DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 101

[Docket No. 96P–0338]

Food Labeling: Health Claims; Soluble Fiber from Certain Foods and Coronary Heart Disease

AGENCY: Food and Drug Administration, HHS.

ACTION: Proposed rule.

SUMMARY: The Food and Drug Administration (FDA) is proposing to authorize the use, on food labels and in food labeling, of health claims on the association between soluble fiber from psyllium husks and reduced risk of coronary heart disease (CHD). FDA is proposing this action in response to a petition filed by the Kellogg Co. (the petitioner). The agency has tentatively concluded that, based on the totality of publicly available scientific evidence, soluble fiber from psyllium husk, similar to beta (β)-glucan soluble fiber from whole oats, when included as part of a diet low in saturated fat and cholesterol, may reduce the risk of CHD by lowering blood cholesterol levels. Therefore, the agency is proposing to amend the regulation that authorized a health claim on soluble fiber from whole oats and the risk of CHD to include soluble fiber from psyllium husks.

DATES: Written comments by August 5, 1997. The agency is proposing that any final rule that may issue based upon this proposal become effective upon its publication.

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

FOR FURTHER INFORMATION CONTACT: Joyce J. Saltsman, Center for Food Safety and Applied Nutrition (HFS–165), Food and Drug Administration, 200 C St. SW., Washington, DC 20204, 202–205–5916.

SUPPLEMENTARY INFORMATION:

I. Background

The Nutrition Labeling and Education Act of 1990

On November 8, 1990, the President signed into law the Nutrition Labeling and Education Act of 1990 (the 1990 amendments) (Pub. L. 101–535). This new law amended the Federal Food, Drug, and Cosmetic Act (the act) in a number of important ways. One of the most notable aspects of the 1990 amendments was that they confirmed FDA's authority to regulate health claims on food labels and in food labeling.

In the **Federal Register** of January 6, 1993 (58 FR 2478), FDA adopted a final rule that implemented the health claim provisions of the act (hereinafter referred to as the 1993 health claims final rule). In that final rule, FDA adopted § 101.14 (21 CFR 101.14), which sets out the rules for the authorization and use of health claims. The agency also adopted § 101.70 (21 CFR 101.70), which establishes a process for petitioning the agency to authorize health claims about a substance-disease relationship (§ 101.70(a)) and sets out the types of information that any such petition must include (§ 101.70(d)). These regulations became effective on May 8, 1993.

In addition, FDA conducted an extensive review of the evidence on the 10 substance-disease relationships listed in the 1990 amendments. As a result of its review, FDA has authorized claims that relate to 8 of these 10 relationships.

In its review of the relationship between dietary fiber and cardiovascular disease (CVD), the agency reviewed all relevant scientific evidence on dietary fiber and its effects on serum cholesterol. The agency started by examining the conclusions and recommendations of the pertinent Federal Government reviews on this topic area: the 1988 ''Surgeon General's Report on Nutrition and Health'' (the Surgeon General's report) (Ref. 3) and the 1989 Food and Nutrition Board, National Academy of Sciences' (FNB/NAS) ''Diet and Health'' (Ref. 4). These two reports (Refs. 3 and 4) provided a comprehensive review of the role of a broad range of nutrients, including dietary fiber, in the development of a number of chronic diseases, including heart disease. Because the FNB/NAS and Surgeon General's report were done independently but concurrently, taken together, they provide an authoritative picture of the state of scientific opinion at the time that they were published in 1988 and 1989. Therefore, the agency began its review of the dietary fiber evidence with studies that had been published since 1988. This evidence included studies on all fibers and did not focus on any particular individual fibers. While the agency denied the use in food labeling of health claims relating total dietary fiber to reduced risk of CVD (58 FR 2552), it authorized a health claim relating diets low in saturated fat and cholesterol and high in fruits, vegetables, and grain products that contain dietary fiber (particularly soluble fiber) to a reduced risk of CHD, one of the most common, most frequently reported, and most serious forms of CVD.

In denying the dietary fiber and CVD health claim, the agency stated that it is difficult to determine the relationship between dietary fiber and heart disease because dietary fiber is a diverse group of chemical substances that may be associated with different physiological functions (58 FR 2552 at 2572). Chemically and physiologically, cellulose, lignin, hemicellulose, pectin, and alginate (all relatively purified fiber types) behave differently. Likewise, wheat bran, oat bran, and rice bran (all heterogeneous mixtures of fibers) are not similar in composition. The agency also noted that it is very difficult to chemically analyze dietary fiber components, and that, consequently, it is hard to correlate the role of specific fiber components to health effects.

Based on its review of numerous authoritative documents, including Federal Government reports and recent research on dietary fiber and CHD, and on its consideration of comments received in response to the proposed rule entitled ''Health Claims; Dietary Fiber and Cardiovascular Disease'' (56 FR 60582, November 27, 1991) (hereinafter referred to as the 1991 dietary fiber and CVD proposal), FDA concluded that the publicly available scientific evidence supported an association between diets low in saturated fat and cholesterol and high in fruits, vegetables, and grain products (i.e., foods that are low in saturated fat and cholesterol and that are good sources of dietary fiber) and reduced risk of heart disease (58 FR 2552 at 2572). The agency further stated that, although the specific roles of the numerous potentially protective substances in such plant foods were not yet understood, populations with diets rich in these foods experience many health advantages, including lower rates of heart disease. The agency noted, however, that there was no scientific agreement as to whether the observed protective effects against heart disease were the result of the combination of nutrient components of the foods, including soluble fiber; of the other components of soluble fiber-rich diets (for example, potassium and magnesium); of the displacement of saturated fat and cholesterol from the diet; or of nonnutritive substances in these foods.

For all these reasons, the agency stated that the fact that these foods contain dietary fiber, particularly soluble fiber, could serve as a useful marker for identifying those fruits, vegetables, and grain products that,

when added to diets low in saturated fat and cholesterol, may help in reducing blood low density lipoprotein (LDL)-cholesterol levels (58 FR 2552 at 2572). Thus, the agency authorized a health claim in § 101.77 (21 CFR 101.77) on the association between diets low in saturated fat and cholesterol and high in vegetables, fruit, and grain products that contain soluble fiber and a reduced risk of heart disease.

In the 1993 dietary fiber and CVD final rule, in response to a comment regarding the apparent hypocholesterolemic properties of specific food fibers, e.g., oats, FDA agreed that the effectiveness of naturally occurring fibers in foods may be documented for specific food products (e.g., oat brans meeting specified parameters) (58 FR 2552 at 2567). Further, the agency stated that if manufacturers could document, through appropriate studies, that dietary consumption of the soluble fiber in their particular food has the effect of lowering LDL-cholesterol, and has no adverse effects on other heart disease risk factors (e.g., high density lipoprotein (HDL)-cholesterol), they should petition for a health claim for their particular product.

In the **Federal Register** of January 23, 1997, FDA published a final rule on the relationship between soluble fiber from whole oats and reduced risk of coronary heart disease (the soluble fiber from whole oats final rule), § 101.81 (21 CFR 101.81) (62 FR 3584 and modified at 62 FR 15343, March 31, 1997). In that document, the agency concluded that the type of soluble fiber in whole oats, β-glucan soluble fiber, is the primary component responsible for the hypocholesterolemic properties associated with consumption of whole oat products as part of a diet that is low in saturated fat and cholesterol (62 FR 3584 at 3585). The agency based its conclusions on the totality of publicly available evidence, taking into account evidence showing that consumption of β-glucan soluble fiber from whole oats has the effect of lowering blood total- and LDL-cholesterol in both humans and animals (62 FR 3584 at 3586).

The agency also acknowledged the likelihood that consumption of β-glucan soluble fiber from sources other than whole oats, as well as that from certain other non β-glucan soluble fibers, will affect, as part of an appropriate diet, blood lipid levels (62 FR 3584 at 3587). Although the agency considered structuring the final rule as one on ''soluble fiber from certain foods'' and the risk of CHD to allow flexibility in expanding the claim to other sources of soluble fiber, it stated that it was premature to do so inasmuch as the agency had not reviewed the totality of evidence on other, non-whole oat sources of soluble fiber. However, FDA structured § 101.81 in a way that, while the regulation covered β-glucan soluble fiber from whole oats, would allow it to be amended as evidence becomes available to support the use of the claim for other sources of soluble fiber.

The present rulemaking is in response to a manufacturer's health claim petition on the relationship between soluble fiber from psyllium and the risk of heart disease.

II. Petition for Health Claim on Psyllium and Reduced Risk of CHD

A. Background

On June 12, 1996, the Kellogg Co. submitted a petition to FDA requesting that the agency authorize a health claim on the relationship between consumption of soluble fiber from psyllium (specifically from psyllium husks) and the risk of CHD (Ref. 1). On September 18, 1996, the agency sent the petitioner a letter stating that it had completed its initial review of the petition, and that the petition would be filed in accordance with section 403(r)(4) of the act (21 U.S.C. 343(r)(4)) (Ref. 2). In this document, the agency will consider whether a health claim on this nutrient-disease relationship is justified under the standard in section 403(r)(3)(B)(i) of the act and in § 101.14(c) of FDA's regulations. The following is a review of the health claim petition.

B. Preliminary Requirements

1. The Substance Is Associated With a Disease for Which the U.S. Population Is at Risk

The regulations authorizing claims on dietary saturated fat and cholesterol and risk of CHD (§ 101.75 (21 CFR 101.75)); fruits, vegetables, and grain products that contain soluble fiber and risk of CHD (§ 101.77); and soluble fiber from whole oats and risk of CHD (§ 101.81) establish that CHD is a disease for which the U.S. population is at risk. In adopting those regulations, FDA stated that CHD remains a major public health problem, the number one cause of death in the United States. Despite the decline in deaths from CHD over the past 30 years, this disease is still exacting a tremendous toll in morbidity and mortality (Refs. 3 through 5). There are more than 500,000 deaths each year for which CHD is an underlying cause, and another 250,000 deaths for which CHD is a contributing cause. About 20 percent of American adults ages 20 to 74 years have blood total cholesterol levels in the ''high'' category (total cholesterol greater than or equal to (≥) 240 milligrams (mg) per (/) deciliter (dL) or LDL-cholesterol ≥160 mg/dL) (Ref. 6). Another 31 percent have ''borderline'' cholesterol levels (total cholesterol between 200 to 239 mg/dL). Therefore, based on these facts as presented in §§ 101.75, 101.77, and 101.81, FDA tentatively concludes that the requirement in § 101.14(b)(1) has been met.

2. The Substance is a Food

Psyllium is a harvestable grain from plants of the *Plantago* genus (Ref. 1, p. 5–6). Different types of psyllium are available, depending on the growing region. It is primarily cultivated in France, Spain, and India, with some small quantities grown in the American Southwest. Psyllium husk (also known as psyllium seed husk), which comes from the dried coat of the psyllium seed, is used as a food or food component in a number of foods in the United States (Ref. 1, p. 9–11) and is the source of psyllium soluble fiber that is the subject of the petition. Psyllium husk is a concentrated source of soluble fiber and contributes certain technical effects (e.g., as a stabilizer) that are retained when it is consumed at levels necessary to justify the petitioned claim.

Therefore, FDA tentatively concludes that the substance satisfies the preliminary requirements of § 101.14(b)(3)(i).

3. The Substance Is Safe and Lawful

The petitioner has also submitted a petition requesting that FDA affirm that the use of psyllium husk in grain-based foods is generally recognized as safe (GRAS) (55 FR 4481, February 8, 1990). The agency notes that this GRAS affirmation petition (GRASP 0G0357) is still under review, and that authorization of a health claim should not be interpreted as affirmation that the petitioned uses of psyllium are GRAS. Such a determination can be made only after the agency has completed its review of the GRAS petition. A preliminary review of the GRAS affirmation petition, however, reveals that it contains significant evidence supporting the safety of the use of this substance at the levels necessary to justify a health claim.

In its GRAS affirmation petition, the petitioner relied heavily on the conclusions about the safety of psyllium by the Life Sciences Research Office (LSRO) of the Federation of American Societies for Experimental Biology (FASEB) (Ref. 1, pp. 12–17). In its 1993 report entitled ''The Evaluation of the Safety of Using Psyllium Husk as a Food Ingredient,'' LSRO reviewed and

evaluated published data, unpublished studies that were in press at that time, and other information and data. Based on this review, LSRO concluded that:

> There is no evidence in the available information on psyllium that demonstrates or suggests reasonable grounds to suspect a hazard to the public when it is used in a number of food categories and at levels of addition that would result in total consumption of as much as 25 g/day of psyllium. However, it is not possible to determine without additional data whether a significant increase in consumption above 20 to 25 g/day would constitute a dietary hazard.

(Ref. 31, p. 57.) The agency is not prepared to disagree with LSRO's conclusions on the safety of psyllium husk.

The agency points out, however, that some concerns about the safety of psyllium do exist. For example, available information suggests that long-term exposure to high levels of psyllium husk may enhance epithelial cell proliferation in the gastrointestinal tract. Rats consuming an elemental diet containing 30 percent fiber supplement, of which 10 percent was Ispaghula (psyllium), had increased cell proliferation in the stomach, distal small intestine, and colon when compared to rats consuming an elemental diet with no fiber supplement (Ref. 36). There is no agreement in the scientific community, however, whether such an increase in cell proliferation is related to an adverse health effect (Ref. 37). FDA requests comments on whether enhanced proliferation of gastrointestinal tract epithelial cells as a result of long-term exposure to psyllium husk is of concern, and whether it would provide a basis for not authorizing a claim.

The agency is also aware that psyllium husk can cause allergic reactions in some people, such as health care professionals, who regularly dispense psyllium containing products in the course of their work. Information provided by the petitioner (Ref. 32) shows that there are at least 13 protein fractions present in psyllium husk preparations. Some of these protein fractions cross react with sera obtained from individuals who experienced allergic reactions to psyllium-containing foods. The information also shows that refinement of psyllium husk preparations, i.e., increasing the purity of psyllium husk, by mechanical sieving can reduce the level of antigenic protein fractions (Ref. 32).

Because of concerns regarding the allergenic potential of products derived from psyllium seed, FDA is proposing specifications for the purity of the psyllium husk that is the subject of this health claim proposal to reduce the potential for allergic reactions to foods containing added psyllium. These specifications are based on information provided in the petition (Ref. 32) and on the specifications used by the petitioner (Ref. 1). FDA requests comments on the adequacy of these proposed specifications to reduce the allergenic potential of psyllium husk consumed as a component of food. Are other steps, such as requiring that a psyllium-containing product that bears a health claim declare on its prinicipal display panel that psyllium is present in the food, necessary?

Additionally, the agency is aware of the potential for gastrointestinal obstruction to occur following consumption of psyllium husk in the absence of sufficient liquid to ensure thorough hydration. However, the 1993 report by LSRO noted that reports of gastrointestinal obstruction have been associated almost exclusively with consumption of bulk laxatives without proper hydration (Ref. 31). Moreover, LSRO stated that there have been no such reports associated with the consumption of psyllium-containing cereals consumed with milk. It also noted that there are no data regarding possible alimentary tract obstruction that could be associated with consumption of psyllium-containing products such as poptarts, waffles, breads, and other foods that may be consumed without a liquid (Ref. 31). LSRO stated that the moderate amount of psyllium in these products would not be expected to cause gastrointestinal obstruction, and that any such possibility would be reduced by a suitable suggestion that these products be consumed with fluids (Ref. 31). The agency is asking for comments on whether psyllium-containing foods should carry a statement advising that the product be consumed with liquids, or whether the potential for blockage is not an issue of concern for psyllium-containing food.

Based on the totality of the evidence, the agency is not prepared, at this time, to take issue with the petitioner's view that the use of psyllium husk is safe and lawful. Although FDA tentatively concludes that the petitioner has provided evidence that satisfies the requirement in § 101.14(b)(3)(ii) that use of psyllium husk at the levels necessary to justify a claim is safe and lawful, the agency requests comment on this tentative conclusion. The agency recognizes that, should this proposed health claim be authorized, there may be an increase in the consumption of psyllium. Therefore, the agency also requests comments on actions, if any, that may be necessary to ensure that longterm consumption of psyllium will be at safe levels, such as establishing a maximum psyllium content that foods may contain to bear the health claim or limiting the kinds of foods that can contain psyllium and bear a claim.

III. Review of Scientific Evidence

A. Basis for Evaluating the Relationship Between Soluble Fiber from Psyllium and CHD

In the 1991 dietary fiber and CVD proposal, the agency set forth the basis for the relationship between dietary fiber and CVD (56 FR 60582 at 60583). In that document, the agency stated that there are many risk factors that contribute to the development of CVD, and specifically CHD, one of the most serious forms of CVD and the leading cause of disability. The agency also stated that there is general agreement that elevated blood cholesterol levels are one of the major ''modifiable'' risk factors in the development of CVD and, more specifically, CHD.

The Federal Government and others who have reviewed the matter have concluded that there is substantial epidemiologic evidence that high blood levels of total cholesterol and LDL-cholesterol are a cause of atherosclerosis (inadequate circulation of blood to the heart due to narrowing of the arteries) and represent major contributors to CHD (56 FR 60582 at 60583, Refs. 3 through 5). Factors that decrease total cholesterol and LDL-cholesterol will also tend to decrease the risk of CHD. High intakes of saturated fat and, to a lesser degree, of dietary cholesterol are associated with elevated blood total and LDL-cholesterol levels (56 FR 60727 at 60728, November 27, 1991). Thus, it is generally accepted that blood total cholesterol and LDL-cholesterol levels can influence the risk of developing CHD, and, therefore, that dietary factors affecting blood total cholesterol levels affect the risk of CHD (Refs. 3 through 5).

When considering the effect that the diet or components of the diet have on blood (or serum) lipids, it is also important to consider the effect that these factors may have on blood levels of high density lipoprotein-cholesterol (HDL-cholesterol). HDL-cholesterol is involved in the regulation of cholesterol transport out of cells and to the liver, from which it is ultimately excreted (Refs. 3 and 33). Therefore, HDL-cholesterol has a protective effect in the body by helping to reduce the risk of CHD.

For these reasons, FDA limited its review of the relationship between soluble fiber from the psyllium husk, hereinafter referred to as ''psyllium,'' and CHD to effects of dietary intake of this substance on blood lipid levels and on the risk of developing CHD. The agency based its evaluation of the relationship between consumption of this substance and CHD on changes in blood total cholesterol, LDL-cholesterol, and HDL-cholesterol, resulting from dietary intervention with soluble fiber from psyllium and with psyllium-containing products. This focus is consistent with that used by the agency in response to the 1990 amendments in deciding on the dietary saturated fat and cholesterol and CHD health claim, § 101.75 (56 FR 60727 and 58 FR 2739); the fruits, vegetables, and grain products and CHD claim, § 101.77 (56 FR 60582 and 58 FR 2552); and the soluble fiber from whole oats and CHD claim, § 101.81 (61 FR 296 and 62 FR 3584).

B. Review of Scientific Evidence

1. Evidence Considered in Reaching the Decision

The petitioner submitted scientific studies evaluating the relationship between soluble fiber from psyllium, consumed as a food and as an ingredient in foods, and serum lipid levels (Ref. 1). These studies were conducted between 1965 and 1996. The petition included tables that summarized the outcome of those studies and a summary of the evidence. Consistent with the approach taken in the dietary fiber/CVD proposed rules, the agency began its review by considering those psyllium studies that were published since 1988 (date of publication of the Surgeon General's report). In addition, in its review of the petition, the agency considered the conclusions of two LSRO reports (Refs. 7 and 8) relative to studies involving psyllium.

2. Criteria for Selection of Human Studies

The criteria that the agency used to select pertinent studies were that the studies: (1) Present data and adequate descriptions of the study design and methods; (2) be available in English; (3) include estimates of, or enough information to estimate, soluble dietary fiber intakes; (4) include direct measurement of blood total cholesterol and other blood lipids related to CHD; and (5) be conducted in persons who represent the general U.S. population (adults with blood total cholesterol levels less than (<) 300 mg/dL).

In selecting human studies for review, 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/dL), individuals taking lipid-lowering medication during treatment periods, children with hypercholesterolemia, and persons who had already experienced a myocardial infarction, were excluded because of questions about their relevance to the general healthy U.S. population. Studies in which psyllium was tested as part of a mixture of other soluble fibers, e.g., oat bran, were also excluded from review because it was not possible to evaluate the influence of psyllium alone on risk factors for heart disease. These criteria are consistent with those that the agency used to evaluate the relationship between other substances and CHD.

3. Criteria for Evaluating the Relationship Between Soluble Fiber from Psyllium and CHD

FDA generally applied the same criteria in evaluating studies on the relationship between soluble fiber from psyllium and CHD that it used in evaluating studies on the relationship between dietary fiber and CVD in the 1991 proposed rule (56 FR 60582 at 60587) and in the January 1996 proposed rule on whole oats and CHD (61 FR 296). The criteria that the agency used in evaluating the studies for this rulemaking include: (1) Reliability and accuracy of the methods used in nutrient intake analysis, including measurements of total dietary soluble fiber and total dietary fiber; (2) estimates of intake of saturated fat and cholesterol; (3) available information on the soluble fiber content of the psyllium test products and control food; (4) measurement of study endpoints (i.e., total cholesterol, LDL-cholesterol, and HDL-cholesterol); and (5) general study design characteristics.

The general study design characteristics for which the agency looked included 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, monitoring body weight and control of weight loss), appropriateness of statistical tests and comparisons, and statistical power of the studies. The agency considered whether the intervention studies that it evaluated had been of long enough duration to reasonably ensure stabilization of blood lipids (greater than or equal to 3 weeks duration). Finally, the agency considered it highly desirable if the available information on a study included information on total dietary soluble fiber content of baseline, treatment, and control diets and on the nutrient intakes of the subjects during the course of the study.

C. Review of Human Studies

FDA has done a comprehensive review of 21 human studies on psyllium (Refs. 9 through 28 and 30) that were submitted with the petition and met the forementioned criteria for selection (Ref. 35). Of these, the agency gave particular weight to seven studies (Table 1 of this document) (Refs. 14, 15, 16, 19, 23, 24, and 30) that were well controlled, reported intakes of saturated fat and cholesterol, and avoided problems associated with small sample size, lack of placebo control, lack of blinding, and other design problems. The studies listed in Table 1 also had run-in periods of 4 or more weeks duration before the treatment period. During the run-in period, subjects consumed a low saturated fat and cholesterol diet without psyllium or placebo to allow time for serum lipid levels to stabilize to the change in dietary intake. Three of the studies in Table 1 were randomized, double blind, placebo-controlled, parallel trials (Refs. 14, 15, and 19). One study was a randomized, double blind, placebo-controlled, crossover trial (Ref. 16), and three studies were randomized, single blind, placebo-controlled, crossover trials (Refs. 23, 24, and 30).

Five of the studies (Refs. 14, 15, 19, 23, and 24) in Table 1 evaluated the effect of psyllium on serum lipid levels in subjects consuming a Step 1 diet (Ref. 5) (i.e., a diet with no more than 30 percent of calories from total fat, less than 10 percent calories from saturated fat, and less than 300 mg cholesterol daily,) and one study (Ref. 30) included psyllium as part of a Step 2 diet (i.e., a diet with no more than 30 percent of calories from total fat, <7 percent of calories from saturated fat, and <200 mg/day (d) cholesterol). One study (Ref. 16) evaluated the effects of psyllium in subjects consuming their usual diets. The source of psyllium in three studies (Refs. 14, 16, and 19) was a bulk laxative. Subjects mixed the psyllium with a liquid (usually water) and consumed it before meals. The placebo in these studies was cellulose.

Four studies (Refs. 15, 23, 24, and 30) incorporated psyllium into breakfast cereals or a variety of foods (e.g., breads,

cereal, pasta). In these studies, the placebo controls were the same or similar foods that did not contain psyllium (e.g., breads, cereal, pasta).

The level of psyllium consumed in the 7 studies ranged from 3.4 grams (g)/d (about 2.6 g/d soluble fiber) (Ref. 15) to about 11.6 g/d (an estimated 8 g/d soluble fiber) (Refs. 23 and 24). The duration of the treatment periods ranged from 4 weeks (Ref. 30) up to 24 weeks (Ref. 15). The male and female subjects in the 7 studies were moderately hypercholesterolemic and ranged in age from 20 to 80 years.

The results of the studies that evaluated psyllium as a supplement to the diet (Refs. 14, 16, and 19) demonstrated that the subjects consuming psyllium daily experienced significant decreases in blood total cholesterol of about 4 percent (Refs. 14 and 16) and 5 percent (Ref. 19) compared to the control group, which consumed a placebo. LDL-cholesterol decreased significantly, from about 5 percent (Ref. 16) to about 7 percent (Ref. 14), compared to the placebo control. In these three studies, the psyllium group consumed 10.2 g/d psyllium (about 7 g/d soluble fiber) (Refs. 14 and 19) or 15.3 g/d (about 10 g/d soluble fiber) (Ref. 16).

One study evaluated the effect of 3 levels of psyllium intake from foods on lipid levels in hypercholesterolemic men and women (Ref. 15). Three groups (Group 1, 2, and 3) consumed a variety of foods (cereal, bread, pasta, and snack bars) that provided 3.4 g, 6.8 g, or 10.2 g/d psyllium (Groups 1, 2, and 3, respectively) as part of a Step 1 diet for 24 weeks. A control group consumed the same foods with no psyllium. Blood total cholesterol was significantly lowered only in Group 3 from 2 to 4 percent compared to the control group. LDL-cholesterol decreased significantly in Groups 1 and 3 (i.e., about 5 percent) compared to the control group. The total soluble fiber intakes for the control and Groups 1, 2, and 3 were 7 g, 10 g, 10.6 g, and 12.4 g/d, respectively. The authors stated that the difference in soluble fiber intake among the psyllium groups was less than expected and suggested that the subjects may have partially substituted psyllium-containing foods for other foods containing soluble fiber. The results of this study suggest that there is a dose-response relationship between psyllium intake and significant reductions in CHD risk factors, but no specific level can be determined from these data because of possible problems with subject compliance in Groups 1 and 2.

The results of three other studies that tested psyllium-containing cereals (Refs. 23, 24, and 30) showed significant reductions in both blood total cholesterol (about 4 to 8 percent) and LDL-cholesterol (about 5 to 10 percent) compared to the placebo control. The subjects in these studies consumed 9.3 g/d psyllium (about 6.8 g soluble fiber) (Ref. 30) and 11 g/d psyllium (about 8 g soluble fiber) (Refs. 23 and 24).

There were no statistically significant differences between the psyllium and placebo groups in HDL-cholesterol in all but one of the studies in Table 1. In the one study (Ref. 19), post-treatment HDL-cholesterol was significantly higher in the placebo group compared to the psyllium group.

In summary, based on the totality of the evidence presented in randomized studies, consumption of psyllium helped to reduce the levels of blood total and LDL-cholesterol, and thus the risk of CHD, in subjects with moderately elevated to high blood total cholesterol who consumed either a Step 1 or Step 2 diet (low saturated fat and cholesterol) or their usual diets. Psyllium did not adversely affect HDL-cholesterol levels.

IV. Decision to Propose a Health Claim Relating Soluble Fiber from Psyllium to Reduction in Risk of CHD

The results of 7 clinical trials with psyllium that were published between 1988 and 1996 (Table 1), as discussed in section III.C, above, consistently supported that there is a relationship between consumption of soluble fiber from psyllium, as part of a diet that is low in saturated fat and cholesterol, and reduced blood cholesterol levels, which in turn may reduce the risk of heart disease. Based on this evidence, FDA has tentatively concluded that there is significant scientific agreement that the available evidence supports that this nutrient/disease relationship is valid. Thus, the agency is proposing to authorize health claims on the relationship between soluble fiber from psyllium and reduced risk of CHD.

FDA points out, however, that in preparing this document, as is its regular practice in health claim proceedings, the agency conferred with other Public Health Service (PHS) agencies with relevant expertise. These agencies have raised issues that merit consideration in this rulemaking.

First, in the seven studies that met the criteria for evaluation, three involved administration of psyllium in the form of a bulk laxative (Refs. 14, 16, and 19), and in only four of the studies was psyllium incorporated into foods (Refs. 15, 23, 24, and 30). One PHS agency raised an issue about the appropriateness of reliance on the former studies, in which psyllium was not consumed as an ingredient of conventional food.

The agency has tentatively decided that reliance on References 14, 16, and 19, in which psyllium was administered in the form of a bulk laxative, is appropriate because in these studies the psyllium was fed at mealtimes, much in the manner of a dietary supplement, and in concentrations similar to those at which psyllium was incorporated into conventional foods in References 15, 23, 24, and 30. Moreover, the effect of consuming psyllium on the risk of heart disease (i.e., about 3 to 5 percent reductions in blood total and LDL-cholesterol) observed in the studies in which this substance was consumed in conventional food, e.g., in cereal (Refs. 15, 23, 24, and 30), was similar to that seen in the studies (Refs. 14, 16, and 19) in which it was consumed as a bulk laxative. These results suggest that the form in which psyllium is consumed is not significant. However, the agency is asking for comments on whether it is appropriate to consider studies in which psyllium was fed in bulk form as evidence in evaluating this substance/disease relationship.

Second, the subject populations in the studies listed in Table 1 had borderline to high blood cholesterol levels. One PHS agency questioned the relevance of these studies to the general population, which includes individuals with normal as well as elevated blood cholesterol levels. The agency has tentatively concluded that the hypercholesterolemic study populations in the studies listed in Table 1 are relevant to the general population because, based on data from the National Health and Nutrition Examination Surveys (NHANES) III, the prevalence of individuals with elevated blood cholesterol (i.e., 200 mg/dL or greater) is high (approximately 51 percent of adults) (Ref. 6). The proportion of adults having moderately elevated blood cholesterol levels (i.e., between 200 and 239 mg/dL) was estimated to be approximately 31 percent, and the proportion of adults with high blood cholesterol levels (240 mg/dL or greater) was estimated to be approximately 20 percent (Ref. 6). It is also estimated that 52 million Americans 20 years of age and older would be candidates for dietary intervention to lower blood cholesterol (Ref. 6). The agency considers the high proportion of Americans that have elevated blood cholesterol levels (i.e., 51 percent) to make up a significant portion of the general population, thus making the subject population in the studies listed in Table 1 relevant to the general population. However, the

agency is asking for comments on this issue.

V. Decision to Propose to Amend § 101.81

As discussed in section I.B of this document, FDA authorized a claim for soluble fiber from whole oats and CHD on January 23, 1997 (62 FR 3584). In that document, the agency stated that it is very likely that soluble fiber from certain foods, in addition to β-glucan soluble fiber from whole oats, may affect serum lipid levels and thus help to reduce the risk of CHD (62 FR 3584 at 3587). The agency further stated that if a manufacturer can document, through appropriate human and laboratory studies, that a soluble fiber has an effect on blood total- and LDL-cholesterol levels, and thereby can be useful in reducing the risk of CHD, the manufacturer may petition to amend § 101.81 to include that source of soluble fiber among the food sources about which claims are authorized (62 FR 3584 at 3587 and 3588). The agency explained that it was necessary to evaluate each source of soluble fiber individually because soluble fiber is a family of very heterogeneous substances that vary greatly in their effect on the risk of CHD.

The agency tentatively concludes that the soluble fiber in psyllium, like β-glucan soluble fiber from whole oats, when consumed as part of a diet low in saturated fat and cholesterol, may help to reduce the risk of heart disease, and that a health claim describing this relationship is warranted. To this end, the agency is proposing to amend § 101.81, as discussed below, to include soluble fiber from psyllium and to broaden the subject of the claim to ''soluble fiber from certain foods'' and risk of CHD.

As discussed in the preamble to the soluble fiber from whole oats final rule, an umbrella regulation for ''soluble fiber from certain foods'' and CHD will provide flexibility for the inclusion of other food sources of soluble fiber when adequate data are provided to demonstrate that consumption of those foods may help to reduce the risk of heart disease (62 FR 3584 at 3588). Moreover, such an umbrella regulation has the advantage of minimizing consumer confusion in that the claim could not be used on the label of all foods that contain soluble fiber. Rather, the claim will be limited to those soluble fiber sources whose consumption has been demonstrated to have a relationship to the risk of CHD.

VI. Description of Modifications to § 101.81

A. Eligible Sources of Soluble Fiber

Section 101.81(c)(2)(ii) (''Nature of the substance. Eligible sources of soluble fiber'') lists the types and sources of soluble fiber that have been demonstrated to the satisfaction of FDA to have a relationship to the risk of CHD. In § 101.81(c)(2)(ii)(A), FDA lists β-glucan soluble fiber from the whole oat sources, along with the method of analysis for β-glucan soluble fiber by the Association of Official Analytical Chemists. Section 101.81(c)(2)(ii)(A)(*1*) through (c)(2)(ii)(A)(*3*) identify the whole oat sources that are eligible to bear the claim. FDA reserved § 101.81(c)(2)(ii)(B) for future use.

In this document, FDA is proposing to add new § 101.81(c)(2)(ii)(B) to specify psyllium husk as a source of soluble fiber eligible to be the subject of this claim. As discussed in section II.B.3 of this document, the agency is aware that psyllium has been associated with allergic reactions in some people, especially in health care professionals who dispense psyllium containing products in the course of their work. The petitioner stated that using psyllium with a purity of 95 percent in cereal significantly reduced the potential for allergenic responses following consumption of psyllium-containing food (Ref. 1, pp. 85–86). Information provided by the petitioner showed that psyllium husk that has a purity of 95 percent has a maximum protein content of 3 percent and total extraneous matter not to exceed 4.9 percent (i.e., 4.5 percent or less of light extraneous matter and 0.5 percent or less of heavy extraneous matter, as determined by USP methods (Ref. 34)).

In this document, the agency is proposing to adopt these specifications for psyllium husk that may be the subject of a claim. Therefore, proposed § 101.81(c)(2)(ii)(B)(*1*) states that ''to qualify for this claim, psyllium husk shall have a purity of no less than 95 percent, such that it has a 3 percent or less protein content, 4.5 percent or less of light extraneous matter, and 0.5 percent or less of heavy extraneous matter, but in no case may the combined extraneous matter exceed 4.9 percent, as determined by U.S. Pharmacopeia (USP) methods'' that are incorporated by reference (Ref. 1, pp. 5–6, and Ref. 34). The agency requests comments on whether the requirements proposed in § 101.81(c)(2)(ii)(B)(*1*) are sufficient to reduce the potential for allergenic responses in individuals sensitive to psyllium.

Proposed § 101.81(c)(2)(ii)(B)(*1*) identifies psyllium husk as the dried seed coat (epidermis) of the seed of *Plantago (P) ovata*, known as blond psyllium or Indian psyllium; *P. indica*; or *P. psyllium*. This information is consistent with that provided by the petitioner (Ref. 1, pp. 5 and 6) and the description of psyllium husk given in the U.S. Pharmacopeia's (USP) ''The National Formulary'' (Ref. 34).

In proposed § 101.81(c)(2)(ii)(B)(*2*), FDA identifies the analytical method that it intends to use to determine the amount of soluble fiber that is provided by psyllium. Because psyllium-containing food products are highly viscous in aqueous solutions and may not be easily filtered, a method for analyzing for soluble and insoluble dietary fiber from psyllium was developed by Lee et al. (Ref. 29). The assay, a modification of method No. 991.31 from ''Official Methods of Analysis of the Association of Official Analytical Chemists'' (AOAC), appeared in the *Journal of the AOAC International*, volume 78, page 724, 1995, and FDA is proposing to incorporate it by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51 in this document.

B. Nature of the Food Eligible to Bear the Claim

Section 101.81(c)(2)(iii)(A) (as modified at 62 FR 15342) states that ''the food product shall include one or more of the whole oat foods from paragraph (c)(2)(ii) of this section, and the whole oat foods shall contain at least 0.75 gram (g) of soluble fiber per reference amount customarily consumed of the food'' (RACC). FDA arrived at this amount of soluble fiber by dividing an intake of 3 g/d soluble fiber from whole oats by 4 eating occasions per day (62 FR 3584 at 3592). The daily intake of 3 g soluble fiber was based on an analysis of data from a dose-response study that showed that an intake of 3 g/d β-glucan soluble fiber from whole oats was associated with a significant reduction (5 percent) in blood total- and LDL-cholesterol levels, and the results of a meta-analysis and other oat studies (61 FR 296 at 308). Based on four eating occasions per day, each serving of the eligible whole oat product would have to provide a minimum of 0.75 g per RACC as part of the requirements to qualify to bear the CHD claim.

The petitioner for the psyllium claim stated that ''the hypocholesterolemic dose-responsiveness of soluble fiber from psyllium (i.e., psyllium husk) has not been extensively studied, but there is evidence to suggest that the greater

the dose, the more pronounced the cholesterol-lowering effects will be'' (Ref. 1, p. 100). The petitioner noted LSRO's (Ref. 7) recommendations for soluble fiber intake for the general U.S. population. LSRO stated that soluble fiber should account for 25 to 30 percent of the total dietary fiber intake and recommended a daily intake of total dietary fiber intake of between 20 to 35 g/d (Ref. 7). Based on these values, an optimal intake of soluble fiber intake would range from 5 g/d to about 10.5 g/d.

The petitioner also reviewed the results of studies that evaluated the effects of different intake levels of psyllium and considered the conclusions of reviews of the literature on psyllium (Ref. 1, pp. 100 through 102). It noted that some overviews of the literature on psyllium and serum cholesterol levels have suggested intake ranges of 10 to 30 g/d of psyllium (Ref. 1, p. 100). The petitioner also noted that the results of the dose-response study by Davidson et al. (Ref. 15) showed that the group consuming 10.2 g/d of psyllium had differences of approximately 4.6 percent for LDL-cholesterol and 3.3 percent for total cholesterol when compared to controls (Ref. 1, p. 101). Based on all of the evidence, the petitioner asserted that an intake of about 7 g/d soluble fiber from 10.2 g/d psyllium may help to reduce the risk of CHD (Ref. 1, p. 102).

The petitioner suggested that, based on a daily intake level of 10.2 g of psyllium, which provides about 7 g soluble fiber, the level in a food to qualify to bear the CHD claim should be 2.5 g of psyllium per RACC (10.2 g/d divided by 4 eating occasions per day), which provides 1.7 g soluble fiber (7 g/d of soluble fiber divided by 4) per RACC. The petitioner noted that the agency has usually assumed that food consumption patterns generally reflect three meals and a snack (58 FR 2302 at 2379, January 3, 1993).

After review of data from studies submitted with the petition, the agency notes that, with the exception of the dose-response study by Davidson et al. (Ref. 15), psyllium was consumed in these studies at levels of 10 or more g/d (soluble fiber was approximately 7 g/10 g of psyllium) (see Table 1 and Ref. 35). In those placebo-controlled studies that tested an intake of psyllium of 10.2 g, the effect on serum blood lipids was consistent, i.e., blood total and LDL-cholesterol levels were significantly lowered, and HDL-cholesterol levels were not affected (Refs. 10, 11, 13 through 15, 18, 19, 22, and 26).

As noted earlier, Davidson et al. (Ref. 15) evaluated the effect of psyllium at levels of 3.4 g (Group 1), 6.8 g (Group 2), and 10.2 g (Group 3) per day from foods consumed as part of a Step 1 diet. The results of the study showed significant lowering of serum lipids in subjects consuming 10.2 g/d psyllium in food. The authors stated, however, that the subjects in the first two groups may not have complied with study protocol, thus confounding the results for them. Because of the potential for confounding in this study, the agency finds that the results of the Davidson study do not provide the information needed to determine a dose-response between the level of psyllium intake, and therefore the level of soluble fiber from psyllium, and the degree of change in blood lipid levels.

In this document, the agency is proposing to amend § 101.81 to add soluble fiber from psyllium, but it does not have the data that were available for β-glucan soluble fiber from whole oats on which to establish a dose-response based qualifying level for the amount of soluble fiber from psyllium necessary for a food to be eligible to bear the claim. As discussed above, relative to whole oat soluble fiber qualifying levels, analysis of data from a dose-response study showed that an intake of 3 g/d whole oat soluble fiber was associated with a 5 percent reduction in blood lipids (61 FR 296 at 308). In the whole oat proposal, the agency explained that a significant reduction in serum lipids of 5 percent is associated with the level that was achieved as a result of a dietary fat and cholesterol-focused intervention in the Multiple Risk Factor Intervention Trial and Lipid Research Council clinical trials (61 FR 296 at 308). The agency does not have similar data from which to determine the amount of soluble fiber from psyllium that is associated with a 5 percent reduction in serum lipids.

In the absence of such data, the agency is tentatively proposing to base the qualifying level of soluble fiber from psyllium on a total daily intake of 10.2 g (about 7 g of soluble fiber), as suggested by the petitioner. This level of intake was shown in the clinical studies to be consistently associated with significant reductions in serum lipids.

Therefore, FDA is proposing that the qualifying level of soluble fiber for foods to bear this claim be 1.7 g soluble fiber from psyllium per RACC (7 g divided by 4 eating occasions per day). The agency does not consider it necessary to propose a qualifying amount of psyllium as suggested in the petition (2.5 g) because the qualifying level of soluble fiber will determine the amount of psyllium that is required. Based on estimates from figures provided in the petition and in the studies, psyllium is about 68 percent or more soluble fiber. Therefore, 1.7 g/RACC of soluble fiber from psyllium would relate to about 2.5 g/RACC of psyllium husk. The agency is asking for comments on whether this approach for establishing a qualifying soluble fiber level for psyllium-containing products is appropriate or for data to support another qualifying level for psyllium.

Health claims help consumers to identify those products that will help them achieve a healthy diet (see, e.g., section 403(r)(3)(B)(iii) of the act). Expanding § 101.81 to include psyllium-containing foods will give consumers an opportunity to select from a wider variety of foods containing those soluble fibers that have been shown to help reduce the risk of CHD. The availability of a variety of foods, in turn, should help consumers increase their daily intake of soluble fiber.

To reflect the agency's tentative decision to propose a qualifying level of soluble fiber from psyllium that is different from that required for whole oats, the agency is proposing to amend § 101.81(c)(2)(iii)(A) (as modified at 62 FR 15342) to set out the qualifying level of soluble fiber from whole oat and psyllium foods. Therefore, in this document, proposed § 101.81(c)(2)(iii)(A) is modified to state ''[T]he food product shall include:'' followed by paragraphs (*1*) and (*2*). Paragraph (c)(2)(iii)(A)(*1*) is modified to state ''one or more of the whole oat foods from paragraph (c)(2)(ii)(A) of this section, and the whole oat foods shall contain at least 0.75 gram (g) of soluble fiber per reference amount customarily consumed of the food product.'' FDA is proposing to state in § 101.81(c)(2)(iii)(A)(*2*): ''psyllium that complies with paragraph (c)(2)(ii)(B) of this section, and the psyllium food shall contain at least 1.7 g of soluble fiber per reference amount customarily consumed of the food product.''

The agency recognizes that foods could be produced with a blend of the eligible soluble fibers listed in paragraph (c)(2)(ii) and would be willing to consider whether such foods should be eligible to bear the health claim. An example of a product that contains a blend of the eligible soluble fibers might be one that contains 75 percent of the qualifying level of β-glucan soluble fiber from whole oats and 25 percent of the qualifying level of soluble fiber from psyllium. However, the agency does not have the data on which to evaluate the relationship between consumption of foods containing both psyllium and whole oats and risk of heart disease. Although

both soluble fiber sources affect the same CHD risk factor (i.e., blood lipid levels), the agency cannot assume that foods containing a blend of these grains would have the same ability to affect blood total and LDL-cholesterol levels that a product containing either whole oats or psyllium apparently has. Therefore, if a manufacturer can demonstrate that a diet that is low in saturated fat and cholesterol that includes a blend of the eligible soluble fibers listed in § 101.81(c)(2)(ii)(A) and (c)(2)(ii)(B) has an effect on the risk of heart disease, the manufacturer should petition to amend § 101.81 further. In addition, because the qualifying level that FDA is proposing for soluble fiber from psyllium differs from that which it adopted for β-glucan soluble fiber from whole oats, the issue of an appropriate qualifying level for a blended product should be addressed in any petition.

In the preamble to the final rule in which it adopted § 101.81, the agency explained that the approach it used to derive the qualifying level of 0.75 g per RACC for whole oat products is somewhat different from the one that it used in authorizing other health claims (62 FR 3584 at 3592). The agency explained that the guiding principle for other health claims was to use the established definition for ''good source'' or ''high in,'' which characterize the amount of a nutrient based on a percentage of the Daily Reference Value (DRV) for the nutrient, in a serving of food as the qualifying level. In this way, products that qualify to bear the claim contain a meaningful level of the substance per serving compared to the recommended intake of the substance from all food sources. However, there is no DRV for soluble fiber. While the agency concluded that the approach it took to establish the qualifying level in § 101.81 was appropriate, it stated that it intends to propose to establish a DRV for soluble fiber, and, once that rulemaking is completed, assuming it results in a DRV, it would revisit the requirements in § 101.81 and propose any changes in its provisions that are necessary. For the purposes of any final rule that results from this rulemaking, the agency will also revisit the requirements of § 101.81(c)(2)(iii) if a DRV is established for soluble fiber.

C. Soluble Fiber From Certain Foods and From Eligible Food Sources

In light of the agency's tentative decision to broaden § 101.81 to include soluble fiber from psyllium, the agency is proposing to modify the section heading of § 101.81 from ''Soluble fiber from whole oats and risk of coronary heart disease'' to ''Health claims: soluble fiber from certain foods and risk of coronary heart disease.'' The statement ''soluble fiber from certain foods'' reflects the fact that the subject of the claim is no longer a specific source of soluble fiber, i.e., β-glucan from whole oats, but rather a broader class of substances that includes those sources of soluble fiber for which there is significant scientific agreement that they may help to reduce the risk of heart disease.

The statement ''soluble fiber from whole oats'' also appears in several paragraphs of § 101.81. The agency is proposing to revise this statement where it appears to state ''soluble fiber from certain foods.'' The paragraphs of § 101.81 that will be affected by this change, if it is adopted, include: (a), (a)(3), (b), (b)(2), (c)(2)(i), (c)(2)(i)(A), (d)(3), and (e).

The agency is proposing to revise the statement ''soluble fiber from whole oats'' in three paragraphs of § 101.81, paragraphs (c)(2)(i)(E), (c)(2)(i)(F), and (d)(2), to read ''soluble fiber from the eligible food sources from paragraph (c)(2)(ii) of this section.'' The agency tentatively finds that the statement ''soluble fiber from the eligible food sources * * *'' more accurately identifies the particular sources of soluble fibers that may be the subject of the claim. For example, § 101.81(c)(2)(i)(E) now specifies that the claim must not attribute any degree of risk reduction for coronary heart disease to diets low in saturated fat and cholesterol that include soluble fiber from whole oats. The eligible food sources in this proposed rule include whole oats and psyllium, so FDA is proposing to revise § 101.81(c)(2)(i)(E) to reflect the broader coverage of the claim.

The agency notes, however, that it is not proposing changes to the model claims in § 101.81(e) (modified at 62 FR 15342). In both example claims, the name of the soluble fiber source from § 101.81(c)(2)(ii) (Eligible source of soluble fiber) is provided, and, if desired, the name of the food product may be provided. For example, § 101.81(e)(1) states ''Soluble fiber from foods such as [name of soluble fiber source from section (c)(2)(ii) of this section and, if desired, the name of the food product], as part of a diet low in saturated fat and cholesterol, may reduce the risk of heart disease.'' Therefore, a claim for a psyllium-containing food may state ''Soluble fiber from foods such as psyllium, as part of a diet low in saturated fat and cholesterol, may reduce the risk of heart disease,'' and thus no change in § 101.81(e)(1) or (e)(2) is necessary to reflect the addition of psyllium to the list of substances eligible to bear the claim.

The agency is proposing to make some minor editorial changes in § 101.81, which have no substantive effect on this regulation.

VII. Environmental Impact

The agency has determined under 21 CFR 25.24(a)(11) 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. This finding is based on information submitted by the petitioner in an environmental assessment prepared using the format described in 21 CFR 25.31a(b)(5).

VIII. Analysis of Impacts

FDA has examined the impacts of the proposed rule under Executive Order 12866 and the Regulatory Flexibility Act (5 U.S.C. 601–612). Executive Order 12866 directs agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). Executive Order 12866 classifies a rule as significant if it meets any one of a number of specified conditions, including having an annual effect on the economy of $100 million or adversely affecting in a material way a sector of the economy, competition, or jobs, or if it raises novel legal or policy issues. If a rule has a significant economic impact on a substantial number of small entities, the Regulatory Flexibility Act requires agencies to analyze regulatory options that would minimize the economic impact of that rule on small entities. FDA finds that this proposed rule is not a significant rule as defined by Executive Order 12866 and finds under the Regulatory Flexibility Act that the proposed rule will not have a significant impact on a substantial number of small entities.

The establishment of this health claim results in benefits and in costs only to the extent that food manufacturers elect to take advantage of the opportunity to use the claim. This rule will not require that any labels be redesigned or that any product be reformulated.

Some manufacturers are currently using FDA's approved health claim regarding the benefits of fruits, vegetables, and grain products. This proposed health claim will allow them to specifically highlight the role of

soluble fiber from psyllium. The benefit of establishing this health claim is to provide for new information in the market regarding the relationship of soluble fiber from psyllium and CHD.

Costs will be incurred by small entities only if they opt to take advantage of the marketing opportunity presented by this regulation. FDA cannot predict the number of small entities that will choose to use the claim. However, no firm, including small entities, will choose to bear the cost of redesigning labels unless they believe that the claim will result in increased sales of their product. Therefore, this rule will not result in either a decrease in revenues or a significant increase in costs to any small entity. Accordingly, under the Regulatory Flexibility Act, 5 U.S.C. 605(b), the Commissioner of Food and Drugs certifies that the proposed rule will not have a significant economic impact on a substantial number of small entities. Therefore, under the Regulatory Flexibility Act, no further analysis is required.

IX. Paperwork Reduction Act

FDA tentatively concludes that this proposed rule contains no reporting, recordkeeping, labeling, or other third party disclosure requirement. Thus, there is no ''information collection'' necessitating clearance by the Office of Management and Budget. However, to ensure the accuracy of this tentative conclusion, FDA is seeking comment on whether this proposed rule to permit health claims on the association between soluble fiber from psyllium and reduced risk of CHD imposes any paperwork burden.

X. Effective Date

FDA is proposing to make these regulations effective upon publication of a final rule based on this proposal.

XI. Comments

Interested persons may, on or before August 5, 1997, 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.

XII. 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 a.m. and 4 p.m., Monday through Friday.

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36. Goodlad, R. A., B. Ratcliffe, C. Y. Lee, and N. A. Wright, ''Dietary Fibre and the Gastrointestinal Tract: Differing Trophic Effects on Muscle and Mucosa of the Stomach, Small Intestine, and Colon,'' *European Journal of Clinical Nutrition*, 49(Suppl. 3):S178–S181, 1995.

37. Wasan, H. S. and R. A. Goodlad, ''Fibre-supplemented Foods May Damage Your Health, Lancet, 348:319–320, 1996.

List of Subjects in 21 CFR Part 101

Food labeling, Incorporation by reference, Nutrition, 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 continues 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, 701 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321, 331, 342, 343, 348, 371).

2. Section 101.81 is amended by revising the section heading, the heading for paragraphs (a) and (b), and paragraphs (a)(3), (b)(2), (c)(2)(i) introductory text, (c)(2)(i)(A), (c)(2)(i)(E), (c)(2)(i)(F), (c)(2)(iii)(A), (d)(2), (d)(3), and (e), and by adding paragraph (c)(2)(ii)(B) to read as follows:

§ 101.81 Health claims: Soluble fiber from certain foods and risk of coronary heart disease (CHD).

(a) *Relationship between diets that are low in saturated fat and cholesterol and that include soluble fiber from certain foods and the risk of CHD.*

* * * * *

(3) Scientific evidence demonstrates that diets low in saturated fat and cholesterol may reduce the risk of CHD. Other evidence demonstrates that the addition of soluble fiber from certain foods to a diet that is low in saturated fat and cholesterol may also help to reduce the risk of CHD.

(b) *Significance of the relationship between diets that are low in saturated fat and cholesterol and that include soluble fiber from certain foods and the risk of CHD.*

* * * * *

(2) Intakes of saturated fat exceed recommended levels in the diets of many people in the United States. One of the major public health recommendations relative to CHD risk is to consume less than 10 percent of calories from saturated fat and an average of 30 percent or less of total calories from all fat. Recommended daily cholesterol intakes are less than 300 mg per day. Scientific evidence demonstrates that diets low in saturated fat and cholesterol are associated with lower blood total and LDL-cholesterol levels. Soluble fiber from certain foods, when included in a low saturated fat and cholesterol diet, also helps to lower blood total and LDL-cholesterol levels.

(c) * * *

(2) * * *

(i) Nature of the claim. A health claim associating diets that are low in saturated fat and cholesterol and that include soluble fiber from certain foods with reduced risk of heart disease may be made on the label or labeling of a food described in paragraph (c)(2)(iii) of this section, provided that:

(A) The claim states that diets that are low in saturated fat and cholesterol and that include soluble fiber from certain foods ''may'' or ''might'' reduce the risk of heart disease.

* * * * *

(E) The claim does not attribute any degree of risk reduction for CHD to diets that are low in saturated fat and cholesterol and that include soluble fiber from the eligible food sources from paragraph (c)(2)(ii) of this section; and

(F) The claim does not imply that consumption of diets that are low in saturated fat and cholesterol and that include soluble fiber from the eligible food sources from paragraph (c)(2)(ii) of this section is the only recognized means of achieving a reduced risk of CHD.

(ii) * * *

(B)(*1*) Psyllium husk from the dried seed coat (epidermis) of the seed of *Plantago (P.) ovata*, known as blond psyllium or Indian psyllium; *P. indica*; or *P. psyllium*. To qualify for this claim, psyllium shall have a purity of no less than 95 percent, such that it contains 3 percent or less protein, 4.5 percent or less of light extraneous matter, and 0.5 percent or less of heavy extraneous matter, but in no case may the combined extraneous matter exceed 4.9 percent, as determined by U.S. Pharmacopeia (USP) methods described in USP's ''The National Formulary,'' USP 23, NF 18, p. 1341, (1995), which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies may be obtained from the U.S. Pharmacopeial Convention, Inc., 12601 Twinbrook Pkwy., Rockville, MD 20852, or may be examined at the Center for Food Safety and Applied Nutrition's Library, 200 C St. SW., rm. 3321, Washington, DC, or at the Office of the Federal Register, 800 North Capitol St. NW., suite 700, Washington, DC;

(*2*) FDA will determine the amount of soluble fiber that is provided by psyllium by using a modification of the Association of Official Analytical Chemists' (AOAC's) method for soluble dietary fiber (991.43) described by Lee et al., ''Determination of Soluble and Insoluble Dietary Fiber in Psyllium-containing Cereal Products,'' *Journal of the AOAC International*, 78(No. 3):724–729, 1995, which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies may be obtained from the Association of Official Analytical Chemists International, 481 North Frederick Ave., suite 500, Gaithersburg, MD 20877–2504, or may be examined at the Center for Food Safety and Applied Nutrition's Library, 200 C St. SW., rm. 3321, Washington, DC, or at the Office of the Federal Register, 800 North Capitol St. NW., suite 700, Washington, DC;

(iii) * * *

(A) The food product shall include:

(*1*) One or more of the whole oat foods from paragraph (c)(2)(ii)(A) of this

section, and the whole oat foods shall contain at least 0.75 gram (g) of soluble fiber per reference amount customarily consumed of the food product; or

(*2*) Psyllium that complies with paragraph (c)(2)(ii)(B) of this section, and the psyllium food shall contain at least 1.7 g of soluble fiber per reference amount customarily consumed of the food product;

* * * * *

(d) * * *

(2) The claim may state that the relationship between intake of diets that are low in saturated fat and cholesterol and that include soluble fiber from the eligible food sources from paragraph (c)(2)(ii) of this section and reduced risk of heart disease is through the intermediate link of ''blood cholesterol'' or ''blood total- and LDL-cholesterol;''

(3) The claim may include information from paragraphs (a) and (b) of this section, which summarize the relationship between diets that are low in saturated fat and cholesterol and that include soluble fiber from certain foods and coronary heart disease and the significance of the relationship;

* * * * *

(e) *Model health claim.* The following model health claims may be used in food labeling to describe the relationship between diets that are low in saturated fat and cholesterol and that include soluble fiber from certain foods and reduced risk of heart disease:

(1) Soluble fiber from foods such as [name of soluble fiber source from paragraph (c)(2)(ii) of this section and, if desired, the name of the food product], as part of a diet low in saturated fat and cholesterol, may reduce the risk of heart disease.

(2) Diets low in saturated fat and cholesterol that include soluble fiber from [name of soluble fiber source from paragraph (c)(2)(ii) of this section and, if desired, the name of the food product] may reduce the risk of heart disease.

Dated: May 15, 1997.

William B. Schultz,

Deputy Commissioner for Policy.

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

TABLE 1.—SUMMARY OF CLINICAL TRIALS WITH HYPERCHOLESTEROLEMICS: PSYLLIUM AND CORONARY HEART DISEASE

Study	Duration Treatment	Number of Subjects	Supplements (Psyllium, Placebo) Soluble Fiber g/d	Diet Intake of groups: Sat fat % E; CHOL mg/d	Magnitude of PSY Effect*	Magnitude of Placebo Effect
Levin et al. (Ref. 19)	Base: 8-wk Step 1; Tx: 16-wk Step 1+supplement	PSY: 30 (26 men) Pla: 28 (23 men)	10.2 g/d bulk laxative, cellulose PSY: ~7 g SF	*Sat fat*: PSY- 6.7%; C- 6.3% *CHOL*: PSY- 166 mg; C- 135 mg	*CHOL*: -13 mg/dL (5.6%) *LDL-C*: -13 mg/dL (8.6%)	CHOL: 0; LDL-C -2.2%; HDL-C: ~+6% (sig from PSY)
Bell et al. (Ref. 14)	Base: 12-wk Step 1; Tx: 8-wk Step 1+supplement	PSY: 40 (20 men) Pla: 35 (18 men)	10.2 g/d bulk laxative, cellulose PSY: ~7 g SF	*Sat fat*: PSY- 8-10%; C- 7.7-8.6% *CHOL*: PSY- 168 mg; C- 206 mg	*CHOL*: -9 mg/dL (4.2%) *LDL-C*: -12 mg/dL (7.7%)	CHOL: 0; LDL-C -0.2%; HDL-C no sig dif (grps)
Davidson et al. (Ref. 15)	Base: 8-wk Step 1; Tx: 24-wk Step 1 + PSY or control food (3 servings/d)	PSY 1 56 (31 men) PSY 2 40 (24 men) PSY 3 43 (28 men) C 59	3.4 g, 6.8 g, 10.2 g/d; incorporated into foods: C foods: no PSY PSY 1: ~2.3 g SF, PSY 2: ~.6 g; PSY 3: ~7 g	*Sat fat*: PSY- 7-8.6%; C- 7-8.6% *CHOL*: PSY 1- 151 mg; PSY 2- 181; PSY 3- 169C- 145 mg	*CHOL*: -3% (PSY 3) *LDL-C*: -5% (PSY 3)	CHOL: +1.7%; LDL-C: +3% HDL-C: No sig dif (grps)
Everson et al. (Ref. 16)	Regular diet; 5-d Base; 2 40-d periods; 11-d washout; crossover	20 men	15.3 g/d bulk laxative, cellulose PSY: ~10 g SF	*Sat fat*: PSY- 12%; C- 13.2 % *CHOL*: PSY- 296 mg; C- 274 mg	*CHOL*: -14 mg/dL (-5%) *LDL-C*: -15 mg/dL (8%)	CHOL: -1.9%; LDL-C: -2.7% HDL-C: No sig dif (grps)
Jenkins et al. (Ref. 30)	Base: 2-mo Step 2; Tx: 2 1-mo Step 2 metabolic diets, crossover, washout	12 Ss (3m/9f)	Mean intake: 9.35 g/d PSY in cereal PSY: 6.8 g SF	*Sat fat*: 4% all grps PSY: 36 mg; C: 29 mg *CHOL* PSY- 36 mg; C-29 mg	*CHOL*: -16.6 mg/dL Tx difference: 3.4% *LDL-C*: -9.3 mg/dL Tx difference: 5.1%	HDL-C: No sig dif (grps)
Stoy et al. (Ref. 23)	4-wk Step 1; Step 1 + (8x5x5 wks): Grp 1: PSY-Pla-PSY; Grp 2: Pla-PSY-Pla	23 men	Estimated 11.6 g/d PSY from cereal: ~8 g SF; Wheat cereal: ~3 g SF	*Sat fat*: PSY: 5.1% (Grp 1) and 5.1% (Grp 2) Wheat: 4.5% (Grp 1) and 5.0% (Grp 2) *CHOL*: PSY 141-165 mg Wheat: 164 mg (Grp 1), 117-170 (Grp 2)	*CHOL*: -10 mg/dL (4%) *LDL-C*: -11 mg/dL (6%)	HDL-C: No sig dif (grps)

TABLE 1.—SUMMARY OF CLINICAL TRIALS WITH HYPERCHOLESTEROLEMICS: PSYLLIUM AND CORONARY HEART DISEASE—Continued

Study	Duration Treatment	Number of Subjects	Supplements (Psyllium, Placebo) Soluble Fiber g/d	Diet Intake of groups: Sat fat % E; CHOL mg/d	Magnitude of PSY Effect*	Magnitude of Placebo Effect
Stoy et al. (Ref. 24)	4-wk Step 1; Step 1 + (8x5x5 wks): Grp 1: PSY-Pla-PSY; Grp 2: Pla-PSY-Pla	22 men	Estimated 11.6 g/d PSY from cereal: ~8 g SF; Wheat cereal: ~3 g SF	*Sat fat*: PSY: 4.8 (Grp 1) and 5.2% (Grp 2) Wheat: 4.7% (Grp 1) and 5.6% (Grp 2) *CHOL*: PSY 155-163 mg Wheat: 133 mg (Grp 1), 169-172 (Grp 2)	*CHOL*: -10 mg/dL (4%) *LDL-C*: -11 mg/dL (6%)	HDL-C: No sig dif (grps)

* Significant differences between treatment and placebo groups unless otherwise indicated.

Abbreviations Used in Table 1

C	Control
CHOL	Blood total cholesterol
d	Day
E	Energy
g	Gram
grp	Group
HDL-C	High density lipoprotein cholesterol
LDL-C	Low density lipoprotein cholesterol
m/f	Number of males, number of females
mg/dL	Milligrams per deciliter
mo	Months
oz	Ounces
Pla	Placebo
Pro	Protein
PSY	Psyllium
Sat fat	Saturated fat
SF	Soluble fiber
Sig Dif	Statistically significant difference
Step 1	≤ 30% kcals fat, 55% CHO, 15% Pro, <300 mg cholesterol
Tx	Treatment
wk	week
~	approximately
%	Percent

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