TABLE 3.—DIETARY FIBER AND COLORECTAL CANCER: COHORT STUDIES

Study	Type and location	Subjects	Methods	Results	Comments
Heilbrun et al., 1989 (Ref. 13).	Cohort study, records reviewed retrospectively. Hawaiian Japanese.	Subjects chosen from a group of 8,006 Hawaiian Japanese. 102 colon cancer cases; 60 rectal cancer cases.	Subjects followed for cancer occurrence for 17-20 yrs. Subjects consumed usual diet. Fiber calculated from a single 24 hr. recall taken upon entry into study in 1965-1968. Range of calculated dietary fiber intake was 1.3-43.2 g/day. Method of calculating dietary fiber not clear from text.	No effect of dietary fiber on relative risk of colon cancer in entire cohort. When group was divided in half (based on median fat intake) fiber conferred a significant protective effect only in the "low fat" half of the cohort. Vegetables/fruits also showed protective effect.	Authors consider results "preliminary" because limited #'s of cases precluded definitive analysis of fat effect. As in many other DF studies, fruits and vegetables also showed a protective effect. Only one 24 hour dietary recall (15 years before end of study) interview used to assess fiber intake. This may not accurately assess habitual diet.
Willet et al., 1990 (Ref 49).	Prospective cohort	88,751 subjects (female nurses, 30-55 years old) available for follow up; 150 cases of adenocarcinoma of colon.	Study of the relationships between intakes of meat, fat, and fiber and colon cancer. Follow up since 1976. Dietary questionnaire used to estimate fiber from usual diets. Used crude dietary fiber or Southgate tables.	No evidence for protective effect of crude dietary fiber on colon cancer. High intake of crude fruit fiber, but not vegetable or cereal fiber, was protective. However, adjusted for red meat consumption, the effect disappeared.	

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21 CFR PART 101

[Docket No. 91N-0099]

RIN 0905-AB67

Food Labeling: Health Claims; Dietary Fiber and Cardiovascular Disease

AGENCY: Food and Drug Administration, HHS.

ACTION: Proposed rule.

SUMMARY: The Food and Drug Administration (FDA) is announcing that after review of the available evidence, it tentatively finds that a basis does not exist on which to authorize the use on foods, including dietary supplements, of health claims relating to the association between dietary fiber and cardiovascular disease. While an association appears to exist between consumption of fiber-rich foods and reduced risk of cardiovascular disease, FDA tentatively finds that it cannot attribute this effect to the fiber itself. Therefore, FDA specifically requests comments on this topic. FDA has reviewed the relationship between this dietary component and this disease under the provisions of the Nutrition Labeling and Education Act of 1990 (the 1990 amendments).

DATES: Written comments by February 25, 1992. The agency is proposing that any final rule that may issue based upon this proposal become effective 6 months following its publication in accordance with requirements of the 1990 amendments.

ADDRESSES: Written comments to the Dockets Management Branch (HFA-305), Food and Drug Administration, rm 1-23, 12420 Parklawn Dr., Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: Joyce J. Saltsman, Center for Food Safety and Applied Nutrition (HFF-265), Food and Drug Administration, 200 C St. SW., Washington, DC 20204, 202-485-0316.

I. Background

A. The Nutrition Labeling and Education Act of 1990

On November 8, 1990, the President signed into law the 1990 amendments (Pub. L. 101-535), which amended the Federal Food, Drug, and Cosmetic Act (the act). The 1990 amendments, in part, authorize the Secretary of Health and Human Services (the Secretary) to issue regulations authorizing nutrient content and health claims on the label or labeling of foods. With respect to health claims, the new provisions provide that a product is misbranded if it bears a claim that characterizes the relationship of a nutrient to a disease or health-related condition, unless the claim is made in accordance with the procedures and standards established under section 403(r)(1)(B) of the act (21 U.S.C. 343(r)(1)(B)).

Published elsewhere in this **Federal Register** is a proposed rule to establish general requirements for health claims that characterize the relationship of nutrients, including vitamins and minerals, herbs, or other nutritional substances (referred to generally as "substance" to a disease or health related condition on food labels and in labeling. In this companion document, FDA has tentatively determined that such claims would only be justified for substances in dietary supplements, as well as in conventional foods, if the agency determines, based on the totality of the publicly available scientific evidence (including evidence from well-designed studies conducted in a manner which is consistent with generally recognized scientific procedures and principles), that there is significant scientific agreement, among experts qualified by scientific training and experience to evaluate such claims, that the claim is supported by such evidence.

The 1990 amendments also require (section 3(b)(1)(A)(ii), (b)(1)(A)(vi), and (b)(1)(A)(x)) that within 12 months of their enactment, the Secretary shall issue proposed regulations to implement section 403(r) of the act (21 U.S.C. 343), and that such regulations shall determine, among other things, whether claims respecting 10 topic areas, including dietary fiber and cardiovascular disease, meet the requirements of the act.

In this document, the agency will consider whether a claim on food or food products, including dietary supplements as well as conventional foods, on the relationship between dietary fiber and cardiovascular disease would be justified under the standard proposed in the companion document entitled "Food Labeling: General Requirements for Health Claims for Food: Proposed Rule."

B. Basis for Considering a Claim Relating Dietary Fiber and Cardiovascular Disease

1. Cardiovascular Disease

Cardiovascular disease is a major public health problem in the United States. Coronary heart disease (CHD) is the most common, most frequently reported, and most serious form of cardiovascular disease. CHD and stroke kill nearly as many Americans as all other diseases combined. Cardiovascular disease, primarily CHD is also among the leading causes of disability. These facts remain true despite the dramatic decline over the past 15 years in the death rate from cardiovascular disease: 35 percent for all cardiovascular disease, 40 percent for CHD, and more than 50 percent for stroke (Ref. 64). Changes in lifestyles, risk factor reduction, and medical intervention are major contributors to this decline (Ref. 64).

In order to be consistent with the magnitude of the public health problem and with the conclusions of the Federal government and other reports from recognized scientific bodies such as the National Academy of Sciences (NAS) and the Life Sciences Research Office (LSRO) (Refs. 40, 48, 63, 65, and 66), the focus of this document is CHD rather than the broader area of cardiovascular disease. CHD is not only considered to be the most common and most serious, but is also the earliest form of cardiovascular disease, frequently producing symptoms and health problems in middle-aged adults (Ref. 48). Despite a declining death rate from CHD since the mid 1960's, CHD still accounts for more deaths than any other disease or groups of diseases (Ref. 63). More than 1.25 million heart attacks occur each year (two-thirds occur in men), and more than 500,000 people die as a result (Ref. 63). In the United States, it is very common for significant pathogenesis of CHD to occur without easily detectable symptoms (Ref. 66). Thus, the total affected population is considerably larger than the statistics on death and illness would indicate. In addition to its impact on the nation's health, CHD costs the U.S. economy over $50 billion annually (Ref. 63).

2. Dietary Fiber

Dietary fibers are comprised of components of plant materials that are resistent to human digestive enzymes (Refs. 39 and 46). These components are predominantly nonstarch polysaccharides and lignin and may include, in addition, associated substances (Ref. 46). To date, the best documented and most accepted nutritional role for dietary fibers is for normal bowel function and health (Refs. 39, 49, and Canadian comments: FDA Docket No. 91N-0099). It is generally assumed that current fiber intakes in the United States of 10 to 15 grams (g) per day (6 to 7 g per 1,000 kilocalories (kcal) are less than optimal for meeting these needs (Refs. 36 and 39). Significant increases in this level of intake have been recommended frequently (Ref. 39).

Based on currently available analytical methods, dietary fiber is frequently measured as total dietary fiber and as the subcomponents of soluble and insoluble fibers (Ref. 39). Until recently, epidemiologic and other studies were not able to evaluate total dietary fiber intake because the majority of food composition tables contained no values for total dietary fiber content of foods. In addition, no standardized definitions of dietary fiber or dietary fiber components have been agreed upon.

Naturally occurring fibers in food are usually a mixture of the insoluble fibers such as cellulose and lignin; soluble fibers such as pectins, gums, and mucilages; and combinations of soluble and insoluble fibers such as hemicelluloses (Ref. 40). The proportions and types of fiber subcomponents vary among foods (e.g., oatmeal contains relatively large amounts of soluble fiber, and whole wheat bread contains relatively large amounts of insoluble fiber), and fiber content also varies within a food item or food group depending on the maturity of the plant, storage and ripening conditions, and food processing techniques used, if any.

In evaluating the biological effects and health consequences of dietary fiber intake, dietary fiber intake has been expressed as:

(a) Total dietary fiber or as the major fiber subcomponents (soluble and insoluble fibers);

(b) Fiber-containing foods (e.g., whole grains, legumes, fruits, vegetables);

(c) Fiber-rich food isolates (e.g., wheat bran, oat bran, corn bran, soy isolates); or

(d) Isolated and purified fibers (e.g., cellulose, pectins, lignin).

3. Relationship of Dietary Fiber and Cardiovascular Disease: Theoretical Basis

Many risk factors contribute to the development of cardiovascular disease, and specifically to CHD. There is general agreement that elevated blood cholesterol levels are one of the major "modifiable" risk factors in the development of CHD (Refs. 63 through 66). Federal government and other review (Refs. 48 and 63 through 66) have concluded that there was substantial epidemiologic and clinical evidence to indicate that high blood levels of total cholesterol and low density lipoprotein cholesterol (LDL-cholesterol) are reliable indicators of the development, severity, and rates of atherosclerosis (inadequate circulation of blood to the heart due to narrowing of the arteries) and constitute a major contributor to CHD (Refs. 48 and 63 through 66). Factors that decrease total blood cholesterol and LDL-cholesterol also tend to decrease the risk of CHD. Thus, it is generally accepted that total blood cholesterol and LDL-cholesterol levels can predict the risk of developing CHD, and that dietary factors affecting blood cholesterol levels are related to CHD (Refs. 48 and 63 through 66).

Populations with relatively low serum cholesterol levels tend to have dietary patterns that are low in fat, especially saturated fat and cholesterol, and that are relatively high in fiber-rich foods (e.g. fruits, vegetables, and whole grain cereals) (Refs. 48 and 63 through 66). Because of the relationship between serum cholesterol and CHD, all current dietary guidelines in the United States recommend dietary patterns that are likely to lower serum cholesterol levels: Reductions in dietary intakes of fat, saturated fat, and cholesterol and increases in intakes of vegetables, fruits, grain products, and cereal products (Refs. 48, 62, 63, and 66).

The association between dietary patterns rich in fibercontaining foods and lower levels of serum cholesterol is the theoretical basis for consideration of the appropriateness of a health claim for dietary fiber and reduced risk of developing CHD. Various beneficial health effects, including effects on lipid (fat) metabolism, have been suggested for fiber-containing foods and for dietary fiber, particularly the soluble dietary fiber component (Ref. 40). For these reasons, FDA limited its review of the relationship of dietary fiber and cardiovascular disease to dietary intake of soluble fiber effect on blood lipid levels and to risk of developing CHD. Based on conclusions from Federal government reviews, total blood and LDL-cholesterol were accepted as valid indicators of risk of developing CHD. This focus is most consistent with current dietary guidelines for the U.S. population (Refs. 48 and 62 through 66).

(The relationship of dietary fiber to cancer is addressed in a companion document published elsewhere in this issue of the **Federal Register**. The relationship of cardiovascular disease to lipids and to omega-3 fatty acids are also addressed in companion documents published elsewhere in this **Federal Register.**)

C. Dietary Fiber: Regulatory and Legislative History

1. Early Claims for use of Dietary Fiber

Health attributes for fiber-containing foods have been claimed for over 100 years. Early interest focused on the benefits of wheat bran as a promoter of regular bowel function. Health claims for wheat bran on breakfast cereal packages became popular in the early 1900's, and the importance of adding "bulk" in the diet by the addition of dietary fiber appeared in advertisements that promoted the benefits of certain fibers as aids to digestion and to help relieve constipation. Such health claims on packages were mostly unregulated until after the act deemed products that carried such claims to be drugs and, therefore, subject to requirements of drug law. As a result, the use of health claims on food products virtually stopped until recently.

In 1941, the agency published regulations that included labeling requirements for "non-digestible carbohydrates" (6 FR 5921). At that time, foods having a high fiber content were valued because, when added to foods such as bread, lower caloric density was achieved. Based on the analytical procedures available at that time, the fibrous plant components of food had to be labeled as "crude fiber."

During the late 1970's, FDA sought to revise its regulations to include as fiber other fractions of carbohydrates, in addition to crude fiber, that are not digested by human enzymes. In doing so, the agency noted that the scientific evidence linking fiber to health outcomes was limited. In the **Federal Register** of December 21, 1979 (44 FR 75991), the agency stated that "* * * the relationship of dietary fiber to health remains controversial." Current § 105.66 (21 CFR 105.66) provides for the declaration of nonnutritive substances, but there is no regulation for declaration of fiber.

2. Food Additive Status

Substances that are added to food may be categorized based on their use as generally recognized as safe (GRAS) ingredients, food additives, or substances subject to a sanction or approval granted by the FDA or the United States Department of Agriculture (USDA) prior to September 6, 1958. The use of substances may be GRAS under the general principles set forth in § 170.30 (21 CFR 170.30), listed as GRAS in part 182 (21 CFR part 182), or affirmed as GRAS in Part 184 (21 CFR part 184). FDA's listings of food additives and affirmations that the use of a substance for direct addition to food is GRAS generally include the particular food categories in which (as defined in § 170.3(n)), and the specific technical effects for which (as defined in § 170.3(o)), the substance may be used.

"Fiber" is not considered to be either a food category or a technical effect according to the above definitions, and ingredients that are added to food are therefore not regulated as "fiber." However, FDA has regulated a number of isolated or purified fibers for specific technical effects in various food categories. For example, xanthin gum is listed as a food additive for use as a stabilizer, emulsifier, thickener, suspending agent, bodying agent, or foam enhancer (§ 172.645 ((21 CFR 172.695)); methyl cellulose is listed as a multipurpose GRAS substance ((21 CFR 182.1480)); and pectins are affirmed as GRAS for use as an emulsifier, stabilizer, or thickener (§ 184.1588). Guar gum is affirmed as GRAS for specific conditions of use that include those as an emulsifier, formulation aid, firming agent, and thickener (§ 184.1339). Guar gum has not been listed for use as a source of fiber, and under some circumstances, it has been shown to cause esophageal blockage and thus to be a health hazard. These and many other gums and fiber sources have no established history of food use, or safety as fiber supplements.

3. Dietary Fiber as Subjects of Health Claims

Prompted by the use (beginning in 1984) of information on high-bran cereal packages that high fiber diets may reduce the risk of cancer and by issuance of interim dietary fiber recommendations by the National Cancer Institute, FDA proposed in the **Federal Register** of August 4, 1987 (52 FR 28843), food labeling regulations to allow the use of health messages on labels and food labeling. The agency stated that food labeling could have an important influence on the public's food choices, and that truthful, nonmisleading health messages could increase consumer's understanding of the health benefits that can result from adhering to a sound and nutritious diet. This proposal set forth criteria for the evaluation of health claims.

In the **Federal Register** of February 13, 1990 (55 FR 5176), FDA published a reproposed rule that revoked the 1987 proposal and proposed to establish procedures permitting valid and reliable consumer information on food labels. The agency noted that the previous proposal was too ambiguous to be workable in preventing misleading claims. FDA thus proposed to tighten the requirements for health claims. The agency also proposed to evaluate the scientific evidence on six possible topics for health claims, including dietary fiber and cardiovascular disease.

On November 8, 1990, the President signed the 1990 amendments, which authorize FDA to issue regulations concerning claims on the label or labeling of foods that characterize the relationship between a substance and a disease or a health-related condition. As stated above, this law identified 10 substance-disease topics, including dietary fiber and cardiovascular disease.

D. Evidence Considered in Reaching the Decision

FDA has reviewed all relevant scientific evidence on dietary fiber and its effects on serum cholesterol. The scientific evidence reviewed by the agency included the summary, conclusions, and recommendations of all recent Federal government comprehensive reviews and dietary guidelines on this topic area: "The Surgeon General's Report on Nutrition and Health" (Ref. 63), the National Cholesterol Education Program's (NCEP) "Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults" (Ref. 65), the NCEP "Population Panel Report" (Ref. 66), the USDA and DHHS' "Nutrition and Your Health: Dietary Guidelines for Americans" (Ref. 62), and the DHHS' "Healthy People 2000, National Health Promotion and Disease Prevention Objectives" (Ref. 64).

The agency also reviewed the evidence and conclusions in other nongovernmental documents: The LSRO report on "Physiological Effects and Health Consequences of Dietary Fiber" (Ref. 39), the National Research Council's (NRC) "Diet and Health, Implications for Reducing Chronic Disease Risks" (Ref. 48), the NRC's "Recommended Dietary Allowances"

(Ref. 49), and World Health Organization's (WHO) "Diet, Nutrition, and the Prevention of Chronic Diseases" (Ref. 71).

The agency updated these reports by independently reviewing all human studies and all reviews published since the Federal government and other authoritative documents completed their reviews of the literature. FDA considered animal studies to the extent that they helped explain possible mechanisms of action. FDA also contracted with LSRO to independently evaluate current evidence since their 1987 fiber report. A summary of the LSRO report, "Dietary Fiber and Cardiovascular Disease" (Ref. 40) is included in this review.

Finally, to ensure that its review of relevant evidence was complete, FDA requested, in the **Federal Register** of March 28, 1991 (56 FR 12932), scientific data and information on the 10 specific topic areas identified in section 3(b)(1)(A) of the 1990 amendments. Dietary fiber and cardiovascular disease were among the 10 subjects for which the agency requested information.

E. Summary of Comments in Response to FDA Request for Scientific Data and Information

FDA received 1 comment in response to the February 13, 1990 reproposed final rule and 19 comments in response to the notice in the **Federal Register** of March 28, 1991 (56 FR 12932), concerning dietary fiber and CHD health claims.

One comment from a representative of industry was received in response to the reproposed final rule. Based on the findings of several authoritative documents and a review of additional references published since 1988, the comment suggested that the currently recommended low fat/low cholesterol diet could be made more effective in lowering blood cholesterol and risk of CHD by the inclusion of soluble fiber.

Of the 19 comments received in response to the March 28, 1991 notice requesting scientific data on dietary fiber and cardiovascular disease (under Docket No. 91N–0099), 13 were from industry; 4 from professional organizations; 1 from a consumer; 2 from health professionals; 2 from scientists; and 1 from the Government of Canada. The industry comments included primarily literature reviews and unpublished studies, which were included in FDA's science review of the scientific evidence. One food company did not support health claims on dietary fiber and risk of developing heart disease because of the multifactorial nature of the disease and the seriousness of the disease and suggested that medical intervention is required for proper diagnosis and monitoring of heart disease. All other industry and trade submissions supported the use of health claims.

Of the six comments from professional organizations, three submitted research reports generally supporting a health claim. Another called attention to the need for caution to avoid consumer misunderstanding. One comment pointed to the need to consider the overall diet context. Another took the position that the data on fiber and cardiovascular diseases are insufficient to support a claim.

The citizen comment included a literature search but no comment about the health claim issue.

The two comments from health professionals were divided. Although both provided data supporting their individual position, one was in favor of health claims and the other was not.

The Director General, Food Directorate, Health and Welfare, Canada, submitted information on the regulatory status of health claims in that country. The Canadian government is not in favor of health claims on fiber-containing foods because it is difficult to disassociate the metabolic effects of complex carbohydrates and the low fat content of these diets from those of dietary fiber. The comment said that this finding does not diminish the importance of diet as a factor in the maintenance of health but reinforces the importance of the whole diet rather than the contribution of individual components. Interactions between nutrients and between nutrients and nonnutrient components of the diet probably alter the likelihood of disease.

II. Review of Scientific Evidence

A. Federal Government Documents

Several Federal government documents (Refs. 62 through 64, 66, and 67) have concluded that the evidence for a role of dietary fiber in lowering the risk of cardiovascular disease, and more specifically CHD, is inconclusive.

The Surgeon General's Report (Ref. 63) comprehensively reviewed human and animal studies on CHD and blood cholesterol and noted that an extensive body of evidence supported by epidemiologic, metabolic, and animal studies has established the relationship among intake of saturated fat, high blood cholesterol, and increased rates of CHD (Ref. 63). The report also noted that based on ecological studies in several countries, dietary intakes that are high in starch (e.g., 60 to 70 percent of calories), such as those in Asian countries, are associated with low plasma cholesterol and a low rate of CHD. These diets tend to be high in fiber, lower in energy, and very low in fat, especially saturated fat and cholesterol. Several short-term clinical studies that were reviewed showed an association between water-soluble fiber fractions, such as oat bran, guar gum, and pectin, and cholesterol-lowering effects in hypercholesterolemic subjects (Refs. 7, 22, and 32). The report concluded that current evidence suggests the prudence of increasing consumption of whole grain foods and cereal products, vegetables (including dry beans and peas) and fruits (Ref. 63).

The recommendations of the NCEP (Refs. 65 and 66) are based on the goals of reducing blood cholesterol, and low density lipoprotein (LDL) cholesterol in particular, and providing a diet that is nutritious and palatable (Ref. 65). The LDL-cholesterol levels are directly correlated with risk for CHD (Ref. 65). The NCEP report concluded that changing American eating patterns will help lower blood cholesterol levels, thus reducing the risk of developing CHD. In this regard, the panel recommended lowering the intake of dietary saturated fatty acids, total fat, and cholesterol, and increasing the intake of fruits, vegetables, whole grain products, and legumes. These food items will help meet nutritional needs for minerals, vitamins, dietary fiber (including soluble fiber), and complex carbohydrates (Ref. 66).

The USDA/DHHS report "Nutrition and Your Health: Dietary Guidelines for Americans" (Ref. 62) concluded that dietary fiber is important for proper bowel function and to reduce symptoms of chronic constipation, diverticular disease, and hemorrhoids. It stated that "populations like ours with diets low in dietary fiber and complex carbohydrates and high in fat, especially saturated fat, tend to have more heart disease * * *" (Ref. 62). The dietary guidelines noted the possibility that the benefit from a diet with more fiber may be from the food or component of the food providing the fiber rather than from the fiber alone. The USDA/DHHS dietary guidelines recommended choosing a diet with plenty of vegetables, fruits, and grain products.

In "Healthy People 2000," the Public Health Service and DHHS identified increased consumption of complex carbohydrates and fiber-containing foods by adults as a specific risk reduction objective (Ref. 64). Recommendations included increasing consumption of vegetables (including legumes) and fruits to five or more servings daily, and increasing consumption of grain products to six or more daily servings. The report noted that dietary patterns with higher intakes of vegetables (including legumes), fruits, and grain products are associated with a variety of health benefits, including decreased risk for some types of cancer (Ref. 65). It was also noted that the association between diets high in complex carbohydrates (and fiber) and reduced CHD and diabetes mellitus is difficult to interpret because such diets tend to be lower in energy (calories) and fats, especially saturated fat and cholesterol. "Further research is needed to clarify whether the effect of dietary fiber on blood lipids is an independent effect, and if so, to quantify the relationship. (Ref. 64).

B. Other Review From Recognized Scientific Bodies

Several other comprehensive reviews from recognized scientific bodies on the role of nutrition and health have been published in recent years (Refs. 39, 40, 48, 49, and 71). The conclusions reached in these reports are similar to those reached in the Federal reports noted above.

In 1985, the Department of national Health and Welfare, Health Protection Branch, of the Canadian government convened an expert advisory committee to evaluate dietary fiber issues (Ref. 46). This committee noted that the relationship between the physico-chemical properties of dietary fibers and their physiological effects is difficult to evaluate partly due to the complexity of the interactions of mixed fibers in foods and in some instances, lack of uniformity in testing procedures. They recommended that manufacturers of food products to which nonnative and/or novel fibers have been added to increase dietary fiber content may be required to provide evidence substantiating the safety and efficacy of these products in terms of accepted physiological effects. Nonnative fibers were defined as fibers from traditional foods but not naturally occurring in the foods to which they have been added; novel fibers are those which have not traditionally been part of the human diet. They also recommended that manufactures of products which have been substantially enriched with native fibers should also be prepared to provide proof of efficacy on request. They noted that evidence is lacking that commercially produced products containing some of these materials will, when consumed, produce effects that the public has come to expect of fiber containing foods. They recommended more research to elucidate physiological forles of dietary fiber.

LSRO, in its 1987 report entitled "Physiological Effects and Health Consequences of Dietary Fiber" (Ref. 39), concluded that dietary fiber is an integral part of a healthy diet. However, LSRO stated that the available evidence is not sufficient to support specific, quantitative recommendations on the role of dietary fiber for the prevention of specific diseases in the general, healthy population. LSRO recommended, therefore, that a wide variety of fiber-rich foods be consumed, such as whole grain products, fruits, vegetables and legumes, because of the diversity of effects of various components of dietary fiber. The report stated that the foods eaten in the amounts suggested would provide about 20 to 35 g of dietary fiber per day (approximately 10 to 13 per 1,000 kcal) for the healthy, adult population (Ref. 39).

The 1989 NRC, NAS report, "Diet and Health—Implication for Reducing Chronic Disease Risk" (Ref. 48) reviewed epidemiologic and clinical studies and noted that increased consumption of fiber-rich foods was associated with a lower risk of developing CHD and other diseases. Diets providing 45 g of dietary fiber from fresh fruits, vegetables, and legumes (Refs. 20, 23, and 29), and with an isocaloric replacement of either sugar or bread with a mixture of vegetables providing 40 g per day of dietary fiber (Ref. 21), were associated with lower blood cholesterol levels. The NAS report concluded that although epidemiologic and clinical studies indicate that a diet consisting of complex carbohydrate and high-fiber foods may be associated with a lower risk of CHD, colon cancer, diverticulosis, hypertension, or gallstone formation, there is "no conclusive evidence that it is dietary fiber, rather than the other components of vegetables, fruits, and cereal products, that reduces the risk of those diseases" (Ref. 48). The NAS report recommended increased consumption of vegetables, fruits, breads, cereals, and legumes (Ref. 48).

The WHO report "Diet, Nutrition, and the Prevention of Chronic Diseases" (Ref. 71), stated that dietary factors are known to influence the development of a wide range of chronic diseases, including CHD. The report stated, the "affluent" type of diet that often accompanies economic development is energy (calorie)-dense. People consuming these diets characteristically have a high intake of fat (especially saturated fats) and free sugars and a relatively low intake of complex carbohydrates (from starchy, fiber-containing foods)." All of these factors influence serum cholesterol and their combined effects "may be important in modifying the rate of progression of atherosclerosis."

Based on direct experimental evidence concerning the association between dietary fiber, stool bulk, and intestinal transit time, WHO recommended a lower limit of intake of 16 grams per day of dietary fiber (nonstarch polysaccharides) and an upper limit of 24 g per day. This goal is consistent with an intake of about 27 to 40 g per day of total fiber, which includes other fiber components (Ref. 71).

The 1991 LSRO report "Dietary Fiber and Cardiovascular Disease" (Ref. 39) reviewed epidemiological studies since LSRO's 1987 report and found no new evidence to support reduced risk of CHD from an intake of dietary fiber and particularly soluble fiber. LSRO found that studies suggest that soluble fiber is hypocholesterolemic, while insoluble fiber is not. "Whether the observed effects result strictly from the fiber or from other components of the fiber-rich food or to a combination of these remains to be determined. (Ref. 39). The report also noted that it is also not known if a fiber present in a food is the same as when it has been extracted and purified.

C. Review of the Scientific Evidence: Evidence for an Association Between Intake of Soluble Dietary Fiber and Coronary Heart Disease

All of the government and other reviews by recognized scientific bodies cited above reviewed the evidence for an association between the intake of dietary fiber and CHD, one of the major cardiovascular diseases. It has been established that appropriate dietary intervention, resulting in lower serum total cholesterol, can reduce the incidence of CHD and hence the incidence of cardiovascular disease (Ref. 66; companion document on proposed rules for Health Claims: Lipids and Cardiovascular Disease). The review of studies that follows will also focus, as in the Federal government and other reviews by recognized scientific bodies, on evidence for the beneficial effects of dietary fiber, specifically soluble dietary fiber, on lowering blood total and LDL-cholesterol levels with the ultimate outcome of reduced risk of developing CHD.

The comprehensive government and other reviews by recognized scientific bodies concluded, based on evidence presented to date, that dietary patterns that included fiber-rich foods were associated with lower levels of blood cholesterol and hence lower rates of CHD. Additionally, these reports suggested that if fiber has an effect on serum cholesterol levels, it is probably related to the soluble dietary fiber component, rather than to total, or insoluble, dietary fiber. However, these reports also noted the lack of evidence that would substantiate that it is the soluble fiber component of these foods, rather than some other concomitant change in nutrient intake or weight control, that is the responsible agent for these associations. For this reason, the nutrition guidelines that have been promulgated have emphasized changes in dietary patterns rather than specifically focusing on changes in soluble fiber intakes.

The agency, therefore, concluded that to provide adequate support for a role for dietary fiber, and in particular soluble dietary fiber, in reducing the risk of CHD, the updated evidence would need to specifically show that soluble dietary fiber at some specific level in the total diet has an effect.

1. Criteria for Selection of Human Studies

The agency evaluated all human data published after 1987, the time at which the NAS report (Ref. 48) completed it's review of the scientific evidence. The criteria that the agency used to select pertinent recent studies required that the studies:

(1) Present primary data and adequate descriptions of study design and methods;

(2) Be available in English;

(3) Include estimates, or enough information to estimate, soluble dietary fiber intakes;

(4) Include direct measurement of blood total cholesterol and other blood lipids related to CHD;

(5) For intervention studies, be conducted for a long enough duration to reasonably assure stabilization of blood lipids (greater than or equal to 3 weeks duration); and

(6) Be conducted in persons who generally represent the healthy U.S. population (adults with blood total cholesterol levels less than 300 miligrams (mg) per deciliter (dl).

2. Criteria for Evaluation of Human Studies

FDA evaluated the results of studies against general criteria for good experimental design, execution, and analysis. The criteria that the agency used in evaluating these studies included reliability and accuracy of the methods used in nutrient intake analysis, including measurements of total dietary soluble fiber and total dietary fiber; measurement of study endpoints (i.e., blood total cholesterol and other blood lipids related to CHD); and general study design characteristics, including randomization of subjects, appropriateness of controls, selection criteria for subjects, attrition rates (including reasons for attrition), potential for misclassification of individuals with regard to dietary intakes, presence of recall bias and interviewer bias, recognition and control of confounding factors (for example, intake of saturated fat and other nutrients, monitoring body weight, and control of weight loss), appropriateness of statistical tests and comparisons, and statistical power of the studies.

The availability of information on the total dietary fiber and total dietary soluble fiber content of baseline, treatment and control diets; the soluble fiber content of the test substance; and nutrient intakes were deemed highly desirable. In many cases, analytical or calculated values were not given for total fiber or for total soluble fiber components of the test diet, although in some cases, it was possible to roughly estimate soluble fiber values above baseline levels from available data on the amount and type of test material added to the diet.

Several research reports were based on studies of only a few weeks duration. To ensure that results were not reflective of transient changes, such as failure of blood cholesterol levels to stabilize to the dramatic changes in dietary patterns that occur with the introduction of large amounts of test substances, studies with treatment periods of less than 3 weeks were not considered in the agency's evaluation of scientific evidence.

The agency excluded studies that were published in abstract form because they lacked sufficient detail on study design and methodologies, and because they lacked necessary primary data. Studies using special population groups, such as insulin-dependent diabetics, individuals with very high serum cholesterol (mean greater than 300 mg per dL), children with hypercholesterolemia, and persons who had already experienced a myocardial infarction were also generally not weighed heavily because the relevance of health claims for the general healthy U.S. population is the key question. (Descriptions of all available studies are, however, included in Table 1).

3. Summary of Human Studies

Responses of blood cholesterol levels to dietary treatment are affected by many factors, including initial (baseline) blood cholesterol levels and dietary factors (i.e., the level of saturated fat and cholesterol in the diet) (Refs. 48, 65, and 66). Previous reviewers have generally concluded that in persons with relatively higher baseline levels of blood cholesterol, responses to treatment protocols tend to be of larger magnitude than is seen in persons with more normal blood cholesterol levels (Refs. 48, 65, and 66). For this reason, FDA separately evaluated studies on mildly to moderately hypercholesterolemic individuals (persons with elevated blood total cholesterol levels of 200 to 300 mg per dL) and normocholesterolemic individuals (persons with normal blood total cholesterol levels, less than 200 mg per dL). Since dietary intakes of saturated fat and cholesterol may also affect blood cholesterol levels, FDA also separated its review of studies on the basis of whether fiber effects are being evaluated as part of a "typical" American diet (approximately 37 percent of calories from fat, 13 percent of calories from saturated fat, and greater than 300 mg of cholesterol daily), or whether the test protocols are incorporated into a Step I or similar (e.g., American Heart Association) dietary regimen (less than 30 percent of calories from fat, less than 10 percent of calories from saturated fat, and less than 300 mg cholesterol daily). Detailed summaries of the reviewed studies are in Table 1.

a. *Hypercholesterolemics: "typical" or "usual" diets.* In two metabolic ward studies of 3 weeks duration (Refs. 3 and 4), soluble fiber intakes of 7 to 8 g per day were associated with reductions of 8 to 12 percent in blood total cholesterol level as compared to baseline levels. In both studies, groups experienced some weight loss (approximately 2 to 3 pounds) during the study period. In one study (Ref. 4), blood total cholesterol levels were measured several times throughout the study. The lowest values were observed at an intermediate time; that is, the initial drop in blood cholesterol levels was followed by a trend towards return to baseline levels at the end of the 3-week test period.

In a randomized, controlled, intervention study where subjects were free-living, Van Horn et al. (Ref. 69) assigned 80 men and women (25 to 76 years; serum cholesterol of 213 to 285 mg per dL) to either a control group (regular diet) or a test group which consumed their regular diet plus a cereal providing 2 g of soluble fiber daily. After 4 weeks of intervention, the test group, as compared to the control group, had significantly different dietary intakes for a number of nutrients, including higher intakes of soluble and total fiber, and lower intakes of saturated fat and cholesterol. Blood total cholesterol and LDL-cholesterol levels in the test group decreased by 6 percent and 9 percent, respectively, with no change in the control group.

Kahn et al. (Ref. 25), in a randomized, controlled, intervention study added four muffins containing a total of 6 g of soluble fiber to the daily diets of 16 free-living men and women. After 3 weeks, there were no significant differences in total blood cholesterol levels between test and control groups.

Kesaniemi et al. (Ref. 27), in a randomized, self-controlled, cross-over, intervention study, monitored 34 free-living men (serum cholesterol 223 to 258 mg per dL) who consumed a low fiber diet (3 soluble fiber daily) or a high fiber diet (13 g soluble fiber) for 8 weeks. When consuming the high fiber diet, blood total and LDL-cholesterol levels decreased significantly (5 percent and 7 percent, respectively). The high fiber group consumed significantly higher levels of vegetables, cereal, fruits, and berries, compared to the low-fiber group.

Kestin et al. (Ref. 28), in a randomized, double-blind controlled, cross-over study, fed diets containing 6, 7, or 10 g of soluble fiber per day to 24 men (29 to 61 years; serum cholesterol 186 to 293 mg per dL) for 4 weeks. The sources of soluble fiber varied among test groups. Compared to baseline, subjects consuming 10 g of soluble fiber per day had a significant decline in blood total cholesterol (5 percent), with the decrease mainly in the LDL-cholesterol fraction. The other levels of soluble fiber did not cause significant lowering of serum cholesterol.

In a 12-week randomized, double-blind, cross-over intervention study with two 6-week test periods and a 3-week washout between treatments, Lo and Cole (Ref. 43) fed diets containing 13 or 24 g total dietary fiber per day to 12 men and 8 women (27 to 60; serum cholesterol of 210 to 279 mg per dL). The difference in total dietary fiber intakes between the two protocols was due to the addition of soy fiber to the test diet. (Soy is a relatively rich source of soluble dietary fiber). The effects on blood cholesterol differed depending on order of dietary treatment. If soy-enriched diets were fed first, blood total and LDL-cholesterol levels decreased by 8 percent and 7 percent, respectively, compared to baseline. A significant decline (5 percent) in the LDL-cholesterol levels of the placebo group is also observed. However, when soy-enriched diets were fed after the base diet, there was no effect on blood cholesterol levels. Thus, most changes in blood cholesterol levels occurred during the first 6 weeks of treatment, regardless of diet group.

The effect of beta-glucan, a particular type of soluble fiber, was evaluated in a randomized, cross-over, intervention study by McIntosh et al. (Ref. 44). Twenty-one men (30 to 59 years; serum cholesterol 209 to 270 mg per dL) received a diet containing either 8 or 1.5 g added beta-glucan daily for 4 weeks. Total soluble fiber intakes from the two diets were held constant at 13 g per day. Treatment order has an effect, with the group receiving the beta-glucan-enriched diet first showing no changes in serum total cholesterol, while those consuming this diet as the second dietary protocol showed a decline in blood cholesterol levels.

The effectiveness of high dietary fiber on the blood cholesterol levels of men who had already suffered heart attacks was studied by Burr et al. (Ref. 13). In a 2-year intervention study, over 2,000 men (mean age 56 years) were randomly assigned to several diet groups. One group was given advice to decrease fat intake to less than 30 percent of calories and to increase the ratio of polyunsaturated fat to saturated fat. Another group was advised to increase cereal fiber intake to 18 g per day. There were no significant differences in total mortality or in blood cholesterol levels between these groups.

Bulk laxatives (e.g., psyllium) or gums have been used in several study protocols as sources of supplemental soluble dietary fiber. Stewart et al. (Ref. 55), in an intervention study, compared blood cholesterol levels of 175 elderly (mean age 77 years) who had consumed a bulk laxative rich in soluble fiber for at least 1 month with those who had not been users of these products. The period of use of the bulk fiber supplement ranged from 1 month to 1 year. Those taking greater than 15 g of supplemental soluble fiber per day had a 4 percent lower total blood cholesterol level than those taking less than 8 g of supplemental soluble fiber per day. The use of supplemental fiber without specification as to amount versus no use of supplemental fiber was not associated with any differences in blood cholesterol levels.

In a controlled intervention study, McIvor et al. (Ref. 45) gradually increased the soluble fiber intakes of 8 obese men and women with noninsulin dependent diabetes (ages 45 to 50 years; mean serum cholesterol 222 mg per dL) by increasing consumption of granola bars enriched with a concentrated source of soluble fiber. Up to 22 g of supplemental soluble fiber were consumed per day in addition to that contained in subject's usual diets. After 6 months, serum total cholesterol levels did not differ significantly from baseline levels.

Superko et al. (Ref 56), in a randomized, single blinded, cross-over study, evaluated the relative effects of two different types of an isolated soluble fiber source on blood cholesterol levels of 50 men (39 to 63 years; serum cholesterol of 205 to 282 mg per dL). The fiber supplement added approximately 10 of soluble fiber daily to the regular diet. Although differences were observed in blood cholesterol levels after 4 weeks, at the end of 8 weeks there was no significant difference between the fiber supplement and the placebo groups.

Twenty-six men (30 to 65 years; serum cholesterol 188 to 314 mg per dL) consumed their regular diets and also consumed either a bulk laxative rich in soluble fiber or a placebo prior to each meal for 8 weeks in a randomized, parallel, double-blinded, placebo-controlled, intervention study (Ref. 8). The fiber supplement added approximately 8 to 9 g of soluble fiber to the regular dietary intake. From baseline, the group on the soluble fiber-enriched protocol had a significant decrease in blood total cholesterol (15 percent) and LDL-cholesterol (20 percent).

In summary, several studies were reviewed in which conventional foods high in soluble fiber (e.g., beans or oatmeal) or enriched with soluble fibers (baked goods with added wheat, barley, or oat brans) (Refs. 3, 4, 13, 25, 27, 28, 43, 44, and 69) were used to increase the soluble fiber intakes of subjects. The study durations ranged from 3 weeks to 8 weeks, except for one 2-year study which was of limited value since it did not provide information on soluble fiber intakes (Ref. 13). Although information on total intakes of soluble fiber was not always provided, there was enough available information to make crude estimates of intake. These estimates suggested that, under study conditions used, intakes of soluble fiber above 6 to 12 g per day were generally associated with reductions in blood total and, when measured, LDL-cholesterol levels. The potential for differences in effectiveness among different sources of dietary fiber when total intakes are similar was suggested by two studies (Refs. 27 and 28) and by the equivocal results from several isolated sources of soluble fiber (Refs. 8, 45, 55, and 56).

Several studies used isolated sources of soluble fiber (psyllium and guar gum) either under standard pharmacological conditions in bulk form with meals (Refs. 8 and 55) or incorporated into baked goods (Ref. 45) to increase soluble fiber intakes. Duration of studies ranged from 8 weeks to 1 year. Generally, much higher intakes of soluble fiber were achieved (15 or more per day) with use of supplements as compared to foods (approximately 2 to 12 g daily). One study of 6 months duration (Ref. 45) showed no effect on blood cholesterol levels, although the small sample size (n=8) may lack adequate statistical power. Another study showed rather small changes in blood cholesterol levels (4 percent) with 175 subjects consuming high (15 g or more) versus low (less than 8 g) of supplemental soluble fiber for 1 month to 1 year. Use versus nonuse of supplements showed no relationship to blood cholesterol levels. A third study showed 15 and 20 percent reductions in blood total and LDL-cholesterol after consuming 8 to 9 g of supplemental fiber for 8 weeks (Ref. 8). Finally, results of a fourth study suggested that effects may be transient (Ref. 56), with effects observed at 4 weeks disappearing by the end of 8 weeks.

b. *Hypercholesterolemics: Step 1 diets.* In several studies, the relative effectiveness of Step 1 diets (less than 30 percent calories as fats, less than 10 percent calories as satuated fat, and less than 300 mg cholesterol daily) with and without added soluble fiber were evaluated. In a metabolic ward study, Anderson et al. (Ref. 5) fed Step 1 diets containing 9 g soluble fiber per day to 10 men (40 to 70 years; serum cholesterol 200 to 320 mg per dL) for 3 weeks. The baseline diet contained 3 g soluble fiber daily. There were no significant decreases in total blood cholesterol following consumption of the high fiber diet, but LDL-cholesterol decreased significantly from baseline levels (8 percent decline).

Little et al. (Ref. 42), in a controlled intervention study, examined the effect of 4 types of dietary intervention on blood total cholesterol levels of 184 free-living men (58 to 61 years; serum cholesterol 240 to 267 mg per dL). After 8 weeks, declines in serum cholesterol were the same (approximately 5 percent) for both a low fat diet alone and for a low fat, high fiber diet (total dietary fiber of 40 to 45 g per day; no data on soluble fiber). The authors suggested that low fat rather than increased levels of dietary fiber were responsible for changes in serum cholesterol.

Demark-Wahnefried et al. (Ref. 16), in a randomized intervention study, monitored blood cholesterol levels in 81 men and women (20 to 65 years, mean baseline serum cholesterol of 271 mg per dL) consuming one of four dietary protocols for 12 weeks: Step 1 diet alone, Step 1 diet plus added soluble fiber from 50 g of oat bran, regular diet plus 50 g of oat bran, and regular diet plus 42 g of processed oat bran. Declines in serum cholesterol occurred in all groups. Blood cholesterol levels of groups consuming diets containing the higher soluble fiber (approximately 4 g added soluble fiber daily) did not differ from groups on a dietary regimen modified only in fat and cholesterol content.

Levin et al. (Ref. 37), in a randomized, double-blind, intervention study, followed 58 men and women (21 to 70 years; baseline serum cholesterol of 235 to 245 mg per dL) who consumed a Step 1 diet for 8 weeks followed by 16 weeks of treatment with a placebo or concentrated soluble fiber source. The total soluble fiber intake of the test diet was estimated at 15 g per day compared to intakes of 6 to 8 g daily on the Step 1 diet alone. The group consuming the high soluble fiber diet showed a significant decrease in total and LDL-cholesterol (6 and 9 percent, respectively) from baseline.

Several studies examined the effect of type of fiber on blood cholesterol levels. Keenan et al. (Ref. 26), in a randomized, controlled, double-blind, intervention study with cross-over, used a 6-week pretreatment period to adapt subjects to a Step 1 diet. Then, holding total soluble fiber intakes constant at approximately 6 to 7 g per day, the relative effectiveness of wheat versus oat cereals as the fiber-enriching source were compared. Effects on blood cholesterol levels varied, depending on the order of feeding of the diets supplemented with oat bran or wheat cereal. Interpretation of results was further complicated by the fact that the control group showed an initial decline in blood cholesterol levels followed by a return to baseline at the end of the study.

Bell et al. (Ref. 12), in a randomized, double-blind controlled, intervention study, compared the effects of three diets containing corn flakes (control), pectin-enriched, or psyllium-enriched cereals. Fifty-eight subjects (24 to 69 years; serum cholesterol 227 to 229 mg per dL) consumed Step 1 diet for 6 weeks followed by 6 weeks on the cereal plus Step 1 diets. Total soluble fiber intake for the three diets was relatively constant at 6 to 8 g per day. Blood total and HDL-cholesterol was decreased significantly (6 percent) on the psyllium-enriched but not the pectin-enriched diet.

Several studies evaluated the effectiveness of beta-glucan, a particular type of soluble fiber found in oat products. In a randomized, controlled, intervention study, 351 men and women (20 to 60 years, serum cholesterol 200 to 300 mg per dL) were assigned to one of three dietary regimens: regular diet, Step I diet, or Step I diet plus the addition of about 10 g total dietary fiber (7 to 8 g soluble fiber as beta-glucans) (Ref. 10). There was variable weight loss among treatment groups. No data were provided on total soluble fiber content of the diets. After 8 weeks, reductions in blood total and LDL-cholesterol (decreases of 8 and 10 percent, respectively) were greater with the Step I diet than with no dietary change. Somewhat higher reductions (decreases of 12 to 15 percent) were observed when beta-glucans were added to the Step I diet.

In a randomized, single-blind, controlled intervention study, 148 men and women (30 to 65 years; serum cholesterol 230 to 319 mg per dL) consumed Step 1 diets with either zero or 5 to 7 g of soluble fiber added by incorporation of various types of cereal products (Ref. 15). After 6 weeks, groups consuming diets containing 4 to 6 g of beta-glucan had significant declines in blood total cholesterol (7 to 10 percent) and LDL-cholesterol (10 to 16 percent) as compared to baseline. Blood total cholesterol levels of groups consuming diets containing 1 to 2.4 g daily of beta-glucan did not differ significantly from baseline.

In summary, in the 4 studies with hyperlipidemics consuming diets low in fat, saturated fat, and cholesterol, the addition of soluble fiber to the diets produced equivocal results on blood cholesterol levels, ranging from no effect (Refs. 16 and 42) to 6 to 9 percent declines in blood cholesterol levels when 15 g of soluble fiber per day were consumed for 16 weeks (Refs. 5 and 37). Source of soluble fiber was evaluated in four studies (Refs. 10, 15, 12, and 26). Results were equivocal in one study and suggestive of a source or specific type of soluble fiber component effect in the other studies.

c. *Normocholesterolemics: "typical" or "usual" diets.* Van Horn et al. (Ref. 65), in an epidemiological cross-sectional survey, evaluated baseline dietary assessment and blood cholesterol data from the Coronary Artery Risk Development in Young Adults (CARDIA) study. Dietary intakes were assessed by diet history. Of the over 5,000 men and women (18 to 30 years; normal blood cholesterol levels), there was an inverse and statistically significant correlation between total dietary fiber intake and blood total cholesterol and LDL-cholesterol levels. Many other nutrient intakes were also correlated with blood cholesterol levels. No data were given on soluble fiber intakes.

Seven men with normal blood cholesterol levels (mean 187 mg per dL) consumed their regular diets for 3 weeks followed by the addition of a supplemental source of soluble fiber for an additional 3 weeks (Ref. 1). The added soluble fiber intake was estimated at 16 to 19 grams per day. Blood cholesterol levels decreased during the pretreatment diet phase. After 3 weeks of supplemental soluble fiber intake, total blood cholesterol levels decreased 16 percent from the level at the end of the pretreatment phase.

Gold and Davidson (Ref. 19), in a double-blind, intervention study, provided 2 muffins containing test fibers (oat bran, wheat bran, or wheat/oat bran combination) to 72 male and female medical students (25 to 37 years; mean blood cholesterol 178 mg per dL) for 4 weeks. Subjects were assigned to one of three treatment groups, depending on soluble fiber intake from the muffins. Group mean supplemental soluble fiber intakes were 2.5, 0.9, and 0.33 g per day. Supplemental total dietary fiber was held constant at about 5 g per day. No data were given on baseline dietary fiber intakes. After 4 weeks, the group consuming 2.5 grams per day of supplemental soluble fiber had significantly lower blood total (5 percent) and LDL-cholesterol levels (9 percent) as compared to baseline levels.

In a controlled, cross-over, intervention study, Taneja et al. (Ref. 58) provided isaqbol husks as supplemental soluble fiber (20 to 22 grams per day) to 11 Indian girls, 16 to 18 years (mean serum cholesterol 182 mg per dL) for 3 weeks. The higher fiber intake was associated with a significantly lower blood total cholesterol level (7 percent) compared to the low fiber diet.

Thirty-four men and women college students (mean age 27 years; normal cholesterol) consumed formula diets standardized to reflect the fat and other macronutrient components of U.S. diets (Ref. 35). Various fiber sources and levels of soluble fiber were added by consuming breads and cereals. Dietary protocols in which soluble fiber intakes were 5 or more per day were associated with reduced levels of blood cholesterol; whereas soluble fiber intakes of 3 g or less per day did not show significant changes in blood cholesterol levels.

Swain et al. (Ref. 57), in a randomized, double-blind, cross-over, intervention trial, fed diets containing 4 or 15 g of soluble fiber per day for 6 weeks added as supplementary oat and wheat bran to subject's regular diets. Both the high and low fiber diets were associated with statistically significant decreases in blood total cholesterol levels as compared to baseline.

In a randomized, single-blind, intervention study to evaluate the effect of beta-glucan, a type of soluble fiber, on blood cholesterol levels, Newman et al. (Ref. 50), provided cereal and baked goods to 14 free-living men (35 years or older; serum cholesterol 141 to 247 mg per dL). Treatment diets were consumed for 4 weeks following 4 weeks of pretreatment with the normal diet. Pretreatment diets contained approximately 5 to 7 g of total dietary fiber. The total dietary fiber content of treatment diets was held constant at approximately 45 g of total dietary fiber; these diets, however, differed considerably in beta-glucan content. The high beta-glucan group also consumed less total fat than the control group. At the end of the 4-week treatment period, the blood cholesterol levels of the high beta-glucan group did not differ significantly from baseline. The blood total and LDL-cholesterol levels of the low beta-glucan group, despite high total dietary fiber intakes, were significantly higher than baseline levels.

In summary, for studies in persons with blood cholesterol levels in the normal to borderline or mild risk levels and consuming their regular diets, and within the context of the study conditions, results tended to show declines in blood cholesterol levels with intakes of soluble dietary fiber (Refs., 1, 19, 35, 57, and 58). One study controlled nutrient intakes by use of formula diets and results generally suggested a dose response to soluble fiber intakes (Ref. 35). Generalization to regular dietary patterns needs to be done cautiously. A study on beta-glucans, however, did not show an effect of this fiber in persons with normal blood cholesterol levels (Ref. 50).

d. *Normocholesterolemics: Step 1 diets.* Van Horn et al. (Ref. 68), in a randomized, intervention study controlled with crossover, stabilized 236 free-living men and women (serum cholesterol 163 to 247 mg per dL) on a Phase II American Heart Association diet (low fat, low saturated fat, low cholesterol). Test diets contained 4.2 g of added soluble fiber. After 8 weeks on the test diet, there were no significant differences in total serum cholesterol levels between groups, although blood cholesterol levels were significantly lower in the test group as compared to the control group at the interim 4-week time.

In a randomized, double-blind, placebo-controlled, parallel intervention trial, 75 men and women (mean blood cholesterol approximately 200 mg per dL) consumed a placebo test fiber for 8 weeks while also consuming a Step 1 diet (Ref. 11). The Step 1 diet provided approximately 6 g of soluble fiber per day; the test fiber supplement provided an additional 8 to 9 g of soluble fiber daily. After 20 weeks on the test diet, blood total and LDL-cholesterol levels were significantly reduced from baseline (4 percent and 8 percent, respectively). A subgroup of 30 subjects continued the intervention for 8 more weeks. Total and LDL-cholesterol levels tended to increase towards baseline in the supplemented group and to increase above baseline in the placebo group. The authors reported excellent compliance of the test substance throughout the study period.

In summary, only two studies were available in which the effect of soluble fiber on blood cholesterol levels was evaluated in persons with normal to mildly elevated levels and consuming diets low in total fat, saturated fat, and cholesterol. Results were equivocal but in both cases seemed to be transient since interim values were lower than final values. This occurred, despite the report of excellent compliance in consuming the test material in one study (Ref. 11).

4. Biological Mechanisms

Several mechanisms have been proposed to explain the claimed hypocholesterolemic effect of soluble fiber. These mechanisms have been reviewed in detail elsewhere (Refs. 17, 34, and 39) and will be briefly summarized here.

a. *Gastrointestinal events.* Dietary fibers affect different aspects of gastrointestinal function, resulting in interference in nutrient absorption and diffusion, altered hormonal responses, and production of short chain fatty acids. "These events could act individually or collectively to decrease serum cholesterol" (Ref. 2). However, effects on gastrointestinal functioning have not been studied adequately in the human body.

Studies outside of the body show that viscous fibers can influence the accessibility of absorbable nutrients to the mucosal surface. There are a variety of demonstrated and potential influences of high dietary fiber intake on both intraluminal and mucosal intestinal physiology that may affect the rate and extent of absorption of nutrients, including dietary lipids and cholesterol.

Dietary fiber may influence nutrient and cholesterol availability in its interaction with digestive enzymes, possibly leading to decreased efficiency of digestion and limited diffusion of absorbable products in the intestinal lumen. In rats, soluble fibers delay gastric emptying and interfere with nutrient exposure to digestive enzymes and absorptive surfaces of the small intestine. Viscous fibers, such as guar gum, show marked influence on lipid digestion in dogs. These fibers decrease the grinding and digestive action of the stomach, allowing poorly digested food to pass into the midintestine, leading to delayed lipid digestion.

Interaction between dietary fiber and the intestinal surface has not been studied adequately in humans. Vahouny and Cassidy (Ref. 75) noted that the effects of various fibers, especially viscous fiber preparations, on the activities of mucosal-associated digestive enzymes have not been consistent.

b. *Binding or sequestering bile acids.* Of all the theories proposed to explain the effects of dietary fiber on serum cholesterol that have been seen in some studies, the theory that fiber binds or sequesters bile acids has received the greatest attention and most extensive evaluation (Ref. 17). Dietary fats, or lipids, are first emulsified in the stomach and then are transferred to the upper part of the small intestine where they are hydrolyzed by pancreatic lipase. The hydrolysis products eventually dissolve in bile acids to form micelles. The micelles are broken at the intestinal wall, and the lipid hydrolysis products are absorbed into the body (Ref. 74). Specific dietary fibers are thought to bind or sequester circulating bile acids, thus interfering with micelle formation required for dietary cholesterol absorption, and thus altering or modifying lipid digestion and absorption. Increased excretion of bile acids in feces results in the conversion of liver cholesterol to bile acids, which eventually leads to decreased serum cholesterol and LDL-cholesterol levels.

In an effort to confirm this hypothesis, Story (Ref. 73) observed that the effects of dietary fiber on bile acid excretion are inconsistent and are not large enough to account for observed changes in serum cholesterol. "However, in some cases (e.g., oat bran in hypercholesterolemic humans), a substantial change in bile acid excretion has consistently accompanied the hypocholesterolemic effects. Clearly, this is not the sole mechanism involved for all sources of dietary fiber and our initial hypothesis concerning adsorption-excretion is not valid for all situations" (Ref. 73).

c. *Effect of fiber fermentation products.* Dietary fibers are partially fermented by bacteria in the human colon. Some of the fermentation products formed include short chain fatty acids, such as acetate, propionate, and butyrate. Short chain fatty acids are almost completely absorbed from the colon. Propionate is extracted by the liver and has been shown to lower plasma cholesterol in rats. In vitro studies in rat liver cells have shown that propionate decreases cholesterol synthesis, but only if acetate is used as a cholesterol precursor (Ref. 72). Venter et al. (Ref. 70) showed that dietary propionate fed to baboons raised total cholesterol, although metabolic effects of dietary propionate may not be the same as propionate derived from microbial fermentation of dietary fiber in the colon.

d. *Summary.* There are several mechanisms proposed (interference with gastrointestinal functions, binding of bile acids, and fiber fermentation) to explain the effects of soluble fiber on serum cholesterol found in some short-term studies. Not only is the mechanism unknown, but it has not been determined if it is the soluble fiber itself, the presence of beta-glucan (the major component of soluble fiber), or some other component in the diet that accounts for the observed effects.

5. Conclusions

Earlier reviews by the Federal government and other recognized scientific bodies generally concluded that diets rich in water-soluble fiber fractions were associated with cholesterol-lowering effects in humans (Refs. 48, 65, and 66). They further noted that high fiber diets are often associated with low fat diets and it is difficult to differentiate the effects of the two nutrients, although the net effect is beneficial and soluble fiber in relatively large amounts may serve as a useful adjunct to low saturated fat and low fat diets. The recent update by LSRO (Ref. 40) noted that recent data reflect results from earlier studies in that results suggest soluble fiber but not insoluble fiber may have cholesterol-lowering properties. Some types of soluble fiber, e.g., betaglucan, may be more effective than other types, although the data are extremely limited at this time. Animal studies are generally supportive. This report also notes that it is not clear whether the observed effects result strictly from the fiber or from other components associated with consumption of fiber-rich foods. The report also noted that there are no data to indicate that a fiber present in a food is the same as when it has been extracted and purified.

FDA reviewed over 30 human studies published in the last several years. Under the study conditions, many studies observed a decline in blood cholesterol levels with increasing intakes of soluble fiber. Most studies, however, were of very short duration and, therefore, cannot confirm long-term benefits from high soluble fiber diets. Indeed, questions of long-term effects were raised by the observation of an initial decline in blood cholesterol levels followed by a return upwards towards baseline in some of the longer studies, even when authors reported excellent compliance for consumption of test substances.

There was some evidence suggesting that different types of soluble fiber have different effects. Additionally there was some evidence of a dose response, although the evidence for this is very limited. There were, however, major design flaws in many of the studies which make it difficult to reach firm conclusions. The objectives of many study protocols seemed to be to evaluate the effectiveness of relatively large amounts of a single type of food or fiber source rich in soluble fiber (e.g., oatmeal, baked beans, oat bran) rather than to look at total soluble dietary fiber intakes or to specifically identify the chemical and physical characteristics of soluble fiber that are most effective in lowering blood cholesterol levels. By adding large amounts of foods to diets (e.g., addition of 1 to 2 cups of baked beans daily), these dietary changes were often accompanied by lower calorie intakes and weight loss. Since weight loss alone can lower blood cholesterol levels, this becomes a serious confounder for interpreting study results. Frequently, also, nutrient intakes, particularly those nutrients related to serum cholesterol levels (saturated fat, total fat, cholesterol) varied among treatment and control groups, again confounding interpretation of results. Information on total soluble fiber intakes is not always provided. Results from studies with crossover designs were often particularly confusing since treatment order effects were often observed.

The LSRO update report (Ref. 40) noted that the recent studies represented, to large degree, a repeat of earlier studies. FDA reached a similar conclusion. Based on the totality of the evidence, FDA has determined that the conclusions of the reports reached by the earlier Federal government and other reviews by recognized scientific bodies provide an insufficient basis to support a health claim relating soluble fiber intake to reductions in blood cholesterol levels and, ultimately, to reduced risk of developing CHD. It is still not clear whether observed reductions in blood cholesterol levels on short-term studies are due to changes in other nutrients intakes and/or to concomitant weight loss. The potential for adaptation and loss of effectiveness with time remains an unanswered question. And, most importantly, the data suggest that some but not all components of dietary soluble fiber may be most effective. Evidence to date is too limited to be able to clearly identify the characteristics of effective soluble fibers.

III. Tentative Decision not to Propose a Health Claim Relating Dietary Fiber to Decreased Risk of Cardiovascular Disease

FDA limited its review of the scientific evidence relating to ingestion of dietary fiber and cardiovascular disease to the topic of soluble dietary fiber and risk of developing CHD. These limitations were deemed appropriate because the previous Federal government and other reviews by recognized scientific bodies had focused on these areas and the majority of research efforts to date have focused on these areas.

FDA has tentatively concluded, based on the totality of the evidence, that there is not a sufficient basis to authorize a health claim for dietary soluble fiber and reduction in risk of developing CHD. Numerous human studies have examined the possible role of dietary fiber intake in CHD. Many correlational studies show a relationship between diets high in plant foods (fruits, vegetables, and grains) and reduced rates of cardiovascular disease. There are a number of dietary intervention studies which are generally conducted for short-time periods, and often with fairly large changes in dietary patterns. Most of these studies show short-term benefits in serum cholesterol lowering with diets high in soluble dietary fiber. However, these studies are often also characterized by other concomitant changes which could also affect blood cholesterol levels, including weight loss and changes in other nutrients intakes which affect blood cholesterol levels. Studies of longer duration (6 weeks to 6 months) tend to be limited in number and results are more equivocal. The relationship of type of soluble fiber as currently measured by commonly used methods such as those of the Association of Official Analytical Chemists is not clear.

It is clear that diets high in soluble fiber-rich foods, including whole grains, fruits, and vegetables, are associated with reduced risk of developing CHD. These diets differ, however, in the levels of many nutrients and in types of dietary soluble fiber making it difficult to ascribe observed nutrient and disease relationships to a single nutrient. Overall, the available data are not sufficient to demonstrate that it is the total soluble dietary fiber, or a specific measurable and quantifiable subcomponent, that is related to lower blood cholesterol levels.

A major limitation in designing and evaluating research studies has been the need for better-defined measures of dietary fiber and standardized descriptions for source, type, and amount of dietary soluble fiber (Ref. 39). Dietary fibers, including soluble fibers, are a heterogeneous family of compounds that vary considerably in chemical composition, physical characteristics, and biological effects (Ref. 39). Processing of foods and fiber sources may also alter the inherent characteristics of the soluble fiber. The commonly used analytical methodologies often do not detect many of the characteristics that vary among fibers and that may be related to biological function (e.g., particle size, chemical composition, or water-holding capacity) (Ref. 39). Analytical methods also do not differentiate between source of fiber. This lack of ability to detect many of the differences that exist among fibers and the general lack of clear evidence as to the mechanisms of action of fibers have raised questions as to the ability of commonly used analytical measures of dietary fiber to adequately predict biological actions of specific fibers (Refs. 12 and 24).

Another problem in evaluating the relationship of dietary fiber intakes to the risk of chronic disease such as CHD is the lack of reference food composition data on the fiber content of foods. Consequently, most human studies have described dietary intakes in terms of amounts of oatmeal, or oat, or wheat brans. In many studies, total soluble dietary fiber intake, or even the soluble fiber content of the test material, was not described.

In summary, the currently available scientific evidence is not sufficiently conclusive or specific for soluble fiber to justify use of a health claim relating intake of dietary soluble fiber to reduced risk of CHD. Federal government (Refs. 63 and 66) and other reviews by recognized scientific bodies (Refs. 39, 40, and 48) are consistent in agreeing that it is difficult to separate the effects of fiber from those of other components present in high fiber foods or in dietary patterns high in plant food. As noted above, the evidence that has become available since publication of these reports is consistent with these conclusions and is, therefore, not sufficient to alter the earlier conclusions. Thus, FDA has tentatively concluded, based on the totality of the scientific evidence, that there is not significant scientific agreement among experts qualified by training and experience to evaluate such a relationship, as to the independent and specific role of dietary soluble fiber in reducing the risk of CHD.

FDA recognizes that CHD is a leading cause of morbidity and mortality in the United States and that changes in dietary patterns can play a significant role in reducing risk of CHD. Virtually all recent dietary guidelines for Americans have encouraged the increased consumption of fiber-rich foods, including whole grain cereals, fruits, and vegetables. FDA has supported and continues to support these recommendations and to encourage dietary guidance consistent with the recommendations. This raises a dilemma, however, for which FDA is requesting comment. To encourage and help consumers to meet dietary guidance recommendations, it would be useful to have appropriate dietary information at point of purchase. The use of health claims on foods (including dietary supplements) to inform consumers of these recommendations, however, is problematic since it is not clear what qualifying and other criteria are necessary to adequately define eligible foods for such a health claim. Congress, in the 1990 amendments, specified that FDA evaluate nutrient and disease relationships. Dietary fiber was specified as one nutrient for evaluation. Yet, FDA has tentatively concluded that the available evidence that is supportive of changes in food patterns cannot be extrapolated to a specific fiber effect at this time.

Given the public health significance of CHD and given the general dietary guidance to increase consumption of fruits and vegetables and whole grain products which are rich sources of dietary fiber, including soluble fiber, and other nutrients, FDA is requesting comments on how best to inform consumers of these issues.

Specifically, should the agency permit a claim on the label or in labeling such as "Diets high in fruit, vegetables, and whole grains are associated with a reduced risk of cancer of the lower bowel and cardiovascular disease"; or alternatively "Research has shown that populations who consume diets that contain several servings each of fruit, vegetables, and whole grains have a decreased risk of certain forms of cancer and cardiovascular disease; or "Choose diets with plenty of fruit, vegetables, and whole grains to help lower your risk of cardiovascular disease and certain forms of cancer." If such statements should be permitted, what criteria should be used to identify foods that are eligible for such statements? For example, should such statements be limited to fresh fruit, vegetables, and milled whole grains, or should processed foods derived from these produces also be included? What measure should the agency adopt to assure that consumers are not mislead as to the benefit of consuming a specific product? FDA is requesting comments on whether it has the authority and should allow health claims on foods as well as nutrients.

Based on the studies reviewed in this document, serum cholesterol responses were affected by a number of factors: Initial serum cholesterol level, base diet, self-initiated changes to base diet (particularly to changes in intake of saturated fat and polyunsaturated fat) during the test period, body weight, exercise, medications, general health, and other lifestyle variables. These confounding factors, which were generally not well controlled within many of the individual studies and which make cross-study comparisons difficult, made it impossible to draw conclusions about the relationship of soluble fiber to serum cholesterol levels.

1. Safety of Fiber Supplements

Concerns have been raised about the potential for risk from isolated or purified forms of fiber (Ref. 39). Side effects and possible adverse health effects of high intakes of dietary fiber have also been hypothesized by NAS (Ref. 48). Excessive consumption of fiber supplements may result in more intestinal problems or poor absorption of trace minerals than would be expected from a high-fiber diet (Ref. 40). Fiber sources, such as psyllium seed, guar gum, pectin and other gums, are not listed as GRAS substances for use as a fiber supplement.

The agency is concerned about changing consumption patterns associated with the development and introduction into the marketplace of new sources of dietary fiber, along with increased use of fiber sources as food ingredients or as supplements of fiber. FDA intends to update its GRAS regulations for sources of fiber in the near future. To deal with this issue, the agency intends to initiate a review of the existing types of isolated dietary fibers and their use as a broad class of foods to identify and assess scientific information on the safety of this use. This review will include consideration of the biological effects of different fibers, the extent to which such effects are significantly different for subclasses of dietary fiber, and whether biological effects are significantly altered by chemical or physical changes and by processing. FDA may use the results of this or other reviews to develop a new strategy for assessing food safety.

2. Significant Scientific Agreement

The Federal government and other authoritative reports reviewed consistently concluded that while dietary patterns high in fiber-rich foods were associated with lower levels of serum cholesterol and decreased risk of CHD, the effect of soluble dietary fiber could not be separated from the effects of other dietary factors, i.e., lower contents of saturated fatty acids and cholesterol and higher intakes of fiber, potassium, and vitamins and minerals. The data that has become available since those reports were completed, as reviewed here by FDA and also as independently reviewed by outside experts (Ref. 40), do not provide sufficient evidence to warrant modifying or changing the conclusions reached earlier by the authoritative reports. Thus, FDA concludes that there is not sufficient scientific agreement, among experts qualified by experience and training, to support a health claim for dietary fiber and cardiovascular disease.

3. Public Health Importance

It is clear that cardiovascular disease, and particularly CHD, are major public health problems in the United States. There is also general agreement that dietary patterns that will lower serum cholesterol levels will also lower risk of these diseases. Dietary patterns high in fiber-containing foods; low in fats, saturated fats, and cholesterol; and associated with maintenance of desirable body weights are also associated with decreased risk of CHD. This association is the basis for the numerous dietary guidelines that recommend these types of dietary patterns. FDA has consistently supported these dietary guidelines and continues to do so. (With the proposed changes in the mandatory nutrition labeling regulations (see companion document published elsewhere in this issue of the **Federal Register**), consumers should be better able to obtain the information needed to select foods to help them meet these goals.)

IV. Environmental Impact

The agency has determined under 21 CFR 25.24(a)(1) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

V. Effective Date

FDA is proposing to make these regulations effective 6 months after the publication of a final rule based on this proposal.

VI. Comments

Interested persons may, on or before (February 25, 1992), submit to the Dockets Management Branch (address above) written comments regarding this proposal. Two copies of any comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document. Received comments may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

VII. Economic Impact

The food labeling reform initiative, taken as a whole, will have associated costs in excess of the $100 million threshold that defines a major rule. Therefore, in accordance with Executive Order 12291 and the Regulatory Flexibility Act (Pub. L. 96–354), FDA has developed one comprehensive regulatory impact analysis (RIA) that presents the costs and benefits of all of the food labeling provisions taken together. The RIA is published elsewhere in this issue of the **Federal Register**. The agency requests comments on the RIA.

VIII. References

The following references have been placed on display in the Dockets Management Branch (address above) and may be seen by interested persons between 9 am and 4 pm, Monday through Friday.

1. Abraham, Z. D., and T. Mehta, "Three-week Psyllium Supplementation: Effect on Plasma Cholesterol Concentrations, Fecal Steroid Excretion, and Carbohydrate Absorption in Men," *American Journal Clinical Nutrition*, 47:67–74, 1988.

2. Anderson, J. W., D. A. Deakins, T. L. Floore, B. M. Smith, and S. E. Whitis, "Dietary Fiber and Coronary Heart Disease," in: Clydesdale, F. M., ed., *Critical Reviews in Food Science and Nutrition*, Vol. 29, New York, pp. 95–137, 1990.

3. Anderson, J. W., N. H. Gilinsky, D. A. Deakins, S. F. Smith, D. S. O'Neal, D. W.

Dillon, P. R. Oeltgen, "Lipid Responses of Hypercholesterolemic Men to Oat-bran and Wheat-bran Intake," *American Journal of Clinical Nutrition*, 54:678–83, 1991.

4. Anderson, J. W., N. J. Gustafson, D. B. Spencer, J. Tietyen, C. A. Bryant, "Serum Lipid Response of Hypercholesterolemic Men to Single and Divided Doses of Canned Beans," *American Journal of Clinical Nutrition*, 51:1013–9, 1990.

5. Anderson, J. W., S. Riddell-Lawrence, T. L. Floore, D. W. Dillon, P. R. Oeltgen, "Effects of Refined Bakery Products on Serum Cholesterol Levels in Hypercholesterolemic Men," unpublished, 1991.

6. Anderson, J. W., D. B. Spencer, C. C. Hamilton, S. F. Smith, J. Tietyen, C. A. Bryant, P. Oeltgen, "Oat-bran Cereal Lowers Serum Total and LDL Cholesterol in Hypercholesterolemic Men," *American Journal of Clinical Nutrition*, 52:495–499, 1990.

7. Anderson, J. W., L. Story, B. Sieling, W. J. L. Chen, M. S. Petro, J. Story, "Hypocholesterolemic Effects of Oatbran or Bean Intake for Hypercholesterolemic Men," *American Journal of Clinical Nutrition*, 40:1146–55, 1984.

8. Anderson, J. W., N. Zettwoch, T. Feldman, J. Tietyen-Clark, P. Oeltgen, C. W. Bishop, "Cholesterol-lowering Effects of Psyllium Hydrophilic Mucilloid for Hypercholesterolemic Men, : *Archives of Internal Medicine*, 148:292–296, 1988.

9. Aro, A., M. Uusitupa, E. Voutilainen, T. Korhonen, "Effects of Guar Gum in Male Subjects With Hypercholesterolemia," *American Journal of Clinical Nutrition*. 39:911–916, 1984.

10. Beling, S., L. Detrick, W. Castelli, "Serum Cholesterol Response to a Processed Oat Bran Cereal Among Hypercholesterolemics on a Fat-modified Diet," Unpublished Clinical Trial Submitted by the Quaker Oats Co., 1991.

11. Bell, L. P., K. J. Hectorn, Reynolds, H., Balm, T. K., Hunninghake, D. B. "Cholesterol-lowering Effects of Psyllium Hydrophilic Mucilloid—Adjunct Therapy to a Prudent Diet for Patients With Mild to Moderate Hypercholesterolemia," *Journal of the American Medical Association*, 261:3419–3423, 1989.

12. Bell, L. P., K. J. Hectorn, H. Reynolds, D. B. Hunninghake, "Cholesterol-Lowering Effects of Soluble Fiber Cereals as Part of a Prudent Diet for Patients With Mild to Moderate Hypercholesterolemia, *American Journal of Clinical Nutrition*, 52:1020–6, 1990.

13. Burr, M. L., J. F. Gilbert, R. M. Holliday, P. C. Elwood, A. M. Fehily, S. Rogers, P. M. Sweetnam, N. M. Deadman, "Effects of Changes in Fat, Fish, and Fibre Intakes on Death and Myocardial Reinfarction: Diet and Reinfarction Trial (DART)," *The Lancet*, pp. 757–761, September 30, 1989.

14. Consensus Development Panel, "Lowering Blood Cholesterol to Prevent Heart Disease," *JAMA*, 253:2080–86, 1985.

15. Davidson, M. H., L. D. Dugan, J. H. Burns, J. Bova, K. Story, K. B. Drennan, "The Hypocholesterolemic Effects of Beta-glycan in Oatmeal and Oat Bran—A dose-controlled Study," *JAMA*, 265(14):1833–39, 1991.

16. Demark-Wahnefried, W., J. Bowering, P. S. Cohen, "Reduced Serum Cholesterol With Dietary Change Using Fat-modified and Oat Bran Supplemented Diets," *Journal of the American Dietetic Association*, 90:223–9, 1990.

17. Furda, I., "Interaction of Dietary Fiber with Lipids—Mechanistic Theories and Their Limitations, in: Furda, I., C. J. Brine, Eds., *New Developments in Dietary Fiber*, New York: Plenum Press, p. 67–80, 1990.

18. Glassman, M., Spark, A., Berezin, S., Schwarz, S., "Treatment of Type IIa Hyperlipidemia in Childhood by a Simplified American Heart Association Diet and Fiber Supplementation," *American Journal of Diseases of Children*, 144:973–76, 1990.

19. Gold, K. V., D. M. Davidson, "Oat Bran as a Cholesterol-reducing Dietary Adjunct in a Young, Healthy Population," *Western Journal of Medicine*, 148:299–302, 1988.

20. Grande, F., J. T. Anderson, A. Keys, "Effect of Carbohydrates of Leguminous Seeds, Wheat and Potatoes on Serum Cholesterol Concentration in Man," *Journal of Nutrition*, 86:313–317, 1965.

21. Grande, F., J. T. Anderson, A. Keys, "Sucrose and Various Carbohydrate-Containing Foods and Serum Lipids in Man," *American Journal of Clinical Nutrition*, 27:1043–1051, 1974.

22. Jenkins, D. J. A., A. R. Leeds, C. Newton, J. H. Cummings, "Effect of Pectin, Guar Gum, and Wheat Fiber on Serum Cholesterol," *The Lancet*, i:1116–1117, 1975.

23. Jenkins, D. J. A., D. Reynolds, A. R. Leeds, A. L. Waller, J. H. Cummings, "Hypocholesterolemic Action of Dietary Fiber Unrelated to Fecal Bulking Effect," *American Journal of Clinical Nutrition*, 32:2430–2435, 1979.

24. Judd, P.A., A.S. Truswell, "Dietary Fibre and Blood Lipids in Man," in: "Dietary Fibre Perspectives: Reviews and Bibliography," A.R. Leeds, A. Avenell, eds, London: John Libbey and Co., pp. 23–39, 1985.

25. Kahn, R.F., K.W. Davidson, J. Garner, R.S. McCord, "Oat Bran Supplementation for Elevated Serum Cholesterol," *Family Practice Research Journal*, 10:37–46, 1990.

26. Keenan, J.M., J.B. Wenz, S. Myers, C. Ripsin, Z. Huang, "Randomized Controlled Crossover Trial of Oat Bran in Hypercholesterolemic Subjects," in Press, 1991.

27. Kesaniemi, Y.A., S. Tarpila, T.A. Miettinen, "Low versus High Dietary Fiber and Serum, Biliary, and Fecal Lipids in Middle-aged Men," *American Journal of Clinical Nutrition*, 51:1007–12, 1990.

28. Kestin, M., R. Moss, P.M. Clifton, P.J. Nestel, "Comparative Effects of Three Cereal Brans on Plasma Lipids, Blood Pressure, and Glucose Metabolism in Mildly Hypercholesterolemic Men," *American Journal of Clinical Nutrition*, 52:661–6, 1990.

29. Keys, A., J.T. Anderson, F. Grande, "Diet-type (Fats Constant) and Blood Lipids in Man," *Journal of Nutrition*, 70:257–266, 1960.

30. "Coronary Heart Disease in Seven Countries," Keys, A., Ed., *Circulation*, 41 (Suppl. 1).

31. Khaw, K., E. Barret-Connor, "Dietary Fiber and Reduced Ischemic Heart Disease Mortality Rates in Men and Women: A 12-year Prospective Study," *American Journal of Epidemiology*, 126:1093–1102, 1987.

32. Kirby, R.W., J.W. Anderson, B. Sieling, E.D. Rees, W.J.L. Chen, R.E. Miller, R.M. Kay, "Oat-bran Intake Selectively Lowers Serum Low-density Lipoprotein Cholesterol Concentrations of Hypercholesterolemic Men," *American Journal of Clinical Nutrition*, 34:824–829, 1981.

33. Kris-Etherton, P.M., D. Krummel, M.E. Russell, D. Dreon, S. Mackey, J. Borchers, P.D. Wood, "National Cholesterol Education Program—The Effect of Diet on Plasma Lipids, Lipoproteins, and Coronary Heart Disease," *Journal of the American Dietetic Association*, 88:1373–1400, 1988.

34. Kritchevsky, D., "Lipid Metabolism and Coronary Heart Disease," in: *Dietary Fibre, Fibre-depleted Foods and Disease*, Trowell, H., D. Burkitt, K. Heaton, Eds., New York: Academic Press. pp. 305–313, 1985.

35. Lampe, J.W., J.L. Slavin, K.S. Baglien, W.O. Thompson, W.C. Duane, J.H. Savoral, "Serum Lipid and Fecal Bile Acid Changes with Cereal, Vegetable, and Sugarbeet Fiber Feeding," *American Journal of Clinical Nutrition*, 53:1235–1241, 1991.

36. Lanza, E., D.Y. Jones, G. Block, L. Kessler, "Dietary Fiber Intake in the U.S. Population," *American Journal of Clinical Nutrition*, 46:790–797, 1987.

37. Levin, E.G., V.T. Miller, R.A. Muesing, D.B. Stoy, T.K. Balm, J.C. LaRosa, "Comparison of Ppsyllium Hydrophilic Mucilloid and Cellulose as Adjuncts to a Prudent Diet in the Treatment of Mild to Moderate Hypercholesterolemia," *Archives of Internal Medicine*, 150:1822–27.

38. "Nutrition, Lipids, and Coronary Heart Disease: A Global View," Levy, R., B. Rifkind, B. Dennis, N. Ernst, Eds., Raven, New York, 1979

39. LSRO, Federation of American Societies for Experimental Biology, "Physiological Effects and Health Consequences of Dietary Fiber," Bethesda, MD, 1987.

40. LSRO, Federation of American Societies for Experimental Biology, "Dietary Fiber and Cardiovascular Disease," Bethesda, MD, 1991.

41. Lipids Research Clinics Program, "The Lipid Research Clinics Coronary Primary Prevention Trial Results II, in "The Relationship of Reduction in Incidences of Coronary Heart Disease to Cholesterol Lowering," *JAMA*, 251:365–74, 1984.

42. Little, P., G. Girling, A. Craven, A. Trafford, "The Effect of a Combination Low Sodium, Low Fat, High Fibre Diet on Serum Lipids in Treated Hypertensive Patients," *European Journal of Clinical Nutrition*, 44:293–300, 1990.

43. Lo, G.S., T.G. Cole, "Soy Cotyledon Fiber Products Reduce Plasma Lipids" *Atherosclerosis*, 82:59–67, 1990.

44. McIntosh, G. H., J. Whyte, R. McArthur, P. J. Nestel, "Barley and Wheat Foods: Influence on Plasma Cholesterol Concentrations in Hypercholesterolemic Men," *American Journal of Clinical Nutrition*, 53:1205–1209, 1991.

45. McIvor, M.E., C.C. Cummings, A.I. Mendeloff, "Long-term Ingestion of Guar Gum is Not Toxic in Patients with Noninsulin Dependent Diabetes Mellitus," *American Journal of Clinical Nutrition*, 41:891–894, 1985.

46. Minister of National Health and Welfare Canada, *Report of the Expert Advisory Committee on Dietary Fibre*,

Canadian Government Publishing Centre, Ottawa, Canada, 1985.
47. Minister of National Health and Welfare Canada, "Nutrition Recommendations: The Report of the Scientific Review Committee 1990," Canadian Government Publishing Centre, Ottawa, Canada, 1990.
48. National Research Council/National Academy of Sciences (NAS), "Diet and Health: Implications for Reducing Chronic Disease Risk," National Academy Press: Washington, DC, 1989.
49. National Research Council (NRC), "Recommended Dietary Allowances," 10th Edition, National Academy Press: Washington, DC, 1989.
50. Newman, R.K., S.E. Lewis, C.W. Newman, R.J. Boik, R.T. Ramage, "Hypocholesterolemic Effect of Barley Foods on Healthy Men," *Nutritional Reports International*, 39:749–760, 1989.
51. Nishina, P.M., R.A. Freedland, "Effects of Propionate on Lipid Biosynthesis in Isolated Rat Hepatocytes" *Journal of Nutrition*, 120:668–673, 1990.
52. Ross, R., "Atherosclerosis" in: *Cecil Textbook of Medicine*, J.B. Wyngaarden, L.H. Smith, eds., W.B. Saunders Co., Philadelphia, PA, pp. 319–320, 1988.
53. Shutler, S.M., G.M. Bircher, J.A. Tredger, L.M. Morgan, A.F. Walker, A.G. Low, "The Effect of Daily Baked Bean (*Phaseolus Vulgaris*) Consumption on the Plasma Lipid Levels of Young, Normocholesterolaemic Men," British Journal of Nutrition, 61:257–65, 1989.
54. Stamler, J., "Nutrition-related Risk Factors For The Atherosclerotic Diseases—Present Status," *Procress in Biochemicol Pharmacology*, 19:245–308, 1983.
55. Stewart, R.B., W.E. Hale, M.T. Moore, F.E. May, R.G. Marks, "Effect of Psyllium Hydrophilic Mucilloid on Serum Cholesterol in the Elderly" *Digestive Disease and Sciences*, 36:329–334, 1991.
56. Superko, H.R., W.L. Haskell, L. Sawrey-Kubicek, J.W. Farquhar, "Effects of Solid and Liquid Guar Gum on Plasma Cholesterol and Triglyceride Concentrations in Moderate Hypercholesterolemia," *American Journal of Cardiology*, 62:51–55, 1988.
57. Swain, J.F., I.L. Rouse, C.B. Curley, F.M. Sacks, "Comparison of the Effects of Oat Bran and Low-fiber Wheat on Serum Lipoprotein Levels and Blood Pressure" *New England Journal of Medicine*, 322:147–52, 1990.
58. Taneja, A., C.M. Bhat, A. Arora, A.P. Kaur, 1989. "Effect of Incorporation of Isabgol Husk in a Low Fibre Diet on Faecal Excretion and Serum Levels of Lipids in Adolescent Girls," *European Journal of Clinical Nutrition*, 43:197–202, 1989.
59. Tuomilehto, J., M. Silvasti, A. Aro, P. Karttunen, C. Gref, C. Ehnholm, M. Uusitupa, "Long Term Treatment of Severe Hypercholesterolaemia With Guar Gum," *Atherosclerosis*, 72:157–162, 1988.
60. Tuomilehto, J., E. Voutilainen, J. Huttunen, S. Vinni, K. Homan, "Effect of Guar Gum on Body Weight and Serum Lipids in Hypercholesterolemic Females," *Acta Medica Scandinavian*, 208:45–48, 1980.
61. J.H. Ullrich, "Evaluation of a High-fiber Diet in Hyperlipidemia: A Review," *Journal of the American College of Nutrition*, 6(1):19–25, 1987.
62. USDA and DHHS, "Nutrition and Your Health: Dietary Guideline for Americans' " 3rd Edition, Home and Garden Bulletin No. 232, U.S. Government Printing Office, Washington, DC.
63. DHHS, Public Health Service, "The Surgeon General's Report on Nutrition and Health," U.S. Government Printing Office, Washington, DC, 1988.
64. DHHS, Public Health Service, "Healthy People 2000: National Health Promotion and Disease Prevention Objectives," Washington, DC, 1990.
65. DHHS, Public Health Service and the National Institutes of Health (NIH), "National Cholesterol Education Program: Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults," NIH, Bethesda, MD, 1989.
66. DHHS, Public Health Service and the National Institutes of Health, "National Cholesterol Education Program: Population Panel Report," Bethesda, MD, 1989.
67. Van Horn, L., C. Ballew, K. Liu, K. Ruth, A. McDonald, J.E. Hilner, G.L. Burke, P.J. Savage, C. Bragg, B. Caan, D. Jacobs, M. Slattery, S. Sidney, "Diet, Body Size, and Plasma Lipids-lipoproteins in Young Adults: Differences by Race and Sex," *American Journal of Epidemiology*, 133:9–22, 1991.
68. Van Horn, L., Emidy, L.A., Liu, K., Liao, Y., Ballew, C., King, J., Stamler, J. 1988, Serum Lipid Response to a Fat-modified, Oatmeal-enhanced Diet, "*Preventive Medicine*, 17:377–386.
69. Van Horn, L., A. Moag-Stahlberg, K. Liu, C. Ballew, K. Ruth, R. Hughes, J. Stamler, "Effects on Serum Lipids of Adding Instant Oats to Usual American Diets," *American Journal of Public Health*, 81:183–88, 1991.
70. Venter, C.S., H.H. Vorster, D.G. Van der Nest, "Comparison Between Physiological Effects of Konjac-glucomannan and Propionate in Baboons Fed Western Diets," *Journal of Nutrition*, 120:1046–1053, 1991.
71. World Health Organization (WHO), "Diet, Nutrition, and the Prevention of Chronic Diseases," World Health Organization, Geneva, Switzerland, 1990.
72. Nishina, P.M., R.A. Freedland, "Effects of Propionate on Lipid Biosynthesis in Isolated Rat Hepatocytes," *Journal of Nutrition*, 120:668–673, 1990.
73. Story, J.A., "Modification of Steroid Excretion in Response to *Dietary Fiber: Basic and Clinical Aspects*, Vahouny, G.V., D., Kritchevsky, Eds., New York: Plenum Press, pp. 253–264.
74. Sugano, M., I. Ikeda, K. Imaizumi, Y. Lu, "*Dietary Fiber—Chemistry, Physiology, and Health Effects*, Kritchevsky, D., Bonfield, C., Anderson, J.W., eds., New York: Plenum Press, p. 137–156, 1990.
75. Vahouny, G.V., M.M. Cassidy, "*Dietary Fibers and Absorption of Nutrients*, *Proceeding of the Society for Experimental Biology and Medicine*, 180:432–446, 1985.

List of Subjects in 21 CFR Part 101

Food labeling Reporting and recordkeeping requirements.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, it is proposed that 21 CFR part 101 be amended as follows:

PART 101—FOOD LABELING

1. The authority citation for 21 CFR part 101 is revised to read as follows:

Authority: Secs. 4, 5, 6 of the Fair Packaging and Labeling Act (15 U.S.C. 1453, 1454, 1455); secs. 201, 301, 402, 403, 409, 501, 502, 505, 701 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321, 331, 342, 343, 348, 351, 352, 355, 371).

2. Section 101.71 is amended by adding paragraph (b) to read as follows:

§ 101.71 Health claims: claims not authorized.

* * * * *

(b) Dietary fiber and cardiovascular disease (insert cite and date of publication in the **Federal Register** of the final rule).

Dated: November 4, 1991.

David A. Kessler,

Commissioner of Food and Drugs.

Louis W. Sullivan,

Secretary of Health and Human Services.

Note: The following tables will not appear in the annual Code of Federal Regulations.

BILLING CODE 4160-01-M

Table 1

Dietary fiber and cardiovascular disease: Effects of soluble fiber on blood cholesterol in humans.

Study	Study Design	Subjects	Methods	Results	Comments
Abraham and Mehta, 1988 (Ref. 1)	Intervention, controlled diet	7 men, free living, with normal blood cholesterol (mean 187 mg/dL; range 132-240 mg/dL)	Subjects consumed controlled meals, based on usual diet, for 3 weeks followed by 3 weeks with psyllium (PSY) husks added to control diet in form of muffins, cookies, fruit drinks, and peanut butter. Gradual ↑ of psyllium starting with 7 grams/day to 21 g/day. Estimated soluble fiber (SF) intake from PSY - 16-19 g/day. Base diet: 30% kcals (kilocalories or Calories) from fat; 16% from protein; 54% kcals from carbohydrate. Cholesterol intake 300-400 mg/day. P/S = 1; total dietary fiber (TDF) 17 g/day.	After 3 weeks, total or serum cholesterol (TC) ↓16% (calculated) (significant (S)); LDL and HDL cholesterols also ↓ significantly. Subjects with the highest baseline serum cholesterol had the greatest TC reductions.	Subjects' cholesterol values were not stabilized, as the authors reported, when psyllium intervention was started. There was no control group during the intervention period. No data on body weight. The short test period limits ability to generalize to long term effects.
Anderson et al., 1988 (Ref. 8)	Intervention, randomized, parallel, double blinded, placebo controlled	26 men, ages 30-65; free living; normo- and hypercholesterolemic (18[illegible]-314 mg/dL)	Subjects consumed regular diet for 2 weeks followed by adding psyllium (Metamucil) or cellulose (control), 3 times a day before meals (3.4 g fiber source/meal), to meals for 8 weeks. Dietary intakes monitored with 24-hour random records. 10.2 g/day of PSY provided an estimated 8-9 g of SF. Base diet: 40% kcals from fat; 20% kcals from protein; 40% kcals carbohydrate; <300 mg/day of dietary cholesterol.	From baseline, soluble fiber from psyllium: TC ↓15% (S); LDL ↓20% (S), and LDL/HDL ratio ↓15% (S). There were also significant differences between the placebo group and the psyllium group. No effect of PSY on HDL.	Psyllium was provided as an adjunct to the regular diet. Steady decline in TC over 8-week test in PSY group. No effect on body weight. Authors report compliance was excellent.
Anderson et al, 1990 (Ref. 4)	Intervention, randomized, self-controlled study on a metabolic ward	24 males, hypercholesterolemic, 37-69 years old. No hypocholesterolemic medications were allowed. 5 subjects exceeded desirable body weight by ≥ 20%.	Subjects consumed typical "American" diet for 7 days as a control period. Diet provided 38% kcals as fat; 19% kcals as protein; 43% kcals as carbohydrate; 420 mg dietary cholesterol; total kcals: 1729-1981/day. After 7 days subjects randomized into 3 groups for 21-day test period: Group A (n=6) received a single serving of canned beans (227 g) at noon, Groups B and C (n=9 each) received 2 divided servings of canned beans (227 g and 182 g, respec-tively). TDF / SF Control diet 13 g / 4 g Diets A and B 23 g / 8 g Diet C 23 g / 7 g	Total Serum cholesterol: ↓ 8-11.6% (S) compared to baseline control period in all three test groups. Overall, the LDL/HDL ratio remained similar to control ratios for groups A, B, and C. The interim TC values were lower (↓13-17% decrease from baseline) than the final values.	Each group experienced some weight loss (approximately 3 pounds). Calorie intakes were approximately 1800 kcals/day. TC was increasing towards baseline at end of 3-week test period. Short test period is a limitation of study design.

TABLE I--CONTINUED

Study	Study Design	Subjects	Methods	Results	Comments
Anderson et al, 1990 (Ref. 6)	Intervention, randomized, self-controlled, cross-over on metabolic ward	12 men; 46-70 years old; hypercholesterolemic (210-326 mg/dL); body mass indices of less than 30; 5 subjects had evidence of cardiovascular disease	Subjects, randomized into 2 groups, consumed typical "American" diet for 2 weeks in addition to test or control cereal followed by crossover to other cereal for 2 weeks. Base diet provided 41% kcals as fat; 20% kcals as protein; 43% kcals as carbohydrate; 355 mg dietary cholesterol. One group started with addition of 56 g oat bran cereal to the diet; the other consumed 56 g of cornflakes (control). Total dietary fiber (TDF) and total soluble fiber (TSF) were: TDF TSF Oat bran cereal 21 g 7.4 g Cornflakes 15 g 4.5 g	Oat bran diet: ↓ TC 5.4% (S) compared to the corn flakes diet. LDL was lowered by 8.5%, and HDL was not significantly lowered.	The intake of carbohydrates, protein, fat and cholesterol were nearly identical in the two groups. Total dietary fiber varied between the two diets. No change in body weight. Short duration of test is a limitation.
Anderson et al, 1990 (Ref. 5)	Intervention, self-controlled, metabolic ward	10 men, ages 40-70 years; mild to high hypercholesterolemia (200-320 mg/dL); 13 enrolled. 3 dropped out: 2 for reasons unrelated to the study, 1 for non-compliance.	Subjects consumed a controlled diet for 7 days (control period) followed by a 3-week test period. Base diet: 30% kcals from fat; 15 kcals from protein; 55% kcals from carbohydrate; 450 mg/day dietary cholesterol; TDF 25 g/day. The test diet consisted of refined wheat bakery products, high in soluble fiber and fruits and vegetables. TDF TSF Bakery diet 25 g 9 g Baseline diet 25 g 3 g	No significant decrease in serum cholesterol on bakery diet; 8 had ↓TC; 2 had ↑TC. Significant (8%) ↓ in LDL. No significant change in the LDL/HDL ratio from control period.	Total fat was controlled but the P/S (poly-unsaturated fat/saturated fat ratio) increased somewhat in the bakery diet. Short time allowed for end-point measures to stabilize to the base diet; the subjects showed a ↓ in TC and ↓LDL during the 7-day control period. Constant body weight maintained by adjusting energy intake.
Anderson et al., 1991 (Ref. 3)	Intervention, randomized, controlled, metabolic ward study	21 men*, ages 38-73 years: hypercholesterolemic (total serum cholesterol: 190 to 347 mg/dL). Body mass indices less than 28.7; no medication for hypercholesterolemia. 1 subject failed to complete study. *14 men had hypertension, CHD, or CVD	Subjects consumed "typical" American diet for 7 days as a baseline (control), then randomized to oat bran (110 g oat bran/day) or wheat bran (40 g wheat bran/day) diets for 21 days; control and treatment diet identical in energy content, and nutrients, differing only in soluble fiber soluble fiber (oat bran) and insoluble fiber (wheat bran). Baseline diet: 41% of kcals from fat, 16% protein, 43% from carbohydrate, 450 mg cholesterol, 14 g/day TDF, 3 g/day SF. Brans were incorporated into muffins and cereals. TDF SF (bran) TSF (diet) g/day Baseline diet 14 5-6 Oat bran 34 7.6 13.4 Wheat bran 34 1.3 7.8	TC % LDL % HDL % OB ↓12.8* ↓12.1* ↑7.4 WB ↓4.4 ↓5.5 ↓3.1 *significant from baseline There was no change in the LDL-HDL ratio in OB group. No effect on HDL in either group.	Authors state the purpose of their study is to compare the effects of soluble fiber (from OB) and insoluble fiber (from WB) keeping TDF constant. Significant weight loss in both groups (about 1 kg from control values).

TABLE 1--CONTINUED

Study	Study Design	Subjects	Methods	Results	Comments
Aro et al., 1984 (Ref. 9)	Intervention, double blind, crossover with placebo	14 men, ages 30-64, free living; severely hypercholesterolemic (301-402 mg/dL) and hypertriglyceridemia	Study designed with two 12-week crossover periods with an initial 4-week period on placebo diet and a 4-week washout between test periods. Subjects consumed normal diet (not defined); no dietary records were kept. Guar gum granules were mixed with water and taken before means; same for placebo. Placebo - wheat flour prepared similar to guar. Guar gum, 15 g/day (estimated 10.5 g soluble fiber) was added to baseline diet; it was consumed in 5-gram doses, after mixing with water, before the 3 main meals.	Guar gum: TC ↓ significantly after 6 weeks (15.3%) and by 8.2% between weeks 6 and 12 as compared to baseline. Most of the ↓ was in LDL (22% after 6 weeks and 14% after 12 weeks). Significant ↑ in mean TC from 6 to 12 weeks of guar gum supplementation. LDL/HDL ratio significantly lower in guar than placebo group. Placebo group experienced ↓ in LDL over the 12 weeks. No significant difference in TC and LDL between treatment and control after 12 weeks.	Weight maintained during the study; no dietary information given; no information on TDF or total SF intakes. Authors reported good compliance. The authors suggest that the attenuated effect of guar over time may reflect compensatory mechanisms in the body.
Beling et al, 1989 (Ref. 10)	Intervention, randomized, controlled	351 men and women, ages 20-60, hypercholesterolemic (total serum cholesterol between 200 and 300 mg/dL); not greater than 50% ideal body weight. 433 enrolled; 351 completed; attrition rates for groups 1,2, & 3 were 17%, 15%, and 24%, respectively. Major reason for attrition was inability to attend classes.	This was an 8-week study with 3 groups: Group 1: no dietary change Group 2: Step I diet, which was introduced during the first 4 weeks of the study and continued for 8 weeks Group 3: Step I diet, which was introduced during the first 4 weeks of the study, plus 2 oz oat cereal, which was added for weeks 5 through 8. Oatcor™, a concentrated oat bran cereal, was provided in 2 packets (1 oz each) to be consumed as a snack or cereal. The oat bran provided 10.6 g total dietary fiber per day; 7-8% total beta-glucans by weight. Group / % kcal - SFA (0 / Tx) 1: 12 / 10-11 2: 11 / 6 3: 12 / 7 (SFA = saturated fatty acids) % kcal - fat (0 / Tx) 1: 38 / 34-36 2: 34 / 23 3: 37 / 25-26 Total Dietary Fiber (0 / Tx) 1: 12 / 12-14 2: 12 / 18-19 3: 9 / 15-16	Total Serum Cholesterol (% Change from baseline) Group / 4 wks / 8 wks 1: ↓2 / ↓2 2: ↓10 / ↓8 3: ↓12 / ↓12 LDL - cholesterol (% change from baseline) 1: ↓3 / ↓5 2: ↓11 / ↓10 3: ↓12 / ↓15 HDL - cholesterol (% change from baseline) 1: ↓1 / ↓1 2: ↓6 / ↓3 3: ↓8 / ↓8	Variable weight loss by treatment: group 1: 2 lbs; group 2: 4 lbs, and group 3: 6 lbs. There was no data on soluble fiber in diets. Not everyone responded similarly; both positive and negative responders and variation in magnitude of effect within treatment groups. Study was unblinded.

TABLE I--CONTINUED

Study	Study Design	Subjects	Methods	Results	Comments
Bell et al., 1989 (Ref. 11)	Intervention, randomized, double blind, placebo controlled, parallel	75 men and women, 50th-90th percentile cholesterol (mean for placebo group was 162 mg/dL; for test group, 207 mg/dL); free living	This was a 20-week study with 12 weeks on step 1 diet, followed by 8 weeks of test fiber or placebo (cellulose). Psyllium (Metamucil powder) (3.4 g/meal) was taken 3 times a day before meals. Dietary intake was assessed with 3-day food records at weeks -6, 0, 8 and 16. <u>Step 1 Diet:</u> Fat 27-38% kcals SFA 7-10% kcals Cholesterol 160-200 mg/day T. Dietary Fiber 19-22 g/day Soluble Fiber 6 g/day Psyllium provided an estimated 8-9 g soluble fiber.	TC ↓4.2% (S) from baseline and ↓4.8% (S) from placebo; LDL ↓7.7% from baseline and ↓8.2% (both S) from placebo. LDL/HDL ratio: ↓10% from placebo and baseline (S). 30 subjects continued the intervention for 8 more weeks. Total and LDL cholesterol in the psyllium group tended to increase during the additional 8 weeks in both groups. TC values ↑ above baseline in placebo group; test group: TC ↑ but was still 7.7% lower than the placebo, but only 1.5% lower than baseline.	Psyllium was given as an adjunct to the diet, not in food form. Step 1 diet did not lower serum cholesterol significantly different in baseline TC values. Long term effectiveness remains a question based on evidence in this study of ↑ cholesterol during weeks 8-16 on psyllium. Both TC and LDL values ↑ above baseline in the placebo group; in test group TC ↑ and was only 1.5% lower than baseline, LDL ↑ and was 5% lower than baseline. Compliance was excellent in both groups.
Bell et al., 1990 (Ref.12)	Intervention, randomized, double-blinded, controlled	58 men; 24-69 years old; free living; with mild to moderate hypercholesterolemia (mean range 227-229 mg/dL)	Subjects consumed a Step 1 diet for 6 weeks; then randomly assigned to pectin-enriched, psyllium-enriched cereal, or corn flakes (control) groups for additional 6 weeks. Three-day dietary intake records taken at -6, 0, and +6 weeks. Cereals were added to Step 1 diet. NCEP step 1 diet: 30% kcals as fat, 55% carbohydrates, 15% protein; approx. 200 mg/day cholesterol. Total Dietary Fiber <u>Baseline</u> <u>Week 6</u> <u>g/ day</u> Placebo 22 19 Pectin 21 16 Psyllium 23 22 Total Soluble Fiber <u>Baseline</u> <u>Week 6</u> <u>g/day</u> Placebo 7 6 Pectin 8 6 Psyllium 8 8	Total Cholesterol Diet Phase / Cereal Phase % from <u>baseline</u> / % from <u>diet phase</u> Placebo ↓ 4 ↑ 0.4 Pectin ↓ 4 ↓ 2 Psyllium ↓ 3 ↓ 6 * * significant from baseline and placebo LDL - cholesterol Diet Phase / Cereal Phase % from <u>baseline</u> / % from <u>diet phase</u> Placebo ↓ 4 ↓ 0.4 Pectin ↓ 5 ↓ 4 Psyllium ↓ 4 ↓ 6 * HDL - cholesterol Diet Phase / Cereal Phase % from <u>baseline</u> / % from <u>diet phase</u> Placebo ↓ 6 ↑ 2 Pectin ↓ 6 ↑ 3 Psyllium ↓ 4 ↓ 2	Excellent compliance reported. Dietary intakes were approximately same among groups, except for total dietary fiber. No change in weight.
Burr et al., 1989 (Ref.13)	Intervention on effects of diet on secondary prevention of myocardial infarction (MI), randomized, controlled	2,033 men, all recovered from MI; mean age 56 years; free living	A 2-year study. Three groups: (1) advice given to ↓ fat intake to 30% of calories and ↑ the P/S ratio to 1.0; (2) advice given to ↑ fatty fish intake to 2 servings/week; (3) advice given to ↑ cereal fiber (not defined) to 18 g/day. Cereal fiber intake in group 3 was twice that in subjects not given fiber advice. Normal diet of subjects was not defined.	No significant difference in total mortality between those given fiber advice and those not given fiber advice. No significant changes in serum cholesterol attributable to fiber advice.	Fiber is not separated into soluble and insoluble components; no assessment of confounding factors, including intakes of other nutrients (e.g., SFA), was provided.

TABLE I--CONTINUED

Study	Study Design	Subjects	Methods	Results	Comments
Davidson et al., 1991 (Ref. 15)	Intervention, randomized, single-blinded, controlled. Purpose to evaluate the effectiveness of soluble fiber fraction, beta-glucan, in lowering serum cholesterol.	156 men and women, aged 30-65, randomized; 148 completed; free living hypercholesterolemic (230-319 mg/dL) with multiple risk factors. Data from only 140 were used, 8 dropped because of lack of compliance. Dropouts: placebo (3), OB-56 (2); OM-28(1); OM-84(1), and OB-84(1).	NCEP Step 1 diet given 8 weeks before randomization to test diet and during the test period. 6 weeks of intervention with oatmeal (OM)or oat bran (OB) in 28 g, 56 g or 84 g servings. 28 g farina as a control. After intervention 6 weeks of follow-up with no supplementation. Step 1 diet: fat: <30% kcal SFA: <10% kcals Groups IDF TSF OM 28 g 16 6 OB 28 g 17 6 OM 56 g 14 5 OB 56 g 20 7 OM 84 g 19 7 OB 84 g 22 7 Farina 28 g 15 0 4-day food records at baseline, week 3,6,12.	Group g. β Glu % TC % LDL 1. OM 28 1.2 -3.9 -5.8 2. OB 28 2.0 -2.7 -4.7 3. OM 56 2.4 -2.7 -3.5 4. OB 56 3.6 -9.5* -15.9* 5. OM 84 4.0 -7.1* -10.1* 6. OB 84 6.0 -6.9* -11.5* 7. FA 28 0.0 +0.6 +0.6 OM=oatmeal OB=oat bran FA=farine Glu=glucan * Only these changes are significantly different from baseline. The groups showed a decrease in total cholesterol and LDL at the higher levels of oat intake.	Lacked control group for each level of oats consumed. Body weight were stable.
Demark-Wahnefried et al., 1990 (Ref. 16)	Intervention, randomized	81 men and women, 20-65 years, hypercholesterolemic (mean of 271 mg/dL), free-living: 13 dropped out.	12 weeks of intervention on oat bran or processed oat bran cereal. Individuals given oat bran (OB) supplements, OB cereal, and a recipe book for fat-modified diets. One group consumed regular diet and did not get recipes. 50 g oat bran per day (estimated 3.7 g soluble fiber) as add-on to test group. 50 g OB and 42.5 g processed cereal had same amount beta-glucan. Diets: Group 1: low fat, low cholesterol diet Group 2: low fat, low cholesterol diet plus 50 g OB Group 3: regular diet plus 50 g OB Group 4: regular diet plus 42.5 g processed oat bran	Although there was a significant drop in serum cholesterol with all groups, there was no significant difference in the final serum cholesterol between any of the four groups. The low fat, low cholesterol control diet alone had the most marked drop in cholesterol (↓17%) from baseline.	Drop out rate is very high (16%). The study size is small; power to detect changes between groups is limited. Variable weight loss among group with the group consuming low fat diet plus oat bran experiencing the greatest weight loss (4-5%). Calorie intake varied from a mean of 1600 Cal/day for low fat, low cholesterol diet to 1900 Cal/day for oat bran. % changes from baseline in saturated fatty acids ranged from 22% for OB group to 51% for low fat, OB group.
Glassman et al., 1990 (Ref. 18)	Intervention	36 children with type IIa cholesterolemia (mean of 257.0 mg/dL).	8 months on Step 1 diet (10% kcals from SFA) (n=14); 1 month washout period, then 8 months on NY Medical Center modified saturated fat diet (fat 10% of kcals) and added soluble fiber from psyllium (PSY) (n=36). PSY was mixed with water twice a day. Children age 7 and older consumed 10 g psyllium (8-9 g soluble fiber estimated) per day; younger children consumed 2.5 g/day (estimated 2-2.5 g SF).	Total cholesterol and LDL ↓ significantly (18% & 23%, respectively) in test group on NY diet with psyllium. Total cholesterol and LDL decreased 6.7 & 8.8% (NS) on step 1 diet for the same duration. Nine obese children lost weight (2.8 kg).	Primary type IIa cholesterolemia is an inherited condition which causes extremely high serum cholesterol levels in children through a metabolic error in the breakdown of cholesterol. The study is not blinded, and there is no placebo.

TABLE I--CONTINUED

Study	Study Design	Subjects	Methods	Results	Comments
Gold and Davidson, 1988 (Ref. 19)	Intervention, double blind	72 male and female medical students; 25-37 yrs old; free-living; normal cholesterol (mean 178 mg/dL)	This was a 4-week intervention study. Subjects consumed 2 muffins/day that contained test fibers (muffins were provided) along with their regular diet. 3-day food records were submitted. Subjects randomized into 3 groups and received muffins made with either oat bran, wheat bran, or a wheat/oat bran combination. Added soluble fiber (S.F.) and dietary fiber (D.F.) from muffins: S.F.* D.F. g oat bran 2.5 5.0 oat/wheat 0.9 5.3 wheat bran 0.33 5.5 *estimated	Oat bran: TC ↓5%* and LDL ↓9% *significant from baseline S.F. from combined oat/wheat and wheat: TC no change; LDL no significant decrease.	No assessment of the dietary intake before or during the test period. No data on total dietary fiber or total soluble fiber intakes in baseline and treatment diets.
Kahn et al., 1990 (Ref. 25)	Intervention, randomized, controlled.	16 men and women, age 51-54, hypercholesterol-emic (215-314 mg/dL); some were diabetic. Free living	One group began immediate intervention on oat bran for 3 weeks; other group was the untreated control for 3 weeks, then they started the intervention for 3 weeks. This was followed by a 6-week washout period during which blood samples were taken. Test subjects consumed 80 g oat bran (estimated 6 g soluble fiber) per day, added to the diet as oat bran muffins (4 per day). Each muffin provided 112 Calories and 20 g oat bran. Subjects' usual diets were not assessed.	All groups, including the control group, had ↓ TC but there was no significant change in serum cholesterol values when the test group was compared to the control group. Results showed a significant ↓ in total cholesterol by 8% and LDL cholesterol by 10% from baseline when individual values were examined.	No dietary assessment before or during test. Subjects experienced some weight loss.

TABLE 1--CONTINUED

Study	Study Design	Subjects	Methods	Results	Comments
Keenan et al., 1991 (Ref. 26)	Intervention, randomized, controlled, double blind with crossover	145 men and women, ages 20-70; free living; hypercholesterolemic (207-267 mg/dL). 15% dropout after randomization.	Study designed with 3 periods (6 weeks each period): period 1: step 1 diet; periods 2 & 3: test periods. Test products were provided. 3 groups: control, wheat, and oat. The control group consumed step 1 diet for entire study period. 4-day food records were collected in week 5 of each period; baseline dietary intake taken by self-administered food frequency questionnaire. Step 1 diet: fat calories: <30% SFA calories: <10% Cholesterol: 240 mg/day 2 ounces of oat bran cereal and 2 ounces of ready-to-eat wheat cereal were test fibers. Oat bran: (3 g SF/day); Wheat cereal (1 gram SF/day)	Total cholesterol and LDL decreased in all groups during step 1 period (↓2.5-4%). Oat-wheat group had a further ↓ in TC of 2% (NS) on oat cereal, followed by a 6% ↑ in TC on wheat cereal. The wheat-oat group had no change in TC on wheat and a 3% decrease on oat. Control group had significant increase in TC back to baseline during test periods. Women under 50 found resistant to oat bran intervention. Control — TSF g/day — % Change in TC* Step 1 — 6.8 — ↓2.5-4 Step 1 — 6.2 — + Step 1 — 6.0 — + Oat-Wheat Step 1 — 6.7 — ↓2.5-4 Oat — 7.7 — N.S. Wheat — 6.1 — ↑ 6 Wheat-Oat Step 1 — 5.8 — ↓2.5-4 Wheat — 6.0 — N.S. Oat — 7.4 — ↓ 3 *Compared to beginning of respective treatment period.	Placebo was needed for diet only group. Control group initially dropped TC and then returned to baseline making it difficult to use as a control. Variability among groups in serum cholesterol levels at beginning of treatment periods.

TABLE I--CONTINUED

Study	Study Design	Subjects	Methods	Results	Comments
Kesaniemi et al, 1990 (Ref.27)	Intervention, randomized, self-controlled, crossover	34 men, free living, normal serum cholesterol (223-238 mg/dL). Helsinki, Sweden; 3 were mildly hypertensive, 3 had gallstones, 1 had history of myocardial infarction, and 1 had maturity onset diabetes mellitus.	Purpose of study to evaluate cholesterol metabolism on high and low mixed-fiber diets. A 16-week study: 8-week low fiber period and an 8-week high fiber period. Diets for both groups were self selected. High fiber diet consisted of unpurified corn products, fruits, vegetables, salads, berries, fiber-cereal (made with oat flakes and guar gum and pectin) and graham biscuits (fortified with bran and carrots). Low fiber diet: avoid eating unpurified cereal products, vegetables, salads, fruits and berries. Low fiber period: 11.6 g per day mean intake total fiber (3 g of which is viscous fiber) High fiber period: 26.2 g per day mean intake total fiber (12.8 g of which is viscous fiber) 7-day food records were kept during week 8 of study.	High fiber diet: TC ↓5%, HDL ↓8% and LDL ↓7%. (all statistically significant)	Dietary intakes of total carbohydrate, energy and protein intake were lower on high-fiber diet. Fat intake did not differ significantly between the groups, but the high fiber diet did contain less total fat, with a higher polyunsaturated to saturated ratio. The high fiber group consumed significantly higher levels of vegetables, cereal, fruits, and berries, compared to the low-fiber group.
Kestin et al., 1990 (Ref. 28)	Intervention, randomized, double blind, controlled with crossover. Purpose to compare separate effects of three cereal brans (wheat, rice, oat) on plasma lipids	24 men, 29-61 years, mild to moderate hyper-cholesterolemia (186-293 mg/dL)	3-week control period prior to test; 4 weeks on each of 3 test diets; no washout. Test fibers, oat bran, wheat bran, rice bran, were provided as bread and muffins; control - low fiber white bread. Fiber supplements were added to individual's normal diet. **Test fibers:** Oat bran: 95 g/d; 5.8 g of soluble fiber per day. Rice bran: 60 g/d; 2.9 g of soluble fiber per day. Wheat bran: 35 g/d; 2.6 g of soluble fiber per day. **Base diet:** % fat calories: 31-37 % SFA calories: 12-13 Cholesterol: 250-300 mg/day TDF: Baseline: 11.2 g/day Test diet: 21 g/day SF: OB diet: 10.3 g/day RB diet: 7.2 g/day WB diet: 6.8 g/day Baselin: 5.7 g/day	Oat bran diet: TC ↓ 5% (significant) compared to baseline. The decrease was mainly in the LDL fraction; HDL increased from baseline in all bran diets. Rice and wheat brans did not cause significant lowering.	The amounts of soluble fiber and insoluble fiber in the three test diets were varied while total fiber was held constant. The oat bran group had higher soluble fiber than the rice, wheat or baseline.

TABLE I--CONTINUED

Study	Study Design	Subjects	Methods	Results	Comments
Lampe et al., 1991 (Ref. 35)	Intervention, controlled, crossover	34 men and women (college students), normal cholesterol; free-living; mean age 27.1 years	Three fiber types (wheat bran, vegetable fiber, sugar beet fiber) were supplements to a controlled liquid base diet for three weeks each, with ≥10-day washout between test periods. Fibers were provided as breads and cereals. Base diet: liquid formula diet providing 35-37% of kcals as fat; 12-14% kcals as saturated fat; 558 mg cholesterol/day; fiber free. Wheat bran: 10 g and 30 g/day (1.1 g and 2.6 g soluble fiber (SF), respectively) Vegetable fiber: 10 g and 30 g (2.7 g and 5.2 g SF) Sugar beet: 30 g (8.2 g SF)	change from baseline TDF / SF (g/day) / %TC Fiber free: 2 / 1 / ↓3 10 g WB: 11 / 1 / ↓4 30 g WB: 29 / 3 / ↓1 10 g VF: 15 / 3 / ↓4 30 g VF: 37 / 5 / ↓8* 30 g SBF: 30 / 8 / ↓14* WB = wheat bran; VF = vegetable fiber SBF = sugar beet fiber *Statistically significant Changes in LDL were similar.	Effect of fiber in a liquid base diet may not reflect fiber effect in regular foods. SFA and cholesterol intakes were higher on fiber free than test diets. Short test periods.
Levin et al., 1990 (Ref. 37)	Intervention, randomized, double blind	58 men and women, 21-70 years old, free living; mildly hypercholesterolemic (235-245 mg/dL)	8 weeks of diet therapy on a step 1 diet (25% kcals as fat; P:S 1.0; cholesterol <200 mg/day, TDF 21-23 g/day; TSF 6.5-8.5 g/day) followed by 16 weeks treatment with psyllium (Metamucil) or cellulose as placebo. PSY or cellulose were consumed in fluids twice a day before meals. TSF in PSY (10.2 g/day) group an estimated 15 g/day.	Psyllium diet: TC ↓6% and LDL ↓9% (both significant) from baseline; placebo group, no change.	The psyllium group showed a small drop (not statistically significant) in dietary fat intake, while the placebo showed no change. There was some weight loss in the psyllium group. Subject compliance was 95%.
Little et al., 1990 (Ref. 42)	Intervention, controlled	184 men, ages 58-61; free living, treated for hypertension and hypercholesterolemia (240-267 mg/dL)	8-week intervention with five groups: Group 1: no dietary change Group 2: high fiber Group 3: low sodium Group 4: low fat (25% cal) Group 5: low fat, high fiber Fiber was not defined. Total dietary fiber, including soluble and insoluble, was 40-45 g/day.	Low fat diet: TC ↓4.7% (S) compared to baseline; Combination low-fat, high fiber diet: TC ↓4.1% (S) compared to baseline; LDL was not ↓ significantly in either diet group and TC lowering for these two groups were not different from each other. High fiber diet: TC ↑1% (NS).	Changes in serum cholesterol were same for low fat diets and for low fat and high fiber diet. Authors suggest low fat was the effective nutrient.

TABLE I--CONTINUED

Study	Study Design	Subjects	Methods	Results	Comments
Lo and Cole, 1990 (Ref. 43)	Intervention, randomized, double blind, crossover	12 men, 8 women ages 27-60; free living; normo- and hypercholesterol-emic (210-279 mg/dL)	12-week study: two 6-week test periods with additional 3-week rest between periods. Soy cotyledon fiber, made into cereal and bread, was supplemented in 3 divided portions to the subjects' normal diet. Soy: 15 g dietary fiber: 4.3 g of soluble fiber and 13 g of insoluble fiber per day placebo supplements: 4-5 g dietary fiber, 1.2 g soluble fiber, 3 g insoluble fiber. Dietary intake assessed from 3-day dietary records. Diets — Placebo — Soy % kcals fat — 32 — 36 Cholesterol — 290 mg — 270 mg TDF — 13 g — 24 g	After first 6 weeks: Soy group: TC ↓8% (S), LDL ↓7% (S). Placebo group: TC ↓2%, LDL ↓5% (S). After crossover, subjects on soy had a non-significant reduction of cholesterol. The greatest cholesterol reduction occurred within the first six weeks.	This study has a placebo group, is double-blinded and randomized. Fat intake in the two groups were borderline significantly different; neither the saturated nor polyunsaturated intakes are measured. The authors did not keep total dietary fiber constant between the groups. Results varied by order of treatment.
McIntosh et al., 1991 (Ref. 44)	Intervention, randomized, crossover; purpose - to compare barley vs wheat foods and their influence on serum cholesterol levels.	21 men, aged 30-59; free living, mild to moderately to high cholesterol (209-270 mg/dL); South Australia	3-week baseline period followed by 4 weeks on each diet. No washout between test periods. Barley and wheat foods were provided. Barley (high in β-glucan) was tested against wheat; dietary intake assessed from 24-hour recall every third day throughout study. Barley diet: 38 g DF, 13 g SF, 25 g insoluble fiber (IF), 8 g β-glucan. Wheat diet: 38 g DF, 13 g SF, 25 g IF, 1.5 g β-glucan. Base diet: 31-35% kcals as fat, 25-26% kcals as saturated fat, P/S 1.6. TDF: 21 g/day; SF: 7 g/day.	Compared to baseline: barley: ↓TC about 2% and LDL ↓1% (both NS); wheat: TC ↑4% and LDL ↑6%. The group consuming barley during the first test period had no difference in serum total cholesterol, then a small increase in cholesterol on wheat. Those consuming wheat first, then barley showed increased serum total cholesterol, then decreased cholesterol on barley.	The authors, in their analysis, controlled statistically for the P/S and fibers. Results difficult to interpret since wheat was used as a control. Comparison to baseline cholesterol shows only a slight effect of barley on TC. The authors account for the difference in response between groups by suggesting that 4 weeks was too short a test period.
McIvor et al., 1985 (Ref. 45)	Intervention, controlled	8 men and women, obese, ages 45-50, with non-insulin dependent diabetes, free living; normal cholesterol (mean 222 mg/dL).	6-month intervention with gradual phase-in of guar gum within first 4-8 weeks. Guar gum added to subjects' normal diets in granola-type bars. Ss began with 1 granola bar/day and increased to 4 bars/day. These were eaten with meals. Control group consumed granola bars without guar gum; no dietary assessment of normal diet. Guar gum intake: up to 32 g/day (4.8 bars/day - each bar had 6.6 g guar gum and estimated 22 g SF).	After 6 months, serum total cholesterol was not significantly different from baseline. LDL and HDL components were not discussed.	Diet was not monitored.

TABLE I--CONTINUED

Study	Study Design	Subjects	Methods	Results	Comments
Newman et al., 1989 (Ref. 50)	Intervention, randomized, single blind; purpose - to compare barley with wheat sources of fiber.	14 men, 35 years or older, free living, normal serum cholesterol 141-247 mg/dL	4 weeks of pretreatment with normal diet (see below) followed by 4 wks of test. Cereal and baked goods containing hulless barley (10% β-glucan) were provided for high fiber, high β-glucan group. Cereal and baked goods containing 75% wheat flour/25% wheat bran (0.5% β-glucan) for low fiber, low β-glucan group. 3-day dietary history recorded last 3 days of study. Pre-treatment diets Groups: Wheat / Barley % fat kcals: 35 / 42 TDF, g: 7.6 / 4.9 Final diets % fat kcals: 34 / 35 TDF, g: 46.4 / 44.0	The wheat group had a significantly higher total cholesterol and LDL at the end of the study than at the beginning. The barley group showed no significant change from the beginning to the end of the study.	Total fat intake was significantly different between the groups initially. Over the course of the study, there is a large ↓ in the test group's fat intake, and no change in the wheat group.
Shutler et al., 1989 (Ref. 53)	Intervention, randomized, self-controlled, not blinded	13 non-smoking men, 18-26 years old; free living; normal cholesterol (mean of 196 mg/dL)	A 42-day study: 2 weeks test with canned beans added to normal diets, followed by a 3-week wash-out period, then a 14-day control with spaghetti, followed by subjects' regular diets for 20 or more days. Beans: 1 can (450 g) per day (soluble fiber not assessed); Spaghetti: 1 can (440 g) per day. 3-day food diary kept for the pre-trial, bean, and spaghetti periods. Diets: Baseline / Beans / Spag. % fat kcals: 36 / 31 / 33 P:S: 0.4 / 0.4 / 0.4 Chol, mg: 290 / 208 / 174 TDF, g: 25 / 60 / 24	Test group, while eating beans: TC ↓12% (S); and HDL ↓15% (S) compared to baseline. After a washout period, the same group, substituting spaghetti for beans showed no effect in cholesterol reduction compared to baseline.	Sat. fat and PUFA (polyunsaturated fatty acids) changes in intake during the test periods were similar. No data on soluble and insoluble fibers. Short test period is a limitation of study.
Stewart et al., 1991 (Ref. 55)	Intervention	Test: 175 men and women, mean age 77 years. Treatment group was selected from ambulatory elderly participants attending a health screening and who had been using psyllium as a laxative or stool softener for at least 1 month. The control group consisted of 741, mean age 75, and was selected from program participants not using psyllium.	The test participants had to be taking psyllium (PSY) for at least one month to one year. The intake of PSY varied from less than 9 g (soluble fiber estimated at 7-8 g) per day to over 19 g (SF estimated at 15-17 g) per day. The regular diet of the participants was not assessed.	Those taking greater than 15-17 g of soluble fiber from psyllium per day had a ↓4.1% in TC (significant). Those taking less than 8 g of soluble fiber from psyllium had no significant change in TC. Comparing taking any amount of psyllium to taking none, did not show a significant difference. intake of PSY was significantly correlated with change in serum cholesterol.	Some selection bias may have occurred since the test group included only regular users of bulk laxative and the control group only regular non-users. The quantity of the psyllium test intake was not controlled. Treatment group were older than controls (77 vs 55 years).

TABLE I--CONTINUED

Study	Study Design	Subjects	Methods	Results	Comments
Superko et al., 1988 (Ref. 56)	Intervention, randomized, single blind with crossover	50 men; aged 39-63; free living; mild to moderately hypercholesterolemic (205-282 mg/dL)	An 8 week study with 3 groups: test group consumed medium-viscosity guar gum (liquid or solid form) for 4 weeks on one diet, then crossover to other form of guar for 4 weeks. Second group: high viscosity guar - consumed in solid form for 4 weeks only. Control group consumed placebo for 8 weeks. Diet was self-selected except for fiber supplements and placebo. Guar gum intake: 15 g/day, (estimated soluble fiber of 10.5 g/day). Placebo intake: 15 g/day. 4-day dietary records were obtained at baseline and at end of each test period.	At 4 weeks: Medium viscosity guar group TC ↓10% (S) and LDL ↓14% (S) from baseline. High viscosity guar group TC ↓15% (S) and LDL ↓18% (S) from baseline. Placebo group TC ↓4% from baseline (NS) and ↓7% drop in LDL (NS). At 8 weeks: the guar groups' total cholesterol levels increased during the second half of the study. Net effect over the 8 weeks of the study: a NS difference between guar groups and the placebo.	Study is blinded and fat intake was measured and assessed for differences between groups. Results differed between the first 4 weeks and the second 4 weeks of guar-supplemented diets making it difficult to draw conclusions about the effect of guar gum on serum cholesterol.
Swain et al., 1990 (Ref. 57)	Intervention, randomized, double blind, crossover	4 male, 16 female hospital employees; 23-49 yrs old; free-living; normal cholesterol: mean 185 mg/dL	6-week test period followed by a 2-week washout, then crossover to other diet for 6 weeks. Oat bran and wheat bran were fiber sources added to subjects' regular diets. Dietary intake assessed with food frequency questionnaire; 4-day food records kept during 5th test week of each test period. Oat bran: 15 g soluble fiber (S.F.)/day Wheat bran: 3.7 g S.F./day Base diet Fat: 31% of kcals; high fiber period had 35% kcals as fat, which came from unsaturated fat in oat bran supplements. Authors contend the additional fat does not affect serum cholesterol.	High fiber: total serum cholesterol (TC): ↓7.5%*+; LDL: ↓9.1%*+ Low fiber: TC ↓7.1%*+; LDL: ↓6.4%*+ *significantly lower from baseline +no difference between groups Authors proposes that substitution of either wheat or oat fiber for dietary saturated fat causes the decrease in TC.	No placebo. Study results limited by small number of subjects and short test period.
Taneja et al., 1989 (Ref. 58)	Intervention, controlled crossover	11 Indian girls, 16-18 years old; free living, normal cholesterol (mean 182 mg/dL)	A 6-week study: 3 weeks on low fiber foods; 3 weeks on high fiber foods. Controlled low fiber diet: refined cereals, dehusked pulses, potatoes, milk, curd, eggs, low fiber vegetables. High fiber diet: same diet with added isagbol husks. Isagbol husks - 25 g (estimated 20-22 g SF) per day.	Higher fiber diet: TC significantly lower (↓7%) compared to low fiber diet. LDL and HDL components are not discussed.	The initial TC levels of each group are not reported. In addition, the fat intake is lower in the high fiber group, and soluble and insoluble components of the isagbol husk diet are not reported.

TABLE I--CONTINUED

Study	Study Design	Subjects	Methods	Results	Comments
Tuomilehto et al., 1988 (Ref. 59)	Intervention, placebo-controlled, crossover	23 men and women, 37-67 years, free living; severely hypercholesterolemic (range 309-553 mg/dL); 4 had type II diabetes, 8 had hypertension, five had familial hypercholesterolemia.	A 1-year study: 1 month placebo period at start, followed by 50 weeks of test with guar gum, then 4 weeks of placebo period. Subjects told to mix guar gum granules with water and take before a meal or mix granules with food. Placebo: granulated wheat flour consumed the same as guar. Guar and wheat granules were added to Ss normal diet (not defined). <u>Guar gum</u>: 15-30 g/day (estimated 10.5-21 g soluble fiber) <u>Wheat flour</u>: 15 g/day Dietary intake monitored by food diary for 4 days before test period and at weeks 17 and 33.	Maximum TC ↓18% (S) after 8 weeks; then ↑ to a final TC level (347 mg/dL) significantly lower (10.5%) than baseline. During final placebo month, serum cholesterol ↑ to pretreatment level. Higher intakes of soluble fiber (14-21 g/day) from 20-30 g guar were not well tolerated. At 34 weeks: LDL ↓15% (S).	Subjects had severely high TC and many with other medical problems. There was some weight loss (4.4 lbs) which was not statistically significant, but must be considered when interpreting the results. Diet was not defined, nor was soluble fiber intake defined.
Van Horn et al., 1988 (Ref. 68)	Intervention, randomized, controlled with crossover	236 men and women, ages 30-65, free living; normo-cholesterolemic (163-247 mg/dL)	A 12-week study: 4 weeks on control diet and 8 weeks on test diet. Both test and control groups consumed the Phase II American Heart Association (AHA) diet throughout the study. The test group consumed 56 g oatmeal/day for for 8 weeks. <u>Phase II AHA diet</u>: total fat: ≤ 30% calories; equal distribution among saturated, mono-unsaturated, and poly-unsaturated fatty acids. Dietary cholesterol: 250 mg/day. 56 g per day oatmeal: 8.4 g dietary fiber and 4.2 g of soluble fiber.	Serum cholesterol levels at baseline and after 4 weeks on the AHA diet were similar for both groups. <u>After 4 weeks:</u> test group had significantly lower serum cholesterol than control group. <u>After 8 weeks: no</u> significant difference in total serum cholesterol between groups. Changes in LDL paralleled changes in total cholesterol. Similar and nonsignificant increases occurred in HDL in both groups. Subgroup analysis showed that subjects in test group with highest baseline serum cholesterol had greater reductions in cholesterol. No change in LDL. The low fat diet was effective in lowering serum cholesterol	No beneficial effect of soluble fiber from oatmeal on serum cholesterol after 8 weeks.

TABLE I--CONTINUED

Study	Study Design	Subjects	Methods	Results	Comments
Van Horn et al., 1991 (Ref. 65)	Epidemiological cross sectional survey	5,111 men and women, 18-30 years; normal cholesterol levels	3 diets: a) lower SFA, high PUFA; b) lower SFA and fish; c) lower SFA and cereal	Dietary fiber is inversely and significantly correlated with TC and LDL; and positively and significantly correlated with HDL in 25-30 year-old white women.	Dietary analyses did not assess soluble and insoluble components of dietary fiber. Also, the study did not control confounders such as smoking, alcohol use, exercise, or fat intake differences between groups. Single samples for cholesterol analysis could not correct for intraindividual variability. Statistical significance was not adjusted for multiple comparisons.
Van Horn et al., 1991 (Ref. 69)	Intervention, randomized, controlled	80 men and women, mild to moderate hypercholesterolemia (213-285 mg/dL)	Two groups: control group consumed regular diet; test group consumed regular diet plus instant oats (2 packets/day - 57 g). IDF SF Insol. F Oatmeal 5.6 g 2.2 g 3.4 g	The test group, while supplementing their diet with oatmeal: TC ↓6% (S); both the LDL and the LDL/HDL ratio ↓9%. The control group showed no change.	The study was not blinded; the test group reduced their intake of total fat, saturated fat and dietary cholesterol, and may have made other lifestyle changes.

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