Council for Responsible Nutrition
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Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

RE: Comments to FDA's Proposed Rule on Food Labeling; Health Claim; Phytosterols and Risk of Coronary Heart Disease [Docket Nos. FDA-2000-P-0102, FDA-2000-P-0133, and FDA-2006-P-0033; Formerly Docket Nos. 2000P-1275, 2000P-1276, and 2000P-0316, Respectively] (75 FR 76526).

The Council for Responsible Nutrition (CRN)[1] is a Washington, DC-based trade association representing the dietary supplement industry. Our members include some of the largest and most well known ingredient suppliers, manufacturers, direct sellers and retailers of dietary supplements. CRN appreciates the opportunity to provide comments on the proposed rule for the health claim on phytosterols and risk for coronary heart disease[2]. CRN supports the FDA's efforts to ensure that health-related claims for dietary supplements are supported by credible scientific evidence. However, CRN has concerns that the Agency's proposed action to exclude all dietary supplement products that contain free phytosterols from bearing the approved health claim does not reflect full consideration of the impact of all delivery matrices on the efficacy of dietary supplements containing free phytosterols.

In addition to tablets, softgels and capsules, dietary supplements can be formulated as dry powders that are intended to be blended into a food or beverage prior to consumption. A free phytosterol powdered dietary supplement that is reconstituted into a food or liquid beverage will overcome dissolution and distribution limitations that may occur with the tablet or capsule form of free phytosterols. Spilburg, et al., 2003 demonstrated that 4-weeks'

[1] The Council for Responsible Nutrition (CRN), founded in 1973 and based in Washington, D.C., is the leading trade association representing dietary supplement manufacturers and ingredient suppliers. CRN companies produce a large portion of the dietary supplements marketed in the United States and globally. Our member companies manufacture popular national brands as well as the store brands marketed by major supermarkets, drug store and discount chains. These products also include those marketed through natural food stores and mainstream direct selling companies. In addition to complying with a host of federal and state regulations governing dietary supplements, our 70+ manufacturer and supplier members also agree to adhere to voluntary guidelines for manufacturing, marketing and CRN's Code of Ethics. Learn more about us at www.crnusa.org.

[2] 75 FR 76526. http://www.federalregister.gov/articles/2010/12/08/2010-30386/food-labeling-health-claim-phytosterols-and-risk-of-coronary-heart-disease

supplementation with a powdered phytosterol that was mechanically blended into a lemonade-flavored beverage prior to consumption significantly reduced LDL-cholesterol as compared to placebo[3]. Furthermore, Kassis, et al., 2008[4] demonstrated that supplementation with a free phytosterol powder that was mixed into margarine and served as a single dose with breakfast significantly lowered plasma total cholesterol and LDL-cholesterol. These data suggest that the delivery matrix used for free phytosterol-containing dietary supplements influences the efficacy of the formulation and that some dietary supplements should be able to bear the health claim relating phytosterols and risk of coronary heart disease[5].

Furthermore, tablet and capsule preparations of free phytosterols that disintegrate efficiently may provide a different effect than tablets or capsules that do not. A closer look at disintegration time and efficacy data reveals that disintegration of the specific dietary supplement delivery matrix is an important variable that needs consideration when evaluating the effect of free phytosterols taken as dietary supplements. It is noteworthy that disintegration time has been an important variable for other FDA approved nutrition-related health claims. The United States Pharmacopeia (USP) has developed a standard for disintegration of dietary supplements[6]. Dietary supplements bearing the FDA-approved health claim for folate and neural tube defects[7] must meet the United States Pharmacopeia (USP) standards for disintegration and dissolution, except that if there are no applicable USP standards, the folate in the dietary supplement shall be shown to be bioavailable under the conditions of use stated on the product label. Therefore, the FDA has set a precedent for the consideration of disintegration and dissolution standards as specific requirements for health claim use.

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[3] Spilburg CA, Goldberg AC, McGill JB, et al. Fat-free foods supplemented with soy stanol-lecithin powder reduce cholesterol absorption and LDL cholesterol. *J Am Diet Assoc* 2003;103:577-581.

[4] Kassis AN, Vanstone CA, AbuMweis SS, Jones PJ. Efficacy of plant sterols is not influenced by dietary cholesterol intake in hypercholesterolemic individuals. Metabolism 2008;57:339-346.

[5] Plant Sterol/stanol esters and Risk of Coronary Heart Disease *(21 CFR 101.83).* http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=101.83

[6] USP General Chapter <2040> Disintegration and Dissolution of Dietary Supplements. http://www.usp.org/pdf/EN/USPNF/gc2040DisintegrationAnd%20DissolutionDS.pdf

[7] Folate and Neural Tube Defects *(21 CFR 101.79).* Dietary supplements shall meet the United States Pharmacopeia (USP) standards for disintegration and dissolution, except that if there are no applicable USP standards, the folate in the dietary supplement shall be shown to be bioavailable under the conditions of use stated on the product label. http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=101.79

Data on dietary supplements containing free phytosterols that meet USP standards for disintegration as compared to products that do not meet this standard demonstrate that dissolution time is a factor influencing efficacy for these products. CRN members have shared with CRN a re-evaluation of the relevant data that the FDA identified as important for examining the effect of free phytosterol dietary supplements. These same data were re-evaluated by determining if the phytosterol interventions met USP standards for disintegration. Interventions that used free phytosterol supplements that met USP disintegration time significantly lowered serum cholesterol while interventions that used preparations that did not meet USP disintegration standards did not. More specifically, interventions in the "tablet" arm of McPherson, et al., 2005[8] and Goldberg, et al., 2006[9] met USP disintegration standards and significantly lowered serum cholesterol while interventions used in Denke,1995[10] and in the "slow-release" arm of McPherson, et al.,2005 did not meet USP dissolutions standards and were not significantly effective at lowering serum cholesterol.

In summary, CRN believes that the phytosterol health claim should be allowed for powdered dietary supplements containing free phytosterols and for dietary supplements in other delivery matrices that meet or exceed USP disintegration time.

Thank you,

Douglas MacKay, ND

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[8] McPherson TB, Ostlund RE, Goldberg AC, et al. Phytostanol tablets reduce human LDL-cholesterol. J Pharm Pharmacol 2005;57:889-896.

[9] Goldberg AC, Ostlund RE Jr, Bateman JH, et al. Effect of plant stanol tablets on low-density lipoprotein cholesterol lowering in patients on statin drugs. Am J Cardiol 2006;97:376-379.

[10] Denke MA. Lack of efficacy of low-dose sitostanol therapy as an adjunct to a cholesterol-lowering diet in men with moderate hypercholesterolemia. Am J Clin Nutr 1995;61:392-396.