Tufts-New England Medical Center
A Lifespan Partner

TUFTS UNIVERSITY
SCHOOL OF MEDICINE

July 15, 2003

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

Re: FDA letter of February 14, 2003 re: health claims for phytosterols; request for reconsideration and comments on guidance that FDA is developing. Docket Nos. OOP-1275 and OOP-1276: Comments, and request to reopen the comment period.

To Whom it May Concern:

Unilever Bestfoods North America has asked that I provide you with my views on the company's comment that "low-fat" or "fat-free" foods that contain unesterified plant sterols or stanols (free phytosterols) should not at this time be eligible to be labeled with a health claim about the relationship between phytosterols and coronary heart disease. The company has set forth its position that this claim should be permitted for such foods only if additional data are submitted to FDA to demonstrate that there is significant scientific agreement that free phytosterols consistently result in meaningful levels of cholesterol reduction when formulated in such foods. I am familiar with this comment and with the data that support it. I am also familiar with the standards for significant scientific agreement that form the basis for the approval of health claims. For the reasons discussed in this letter, I fully support this comment.

My professional experience is in the field of internal medicine (residency at Mt. Sinai Hospital, New York), endocrinology and metabolism (fellowship at the National Institutes of Health), and cholesterol and heart disease prevention (Director, Lipid and Heart Disease Prevention Clinic, Tufts-New England Medical Center). I am a Professor of Medicine at Tufts University School of Medicine and a Professor of Nutrition at the Friedman School of Nutrition Science and Policy at Tufts University in Boston. I do research in the area of nutrition, genetics, lipoprotein, and heart disease prevention, and served on the Nutrition Committee of the American Heart Association, as well as the First and Second Adult Treatment Panels of the National Cholesterol Education Program (NIH). Based on my professional experience, I am familiar with scientific standards for reviewing studies of cholesterol-reducing agents and with views on this topic held by others in the scientific and medical community.

OOP-1275 C25

Atherosclerosis Research Laboratory

Lipid and Heart Disease Prevention Clinic

Ernst J. Schaefer, MD
Director, and
Head, Lipid Clinic

Bela F. Asztalos, PhD
Head, Biochemistry Section

Margaret E. Brousseau , PhD
Head, Genetics Section

Stefania Lamon-Fava, MD, PhD
Head,
Hormone Replacement Section

Alice H. Lichtenstein, DSc
Head, Nutrition Section

Julian B. Marsh, MD
Head, Metabolism Section

Judith, R. McNamara, MT
Supervisor,
Atherosclerosis Research Laborato

Jose M. Ordovas, PhD
Head, Molecular Biology Section

Francine K. Welty, MD PhD
Head, Kinetic Modeling Section

Joi L. Augustin, MS, RD
Head,Nutritional Counseling
617 636-0128

Clinic Phone 617 556-3100
750 Washington Street
Tufts-NEMC Box #216
Boston, Massachusetts 02111

Office Phone
Tel 617 556-3100
Fax 617 556-3103

In my opinion, the published data are inconclusive with respect to whether free phytosterols consistently result in meaningful levels of cholesterol reduction when formulated in fat-free or low-fat foods or beverages. As indicated by Unilever Bestfoods North America, the studies by St-Onge et al (in press, Journal of Lipid Research 2003) and Denke (American Journal of Clinical Nutrition 1995;61:392-396) demonstrate a lack of efficacy of free phytosterols, whereas the study by Nestel et al (European Journal of Clinical Nutrition 2001;55:1084-1109) suggests that free phytosterols in low-fat foods are less effective than esterified sterols.

Other published studies do not enable a proper evaluation of the cholesterol-lowering efficacy of free phytosterols in low-fat foods. For example, in the study by Maki et al (Maki KC, Shinnick F, Seeley MA, Veith PE, Quinn LC, Hallissey PJ, Temer A, Davidson MH. Food products containing free tall oil-based phytosterols and oat beta-glucan lower serum total and LDL cholesterol in hypercholesterolemic adults (J Nutr 2003;133:808-13) a combination of treatments was studied, not allowing for interpretation of the net effect of the free phytosterols.

In the study by Tikkanen et al (Tikkanen MJ, Hogstrom P, Tuomilehto J, Keinanen-Kiukaanniemi S, Sundvall J, Karppanen H) Effect of a diet based on low-fat foods enriched with nonesterified plant sterols and mineral nutrients on serum cholesterol. Am J Cardiol 2001;88:1157-62), the 'low-fat foods' are not being described so that it is unclear what the composition has been of the foods being used.

Considering these published studies together, and based on my familiarity with the scientific literature and with the conduct of research in this field, it is my opinion that the available data do not at this time permit a conclusion to be drawn as to whether free phytosterols consistently and meaningfully reduce cholesterol levels when formulated in low-fat or fat-free products. I believe that others in my professional field, reviewing the same data, would reach a similar conclusion. I therefore support Unilever Bestfoods North America's request that foods that contain free phytosterols should be eligible to be labeled with the health claim only if the foods are not "low-fat" or "fat-free", and that additional clinical data need to be generated to support a health claim about free phytosterols in "low-fat" or "fat-free" foods.

Sincerely,

Ernst J. Schaefer, M.D.
Professor of Medicine
Chief, Lipid Research Laboratory
Director, Lipid and Heart Disease
Prevention Program
EJS/sp