

Appendix A



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Dockets Management Branch (HFA-305)
Food and Drug Administration
Parklawn Building
Room 1061
5630 Fishers Lane
Rockville, MD 20852

RE: Dockets 00P-1275 and 00P-1276
Health Claims: Plant Sterol/Stanol Esters and Coronary Heart Disease

Dear Sir or Madam:

Reference is made to the September 8, 2000 *Federal Register* concerning the FDA's interim final rule on allowing health claims for the role of plant sterol/stanol esters in the reducing the risk of coronary heart disease.

McNeil Consumer Healthcare, as one of the petitioners cited in the interim final rule, commends FDA's expeditious approval of these claims and submits the attached comments and suggestions on how this rule may be fully applied to provide the best information in the interest of the public health.

It is our understanding that Raisio Benecol, Ltd. will submit comments to this docket. While Raisio's approach differs from McNeil's, we believe that they arrive at a similar conclusion concerning the argument for parity for minimum daily intake.

Sincerely
MCNEIL CONSUMER HEALTHCARE

Gilbert A. Leveille
Vice President, Worldwide Scientific & Regulatory Affairs

enc.

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I. INTRODUCTION

McNeil Consumer Healthcare is one of the petitioners cited in the September 8, 2000 *Federal Register* Interim Final Rule for health claims concerning plant sterol/stanol esters and coronary heart disease (CHD) (Docket No. 00P-1276).

As FDA stated in previous rules (21 CFR 101.75, 101.77, 101.81 and 101.82), CHD remains a major health problem and, with over 500,000 victims a year, the number one cause of death in the United States. FDA also provides the figures that one in five American adults, between the ages of 20 and 74, are at high risk, based on their total blood cholesterol levels. An additional 31 percent of adults have "borderline" total blood cholesterol levels, along with other risk factors. This equates to 51 percent of the adult population in the United States being at risk for developing CHD or related illnesses.

Based on its review of the scientific literature, FDA has concluded that foods and dietary supplements containing plant stanol esters may assist consumers in reducing their risk of CHD by lowering serum cholesterol levels. To fulfill the inherent public health benefit of the Rule, McNeil emphasizes the importance of the following six points:

1. The data demonstrate the equivalent cholesterol-lowering effect of dietary plant stanol esters and plant sterol esters. McNeil, therefore, recommends replacing the current two-tier designation with a single minimal daily effective level, thus treating plant sterol esters and plant stanol esters as a single class of compounds. To treat them differently within the same Rule is also potentially confusing to the consumer.
2. McNeil urges that the type of foods eligible to bear the health claim be expanded beyond spreads, salad dressings and snack bars, thereby encouraging consumer use through a broader array of foods. As with points 3 through 5 below, such a provision will provide consumers with greater choices and product diversity to more easily realize the cholesterol-lowering capability of plant stanol esters.
3. McNeil is requesting a broader exception from the minimum nutrient contribution for foods allowed to bear the health claim based on their stanol esters content [21 CFR 101.14(e)(6)]. Such an exception will benefit consumers by encouraging development of a greater number of food forms containing stanol esters. This will facilitate consumers' ability to attain a stanol esters intake which will provide a cholesterol-lowering health benefit.
4. While the Interim Final Rule exempts spreads and dressings for salad from the disqualifying level for total fat per 50g of food, the exception should be extended to include all foods with a serving size of two tablespoons or less, or 30g or less.
5. McNeil supports FDA's target of two servings of plant stanol ester-containing foods taken at different times during the day.
6. We agree with the inclusion of the plant stanol ester-containing dietary supplement as a product approved to bear the health claim.

I. **COMMENTS ON INTERIM FINAL RULE**

A. ***Cholesterol-Lowering Parity of Plant Sterol/Stanol Esters***

The agency has evaluated the pertinent scientific literature in determining the minimum daily effective dietary intake of plant stanol esters or plant sterol esters to lower blood cholesterol levels. Specifically, the agency specified in the Interim Final Rule that the minimum total daily intake for plant stanol esters be at a level of 3.4g [stated at §101.83(e)(2)], while the minimum total daily intake for plant sterol esters be at 1.3g [stated at §101.83(e)(10)]. McNeil believes that this substantial intake difference between the two substances is not justified by available science. It also creates a perceived disparity in value and efficacy, potentially leading to consumer confusion. We therefore request that the agency revise the Interim Final Rule to provide that minimum intake amounts be the same for plant stanol esters and plant sterol esters.

The similarity of plant stanol esters and plant sterol esters in their cholesterol lowering ability is supported by the available science, which includes additional, relevant data published since the original health claim petitions for these ingredients were filed (Hallikainen, et al 2000; Plat, et al 2000; and Normén, et al 2000). The rationale for considering plant stanol esters and plant sterol esters as a single class of compounds in assessing their cholesterol-lowering activity is as follows:

- 1) ***Similar Mechanism of Action:*** The science developed in experimental animals and *in vitro* systems demonstrates that both plant stanol esters and plant sterol esters inhibit cholesterol absorption by competing with cholesterol for incorporation into the micelles.
- 2) ***Similar Clinical Effects:*** Studies in which cholesterol absorption is directly measured have clearly shown that plant sterols and plant stanols, singly or in ester form, inhibit cholesterol absorption by the same mechanism and to the same extent. Additionally, three published clinical trials directly comparing the cholesterol-lowering potential of similar amounts of dietary plant stanol esters and plant sterol esters show that both substances reduce serum LDL-cholesterol (LDL-C) to a similar extent.
- 3) ***Statistical Equivalence:*** A statistical analysis of relevant data shows that there is a significant relationship between the amount of plant stanol esters and plant sterol esters ingested and the reduction of LDL-C. The analysis further shows that there is no statistically significant difference between the LDL-C lowering response for plant sterol esters and plant stanol esters.
- 4) ***Consumer Confusion:*** Different per serving guidelines for plant sterol esters and plant stanol esters creates consumer confusion.

1. Similar Mechanism of Action

Experimental evidence from *in vitro* systems and in laboratory animals indicates that plant stanols and plant sterols inhibit cholesterol absorption by competing with cholesterol for incorporation into intestinal micelles. Stanols and sterols have a higher affinity for mixed micelles than does cholesterol (von Bergmann, et al 1999). This suggests that these compounds successfully compete with cholesterol for micellar incorporation, leading to a reduction in cholesterol absorption.

Sugano, et al (1977) compared the hypocholesterolemic effects of sitosterol and sitostanol in rats fed diets with added cholesterol and found that both compounds lowered serum cholesterol. Ikeda and Sugano (1978), using radio-labeled sitosterol and sitostanol administered orally or intravenously to rats, found that the interference with cholesterol absorption appeared to be mechanistically similar for both compounds.

Bhattacharyya and Eggen (1988) examined plant sterol absorption in rhesus monkeys. Their results indicate that both cholesterol and campesterol were contained in the micellar fraction. The authors concluded that the two necessary steps in the process of sterol absorption, namely, the amounts of sterols solubilized in micelles and their esterification within the mucosal cells are responsible for sterol absorption.

Ikeda, et al (1989) studied the influence of sitosterol and sitostanol on the solubility of cholesterol in mixed bile salt micelles *in vitro* and *in vivo*. The investigators reported that both sitosterol and sitostanol decreased micellar solubility of cholesterol to a similar extent *in vitro*. They further confirmed these findings in rat studies in which both compounds significantly decreased liver cholesterol, thus showing the inhibitory effect each had on cholesterol absorption. Solubility of cholesterol in the micellar aqueous phase of rats fed cholesterol plus sitostanol and cholesterol plus sitosterol averaged 53% and 24% lower, respectively, than that in rats fed cholesterol alone. The results of these studies clearly show that individual plant sterols and plant stanols block cholesterol absorption via entry into mixed micelles in the rat model.

Ling and Jones (1995) summarized the available evidence for the mechanism for reduced cholesterol absorption by phytosterols. They indicate that reduced cholesterol solubilization in bile salt micelles appears to be a major factor in inhibiting cholesterol absorption by these compounds.

These findings from the *in vitro* and animal studies demonstrate that both plant sterols and plant stanols reduce cholesterol absorption by a similar mechanism, i.e., by competing with cholesterol entry into intestinal micelles.

2. Similar Clinical Effects

Data from human trials confirm the *in vitro* and animal study finding that plant stanol esters and plant sterol esters inhibit cholesterol absorption by a similar mechanism and to a similar extent. Additionally, clinical trials demonstrate no significant differences in LDL-C lowering when plant stanol esters are compared to plant sterol esters.

Heinemann, et al (1991) compared the effects of sitosterol and sitostanol on inhibition of cholesterol absorption in 10 male volunteers divided into two groups, each intubated with triple lumen tubes, and fed liquid formula diets alone or with added sitosterol or sitostanol. Cholesterol absorption was similar and not statistically different between subject groups during the control period (averaging 34% and 31%, respectively). Both sitosterol and sitostanol infusions reduced cholesterol absorption 50-85%, demonstrating that both sitostanol and sitosterol are effective in reducing cholesterol absorption in human volunteers.

Jones, et al (2000) [FDA reference 58]* examined cholesterol absorption, synthesis and turnover, in addition to measuring serum levels of lipids, sterols and stanols. Fifteen hypercholesterolemic men were fed, in random order, nutritionally adequate diets containing: a control margarine-like spread; the same spread with added plant sterol esters; or plant stanol esters. Daily consumption was 1.84g of sterols or stanols (2.94g sterol esters/3.13g stanol esters). Cholesterol absorption was significantly decreased compared to control period (36.2% and 25.9% reduction in cholesterol absorption for sterol esters and stanol esters, respectively), with no significant differences between treatments.

Normén, et al (2000), in a trial published subsequent to submission of McNeil's plant stanol ester health claim petition, measured small bowel cholesterol absorption, sterol excretion, and hepatic cholesterol synthesis in subjects with ileostomies. The daily intake of plant sterol esters and plant stanol esters in this randomized, controlled, crossover study corresponded to 1.5g of plant sterols/stanols per day (equivalent to \approx 2.5g as esters). Ileostomy bags from seven subjects were collected every other hour and frozen for analysis of nutrients and sterols. Cholesterol absorption was 56% (43-65%) in the control period, decreasing to 38% (32-46%) in the sterol esters period, and 39% (30-48%) in the stanol esters period. Sterol esters and stanol esters were thus shown to inhibit cholesterol absorption to the same extent.

Three human studies directly compared the serum cholesterol-lowering potential of plant sterol esters and plant stanol esters and showed no significant differences in LDL-C reduction. The following describes changes in LDL-C, rather than changes in serum total cholesterol, because LDL-C is generally accepted to be the serum measurement most closely associated with heart disease risk. Total cholesterol decrements followed the same pattern as changes in LDL-C.

*Bracket [] citations to FDA reference numbers correlate directly with "Section XI. References" of the September 8, 2000 *Federal Register Notice*, "Food Labeling: Health Claims; Plant Sterol/Stanol Esters and Coronary Heart Disease; Interim Final Rule."

Weststrate and Meijer (1998) [FDA reference 67] compared the lipid-lowering effects of margarine-type spreads containing plant sterol esters or plant stanol esters. Results showed that both margarines were effective in lowering LDL-C approximately 13% compared to control margarine. The authors concluded that margarines with plant sterol esters or plant stanol esters were equally effective.

Hallikainen, et al (2000), published a study after issuance of the Interim Final Rule. They investigated whether two spreads containing plant stanol esters or plant sterol esters were equally effective in lowering serum LDL-C concentrations as part of a low fat, low cholesterol (Step 1) diet. The study was a randomized, double-blind, placebo-controlled, crossover trial in hypercholesterolemic subjects. After a two-week Step 1 diet run-in period, subjects were randomized to consume each of the test spreads for periods of four weeks. The two test spreads were matched with respect to fatty acid composition and degree of esterification. Mean daily intakes were 2.01g of stanols per day and 2.04g of sterols per day, as esters, for the 34 subjects completing the study. There were no significant differences in serum lipid responses between the two test spreads, although both lowered LDL-C significantly relative to control spread. Serum LDL-C was reduced by 12.7% at end of the stanol esters spread period and 10.4% after the sterol esters spread period relative to control. The authors concluded that as part of a Step 1 diet, plant stanol esters and plant sterol esters spreads reduced LDL-C concentrations significantly and equally.

In the Jones, et al (2000) study referenced above, serum lipid measurements were made in addition to the direct measurement of cholesterol absorption. In this study, the control diet reduced LDL-C levels by 3.9%. The plant sterol esters reduced LDL-C by 12.9%, which was significantly different from control. The plant stanol esters reduced LDL-C by 7.9%, which was neither significantly different from control, nor significantly different from sterol esters. However, both sterol and stanol esters spreads significantly reduced LDL-C levels from baseline. The authors concluded that both esterified sitosterol and esterified sitostanol are efficacious in favorably reducing circulating cholesterol concentrations in hyperlipidemic males.

A review by Law (2000) [FDA reference 100], summarized 14 published, peer-reviewed, randomized, double-blind clinical trials in adults. These trials compared the effects of margarines with and without added plant sterol esters and/or plant stanol esters on LDL-C reduction. Law noted the similar extent to which LDL-C reduction occurred. In a plot of sterol or stanol intake against LDL-C reduction, he notes the continuous relationship of dose and response up to about 3.4g daily intake.

The clinical data are predictable on the basis of the *in vitro* data and animal studies. Similar intakes of plant stanol esters or plant sterol esters reduced LDL-C levels and inhibited intestinal cholesterol absorption to an equivalent degree.

3. Statistical Equivalence

The science described above supports the principle that plant sterol esters and plant stanol esters inhibit cholesterol absorption to an equivalent extent, thereby lowering LDL-C to a similar degree. It, therefore, follows that a single minimum effective daily intake of either ingredient is appropriate. A statistical analysis conducted on relevant clinical data provides additional substantiation for establishing a common minimum daily intake for plant stanol esters and plant sterol esters (Appendix B).

The following criteria were used in selecting data points utilized for the statistical analysis. Data from all studies considered relevant by FDA in the Interim Final Rule were used, with the following exceptions:

- Studies utilizing free stanols [FDA reference 97] or free sterols [FDA references 65, 75] or mixtures [FDA reference 74] were excluded.
- Data where the results for LDL-C were not significantly reduced compared with placebo were excluded (one data point from each of the following FDA references: 88, 94, 77).
- Studies where LDL-C was not reported were excluded. (FDA reference 91).
- The data point from FDA reference 78 where stanol ester was incorporated into butter was excluded.

Additionally, FDA references 64 and 65 were excluded based on FDA's determination that these studies were difficult to interpret and the results inconsistent. FDA references 81 and 82 were also excluded, based on FDA's determination that these reports lacked sufficient detail on the reason for the varying number of control subjects.

Additionally the data from two studies published subsequent to the Interim Final Rule were included, as these studies satisfy FDA's criteria as specified in Section III.B.2 of the Rule. (Hallikainen, et al 2000 and Plat, et al 2000).

In all, 21 data points from 12 studies were included for plant stanol esters [FDA references 58, 67, 77, 78, 80, 88, 89, 90, 92, 94, Hallikainen, et al (2000), and Plat, et al (2000)], and nine data points from six studies for plant sterol esters [FDA references 51, 57, 58, 61 and 62, 67 and Hallikainen, et al (2000)].

One of the two studies published subsequent to the Interim Final Rule (Hallikainen, et al 2000), was summarized above. The second study (Plat, et al 2000) was a randomized, double-blind, placebo-controlled, cross-over study of 39 healthy normocholesterolemic or mildly hypercholesterolemic subjects. The results demonstrated that the LDL-C lowering effects of 2.5g/daily of plant stanols (4.25g plant stanol esters) consumed in a single, midday dose did not differ significantly from that obtained when the same plant stanol esters intake level was divided over three meals daily. LDL-C was reduced by 9-10% versus control intakes.

In the statistical analysis (Appendix B), all three variables (grams of sterol esters per day, grams of stanol esters per day, and the percentage change in LDL-C level) represent the average level of intake or the average percent reduction in LDL-C for an individual study. A regression analysis was conducted and showed a highly significant relationship between sterol/stanol esters intake and percent LDL-C reduction ($R^2 = 0.352$; $p = 0.003$). This observation permitted an additional analysis to test whether the effects of the two esters were different from each other. The effect of type of ester (stanol vs sterol) was modeled, using all plotted data. This second analysis indicated that the slopes of the lines of best fit for the plant sterol esters data and for the plant stanol esters data were not significantly different from each other. Therefore, the overall statistical analysis reinforces the conclusions from the published scientific literature demonstrating the equivalency of dietary stanol esters and sterol esters in reducing LDL-C.

4. Consumer Confusion

Based on a recent research sampling, the differing health claims specified in the Interim Final Rule, lead to significant confusion in two-thirds of consumers (Appendix C).

According to key findings, when asked if one product "would be better than the other at helping to reduce the risk of heart disease," 39% of consumers thought that one product would be more effective than the other; 27% were unsure; and only 34% thought the products were equally effective. This means that fully 66% of the 303 consumers in the study were confused about the risk reduction potential of the products.

Based on these observations, the health claims specified in the Interim Final Rule are confusing to consumers. Consumer understanding would be enhanced by a uniform daily intake amount for plant stanol esters and plant sterol esters which allows for a clear and equal message of risk reduction to be provided to the public.

Conclusion: The analysis of relevant scientific data leads to the conclusion that similar amounts of dietary stanol esters or sterol esters lower LDL-C to the same extent. Furthermore, consumer research shows that health claims based on differing minimum daily intakes directly leads to consumer confusion.

McNeil, therefore, believes the Final Rule should specify a single minimum daily effective level that would apply to both plant stanol esters and to plant sterol esters. The level selected should be high enough to effect a meaningful reduction in LDL-C.

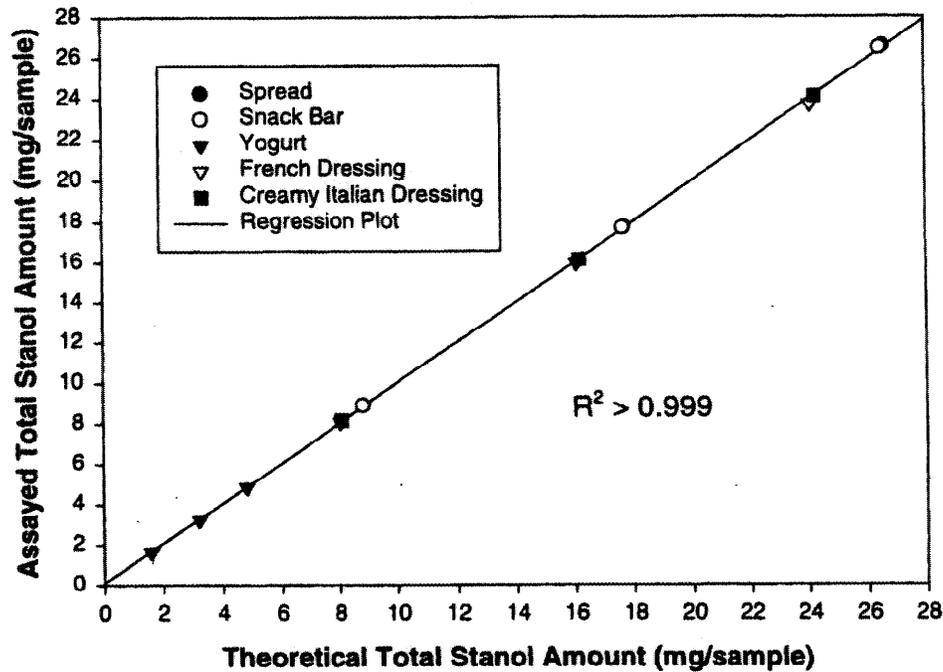
B. General Food Use of Plant Stanol Esters

The Interim Final Rule provides in Part V Section D(1)(b) that the foods eligible to bear the health claim for plant stanol esters and coronary heart disease are spreads, dressings for salad, snack bars, and dietary supplements in softgel form. It additionally states that FDA will consider expanding foods eligible to bear the health claim "...if comments on this rule provide a validated analytical method that permits accurate determination of the amount of plant stanol esters in other foods." McNeil has provided as Appendix D-1 a validated analytical method to permit the analysis of any food for the qualifying level of plant stanol esters per reference amount customarily consumed (RACC).

The methodology for plant stanol analysis in stanol ester-containing spreads, dressing, snack bars (previously reviewed by FDA as part of McNeil's health claim petition) and yogurt (Appendix D-2) is identical in saponification, extraction and derivatization procedures. Gas Chromatographic detection and plant stanol quantification are also comparable across stanol ester-containing foods. The only procedural points of difference for analysis of stanol ester-containing foods are the initial blending of the sample and the amounts of sample and Internal Standard introduced into the assay. Given the uniform procedure for plant stanol analysis in stanol ester-containing foods, McNeil Analytical Method 88-AM-901, Determination of Stanols and Sterols in Benecol Foods was developed for determination of plant stanols in any stanol ester-containing food.

This single analytical method for measuring plant stanols in any stanol ester-containing food is supported by method validation studies in multiple stanol ester-containing food systems. Method validation studies were performed in dairy, oil and grain based multi-component stanol esters food systems. Spread and dressing were selected as representative oil-water emulsions; snack bars as model grain-based systems; and yogurt as a representative dairy system. Method validation demonstrates that analysis of plant stanols is linear, accurate and precise across stanol ester-containing food systems (see linearity graph below). Analysis of foods not containing stanol ester and mass spectra of sitostanol and campestanol from stanol ester-containing foods demonstrate specificity of the analytical methods for plant stanols. The singular analytical approach across food systems and method validation studies in dairy, oil and grain based multi-component foods verify this method for quantitative analysis of plant stanols in foods containing plant stanol esters.

**Linearity Plot of Assayed Total Stanol Amount Versus
Theoretical Total Stanol Amount**



Conclusion: McNeil has provided a validated method for analysis of plant stanol esters in any food. We therefore urge that the health claim for plant stanol esters be extended to all foods, encouraging manufacturers to provide a greater number and variety of foods than provided for in the Interim Final Rule. A broader array of foods will enable consumers to more easily incorporate plant stanol esters their diets and promote healthful eating patterns.

C. Minimum Nutrient Contribution Requirement

Currently marketed food products eligible to bear the health claim under the provisions of the Interim Final Rule include spreads and bars. The provisions of the Interim Final Rule state at §101.83(H)(iii), subsection (D): "The food must meet the minimum nutrient contribution requirement in §101.14(e)(6) unless it is a dressing for salad...." Spreads and bars do not meet this requirement, yet they are not designated as an exception as are dressings for salad. McNeil requests clarification from FDA on this point.

Section §101.14(e)(6) prohibits health claims for a food unless the food contains 10 percent or more of the recommended daily intake or DRV for vitamin A, vitamin C, iron, calcium, protein or fiber per RACC, prior to any nutrient addition. McNeil's petition requested a general exception from this requirement. FDA did not grant the requested general exception, nor did it grant an exception of McNeil's spread and bar products. In its comments, the agency pointed out that the minimum nutrient contribution requirements were intended to ensure that the value of health claims would not be trivialized; that the petitioner's rationale did not justify any exception; and that manufacturers of foods not meeting this requirement could petition the agency on a case-by-case basis to request an exception.

It is McNeil's position that the exception apply to spreads and bars, as well as be extended to all food products. McNeil is requesting that FDA allow an exception to the provision that the minimum nutrient contribution requirement be met with nutrients "inherently" present in the food. We are requesting that the requirement be allowed to be met by nutrient addition to the final food product, providing compliance with FDA's fortification policy is also met. By applying the food fortification policy at 21 CFR 104.20, the exception can be extended to all foods without trivializing the health claim. The provisions of that regulation provide appropriate guidelines for fortification of food products; therefore, foods meeting the minimum nutrient requirements through fortification would be eligible to bear the health claim.

Providing for exceptions only on a case-by-case basis, as FDA currently suggests, fails to provide a viable alternative, unless an expedited review procedure is specified as part of this health claim regulation. An expedited review process could, for example, be based on the notification procedure found elsewhere in the regulations and provide that manufacturers or others applying for an exception submit a notification of intent to apply the stanol esters health claim to a non-qualifying food. This notification would include information supporting the position that the food should be excepted. Absent agency response setting forth reasons why the food should not be included in the exception, the notification would be deemed as constituting approval.

If these requested exceptions are not allowed, and an expedited review procedure is not defined in this regulation, case-by-case evaluations could only be initiated and proceed as amendments to the health claim regulation, requiring adherence to all procedural and time requirements. Such a process could operate only to delay or substantially hinder the development of additional food forms and, as a practical matter, would not enable new product development to proceed until the amendment process had been completed, if at all.

Conclusion: McNeil requests that:

- . FDA clarify that the exception from the minimum nutrient requirements applies to spread and bar forms already marketed and found to be appropriate to bear the health claim.
- . FDA consider excepting all foods from the provision of "inherently present nutrients" and allow for meeting the nutrient contribution requirement by addition of nutrients, consistent with the agency's fortification policy.
- . Should FDA not extend the exception to all foods, an expedited notification review process should be made part of this health claim regulation to permit timely exception consideration.

D. Fat Content Requirements

In the Interim Final Rule, FDA granted two exceptions from NLEA fat content requirements: 1) An exception that foods bearing the health claim meet the low fat nutrient content claim; and 2) An exception from the disqualifying level for total fat per 50g of food for spreads and dressings for salad, but for no other food products or forms.

McNeil agrees with FDA's decision to except foods from the nutrient content requirements for low fat foods. By doing so, FDA acknowledges the public health benefits of plant stanol esters and provides for their increased use in foods.

In our health claim petition, McNeil requested an exception from the small serving size total fat requirement. We do not agree that the exception for total fat for small serving sizes (less than or equal to 2 tablespoons or 30g per RACC) should be limited only to spreads and dressings for salad. The agency did not permit a blanket exception for all foods with small serving sizes, based on its concern that such an exception would open the door to increased consumption of high fat foods. There are a number of reasons McNeil urges FDA to reconsider exempting all foods with small serving sizes from the requirement of no more than 13g total fat per 50g.

First, all foods bearing the health claim will be required to be low in saturated fat and cholesterol, which is consistent with the recently distributed Dietary Guidelines for Americans, 2000 and the requirements for all other health claims relating to CHD. As stated in the Interim Final Rule, "the 2000 Dietary Guidelines Advisory Committee concluded that the scientific evidence on dietary fat and health supports assigning first priority to reducing saturated fat and cholesterol intake, not total fat intake."

Second, if all foods with small serving sizes were excepted, they would continue to be required to meet all disqualifying levels, including total fat, per RACC and per serving. This requirement alone will limit the number of high fat foods eligible to bear the health claim. In addition, the disclaimer, "See nutrition information for fat content," would apply and appear on labels of products with small servings that bear the health claim and exceed the disqualifying level for fat. This is consistent with the public health recommendation FDA cites as the basis for allowing the disclosure for spreads and dressings for salad, namely the expert opinion on total fat intake, the risk of CHD, and general health. Although diets high in saturated fat and cholesterol are implicated in CHD, current scientific evidence does not indicate that diets high in unsaturated fat are associated with CHD.

Finally, the labels of all products containing plant stanol esters clearly specify the number of servings recommended per day to obtain the health benefit, along with the amount of plant stanol esters provided per serving. This information is required to appear on the principle display panel as part of the health claim and this prominence will serve as a primary means of informing consumers exactly how many servings of a product with a small serving size are recommended.

Unless an exception for additional foods with small serving sizes is granted as part of this rulemaking, FDA will need to evaluate such foods on a case-by-case basis. Absent an expedited notification process, a potentially lengthy procedure would provide a disincentive for manufacturers to develop additional plant stanol ester-containing foods, thereby depriving consumers of variety and the opportunity to consume foods that may reduce the risk of heart disease.

Conclusion: McNeil recommends that FDA except all foods with small serving sizes from the disqualifying levels for total fat on a 50g basis in order to bear the health claim. Importantly, we are not suggesting that such foods be excepted from the total fat disqualifying level per serving or per RACC.

E. Daily Serving Guidelines

In the Interim Final Rule, FDA specifies that the daily intake of plant stanol/sterol esters "should be consumed in at least two servings eaten at different times during the day with other foods," as stated in Part V Section B, "Description and Rationale for Components of the Health Claim." McNeil supports FDA's two serving per day target.

Importantly, consumers can easily understand and maintain a diet that incorporates at least two servings of plant stanol esters a day, thus encouraging long-term compliance culminating in substantial health benefits.

F. *Inclusion of Dietary Supplements*

We fully support the inclusion of plant stanol ester-containing dietary supplements as products qualifying for the claims as provided in Part II Section A(3)(b)(ii) and stated in Part V Section D (1)(b), "Nature of the Food Eligible to Bear the Claim."

This addition to the foods eligible to bear the health claim offers consumers with yet another straightforward and convenient way to incorporate plant stanol esters into their diet, encouraging a greater number of consumers to use products providing demonstrated health benefits.