

PATTON BOGGS LLP
ATTORNEYS AT LAW

Patton Boggs LLP
Washington, DC 20004
202 457 8000
pattonboggs.com

July 6, 1999

Stuart M. Pape
(202) 457-5240
sp.pape@pattonboggs.com

VIA FACSIMILE AND REGULAR MAIL

Ms. Christine Lewis (IFS-451)
Deputy Director
Office of Special Nutritionals
Center for Food Safety and Applied Nutrition
Food and Drug Administration
200 C Street, S.W.
Washington, DC 20204

Re: *General Mills, Inc.; Whole Grain Foods Authoritative Statement Claim Notification*

Dear Ms. Lewis:

On behalf of General Mills, Inc. ("General Mills"), I make the following supplements to the "Whole Grain Foods Authoritative Statement Claim Notification," submitted by Patton Boggs LLP, on behalf of General Mills, on March 10, 1999. These amendments are made without prejudicing the 120-day notification period set forth in section 303 of the Food and Drug Administration Modernization Act of 1997 ("FDAMA").¹

1. Difference from Existing Claims

The notification is amended to include the following statement on page 27, immediately following the last paragraph of section VII, "Consistency with Currently Authorized Health Claims," and preceding section VIII, "Conclusion":

"The whole grain foods claim is not equivalent to any authorized health claims, including those for fiber. The whole grain foods claim refers to 'diets rich in whole grain foods and other plant foods,' as opposed to fiber-containing foods. Rather than fiber being a food component referred to in the claim as necessary for the beneficial relationship, the whole

¹ Pub. L. No. 105-115 (November, 21, 1997).

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SEATTLE, WASHINGTON

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grain claim recognizes the explicit wording, and intended meaning, of the authoritative statement: whole grain foods themselves have a beneficial effect that cannot be attributed to fiber, or any other single component of the foods. Furthermore, because diets that satisfy the whole grain claim, do not necessarily satisfy the fiber claims, and vice versa, the claims are clearly mutually exclusive. Thus, the proposed whole grain foods claim satisfies FDAMA's requirements because it is appropriately based on an authoritative statement, and is not equivalent to an already-authorized health claim."

2. Model Claim

The model claim set forth on page 10 of the notification is amended to read:

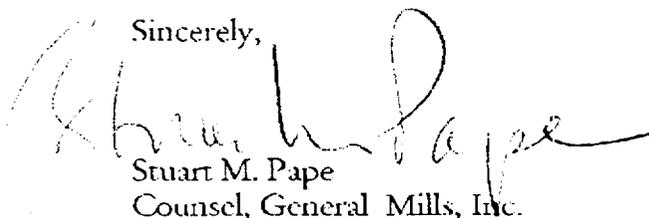
Diets rich in whole grain foods and other plant foods and low in total fat, saturated fat, and cholesterol, may help reduce the risk of heart disease and certain cancers.²

The amended model claim includes the concept that a diet should be low in saturated fat and cholesterol (as well as low in total fat and rich in whole grain foods and other plant foods) in order to have the potentially beneficial effects on heart disease risk.

3. Confidentiality

General Mills does not object to the Food and Drug Administration making public the March 10, 1999, notification, and this letter, on July 8, 1999, the day the 120-day notification period set forth in FDAMA expires and the claim takes effect.

Sincerely,



Stuart M. Pape
Counsel, General Mills, Inc.

SMP/Sro449573

² The claim would not need to refer to "saturated fat and cholesterol" if the disease endpoint in the claim were only "certain cancers."

APPENDIX B

**1999 Whole Grains Health Claim Notification
(General Mills)**

PATTON BOGGS LLP
ATTORNEYS AT LAW

64085

2550 M Street, NW
Washington, DC 20037-1350
202-457-6000

Facsimile 202-457-6315

March 10, 1999

Stuart M. Pape
(202) 457-5240
spape@pattonboggs.com

VIA COURIER

Center for Food Safety and Applied Nutrition
Food and Drug Administration
200 C Street, SW
Washington, DC 20204

CONFIDENTIAL

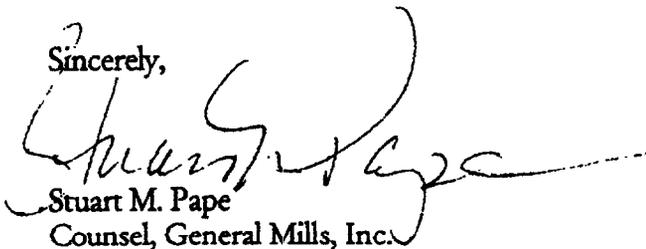
Re: *Authoritative Statement Claim Notification*

Dear Ladies and Gentlemen:

On behalf of General Mills, Inc., we hereby submit the enclosed Whole Grain Foods Authoritative Statement Claim Notification. This notification is submitted pursuant to section 403(r)(3) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 343(r)(3)).

If you have any questions, please feel free to contact me at the above number. Thank you for your consideration of this matter.

Sincerely,



Stuart M. Pape
Counsel, General Mills, Inc.

SMP/jjs

Enclosure

99P-2209

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**WHOLE GRAIN FOODS
AUTHORITATIVE STATEMENT CLAIM
NOTIFICATION**

Before the
Center for Food Safety and Applied Nutrition
Food and Drug Administration
200 C Street, SW
Washington, DC 20204

Submitted on behalf of
General Mills, Inc.

By
Stuart M. Pape
Daniel A. Kracov
Jennifer J. Spokes
Patton Boggs LLP
2550 M Street, NW
Washington, DC 20037
(202) 457-6000

March 10, 1999

***NOTIFICATION FOR A HEALTH CLAIM BASED ON AN
AUTHORITATIVE STATEMENT***

**CONFIDENTIAL
NOT FOR PUBLIC DISCLOSURE**

**Notification for a Health Claim Based on an Authoritative Statement
Pursuant to 21 U.S.C. 343(r)(3)**

I. Executive Summary

A. The Proposed Authoritative Statement Claim

General Mills, Inc. ("General Mills") proposes to use the following authoritative statement claim relating to diets containing whole grain foods, and coronary heart disease ("CHD") and certain cancers:

Low fat diets rich in whole grain foods and other plant foods may reduce the risk of heart disease and certain cancers.

The authoritative statement claim notification includes a definition for whole grain foods that ensures that the food bearing the claim contains whole grain(s) as the predominant ingredient. Also, the notification sets forth appropriate criteria to permit the Food and Drug Administration ("FDA" or the "agency") to ensure compliance.

B. The Claim Derives From An Authoritative Statement from the National Academy of Sciences *Diet and Health* Report

The support for the whole grain foods authoritative statement claim derives from an authoritative statement from the National Academy of Sciences ("NAS") *Diet and Health: Implications for Reducing Chronic Disease Risk* report. The statement concludes that "(d)iets 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." The proposed authoritative statement claim repeats the importance of diets high in plant foods, and specifies "whole grain foods" as an example of a plant food cited in the statement as

beneficial.

The *Diet and Health* report reflects a comprehensive and deliberative review by the NAS Committee on Diet and Health, of the scientific literature on diet and major associations between diet and health. In reaching its conclusions about plant foods, including whole grain foods, the nineteen-member Committee considered direct and indirect evidence including epidemiological, animal, and human studies related to carbohydrates, dietary fiber, fat-soluble vitamins, water-soluble vitamins, cholesterol, and fat intake. Since the publication of the report, both the statement and its scientific basis continue to receive support from scientific studies, including those addressing whole grain foods alone. Thus, the authoritative statement, and the significant scientific agreement supporting the statement, provide a substantial basis for the whole grain foods authoritative statement claim.

C. The Proposed Claim Will Lead to Increased Consumption of Whole Grain Foods

Whole grain foods are consistently recommended as components of a healthy diet. The positive effect of whole grain foods on disease risk is well-recognized, and whole grain foods provide a variety of vitamins, minerals, and other dietary substances that are otherwise important for good health. This authoritative statement claim will encourage increased consumption of plant foods, especially whole grain foods, and thus provide a substantial benefit to public health.

FDA has approved health claims for fruits and vegetables, together with grains, for certain cancers and coronary heart disease. However, whole grain foods consumption has not significantly increased since approval of the claims, and remains below desired levels. In contrast, consumption of other plant foods, such as fruits and vegetables, has increased.

Consumer disinterest in whole grain foods, as compared to fruits and vegetables,

likely results from consumers not recognizing the potential benefits derived from consumption of whole grain foods. Consumers do not recognize the benefits of whole grain foods, as compared to fruits and vegetables, because the benefits of fruits and vegetables have been given significantly more attention than the benefits of whole grain foods. For example, while a health claim exists that addresses fruits and vegetables alone, whole grain foods are incorporated into health claims only as part of the "fiber-containing fruits, vegetables, and grains" claims. A health claim for whole grain foods and other plant foods will emphasize to consumers the benefits of consuming a low fat diet rich in whole grain foods. The proposed claim will impress upon consumers that not only plant foods in general, but whole grain foods themselves, are an important component of the diet, and that consumption of fruits and vegetables does not eliminate the need to consume whole grain foods.

D. The Claim is Consistent with Currently Authorized Health Claims

The proposed claim is consistent with already-approved claims about the relationships between fiber-containing foods and soluble fiber from whole oats, and risks of CHD and cancer. The claim broadly addresses whole grain foods and other plant foods, rather than a particular component of whole grains, such as fiber. Although fiber is one component of whole grain foods and other plant foods that might be primarily responsible for reducing the risk of heart disease and cancer, the effects on these diseases do not likely result from the food's fiber content alone. Because consumers associate fiber with laxation, and thus might not find the idea of increased fiber consumption appealing, it is important to emphasize to consumers the other benefits of whole grain foods.

In addition, the proposed claim complements existing claims about diets low in dietary lipids, saturated fat, and cholesterol, reducing the risks of CHD and certain cancers. The claim addresses the plant foods, and specifically whole grain foods,

component of a low fat diet, and therefore draws particular attention to the importance of these foods. Thus, the proposed claim educates consumers about a category of foods that they should seek out and recognize in order to make healthy food choices.

E. Conclusion

The proposed claim appropriately reflects an authoritative statement of a scientific body that addresses the relationship between whole grain foods and other plant foods, and reduced risk of CHD and certain types of cancers. As indicated by the authoritative statement, scientific evidence supports the benefits of eating healthy diets rich in these foods. However, consumption of whole grain foods remains below recommended levels. Consumers will benefit greatly from a claim indicating a relationship between consumption of whole grain foods and a reduction in disease risk. The proposed claim will draw consumer attention to whole grain foods and the need to increase their consumption, and will lead to enhanced public health.

II. Introduction

General Mills intends to make an authoritative statement claim about the relationship of plant foods, and specifically whole grain foods, with coronary heart disease ("CHD") and certain cancers. An expert panel of the National Research Council ("NRC"), a subdivision of NAS, recognized these relationships and included them in NRC's renowned *Diet and Health* report on diet and disease relationships. The positive effect of whole grain foods on disease risk is consistently recognized by scientific experts. Additionally, whole grain foods provide a variety of vitamins, minerals, and other dietary substances that are otherwise important for good health.¹ In fact, an important new study shows that whole grain consumption is inversely related to total mortality.²

Experts continue to urge whole grain foods as an important component of a healthy diet. However, despite long-standing and general agreement that people benefit significantly from increased consumption of whole grain foods, consumption remains below desired levels. This authoritative statement claim will raise consumer awareness of the potential benefits from consuming whole grain foods. The claim will encourage increased whole grain consumption and thus, will provide a substantial benefit to public health.

¹DEPARTMENT OF AGRICULTURE AND DEPARTMENT OF HEALTH AND HUMAN SERVICES, NUTRITION AND YOUR HEALTH: DIETARY GUIDELINES FOR AMERICANS, December 1995, at 22.

² Jacobs, David R., et. al., "Is Whole Grain Intake Associated with Reduced Total and Cause-Specific Death Rates in Older Women? The Iowa Women's Health Study", *American Journal of Public Health*, 1999; 89:322-329.

III. Background

National dietary recommendations advise a shift to a low fat, plant-based diet, founded on the consumption of adequate amounts of grain foods. Indeed, grain foods form the base of the Food Guide Pyramid, with the United States Department of Agriculture ("USDA") and the Department of Health and Human Services ("HHS") recommending 6-11 servings of grains per day – more servings than any other food type.³ Public health policy goals as specified in *Healthy People 2000: National Health Promotion and Disease Prevention Objectives*, include reducing deaths from coronary heart disease and reversing the rise in cancer deaths through dietary measures that include increasing consumption of foods such as grains.⁴

Experts advise that of the recommended 6-11 servings of grain per day, several servings should consist of a variety of whole grain foods.⁵ In fact, it has been proposed that the Food Guide Pyramid should be revised to further emphasize whole grain foods.⁶ Other national nutrition policy documents also recognize the key role that whole grain foods play in achieving an optimal diet. Increased whole grain consumption is recommended in USDA's *Dietary Guidelines for Americans*,⁷ the NRC's *Recommended Dietary Allowances*⁸ and *Diet and Health*⁹ reports, and the Surgeon General's *Report on*

³ DIETARY GUIDELINES FOR AMERICANS, *supra* note 1.

⁴ HHS, HEALTHY PEOPLE 2000: NATIONAL HEALTH PROMOTION AND DISEASE PREVENTION OBJECTIVES, 118-119 (1990).

⁵ DIETARY GUIDELINES FOR AMERICANS, *supra* note 1, at 25. See also Schwartz, Nancy E., "Narrowing the Gap: Practical Strategies for Increasing Whole-Grain Consumption", *Critical Reviews in Food Science and Nutrition*, 34(5&6):513-516 (1994); Welsh, Susan, et.al., "Achieving Dietary Recommendations: Whole-Grain Foods in the Food Guide Pyramid", *Critical Reviews in Food Science and Nutrition*, 34(5&6):441-451 (1994).

⁶ Willet, Walter C., "The Dietary Pyramid: Does the Foundation Need Repair?", Editorial, *American Journal of Clinical Nutrition*, 1998:68:218-219. See Schwartz, *supra* note 5; Welsh, *supra* note 5.

⁷ DIETARY GUIDELINES FOR AMERICANS, *supra* note 1, at 25.

⁸ SUBCOMMITTEE ON THE TENTH EDITION OF THE RDAs, NAS, RECOMMENDED DIETARY ALLOWANCES, 10TH ed., 42 (1989).

⁹ COMMITTEE ON DIET AND HEALTH, NAS, DIET AND HEALTH: IMPLICATIONS FOR REDUCING CHRONIC DISEASE RISK, at 8 (1989).

Nutrition and Health.¹⁰ In addition, the American Cancer Society¹¹ and American Dietetic Association¹² recommend an increased intake of whole grain foods.

Although a majority of consumers know about the Food Guide Pyramid's recommendations,¹³ consumer intake of whole grain foods falls far below recommended levels.¹⁴ Furthermore, only 30 percent of Americans report trying to include more whole grains in their diets, less than those trying to avoid too much fat in their diets, or trying to include more variety of foods in their diets.¹⁵ Thus, consumers clearly need to increase their understanding of the benefits in order to increase their consumption of whole grain foods.

The authoritative statement that serves as the basis for this claim identifies the benefits of plant foods, including whole grain foods, fruits, vegetables, and legumes, in reducing CHD and cancer risk. However, despite the long-standing recognition of the value of these foods, consumption of whole grain foods remain below that of other plant foods such as fruits and vegetables. Even after FDA's 1993 approval of health claims for fruits, vegetables, and grains, with certain cancers and coronary heart disease,¹⁶ whole grain foods consumption remained below the Food Guide Pyramid recommendations.

Results from a study conducted from 1994 through 1996 show that Americans ate an average of only about 6-2/3 servings of grain products daily.¹⁷ Importantly, whole

¹⁰ SURGEON GENERAL, HHS, THE SURGEON GENERAL'S REPORT ON NUTRITION AND HEALTH: SUMMARY AND RECOMMENDATIONS, Pub. No. 88-51211, 12-13 (1988).

¹¹ AMERICAN CANCER SOCIETY, GUIDELINES ON DIET, NUTRITION AND CANCER PREVENTION: REDUCING THE RISK OF CANCER WITH HEALTHY FOOD CHOICES AND PHYSICAL ACTIVITY, 1996.

¹² See Schwartz, *supra* note 5.

¹³ In a recent survey, 60 percent of Americans knew of the Food Guide Pyramid recommendations. Gallup Survey of Changing Food Preparation and Eating Habits. Multi-Sponsored Surveys, Inc. Princeton, NJ, 1998.

¹⁴ Jacobs, *supra* note 2; Albertson A.M., Tobelmann, R.C., "Consumption of Grain and Whole Grain Foods by an American Population During the Years 1990 to 1992", *Journal of the American Dietetic Association*, 1995;95:703-704.

¹⁵ Gallup Study of Changes in Food Preparation and Eating Habits, *supra* note 13.

¹⁶ 21 C.F.R. § 101.76, § 101.77.

¹⁷ USDA, Agricultural Research Service. 1997. Pyramid Servings Data: Results from USDA's 1995 and 1996 Continuing Survey of Food Intakes by Individuals. On 1994-1996 Continuing Survey of Food

grain foods comprised only 1 of these servings.¹⁸ Furthermore, 36 percent of the adults surveyed reported consuming no whole grain foods during the two non-consecutive reporting days.¹⁹ Another study, conducted in 1995, reported a mean whole grain foods intake of only 0.5 eatings per day for adults.²⁰ Less than 2 percent of the study population consumed 2 or more eatings per day, and 23 percent consumed no whole grains over the 14-day collection period.²¹

In contrast, the consumption of fruits and vegetables increased as a result of the 1993 health claims and related promotional campaigns.²² Fruits and vegetables intake increased from 3.4 servings per day before approval of the health claims,²³ to 4.9 servings per day after approval of the health claims.²⁴ From 1994-1996, while 60-76 percent of men and women perceived it important to follow dietary guidelines to consume plenty of fruits and vegetables, only 26-35 percent perceived it as important to consume plenty of bread, cereal, rice, and pasta.²⁵ Currently, 52 percent of Americans believe eating more fruits and vegetables is the most important dietary habit, while only 6 percent believe that eating more whole grain foods is the most important dietary habit.²⁶

Lack of understanding of the benefits of whole grain foods might be one of the primary reasons consumers do not perceive whole grain foods to be as necessary and beneficial to the diet as fruits and vegetables. According to a recently conducted

Intakes by Individuals and 1994-1996 Diet and Health Knowledge Survey. CD-ROM.

¹⁸Contribution to this 1 serving derived from a variety of foods including breads, snacks, ready-to-eat cereals, hot cereals, sweet snacks/pancakes, and rice/pasta/tortillas. *Id.*

¹⁹*Id.*

²⁰Albertson, *supra* note 14.

²¹*Id.*

²²An example of a promotional campaign is the "5 A Day for Better Health Program", sponsored by the National Cancer Institute and the Produce for Better Health Foundation, which encourages consumers to eat five or more servings of fruits and vegetables per day.

²³USDA, Continuing Survey of Food Intake by Individuals, 1988-1991.

²⁴USDA's 1994-96 Continuing Survey of Food Intake by Individuals and 1994-96 Diet and Health Knowledge Survey, Food Surveys Research Group, Beltsville Human Nutrition Research Center, ARS, Riverdale, MD.

²⁵*Id.*

²⁶Market Facts, Inc., Chicago IL, 1998 (see Attachment 1).

survey, 67 percent of consumers indicate a willingness to eat whole grain products more often if they believed they could help reduce their risk of heart disease and cancer.²⁷ An authoritative statement claim specifying whole grain foods as a type of plant food would help to educate consumers about whole grain foods and their benefits, and lead to more widespread and frequent consumption of whole grain foods.²⁸ Increased consumer awareness and demand for whole grain foods also will encourage development of more whole grain products by the food industry.²⁹

In addition to approving health claims encompassing fruits, vegetables, and grains,³⁰ FDA also approved a health claim specific to fruits and vegetables and cancer.³¹ FDA has not, however, approved a health claim specific to grains, nor whole grain foods. An authoritative statement claim highlighting whole grain foods would focus consumer attention on whole grain foods specifically, just as the fruits and vegetables health claim does for those foods. The claim would emphasize the benefits of whole grain foods as an important element of a healthy diet.

Finally, the ability to identify whole grain foods may also be a barrier to consumers achieving an adequate intake of whole grain foods. Consumers may not clearly understand which foods are significant sources of whole grains and which are not. An authoritative statement claim on qualifying products would help Americans

²⁷ *Id.*

²⁸ General Mills research and market share data indicate increased awareness of health benefits and increased purchases of CHEERIOS® following approval and placement on the package of the soluble fiber from whole oats and CHD health claim (21 C.F.R. § 101.81). Approximately four to six months following the announcement of the approval of the soluble fiber from whole oats health claim, the CHEERIOS® base business increased 5 to 6 percent.

²⁹ See Levy, Alan S., et. al., Division of Market Studies, Center for Food and Applied Nutrition, "Consumer Impacts of Health Claims: An Experimental Study", January 1997.

³⁰ 21 C.F.R. § 101.76, 101.77.

³¹ 21 C.F.R. § 101.78. FDA approved the fruits and vegetables/cancer claim because, although FDA did not find significant scientific agreement that antioxidant vitamins, specific component of fruits and vegetables, reduce the risk of cancer, FDA did find that the foods in their whole form may reduce the risk of cancer. Thus, FDA approved a health claim for the foods despite not knowing the exact mechanism in the foods causing the reduced risk. Similarly, even though scientists might not agree on the mechanisms that cause whole grains to have beneficial effects, scientists and governmental bodies do agree that whole grain foods may reduce the risks of CHD and certain cancers. 58 Fed. Reg. 2639 (January 6, 1993).

identify these foods across a variety of categories, while restating an important nutrient/disease relationship recognized by the NRC in the *Diet and Health* report.

IV. Statutory Basis for Authoritative Statement Claim

Section 303 of the Food and Drug Administration Modernization Act of 1997 ("FDAMA")³² permits health claims without prior FDA approval if the claim refers to a relationship between a nutrient and a disease, about which a qualified governmental scientific body has published an authoritative statement. The provision requires that the scientific body making the statement belong to the United States government and have official responsibility for public health protection or research directly relating to human nutrition, or be NAS or any of its subdivisions.³³ The authoritative statement must be published, currently in effect, and about the nutrient and disease or health-related condition to which the claim refers.³⁴ The claim and its referenced food must comply with existing regulations.³⁵ The claim must accurately represent the authoritative statement so as to enable the public to comprehend the information provided in the claim and to understand the relative significance of such information in the context of the total daily diet.³⁶

V. The Authoritative Statement Claim

General Mills intends to make the following model authoritative statement claim:

**Low fat diets rich in whole grain foods and other plant foods
may reduce the risk of heart disease and certain cancers.**

The authoritative statement claim is based on the authoritative statement made in the

³²21 U.S.C. 343(r)(3).

³³21 U.S.C. 343(r)(3)(C)(i).

³⁴*Id.*

³⁵21 U.S.C. 343(r)(3)(C)(iii).

³⁶21 U.S.C. 343(r)(3)(C)(iv).

NAS publication, *Diet and Health: Implications for Reducing Chronic Disease Risk*.³⁷ This report states that "(d)iets 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."³⁸ Furthermore, it states that the mechanisms for this effect, although not fully understood, might be explained by the low saturated fatty acid and cholesterol content of such diets, as well as high levels of complex carbohydrates, certain vitamins and minerals, trace elements, and nonnutritive constituents.³⁹

For purposes of this claim, "whole grain foods" means foods which contain 51 percent or more whole grain ingredient(s) by weight per Reference Amount Customarily Consumed ("RACC").⁴⁰ To consider a food as a "whole grain food", whole grain should be present in sufficient quantity to characterize the food. The "whole grain foods" definition conforms to the policy that a food is characterized by its predominant ingredient(s).⁴¹ Such a definition also ensures that the food provides a minimum of 16 grams of whole grain (the equivalent of a whole grain food serving under the USDA's research relating to the Food Guide Pyramid).⁴²

The definition measures whole grain percentage by weight per RACC because the RACC provides a consistent point of reference for foods of the same type. The

³⁷DIET AND HEALTH, *supra* note 9 (See Attachment 2).

³⁸*Id.*

³⁹*Id.*

⁴⁰ General Mills interprets the term "whole grain foods" to be interchangeable with the term "whole grain products". Note that foods bearing the claim must also be low in fat and meet the other general health claim requirements of 21 C.F.R. § 101.14.

⁴¹ See letter to Dr. Michael F. Jacobson, Center for Science in the Public Interest, from David A. Kessler, M.D., Commissioner of Food and Drugs, Food and Drug Administration, November 1, 1993. The Commissioner was responding to a citizen's petition requesting that FDA regulate the use of the term "whole wheat." Although General Mills does not adopt the petition in its entirety, the whole grain foods definition suggested here parallels the proposal to limit the "whole wheat" claim to products containing whole wheat flour as the predominant ingredient. For an analogous example, see 7 U.S.C. 6505(c)(1); the Organic Foods Production Act of 1990 characterizes a food as "organic" if it contains at least 50 percent organically produced ingredients.

⁴² USDA Pyramid Servings Data, *supra* note 17.

RACC currently serves as the measurement standard for other health claims.⁴³ Furthermore, the RACC measurement produces a better representation of the foods providing whole grain benefits because the RACC, unlike the serving size, will not result in foods being disqualified merely due to moisture content. For example, using bread's standard serving size of 30 – 35 grams, the majority of whole grain breads would not qualify as whole grains foods. However, using the 50 gram RACC, whole grains breads, which serve as important sources of whole grains, do qualify for the claim.

Compliance with the "whole grain foods" definition will be determined by reference to the fiber level of whole wheat. Whole wheat is the predominant grain in the U.S. diet, containing 11 grams of fiber per 100 grams of whole wheat. The fiber content creates a measure by which FDA can ensure that a product meets the definition; at the specified levels of fiber, whole grains clearly constitute the predominant ingredient(s). Thus, compliance can be verified by comparing the food's fiber content to the following compliance formula: $(11 \text{ grams} \times 51\% \times \text{RACC}) / 100$. For example:

$$(11 \text{ grams} \times 51\% \times 55 \text{ grams}) / 100 = 3.0 \text{ grams fiber}$$

$$(11 \text{ grams} \times 51\% \times 50 \text{ grams}) / 100 = 2.8 \text{ grams fiber}$$

$$(11 \text{ grams} \times 51\% \times 45 \text{ grams}) / 100 = 2.5 \text{ grams fiber}$$

$$(11 \text{ grams} \times 51\% \times 30 \text{ grams}) / 100 = 1.7 \text{ grams fiber}$$

The fiber level will be determined according to the methods and procedures set forth in 21 C.F.R. § 101.9(g)(2).

General Mills intends to display this authoritative statement claim on the labels of qualifying whole grain cereals listed in Attachment 3, as well as Pop Secret 94% Fat Free popcorn.⁴⁴ General Mills asserts that to the best of its knowledge, labels bearing the claim will not be false or misleading. General Mills also asserts that to the best of its knowledge, foods bearing the claim will comply with the provisions of 21 C.F.R.

⁴³ 21 C.F.R. §§ 101.76, 101.77, 101.81.

⁴⁴ Attachments 3 and 4 also set forth other products that would be eligible to bear the claim.

§ 101.14.

This claim qualifies as an authoritative statement claim by referring to a relationship, between a nutrient and a disease, about which a qualified scientific body has published an authoritative statement. The claim refers to the relationship between whole grain foods and CHD and certain cancers.⁴⁵ The statement was made by NRC, a subdivision of NAS, and published by NAS in the *Diet and Health* report. NAS and its subdivisions are specifically cited by the FDAMA provision as qualified scientific bodies.⁴⁶

The statement qualifies as authoritative because it reflects a deliberative review of plant foods, including whole grain cereals, and their relationship to CHD and cancer. The *Diet and Health* report constitutes a comprehensive analysis of the scientific literature and of the strength of evidence on major associations between diet and diseases undertaken by the NRC's 19-member Diet and Health Committee. Committee members possessed expertise in areas including biochemistry, biostatistics, clinical medicine, epidemiology, foods and food consumption patterns, human genetics, metabolism, nutrition, public health, and toxicology.⁴⁷ The Committee's conclusions on foods containing complex carbohydrates derived from a review of direct and indirect evidence, including epidemiologic, animal, and human studies related to carbohydrates, dietary fiber, fat-soluble vitamins, water-soluble vitamins, cholesterol, and fat intake.⁴⁸ The report was reviewed by additional scientists using procedures approved by the

⁴⁵Although FDAMA stipulates that the statement relate to a "nutrient", FDAMA also stipulates that the claim be made "with respect to" a food. Thus, a claim about a type of food containing a particular nutrient would qualify. Furthermore, in FDA's health claim regulations, FDA permits claims for "substances," including foods that refer either expressly or implicitly to a substance within the food, *i.e.*, fiber-containing fruits and vegetables. 58 Fed. Reg. 2478, 2480 (January 3, 1993).

⁴⁶FDA requests that an authoritative claim notification provide additional proof of consensus within a scientific body if a subdivision of the body made the statement. See "Guidance for Industry Notification of a Healthy Claim or Nutrient Content Claim Based on an Authoritative Statement of a Scientific Body," June 11, 1998, at 2. However, because FDAMA specifies that NAS subdivisions themselves qualify as acceptable scientific bodies, there is no need to further demonstrate consensus.

⁴⁷DIET AND HEALTH, *supra* note 9, at x.

⁴⁸*Id.* at 8.

NAS, National Academy of Engineers, and Institute of Medicine Report Review Committee.⁴⁹

The 1989 report makes clear that the whole grain foods/CHD and cancer relationships have been recognized for at least ten years. The most current scientific literature supporting these relationships, along with the absence of contradictory literature or statements, show that the statement is currently in effect. Furthermore, the statement does not merely reflect preliminary results, inconclusive research, or guidance for future research. As is clear from the statement itself, the context of the statement in the report, and the relevant scientific literature, the statement reflects conclusive scientific consensus supporting the relationship. In fact, as stated in the report, any uncertainty about the effects of whole grain foods relates solely to details about the particular *mechanisms* that contribute to or cause the health benefits, not to the effects of plant foods including whole grain foods on CHD and certain cancers. Thus, under FDAMA, this statement creates a valid basis for an authoritative statement claim.⁵⁰

The claim itself accurately represents the authoritative statement. The authoritative statement acknowledges the benefit of diets high in plant foods, including whole grain cereals, fruits, vegetables, and legumes. The claim parallels the statement by recognizing the value of diets rich in plant foods, and highlights one type of plant food mentioned in the statement: whole grain foods.⁵¹ Although the claim specifically

⁴⁹*Id.* at ii.

⁵⁰See *id.*, at 8. Although FDA had available the *Diet and Health* report in 1993 when it reviewed the existing research regarding diet/disease relationships for potential health claims under the Nutrition Labeling and Education Act, FDA did not review the literature with whole grain food claims in mind. FDA responded to Congress's mandate to review certain nutrients and foods for potential claims, and these did not include whole grains. Thus, FDA concentrated on the mandated nutrients with particular attention to fruits and vegetables, not whole grain foods. The *Diet and Health* report statement represents a comprehensive review of plant foods and whole grains, and the current scientific literature supports this statement.

⁵¹While the claim uses the term "whole grain foods", the authoritative statement references "whole grain cereals." However, the term "whole grain cereals" encompasses all whole grains such as barley, oatmeal, rye, and other whole grains. See M.J. Hill (1997), "Cereals, Cereal Fibre and Colorectal Cancer Risk: A Review of the Epidemiological Literature," *European Journal of Cancer* 6: 219-225, Benito, et. al.,

recognizes one example of plant foods from the statement, the claim does not ignore the importance of all plant food types in the diet, and encompasses other plant foods such as fruits, vegetables, and legumes, through the term "plant foods". As does the statement, the claim recognizes the benefits to both CHD and certain cancers.⁵²

Finally, the claim enables the public to comprehend the information provided in the claim and to understand its relative significance in the context of the total daily diet. The claim specifies whole grain foods as a type of plant food, because consumers are more apt to perceive fruits and vegetables as plant foods, than to perceive whole grain foods as plant foods. However, the claim makes it clear that a diet low in fat and high in whole grain foods should include other plant foods.

VI. Scientific Literature Relating to Whole Grain Foods/Disease Relationships⁵³

The *Diet and Health* report provides strong evidence that diets high in plant foods reduce the risk of CHD and certain cancers. The report includes whole grain foods in its examples of plant foods, and strong evidence verifies that whole grain foods are an

"A Population-Based Case-Control Study of Colorectal Cancer in Majorca. I. Dietary Factors", *International Journal of Cancer* 45:69-76, 1990. Because the proposed definition of "whole grain foods" requires 51 percent whole grain components, "whole grain foods" merely characterizes the food group that contains significant amounts of "whole grain cereals". Consumers will benefit more from use of the term "whole grain foods" because consumers often identify "cereals" with a narrower group of breakfast food that does not include other foods containing whole grains, such as bread and rice.

⁵²Under the statute, a health claim refers to "a nutrient" and "a disease". However, under FDA's health claim regulations, health claims refer to the relationship between a substance and a disease, because FDA inferred that Congress intended to permit health claims for substances other than just nutrients. 58 Fed. Reg. at 2480. Similarly, Congress clearly did not state nor intend to exclude from the definition of health claim any claims that refer to more than one disease, but rather intended that any claims about the relationship between a nutrient and a disease qualify as health claims. Furthermore, already-approved claims such as the cancer claims and the folic acid claim encompass several diseases (different types of cancers, and anencephaly and spina bifida). 21 C.F.R. § 101.73(a), 101.79(a). Finally, if FDA adopted a policy that health claims can only refer to one disease despite the proven benefits for more than one disease, manufacturers would be forced to include several claims on their labels, making the claims less effective and potentially leading to consumer confusion. Thus, the proposed claim not only mimics the authoritative statement, but reflects Congress's clear intent that claims may encompass more than one disease.

⁵³See Attachment 5 for a comprehensive bibliography of scientific literature on the relationship of whole grain foods to CHD and certain cancers (short cites in the text and footnotes, consisting of the author's last name and year of publication, are cited in full in the bibliography).

integral part of a diet high in plant foods.⁵⁴ The *Diet and Health* report reaches its conclusions based on numerous studies existing at the time documenting the association between whole grain food intake and reduced risk of CHD and certain cancers. These relationships continue to be supported by scientific literature published since the *Diet and Health* report (see e.g., Chatenoud, et. al., 1998; Hill, 1998; Jacobs et. al., 1998; Slavin et. al., 1997; Hill, 1997; Jacobs, et. al., 1995).

The studies consistently demonstrate reduced risk for cancer and CHD when demographic and other lifestyle factors (fruits and vegetables, energy and exercise) are controlled or adjusted in the statistical model, and regardless of the dietary questionnaire used to collect dietary data. For example, the findings are consistent for males and females across a variety of populations in the United States and Europe, and consistent in countries with dietary consumption patterns ranging from relatively high to low whole grain food intake. The scientific evidence is strongest for those studies that assess digestive cancers; however, the consistency and magnitude of association is similar to other types of cancer. Studies which examined the effect of whole grain food consumption on lower blood cholesterol levels further support the inverse relationship between higher whole grain intake and reduced risk for CHD. Thus, the studies reflect significant scientific agreement that low-fat diets rich in whole grain foods may help reduce the risk of CHD and certain cancers.

A. Supporting Scientific Evidence: Cancer

Thirty-seven case-control studies, one ecologic study, and three review articles published to date pertaining to whole grain food intake support a relationship between whole grain intake and reduced risk for various types of cancer (Chatenoud, et. al.,

⁵⁴ Kune, 1987; Potter, J.D., "Food and Phytochemicals, Magic Bullets and Measurement Error: A Commentary", *American Journal of Epidemiology* 1996;144:1026-1027; Reddy, B.S., "Diet and Colon Cancer: Evidence From Human and Animal Model Studies, in B.S. Reddy and L.A. Cohen, eds. "Diet, Nutrition, and Cancer – A Critical Evaluation", Vol. 1: Macronutrients and Cancer, CRC Press: Boca Raton, FL, 1986; Slavin, 1997.

1998; Jacobs, et. al., 1998; Goodman, et. al., 1997; Slattery, et. al., 1997; Slavin, et. al., 1997; Tavani, et. al., 1997; Witte, et. al., 1996; Jacobs, et. al., 1995; Giles, et. al., 1994; Boeing, et. al., 1993; Hansson, et. al., 1993; Levi, et. al., 1993; Levi, et. al., 1993; Bidoli, et. al., 1992; Franceschi, et. al., 1992; Tuyns, et. al., 1992; Boeing, et. al., 1991; Boeing, et. al., 1991; Bueno de Mesquita, et. al., 1991; Franceschi, et. al., 1991; Serraino, et. al., 1991; Wu-Williams, et. al., 1990; Franceschi, et. al., 1989; LaVecchia, et. al., 1989; Olsen, et. al., 1989; Peters, et. al., 1989; LaVecchia, et. al., 1988; LaVecchia, et. al., 1988; McLaughlin, et. al., 1988; Tuyns, et. al., 1988; Yu, et. al., 1988; Decarli, et. al., 1987; LaVecchia, et. al., 1987; LaVecchia, et. al., 1987; LaVecchia, et. al., 1986; Mack, et. al., 1986; Gold, et. al., 1985; Rosen, et. al., 1988; Trichopoulos, et. al., 1985; Pickle, et. al., 1984; Winn, et. al., 1984). Only three studies do not support such a relationship (Centonze, et. al., 1994; Talamini, et. al., 1992; LaVecchia, et. al., 1987). Of these studies, one used a daily dose of whole grain too low to show an association with colon cancer (Centonze, et. al., 1994), and the other two studies (on breast and prostate cancer) had odds ratios under 1.0.

In addition, twenty-four studies of cereals/cereal fiber support an inverse relationship with colon cancer (Hill, 1998; Hill, 1997; Olsen, et. al., 1994; Meyer and White, 1993; Zaridze, et. al., 1993; Arbman, et. al., 1992; Thun, et. al., 1992; Freudenheim, et. al., 1990; Willett, et. al., 1990; Heilburn, et. al., 1989; Kune, et. al., 1987; Risch, et. al., 1985; McKeown-Eyssen and Bright-See, 1984; Englyst, et. al., 1982; Jensen, et. al., 1982; Bingham, et. al., 1979; Liu, et. al., 1979; Yanai, et. al., 1979; IARC Working Party, 1977; Knox, 1977; Schrauzer, 1976; Howell, et. al., 1975; Armstrong, et. al., 1974; Irving and Drasar, 1973).⁵⁵ Seven do not, of which most were foreign studies in countries where the intake was probably not high enough to reduce

⁵⁵Substantial evidence exists in whole grain studies to demonstrate scientific agreement about the benefits of whole grain foods. In addition, throughout time, numerous studies on whole grain wheat referred to whole grain as "cereal fiber". See Hill, 1997, at 223. Thus, cereal fiber study results pertain to whole grain foods and should be included in any evaluation of whole grain studies.

colon cancer risk (Benito, et. al., 1990; Freudenheim, et. al., 1990; Macquart-Moulin, et. al., 1986; Potter and McMichael, 1986; Bingham, et. al., 1985; Miller, et. al., 1983; Martinez, et. al., 1975). Taken as a whole, these studies demonstrate the significant scientific agreement linking whole grain food intake to reduced cancer risk.

An analysis of the scientific literature published between 1984 and 1997 (Jacobs, et. al., 1998) evaluating the relationship between various forms of whole grain food intake and 20 types of cancer, and using a statistical analysis controlling for confounding variables (demographic, BMI, lifestyle behaviors, reproductive and/or dietary factors), indicates the following:

(1) Reduced risk for cancer is observed for higher whole grain food intake despite the type of dietary intake methodology used.

(2) There is a strong consistency and moderately strong magnitude of association (approximately 30%) between whole grain food intake and reduced risk for cancer.

(3) There is a moderately strong dose-response relationship between increased whole grain food intake and reduced risk for various cancers.

(4) The association between whole grain food intake and reduced risk of cancer persists even when other confounding variables (e.g. diet, exercise, smoking, alcohol use) are controlled. Confounding with other dietary and lifestyle factors does not explain the apparent protective effect of whole grain foods against cancer. Many studies tested associations for confounding with a variety of variables; risk indicators for high versus low whole grain food intake did not decrease as the number of adjusting factors increased.

Of particular significance is a very recent study finding that a higher frequency of whole grain food intake is an indicator of reduced risk of several neoplasms. Using data from an integrated series of case-control studies conducted in northern Italy between 1983 and 1996, Chatenoud, et. al. (1998) found with statistical significance that high

intake of whole grain foods consistently reduced risk of neoplasms by 30-70% (oral cavity and pharynx, esophagus, stomach, colon, rectum, liver, gallbladder, larynx, breast, ovary, prostate, bladder, kidney, and non-Hodgkin's lymphomas). No significant heterogeneity was found for age of diagnosis, gender, education, smoking habits, alcohol intake, and body mass index. The study found only negligible effects of fruits and vegetables on the association of whole grain food intake and reduced risk for these cancers.

B. Supporting Scientific Evidence: Coronary Heart Disease

The available scientific evidence clearly supports the relationship between higher whole grain food intake and reduced risk of CHD. Large prospective epidemiological studies which controlled for demographic and other lifestyle variables demonstrate an inverse association for CHD with high versus low whole grain food intake. In addition, ecologic and case-control studies, along with experimental and clinical interventions, have shown a positive effect on CHD risk factors with higher whole grain food intake.

To date, fourteen studies support the relationship between whole grain foods and reduced risk of CHD and CHD risk factors (Jacobs, et. al., 1998; Johnston, et. al., 1998; Appel, et. al., 1997; Pietinen, et. al., 1996; He, et. al., 1995; Fraser, et. al., 1992; Ripsin, et. al., 1992; Davidson, et. al., 1991; Van Horn, et. al., 1991; Reynolds, et. al., 1989; Van Horn, et. al., 1988; Van Horn, et. al., 1986; Fraser, et. al., 1981; De Groot, et. al., 1963). Only two studies do not support the relationship (Gramenzi, et. al., 1990; Judd and Truswell, 1979).⁵⁶ Ten published studies on whole grain cereal fiber support the relationship (Salmeron, et. al., 1997; Salmeron, et. al., 1997; Rimm, et. al., 1996; Ripsin, et. al., 1992; Davidson, et. al., 1991; Karlstrom, et. al., 1984; Burr and Sweetnam, 1982;

⁵⁶The *Diet and Health* report considered the Judd et. al., 1979 study and still concluded that whole grain foods reduce CHD risk. Similarly, the Gramenzi, et.al.1990 study has not changed perceptions of the overwhelming evidence that whole grain foods reduce CHD risk.

Anderson and Ward, 1979; Morris, et. al., 1977; Knox, 1977).⁵⁷

The studies on the effects of whole grain foods and cereal fiber on CHD indicate:

(1) Strong prospective epidemiological evidence supporting the association between whole grain foods intake and reduced risk for CHD. De novo analyses conducted in the large prospective Iowa Women's Health Study (Jacobs, 1998), and a Finnish study of rye food intake, suggest whole grain food intake reduced risk for CHD by about 25-30 percent (Pietinen, et. al., 1996). Another prospective study of Seventh Day Adventists (Fraser, et. al., 1992) reported reduced CHD risk in those who preferred whole grain bread to white bread. A large prospective study, Rimm et. al. (1996) examined the association between whole grain cereal fiber intake and risk for myocardial infarction ("MI"). Cereal fiber was associated with reduced risk for MI with 29% decrease in risk for each 10 grams increase in cereal fiber intake.

(2) Strong clinical evidence indicating that whole grain foods modify risk factors for CHD. Numerous randomized clinical studies have demonstrated that whole grain oats reduce total blood cholesterol (Johnston, et. al., 1998; Van Horn, et. al., 1991; Reynolds, et. al., 1989; Van Horn, et. al., 1988; Van Horn, et. al., 1986). Another study by Fraser et. al. (1981) found a reduction of 9 mg/dl in serum cholesterol using a diet containing whole wheat (40 g/day), popcorn and cornmeal plus germ (30 g/day), and oatmeal (30 g/day).

Several studies demonstrate an association between cereal fiber intake and reduced risk for diabetes--a major risk factor for CHD. (Salmeron, et. al., 1997; Salmeron, et. al., 1997). This research further suggests whole grain foods should be consumed, rather than consuming grains lower in known and unknown protective components. In the dietary clinical trial DASH (Appel, et. al., 1997), whole grain foods administered as part of a total diet elicited a blood pressure reduction of both systolic and diastolic pressures by 5.5/3.0 mm Hg. Although total grain intake did not differ

⁵⁷See note 55.

between treatment groups, whole grain foods were increased in the DASH dietary pattern (Sacks, et. al., 1995) as well as fruits, vegetables and low fat dairy products.

(3) One clinical study has directly assessed the effect of whole grain food intake on risk for CHD. The randomized clinical trial, DART, linked the effect of whole-grain intake to a clinical outcome (Burr, et. al., 1989; Burr, et. al., 1989). While DART results are not definitive in ascribing health benefits to whole grain foods intake alone, the results are supportive of the notion that whole grain foods intake together with other healthful dietary practices (which is the context of the authoritative statement claim proposed) may be beneficial. Based on clinical, prospective, and experimental studies, the weight of evidence indicates whole grain foods consumption reduces risk for CHD.

C. Potential Whole Grain Food Mechanisms

The exact mechanisms for whole grain food action are not known. The physiological and nutrient roles of the whole grain food constituents have not been defined, but it is likely that at least some of the constituents act synergistically when consumed by humans.⁵⁸ In fact, it is considered advantageous to consume the nutrients and non-nutrients found in whole grains in the native whole grain form, as many potentially important whole grain components are not present in refined grains.⁵⁹ Numerous epidemiological, clinical and experimental studies support a role for individual components of whole grain foods in reducing risk for chronic diseases such as cancer and CHD.⁶⁰

For example, poorly-absorbed carbohydrates present in whole grains such as resistant starch are fermented in the gut to short chain fatty acids, which have been shown to lower serum cholesterol and which may protect against colon cancer.⁶¹

⁵⁸ Potter, *supra* note 54

⁵⁹ Jacobs, *supra* note 2.

⁶⁰ Slavin, et. al., 1997; Thompson, L. U. "Antioxidants and Hormone-Mediated Benefits of Whole Grains " *Critical Review of Food and Science Nutrition*, 1994; 34: 473-497.

⁶¹ Stephen, A., "Whole Grains--Impact of Consuming Whole Grains on Physiological Effects of Dietary

Whole grain components may provide a protective effect by binding carcinogenic compounds and blocking DNA damage.⁶² Whole grains also are rich sources of antioxidants that can delay the onset or slow down the rate of oxidation in biological systems, and thus may reduce cancer risk.⁶³

Whole grains contain nonnutrients which previously were thought to have only negative consequences. More recently, protease inhibitors, phytic acid, phenolics and saponins, all classified as nonnutrients and present in whole grains, have been found to reduce risk of cancer of the colon and breast in animal models. Phytic acid, phenolics, amylase inhibitors and saponins have been found to lower plasma glucose, insulin and/or plasma cholesterol and triglycerides.⁶⁴ Plant sterols in whole grains such as beta sitosterol may lower cholesterol in humans,⁶⁵ and tumor incidence in rats.⁶⁶

Two recent studies emphasize that the protective effects of whole grains may reflect in part unknown or unmeasured dietary constituents in whole grain foods (Slattery, et. al., 1997; Witte, et. al., 1996). After controlling for several nutrients and other constituents abundant in whole grains, these studies found that whole grain food intake remained protective against polyps and colon cancer in men. These findings

Fiber and Starch," in Clydesdale, F.M. ed. *Critical Reviews in Food Science and Nutrition* 1994; 34:499-511; McIntyre, A., Gibson, P.R., and G.P. Young, "Butyrate Production From Dietary Fibre and Protection Against Large Bowel Cancer in a Rat Model." *Gut*, 1993; 34:386-391; Cummings, J., Bingham S., Heaton, K., Eastwood, M. "Fecal Weight, Colon Cancer Risk and Dietary Intake of Nonstarch Polysaccharide (Dietary Fiber). *Gastroenterology*, 1992; 103:1783-1787.

⁶² Wattenberg, L.W., "Chemoprevention of Cancer By Naturally Occurring and Synthetic Compounds." *Proceedings of the American Association of Cancer Research*, 1990; 32:461-463; Wattenberg, L. W., "Chemoprevention of Cancer." *Cancer Research*, 1985; 45:1-8.

⁶³ Thompson, *supra* note 60.

⁶⁴ Onyeneho, S.N., and N. S. Hettiarachchy, "Antioxidant Activity of Durum Wheat Bran." *Journal of Agricultural Food Chemistry*, 1992; 40:1496-1500; Steinmetz, K.A., and J.D. Potter, "Vegetables, Fruit, and Cancer. II. Mechanisms." *Cancer Causes and Control*, 1991; 2:427-442.

⁶⁵ Jones, P.J., MacDougall, D.E., Ntanos, F., and C.A. Vanstone, "Dietary Phytosterols as Cholesterol-Lowering Agents in Humans." *Canadian Journal of Physiology & Pharmacology*, 75:217-27, 1997; Heinemann, T., Leiss, O., and K. von Bergmann, "Effect of Low-Dose Sitostanol on Serum Cholesterol in Patients with Hypercholesterolemia." *Atherosclerosis*. 1986; 61:219-223; Mattson, F.H., Grundy, S.M., and J.R. Crouse, "Optimizing the Effect of Plant Sterols on Cholesterol Absorption in Man." *American Journal of Clinical Nutrition*, 1982; 35:697-700.

⁶⁶ Raicht, R.F., Cohen, B.J., Sarwal, A.N., Fazzini, E.P., Takahashi, M., "Protective Effect of Plant Sterols Against Chemically Induced Colon Tumors in Rats", *Cancer Research*, 1980; 40:403-405.

suggest that any protective effect of whole grains on cancer does not simply reflect dietary fiber or commonly measured antioxidants in foods.⁶⁷ Unknown constituents of whole grain foods may be protective, and constituents may act synergistically (Slavin, et. al., 1997; Jacobs, et. al., 1995; Jacobs et. al., 1998).

D. Scientific Conclusion

Based on epidemiological studies and known biologically plausible mechanisms identified in feeding and physiological studies, the scientific evidence shows that whole grain foods intake provides a health benefit in terms of reduced rates of CHD and several forms of cancers. Taken as a whole, the epidemiologic and constituent studies are consistent in finding that people who eat more whole grain foods have a reduced risk of CHD and cancer compared to people who eat less whole grain foods. Thus, there is significant scientific agreement that diets rich in whole grain foods are associated with a decreased risk of CHD and some types of cancer. Given the current scientific hypothesis that plant food diets involve components of whole grain foods, legumes, fruits, and vegetables that may work synergistically,⁶⁸ it would be prudent for Americans to eat more whole grain foods.

VII. Consistency with Currently Authorized Health Claims

FDA has taken the view that if the agency has already approved a health claim for a nutrient/disease relationship, then a prospective authoritative statement claim must not conflict with the previous claim.⁶⁹ In a recent authoritative statement health claim notification, FDA found that a proposed claim about calcium increasing bone density to prevent fractures was not consistent with an already existing claim because the

⁶⁷ Potter, *supra* note 54.

⁶⁸ Jacobs, et. al., 1998; Slavin, et. al., 1997; Potter, *supra* note 54, Kune, et. al., 1987; Reddy, et. al., 1986.

⁶⁹ 63 Fed. Reg. 34084 (June 22, 1998).

proposed claim mischaracterized the mechanism by which calcium consumption reduces the risk of osteoporosis.⁷⁰ Unlike that claim however, the whole grain foods claim is consistent with, and complements, existing claims. The whole grain foods claim is consistent with already-approved claims about (1) dietary lipids and cancer;⁷¹ (2) saturated fat and cholesterol and risk of CHD;⁷² (3) fiber-containing grain products, fruits, and vegetables and cancer;⁷³ (4) fruits, vegetables, and grain products that contain fiber, particularly soluble fiber, and risk of CHD;⁷⁴ (5) fruits and vegetables and cancer;⁷⁵ and (6) soluble fiber from whole oats and risk of CHD.⁷⁶

First, the whole grain foods claim complements both the dietary lipids/cancer claim and the saturated fat and cholesterol/CHD claim. Whole grain foods are low in both fat and cholesterol, and thus, the whole grain foods claim is consistent with the fat and cholesterol claims. The fat and cholesterol claims however, do not specify qualifying foods in the model claims. The whole grain foods claim complements the fat and cholesterol claims because it specifies whole grain foods as desirable foods, and thus educates consumers about a food type they should seek and recognize in order to make healthy food choices. Furthermore, the whole grain foods claim effectively combines two diseases, cancer and CHD, so consumers focus their attention on the importance of whole grain foods, rather than get confused by two different claims each specifically referring to whole grain foods.

The whole grain foods claim is consistent with and complements the fruits and vegetables/cancer claim. Experts have consistently cited diets rich in fruits and vegetables and whole grains as beneficial in preventing cancer. The existing fruits and vegetables claim separates fruits and vegetables specifically from the

⁷⁰*Id.*

⁷¹21 C.F.R. §101.73.

⁷²21 C.F.R. § 101.75.

⁷³21 C.F.R. § 101.76.

⁷⁴21 C.F.R. § 101.77.

⁷⁵21 C.F.R. § 101.78.

⁷⁶21 C.F.R. § 101.81.

fruits/vegetables/grains claim, focusing consumer attention solely on fruits and vegetables and making clear that consumers should choose fruits and vegetables. Thus, the whole grain foods claim will impress upon consumers that whole grains themselves are an important component of the diet and that consumption of fruits and vegetables alone does not eliminate the need to consume whole grain foods.

The whole grain foods claim is also consistent with, and complementary of, the fiber-containing grain products, fruits, and vegetables/cancer claim and the fruits, vegetables, and grains containing fiber/CHD claim. The existing claims reference grains generally, but do not reference whole grains specifically. The whole grain foods claim emphasizes the importance of whole grain foods, because whole grains confer special benefits beyond those conferred by all grains. Authoritative bodies recognize the need for whole grain foods specifically, and recommend that whole grain foods comprise a portion of the recommended grain foods consumed each day.⁷⁷

The whole grain foods claim will allow consumers to focus on the benefits of whole grain foods in the diet. A consumer study conducted by General Mills showed the benefits of the proposed claim in increasing consumer awareness of whole grain foods.⁷⁸ Consumers viewed either one of the already-existing "fruits, vegetables, and grain products" claims, or a claim referencing "whole grain cereals and other plant foods." Consumers were then asked for unaided recall of the message conveyed. More than twice as many consumers mentioned "whole grains" as unaided recall from the "whole grain cereals and other plant foods" claim than from the other two claims. Clearly, the proposed claim would draw more consumer attention to the benefit of whole grain foods than that drawn by already-existing claims.

The whole grain foods claim complements the fiber-containing food health claims and the above soluble fiber from whole oats claim,⁷⁹ because it incorporates whole grain

⁷⁷ See, e.g., NUTRITION AND YOUR HEALTH, *supra* note 1, at 25.

⁷⁸ See Attachment 6.

⁷⁹ 21 C.F.R. § 101.81.

foods rather than grain products containing fiber. "Whole grain foods" is not only broader than "fiber", but has different connotations from fiber. "Whole grain foods" will likely appeal to more consumers than the term fiber. Consumers associate fiber with bran, unfavorable taste, and laxation. Thus, consumers might not choose to consume fiber for fear of unfavorable effects, and might recognize a need for fiber only if they suffer from gastrointestinal ailments. However, by using the broader term "whole grain foods", consumers will recognize a type of food that provides substantial health benefits to the general population beyond fiber.

Although fiber is one component of whole grain foods that may contribute to reducing the risk of CHD and some cancers, the effects of whole grain foods on these diseases do not likely result from the fiber content alone.⁸⁰ FDA itself has stated that fiber is not the only component of whole grains that affects serum lipids and thus, CHD ("β-glucan soluble fiber is the primary, but not the only, component in whole oats that affects serum lipids").⁸¹ Furthermore, FDA denied a dietary fiber/cancer health claim because FDA recognized that scientific evidence does not indicate conclusively that fiber itself reduces cancer risks.⁸² However, FDA permits claims for certain foods containing fiber because FDA acknowledges that a low fat diet rich in these foods reduces cancer risks.⁸³

Like with fiber-containing foods, scientists do not know the exact mechanisms of

⁸⁰NATIONAL RESEARCH COUNCIL, NATIONAL ACADEMY OF SCIENCES, CARCINOGENS AND ANTICARCINOGENS IN THE HUMAN DIET, 1993, at 83 (stating that the beneficial effects of whole grains may be due to lignan precursors and other phytoestrogens); UNITED STATES DEPARTMENT OF AGRICULTURE AND UNITED STATES DEPARTMENT OF HEALTH AND HUMAN SERVICES, EATING RIGHT WITH THE DIETARY GUIDELINES, 1992 (stating that "some of the benefit from a high fiber diet may be from the food that provides the fiber, not from the fiber alone"); COMMITTEE ON DIET AND HEALTH, FOOD NUTRITION BOARD, COMMISSION ON LIFE SCIENCES, NATIONAL RESEARCH COUNCIL, NATIONAL ACADEMY OF SCIENCES, DIET AND HEALTH: IMPLICATIONS FOR REDUCING CHRONIC DISEASE RISK, National Academy Press, Washington D.C., 1989, at 8 (stating that certain diets, including those rich in whole-grain cereals, lowering the occurrence of heart disease and certain cancers may be explained by the high levels of complex carbohydrates, vitamins, minerals, trace elements, and nonnutritive constituents).

⁸¹62 Fed. Reg. 3584, 3585 (January 23, 1997).

⁸²58 Fed. Reg. 2537 (January 6, 1993).

⁸³*Id.*

the beneficial effects of whole grain foods. However, studies suggest that fiber alone does not cause the beneficial effects of whole grains on certain cancers and CHD.⁸⁴ Thus, this authoritative statement claim is both different from, and broader than, existing health claims for fiber products in that it addresses a low fat diet containing whole grain foods and other plant foods. This authoritative statement claim is not inconsistent with, and properly complements, the fiber-containing foods claims and other already-approved health claims.

VII. Conclusion

For many years, significant scientific agreement has supported the proposition that consuming a low fat diet rich in whole grain foods and other plant foods may help reduce the risk of CHD and certain cancers. The NRC, a scientific body qualified to make an authoritative statement under FDAMA, published an authoritative statement about this relationship in its *Diet and Health* report. *Diet and Health* represents a deliberative review of the scientific evidence on diet and disease relationships. Current literature shows that significant scientific agreement on this relationship continues to exist today.

Despite repeated recommendations by scientists and government bodies to consume more whole grain foods, consumption of whole grain foods remains low. The proposed authoritative statement claim for whole grain foods will raise consumer awareness of whole grain foods and their benefits. The claim will encourage consumer adherence to dietary recommendations and thus, will further important government goals and policies to enhance public health.

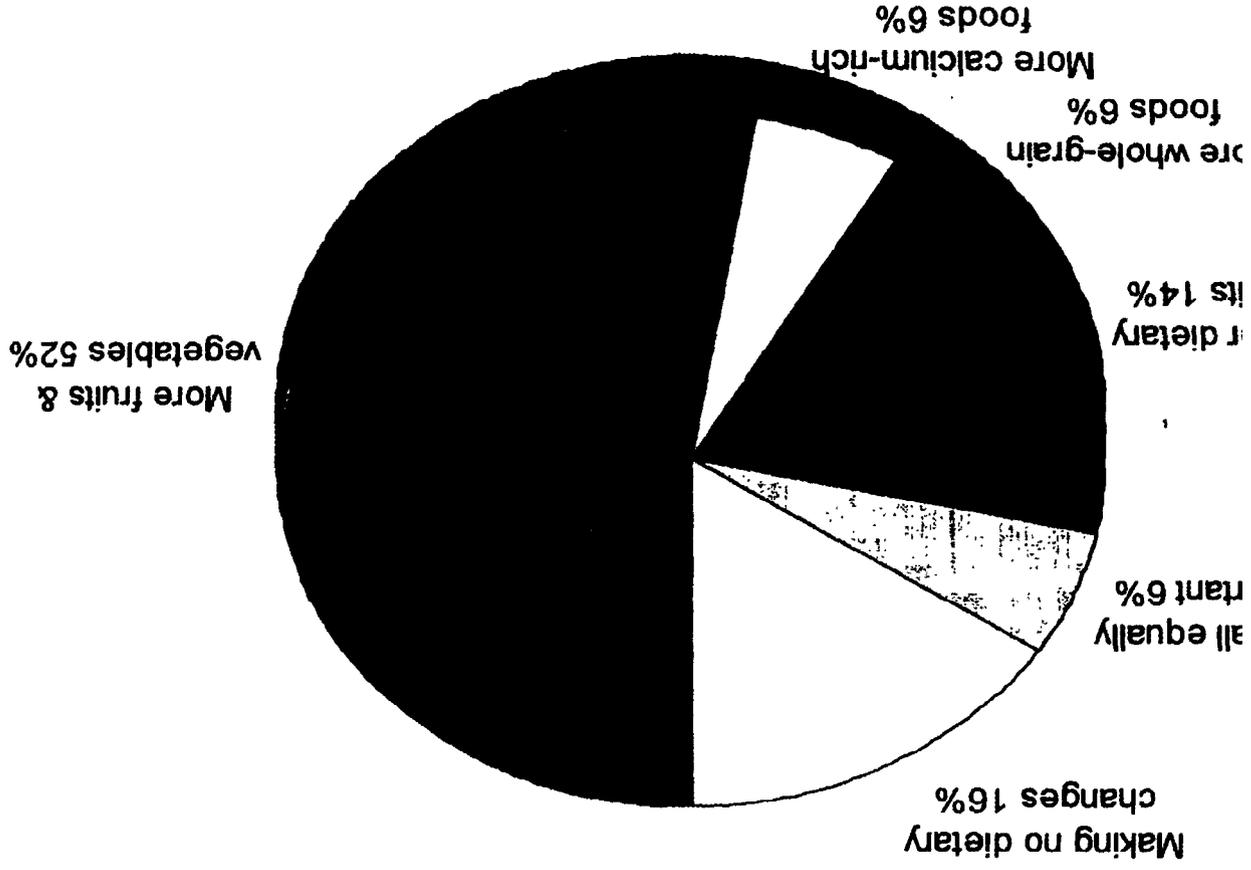
Respectfully submitted,

General Mills, Inc.

⁸⁴ See Section VI.C. above for the potential mechanisms that may contribute to the beneficial effects of whole grain foods.



bit which is most important





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Qualifying Whole Grain Products*
Cereals

Product	RACC Serving (grams)	Whole Grain (grams)	Fiber (grams)
GMI			
Wheat Chex	55	46	4.9
Crispy Wheaties & Raisins	55	35	3.8
Oatmeal Crisp with Raisins	55	33	3.3
Cheerios	30	28	2.8
Wheaties	30	27	3.4
Whole Grain Total	30	26	3.0
Oatmeal Crisp with Apple	55	21	2.9
Multigrain-Cheerios Plus	30	18	1.8
Kellogg's			
Healthy Choice Toasted Brown Sugar Squares	55	49	5.3
Raisin Squares	55	41	4.4
Frosted Mini Wheats Bite Size	55	40	4.3
Frosted Mini Wheats	55	40	4.3
Nutrigrain Almond Raisin	55	39	
Apple Cinnamon Squares	55	37	4.0
Low Fat Granola w/o Raisins	55	32	3.2
Healthy Choice Almond Crunch w/ Raisins	55	32	3.4
Nutrigrain Golden Wheat	30	30	3.2
Post			
Spoon Size Shredded Wheat	55	54	5.8
Shredded Wheat	55	54	5.8
Shredded Wheat & Bran	55	54**	5.8
Fruit & Fibre Peaches /Raisins/ Almonds	55	29**	3.1
Grape Nuts Flakes	30	26	2.8
Grape Nuts	55	41	4.4
Frosted Shredded Wheat - Bite Size	55	24	2.6
Raisin Bran	55	20**	2.2
Quaker			
Shredded Wheat	55	54	5.8
Oatmeal Squares	55	44	4.3
Oatmeal, Regular (Hot)	40	40	4.0
Toasted Oatmeal Honey Nut	55	36	3.6
Natural Low Fat Granola with Raisins	55	33	3.6
Life	30	18	1.8
Cinnamon Life	30	18	1.9
Malt-O-Meal			
Toasty-O's	30	28	2.8

*Based on USDA Food Guide Pyramid Research.

**These levels may be over estimated as they include the bran as well as whole grain.



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Qualifying Whole Grain Products*
Breads, Snacks, Grains

Product	RACC Serving (grams)	Whole Grain (grams)	Fiber (grams)
Breads, Rolls			
Whole Wheat Bread (56% WG)	50	28	3.0
Whole Wheat Pita	50	34	3.7
Whole Wheat English Muffin	55	33	3.5
Whole Wheat Bagel	55	31	3.3
Whole Wheat Roll	50	29	3.1
Whole Wheat Biscuit	55	29	3.1
Snacks / Crackers			
Whole Wheat Cracker (i.e., Triscuits)	30	27	2.9
Whole wheat blend crackers (e.g. Wheat Thins)	30	---	2.0
Tortilla Chips, baked	30	23	2.2
Popcorn, low fat (popped)	30	27	4.3
Grains (Pasta, Rice, etc.)			
Whole Wheat Tortilla	55	33	3.5
Whole Wheat Macaroni, Prepared (55gm.dry)	140	32	3.4
Whole Wheat Spaghetti, Prepared (55gm.dry)	140	32	3.4
Whole Wheat Noodles, Prepared (55gm.dry)	140	28	3.0
Wild Rice, Prepared (45gm.dry)	140	34	2.5
Brown Rice, Prepared (45 gm. dry)	140	24	2.0-2.5
Bulgur, Prepared (45gm.dry)	140	33	>3.0

*Based on USDA Food Guide Pyramid Research.



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In-Store Concept Test

Marketing Roundtables Inc. Minneapolis, MN December 1998

Methodology

A concept test was conducted among consumers in Minneapolis grocery stores. They were each presented one of three concepts (**code 10, code 20, or code 30**). The concept was removed, and they were asked to describe in their own words what was the main or most important message the statement was telling them.

The following claims each appeared on a board picturing four cereal boxes:

Code 10 (FDA) – “Diets high in fiber-containing grain products, fruits and vegetables, and low in fat may reduce the risk of some cancers, a disease associated with many factors.”

Code 20 (FDA) – “Diets rich in fiber-containing grain products, fruits and vegetables and low in saturated fat and cholesterol may reduce the risk of heart disease, a disease associated with many factors.”

Code 30 (Authoritative) – “Diets rich in whole grain cereals and other plant foods may reduce the risk of coronary heart disease and certain cancers.”

Code 10 and Code 20 are current FDA-approved claims. **Code 30** represents the authoritative statement from the NAS Diet and Health Report (NAS, 1989).

Results

The table below sets forth the percentages of consumers mentioning whole grain as part of their message recall.

Conclusion

The proposed claim (NAS, 1989), **code 30**, succeeded in more than doubling consumer recall of whole grain as part of the message.

PATTON BOGGS LLP
ATTORNEYS AT LAW

July 6, 1999

Susan M. Pape
(202) 457-5240
spape@pattonboggs.com

VIA FACSIMILE AND REGULAR MAIL

Ms. Christine Lewis (IFS-451)
Deputy Director
Office of Special Nutritionals
Center for Food Safety and Applied Nutrition
Food and Drug Administration
200 C Street, S.W.
Washington, DC 20204

Re: *General Mills, Inc.; Whole Grain Foods Authoritative Statement Claim Notification*

Dear Ms. Lewis:

On behalf of General Mills, Inc. ("General Mills"), I make the following supplements to the "Whole Grain Foods Authoritative Statement Claim Notification," submitted by Patton Boggs LLP, on behalf of General Mills, on March 10, 1999. These amendments are made without prejudicing the 120-day notification period set forth in section 303 of the Food and Drug Administration Modernization Act of 1997 ("FDAMA").¹

I. Difference from Existing Claims

The notification is amended to include the following statement on page 27, immediately following the last paragraph of section VII, "Consistency with Currently Authorized Health Claims," and preceding section VIII, "Conclusion":

"The whole grain foods claim is not equivalent to any authorized health claims, including those for fiber. The whole grain foods claim refers to 'diets rich in whole grain foods and other plant foods,' as opposed to fiber-containing foods. Rather than fiber being a food component referred to in the claim as necessary for the beneficial relationship, the whole

¹ Pub. L. No. 105-115 (November, 21, 1997).

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PATTON BOGGS LLP
ATTORNEYS AT LAW

Ms. Christine Lewis
July 6, 1999
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grain claim recognizes the explicit wording, and intended meaning, of the authoritative statement: whole grain foods themselves have a beneficial effect that cannot be attributed to fiber, or any other single component of the foods. Furthermore, because diets that satisfy the whole grain claim, do not necessarily satisfy the fiber claims, and vice versa, the claims are clearly mutually exclusive. Thus, the proposed whole grain foods claim satisfies FDAMA's requirements because it is appropriately based on an authoritative statement, and is not equivalent to an already-authorized health claim."

2. Model Claim

The model claim set forth on page 10 of the notification is amended to read:

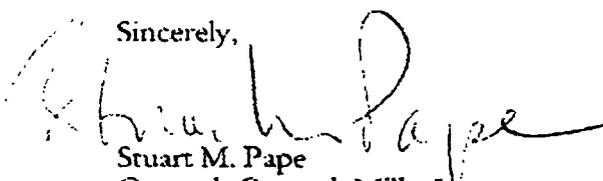
Diets rich in whole grain foods and other plant foods and low in total fat, saturated fat, and cholesterol, may help reduce the risk of heart disease and certain cancers.²

The amended model claim includes the concept that a diet should be low in saturated fat and cholesterol (as well as low in total fat and rich in whole grain foods and other plant foods) in order to have the potentially beneficial effects on heart disease risk.

3. Confidentiality

General Mills does not object to the Food and Drug Administration making public the March 10, 1999, notification, and this letter, on July 8, 1999, the day the 120-day notification period set forth in FDAMA expires and the claim takes effect.

Sincerely,


Stuart M. Pape
Counsel, General Mills, Inc.

SMP/Sro449573

²The claim would not need to refer to "saturated fat and cholesterol" if the disease endpoint in the claim were only "certain cancers."

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); fourth, foods would contain less than 6.5 grams of total fat and 0.5 grams or less trans fat per RACC (following standard rounding rules); and fifth, foods would meet all general requirements for health claims in 21 CFR § 101.14. 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 health claim, thereby facilitating a total fat intake that is consistent with dietary guidelines. Specifically, the less than 6.5 grams per RACC criterion will ensure that increased consumption of whole grain foods prompted by the health claim will not result in excessive intakes of total fat.⁵ Moreover, Kraft anticipates that the physical nature of whole grain products, together with the proposed saturated fat limitation, will act as significant practical restraints on the fat levels of foods bearing the claim.

With regard to trans fat, Kraft is limiting those foods that will bear the claim to those that contain 0.5 grams or less of trans fat per RACC. This criterion reflects FDA’s recent recognition of a link between trans fat consumption and increased serum low density lipoprotein cholesterol levels, a risk factor for CHD. See, e.g., Final Rules; Trans Fatty Acids in Nutrition Labeling, Nutrient Content Claims, and Health Claims, 68 Fed. Reg. 41434 (July 11, 2003).

⁵ In this regard, Kraft notes that the restriction on total fat content to less than 6.5 grams per RACC is intended as a quantitative reflection of the amount of fat on an individual food basis that is consistent with moderate intakes of total fat in the overall diet. The 6.5 gram criterion is not, and should not be interpreted as, a judgment by Kraft that fat levels of 6.5 grams or higher in an individual food are inconsistent with healthy dietary practices.

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 – 6.0	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 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.

C. Trans fat criterion and labeling

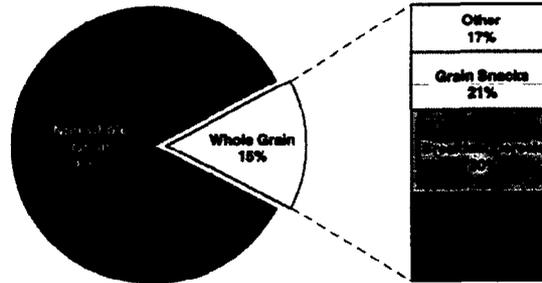
As noted earlier, foods that bear the claim will be restricted to 0.5 grams or less trans fat per RACC and will bear labeling in the manner required by the final rule published in the July 11, 2003 *Federal Register* (68 Fed. Reg. 41434 (amending 21 C.F.R. § 101.9)). The required information concerning 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. These criteria will limit the trans fat content of foods bearing the claim and will effectively mandate early compliance with the final trans fat labeling rule for those foods, thereby ensuring 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 provides 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 3).

Table 3
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 et al (1982) Kushi et al (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 et al (2000) Michels et al (2002)	4	Liu <i>et.al.</i> (1982) Kromhout <i>et.al.</i> (1984) Rimm <i>et.al.</i> (1996) Pietinen et al (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 3 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 results.⁶ 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 there is no compelling evidence to show that it does.

⁶ 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 4

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, “[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.” (*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.⁷ These shifts are reflected in current nutrition science, nutrition public policy, and regulatory precedent.

⁷ 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.”⁸

⁸ 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.

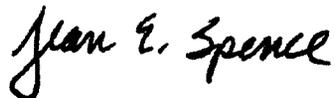
IX. SUMMARY AND CONCLUSIONS

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,



Jean E. Spence
Senior Vice President
Research and Development
Kraft Foods North America, Inc.

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