (e.g. fat) and health outcomes such as CHD, but they are *not* capable of proving a cause and effect relationship. Therefore, by definition, these studies cannot provide conclusive evidence on a possible interaction

between dietary fat and whole grains on the risk of CHD. Despite this *a priori* limitation, an analysis of the available observational studies with respect to this question was conducted (see Table 4).

Table 4

Analysis of observational studies with respect to evidence concerning dietary fat and the cardioprotective properties of whole grain and fiber-containing foods.

Study finding	Study with whole grain data		Study with dietary fiber data only	
	Number of studies	Reference	Number of studies	Reference
Total fat intake with no apparent association with CHD risk			2	Khaw <i>et al.</i> (1987) Morris <i>et al.</i> (1977)
Protective effect remains after adjustment for type of fat	1	Liu <i>et al.</i> (1999)		
No effect of whole grain/fiber regardless of total dietary fat	2	Gramenzi <i>et al.</i> (1990) Jacobs <i>et al.</i> (2000)	2	Kromhout <i>et al.</i> (1982) Kushi <i>et al.</i> (1985)
Insufficient data to assess (e.g. study provided no data on total dietary fat intake)	8	Burr & Sweetnam (82) Fraser <i>et al.</i> (1992) Jacobs <i>et al.</i> (1998) Liu <i>et al.</i> (2000) McKeown <i>et al.</i> (2002) Liu <i>et al.</i> (2003) Hu <i>et al.</i> (2000) Michels <i>et al.</i> (2002)	4	Liu <i>et al.</i> (1982) Kromhout <i>et al.</i> (1984) Rimm <i>et al.</i> (1996) Pietinen <i>et al.</i> (1990) Morris <i>et al.</i> (1977)
Protective effect no longer significant after adjustment for total fat, but multiple adjustments made simultaneously	2	He <i>et al.</i> (1995) Jacobs <i>et al.</i> (1999)	1	Liu <i>et al.</i> (2002)

Analysis of the observational studies summarized in Table 4 shows that there is no evidence that consumption of moderate-fat whole grain food containing diets, low in saturated fat and cholesterol, would be less cardioprotective than their low-fat counterparts. One study found that total dietary fat was not associated with CHD risk thus providing evidence that the fat content of fiber or whole grain food-containing diets does not alter their cardioprotective properties.

One study found that an inverse association between whole grain foods and CHD remained statistically significant after the data were corrected for total fat intake. This observation essentially means that whole grains were protective at

all levels of dietary fat studied, and supports the notion that moderate-fat whole grain diets would be beneficial.

Four studies did not find a direct association between whole grain foods and CHD so that the question of dietary fat becomes moot. Thirteen studies did not provide information on dietary fat or use it to statistically adjust their data. It is not possible, therefore, to assess the impact of fat on the results⁵. Finally, three studies found that correction of the data for dietary fat as well as multiple confounding factors attenuated the protective association found with the uncorrected data. One of these studies examined dietary fiber and not whole grains (Liu *et.al.*, 2002). The other two studies (He *et.al.*, 1995; Jacobs *et.al.*, 1999) pertained to whole grain foods, but adjusted the data for numerous variables simultaneously so that it is not possible to determine whether total fat or one of the other variables (e.g., saturated fat) was responsible for eliminating the statistical significance of the association.

Dietary intervention studies *do* have the capability to demonstrate a cause and effect relationship between a dietary component and a disease outcome or risk factors. An analysis of dietary intervention studies involving fiber or whole-grain containing diets and moderate levels of fat content does not lessen their cardioprotective properties, and no compelling evidence to show that it does.

⁵ The fact that total dietary fat was not used to statistically adjust the data in these studies may be due to the fact that it is not regarded as a CHD risk factor other than as a potential carrier of saturated fat (see Part VIII).

Table 5

Analysis of dietary intervention studies with respect to evidence concerning dietary fat and the cardioprotective properties of whole grain and fiber-containing foods.

Study finding	Study with whole grain data		Study with dietary fiber data only	
	Number of studies	Reference	Number of studies	Reference
No effect regardless of dietary total fat intake			1	Judd and Truswell (1981)
Total fat similar in experimental and control diets	6	Fraser <i>et al.</i> (1981) Anderson <i>et al.</i> (1986) Van Horn <i>et al.</i> (1986) Davidson <i>et al.</i> (1991) Johnston <i>et al.</i> (1998) Jang <i>et al.</i> (2001)	2	Grande <i>et al.</i> (1965) Karsltrom <i>et al.</i> (1984)
Insufficient data to assess (e.g. study provided no data on dietary fat intake)	3	De Groot <i>et al.</i> (1963) Van Horn <i>et al.</i> (1988) Jacobs <i>et al.</i> (2002)	2	Challen <i>et al.</i> (1983) Burr <i>et al.</i> (1989)
Multiple dietary differences make it impossible to assess the impact of dietary fat	4	Van Horn <i>et al.</i> (1991) Keys et al (1960) Schweizer et al (1983) Kay et al (1985)		

Eight studies used diets with the same fat content for all interventions. Total dietary fat is not a variable in such studies so they cannot be used to assess its potential interaction with the cardioprotective properties of whole grain foods. Five studies did not provide information on the fat content of their diets, and four studies had small but statistically significant differences in multiple dietary components between the control and experimental diets so that it is not possible to assess the impact of dietary fat *per se*.

In conclusion, as noted above, the available literature supports a conclusion that the total fat content of fiber or whole grain food-containing diets is unrelated to CHD, and provides no evidence that diets low in saturated fat and cholesterol, but not necessarily low in total fat, are any less effective in reducing the risk of CHD than their low-fat counterparts.

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 *Diet and Health*. The proposed claim and eligibility criteria are also consistent with the underlying studies that provided the basis for the whole grains statement made in *Diet and Health*. Since publication of *Diet and Health*, numerous recommendations and other evidence concerning whole grains, saturated fat, cholesterol, and total fat have emerged. These recommendations and related evidence confirm that (1) continued emphasis should be placed on diets low in saturated fat and cholesterol, and (2) whole grains continue to be a public health priority.

A. Recommendations regarding fat intake

Diet and Health reflected significant scientific agreement that total fat intake may influence CHD risk to the extent that it influenced saturated fat intake. According to the FNB, “[i]ntake of total fat *per se*, independent of the relative content of the different types of fatty acids, is not associated with high blood cholesterol levels and coronary heart disease.” (*Diet and Health*, at 7). Since the FNB issued this finding, additional support for this conclusion has steadily amassed, resulting in significant shifts in dietary recommendations and policy.⁶ These shifts are reflected in current nutrition science, nutrition public policy, and regulatory precedent.

⁶ These shifts have resulted in a moderation of recommendations concerning the percent of energy that should be obtained from fat. At the time of *Diet and Health*, it was suggested that no more than 30% of calories should be obtained from fat; under current recommendations, low-saturated fat diets with moderate amounts of total fat (up to 35% of total energy) are recognized as healthful and appropriate. The recognition that moderate fat diets may be appropriate does not affect the principles outlined in *Diet and Health* regarding whole grains, saturated fat, and cholesterol, but it does further support the proposition that foods containing moderate amounts of fat may be included as part of a healthy diet.

1. Current nutrition science

Serum total cholesterol (T-C) and low-density lipoprotein cholesterol (LDL-C) are well-accepted biomarkers for predicting the risk of CHD. Many of today's dietary recommendations are based on lowering the concentration of these factors in the population. The effect of diet on CHD biomarkers has been studied for many years. Keys (1984) and Hegsted (1986) analyzed data from dietary interventions studies and developed equations that can be used to predict the effect of dietary fats on T-C. These equations reflect the evidence showing that dietary saturated fatty acids (and to a lesser extent cholesterol) increase the concentration of T-C while unsaturated fatty acids (especially polyunsaturated fatty acids) lower it. Total fat would not be expected to influence T-C based on these equations. Epidemiologic studies have repeatedly shown that saturated fat, but not total fat, is associated with reduced incidence of CHD in humans, and numerous clinical trials have confirmed these observations (Hu *et. al.* 2000).

2. Nutrition public policy

Public health authorities have long recommended a low-fat, high carbohydrate diet as a means to reduce the risk of CHD. 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 report of the National Cholesterol Education Program (1994).

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 quasi-governmental authorities universally recognize the appropriateness of low-saturated fat diets with

moderate amounts of total fat (i.e. up to 35% of total energy) as alternatives to low-fat, high-carbohydrate diets for the management of CHD.

a. The Dietary Guidelines for Americans

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 latest edition of the Guidelines (U.S. Department of Agriculture and the U.S. Department of Health and Human Services, 2000). Americans are now 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.

b. The National Institutes of Health

The National Heart Lung & Blood Institute (NHLBI) has also concluded that total fat is not related to CHD risk. Recently updated recommendations to health professionals from this organization were published in a report entitled "Adult Treatment Panel III" (ATP III) (National Cholesterol Education Program, 2001). This report states,

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 (National Cholesterol Education Program 1993, 1994) 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.

The report also makes the following recommendation:

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.*

This conclusion is reflected in new dietary recommendations from this group, which increase the upper range of acceptable fat intake from 30 to 35 percent of total calories. These guidelines also reduced recommendations for dietary saturated fat from ten to seven percent of energy consumed.

c. The National Academy of Sciences/Food and Nutrition Board

NHLBI's conclusions are consistent with those provided in the recent "Macronutrient" report from the Institute of Medicine of the National Academy of Sciences (Food and Nutrition Board, 2002). This report concludes that total fat, *per se*, is not associated with the incidence of CHD, but that diets with more than 35% energy from fat tend to provide excessive amounts of saturated fatty acids:

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.

The Macronutrient Report established recommendations, in the form of an "Acceptable Macronutrient Distribution Range" (AMDR), for total fat for adults of 20 to 35 percent of energy. The upper range of the AMDR was intended to accommodate diets low in saturated fat, but moderate in total fat (predominantly from unsaturated fatty acids) which have been shown to have a beneficial affect on CHD.

These recommendations provide a compelling scientific basis for authorizing use of an appropriate whole grain health claim for foods that are low in saturated fat and cholesterol, but that do not necessarily meet the technical definition of "low fat" as defined by FDA.

3. Regulatory precedent

The shift in U.S. nutrition policy toward moderate fat diets is reflected in several recent rulemakings for CHD-related health claims. For example, the agency concluded that spreads and salad dressings should not be required to comply with the total fat disqualifier level in order to qualify for the sterol/stanol ester and CHD health claim (65 Fed. Reg. 54686, 54709 (Sept. 8, 2000)). In doing so, 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 (Refs. 103 and 108). 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 (Ref 108). In fact, the new guideline for fat intake in the Dietary Guidelines for Americans, 2000 (Ref 103) states, "Choose a diet that is low in saturated fat and cholesterol and moderate in total fat."

FDA recently extended this approach to a proposal 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 (Letter from C. L. Taylor, Ph.D., to F. L. Shinnick, Ph.D.). FDA stated that it would consider the exercise of enforcement discretion with respect to vegetable oils that bear the health claim so long as the labels contained a disclosure statement that complies with 21 C.F.R. § 101.13(h).

Similarly, in identifying the foods that qualify for a health claim concerning soy protein and CHD, the agency 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.

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

B. Whole grains as a public health priority

1. Recommendations for whole grain intake

The scientific information documenting the health benefits of whole grains has prompted public health officials, professional organizations and academic experts to place increased emphasis on recommendations intended to increase the consumption of these foods. Recommendations for consumption of whole grain

foods are included in the Dietary Guidelines for Americans, the Food Guide Pyramid for Young Children, and Healthy People 2010, as well as guidelines of the American Cancer Society, American Diabetes Association, American Dietetic Association, and American Heart Association.

a. The Dietary Guidelines for Americans

The nutritional benefits of whole grains prompted the U.S. Department of Agriculture (USDA) and the U.S. Department of Health and Human Services (USDHHS) to modify the "Dietary Guidelines for Americans" to include a guideline specifically devoted to grains (including whole grains) for the first time in 2000 (USDA/USDHHS, 2000). The 1995 guideline, "Choose a diet with plenty of grain products, vegetables and fruits" was divided into separate guidelines for fruits and vegetables and another for grains. The new guideline for grains states, "Choose a variety of grains daily, especially whole grains." The text of the Dietary Guidelines advises Americans to consume "several servings of whole grain foods" daily to help protect against "many chronic diseases".

b. The Food Guide Pyramid for Young Children

The Food Guide Pyramid for Young Children 2 to 6 Years Old was released by USDA in 1999. The purpose of this educational tool is to communicate the same general messages as the adult Food Guide Pyramid using foods and servings sizes more appropriate for young children. Whole grains are prominently pictured on the Pyramid graphic, and the accompanying text includes the following recommendation, "Offer whole or mixed grain products for at least three of the six grain group choices the Pyramid recommends each day."⁷

⁷ The Food Guide Pyramid for adults booklet (USDA, 1996) also specifically advises Americans to consume whole grains. This booklet states, "To get the fiber you need, choose several servings a day of foods made from whole grains, such as whole wheat bread and whole grain cereals." USDA has announced that it is likely to revise the Food Guide Pyramid shortly after revision of the Dietary Guidelines for Americans in 2005, and it is likely that whole grains will be given greater prominence.

c. Healthy People 2010

The purpose of the "Healthy People" publications (U.S. Department of Health and Human Services, 1990, 2000) is to define a national strategy for significantly improving the health of the nation. The first publication (Healthy People 2000) did not specifically address whole grain intake, but included the following broad objective:

Objective 2.6 and 16.8

Increase complex carbohydrate and fiber-containing foods in the diets of adults to 5 or more daily servings for vegetables (including legumes) and fruits, and to 6 or more daily servings for grain products. (Baseline: 2 ½ servings of fruits and vegetables and 3 servings of grain products for women aged 19 through 50 in 1985)

This objective was revised in Healthy People 2010 to reflect a greater understanding of the relationship between whole grain consumption and public health as reflected in the 2000 Dietary Guidelines for Americans.

Objective 19-7

Increase the proportion of persons aged 2 years and older who consume at least six daily servings of grain products, with at least three being whole grains.

Target: 50 percent

Baseline: 7 percent of persons aged 2 years and older consumed at least six daily servings of grain products, with at least three being whole grains in 1994-96 (age adjusted to the year 2000 standard population).

d. The American Cancer Society

Guidelines for the prevention and early detection of cancer from the American Cancer Society (2002) recommend whole grains:

Choose whole grains in preference to processed (refined) grains and sugars. Choose whole grain rice, bread, pastas and cereals.

e. The American Diabetes Association

The American Diabetes Association's (2003) most current recommendations for the treatment and prevention of diabetes emphasize the importance of whole grains in the diet of all Americans:

As for the general population, people with diabetes are encouraged to choose a variety of fiber-containing foods, such as whole grains, fruits and vegetables, because they provide vitamins, minerals, fiber, and other substances important for good health.

f. The American Dietetic Association

The American Dietetic Association (2002) recently emphasized the importance of whole grain foods in its position statement on dietary fiber:

There is substantial scientific evidence suggesting that vegetables, fruits and whole grains reduce risk of chronic diseases, including cancer and heart disease...Additionally, recent studies suggest that whole foods offer more protection against chronic diseases than dietary fiber, antioxidants, or other biologically active components in foods.

g. The American Heart Association

Revised dietary guidelines from the American Heart Association (Krauss *et.al.*, 2000) specifically recommend frequent consumption of whole grain foods:

Consume a variety of grain products, including whole grains; choose 6 or more servings per day.

Grain products provide complex carbohydrates, vitamins, minerals, and fiber. Dietary patterns high in grain products and fiber have been associated with decreased risk of cardiovascular disease.

In summary, whole grains have been given increasingly greater prominence in guidelines and recommendations from public health authorities. This higher priority reflects an increased understanding of the ability of whole grains to reduced risk of chronic diseases, coupled with a lack of understanding of these benefits by many Americans.

2. Inadequate whole grain consumption in the United States

Despite the considerable evidence that regular consumption of whole grains can reduce the risk of CHD and other chronic diseases, most Americans appear unaware of these benefits and the intake of whole grain products remains well below current dietary recommendations (Jones *et.al.*, 2002). An analysis of data from the 1994-96 Continuing Survey of Food Intake by Individuals (CSFII) found that average consumption of whole grains among U.S. adults was only one serving per day, and only eight percent of this group met the current recommendation to eat at least three servings per day (Cleveland *et.al.*, 2000).

Whole grain consumption also differs by demographic group. Kantor *et.al.* (2001) reported that the mean number of servings of whole grains eaten per day tends to be higher among U.S. Caucasians (1.1) compared to non-Native

American minorities (0.7). In addition, whole grain intake was associated with education level (1.2 servings/d for people with post-high school education vs. 0.8 for those who did not finish high school) and household income (0.8 vs. 1.2 servings/d for people with incomes <130% of the poverty level compared to those with >350%, respectively). Cleveland *et.al.* (2000) found that health conscious consumers (e.g. exercisers, non-smokers, vitamin and/or mineral supplement users and non-overweight individuals) tended to eat more servings of whole grains than their less health conscious counterparts. These findings suggest that a significant portion of the population stands to benefit from increased consumption of whole grain foods.

3. Barriers to whole grain consumption

The most frequently cited barriers to increased consumption of whole grain foods by U.S. consumers are low awareness of their benefits, inability to identify such foods in the marketplace and unwillingness to sacrifice good taste (Adams and Engstrom, 2000; Kantor *et.al.*, 2001). Nevertheless, consumers are receptive to messages about nutrition and health. A recent survey (IFIC, 2002) found that 93% of Americans believe that some foods have health benefits beyond basic nutrition (i.e. vitamins and minerals), and 85% are interested in learning more about such foods. These results suggest that consumers may respond to compelling messages about whole grains that address the existing barriers to increased consumption. Increased consumer and health professional education and increased availability of better-tasting products have been identified as strategies to increase the consumption of whole grain foods (Adams and Engstrom, 2000). Kantor *et.al.* (2001) concluded that the FDA-sanctioned health claims have the potential to address all three of these strategies.

Taste is considerably influenced by fat, a major contributor to the palatability of many foods, including whole grains. In addition to bringing out the flavor of such products, fat contributes significantly to their texture and mouth feel and results in improved consumer acceptability.

Fat is especially important in processing crackers and other baked products with significant whole grain content:

- Fat is needed to process and sheet the dough
- Low fat, whole grain dough will not flow and become dry and crumbly
- The fiber in whole grain has binding properties for both water and fat
- Adding more water does not aid in processing because the dough becomes very sticky and the increased bake time to eliminate the additional water leads to a very dry hard texture that is unacceptable to consumers

Use of a whole grains health claim on popular products that contain moderate amounts of fat, such as nut-containing cereals, Triscuit™ brand whole grain crackers, and other whole grain foods would expose more consumers to the benefits of whole grains. It also would call attention to additional dietary sources of whole grains that may previously have been unrecognized.

In summary, consumption of a diet rich in whole grains is widely recommended, but intake of whole grain foods in the United States continues to fall below recommended levels. Exposure of consumers to a variety of whole grain foods, including foods that may currently be unrecognized as containing whole grains, is one strategy for furthering public health goals concerning diets rich in whole grains.

IX. SUMMARY AND CONCLUSIONS

In summary, the greatest possible benefit for all stakeholders is made possible by a health claim that focuses on the relationship between CHD and diets rich in whole grains but low in saturated fat and cholesterol. Such a claim reflects not

only *Diet and Health*, but also the latest nutrition science confirming that saturated fat intake (and to a lesser extent cholesterol) is related to CHD risk factors, but that dietary total fat, *per se*, is not. It is also consistent with government nutrition policy concerning such science, mirrors statements from scientific and professional organizations, follows precedent established by FDA for other CHD-related health claims, and would have a minimal effect on total dietary fat intake.

Furthermore, use of the claim on products that are low in saturated fat and cholesterol, but not necessarily low in total fat, will provide food manufacturers with greater opportunities to increase whole grain consumption. Use of the claim on a wider range of products will help educate consumers about the benefits of whole grains, and availability of the claim for slightly higher fat products will provide industry with the opportunity and additional incentives to develop new and better tasting whole grain foods.

Respectfully submitted,



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