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Notice of Assessment of Certain Categories of Foods Containing Added Phytosterols

Bureau of Nutritional Sciences
Food Directorate, Health Products and Food Branch
Health Canada

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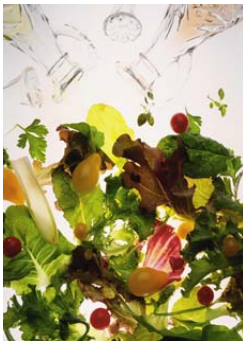


Canada

Introduction:

This document summarizes Health Canada's safety assessment of certain foods containing added phytosterols and invites manufacturers to seek authorization to sell and advertise these novel foods in Canada.

The term "phytosterols" is used in this document as a collective term for plant sterols, and their hydrogenated stanol forms, whether used in the free sterol form or esterified with fatty acids (also known as sterol esters or phytosterol esters). There is a diversity in the composition of phytosterols and over 40 phytosterols have been identified in nature. The safety assessment considered phytosterols and stanols as a group.

Phytosterols occur naturally in plants, and vegetable oils are the major source of phytosterols in Canadian diets. Phytosterols, when consumed at sufficiently high levels, have been shown to reduce serum total and LDL cholesterol levels.

In Canada, the regulatory status of foods with added phytosterols has evolved over the past ten years. Phytosterols sold in isolated form have a history of sale and use as drugs and, later, when the Natural Health Product Regulations came into effect, as natural health products under the Food and Drugs Act to treat hypercholesterolemia. When it was first proposed that a food containing added phytosterols be sold the product was considered a drug on the basis that it was manufactured for a therapeutic purpose, i.e., interfering with the absorption of intestinal cholesterol (modifying an organic function) with the intent of reducing elevated serum cholesterol levels. As a result, no novel food review was completed. At the time, data and information to support the safety of foods containing phytosterols, particularly long term studies, were lacking.

Health Canada has recently reconsidered the classification of such products in light of recently clarified principles for the classification of foods at the Food-Natural Health Product interface; and the developments in what is known about these products. It was determined that where a substance with a food purpose or dietary origin is added to a product in controlled amounts to allow for safe consumption as a food and food has substantiated health effects, the product may be classified and regulated as a food. In these circumstances, the use of a disease risk reduction claim or therapeutic claim would not be sufficient to classify the food as a natural health product.

Completion of this novel food class assessment has also become possible because, very importantly, data and information considered critical to the establishment of the safety of phytosterols for use as ingredients in foods has recently become available.

The safety of phytosterols was assessed according to Division 28 of the Food and Drug Regulations (FDR), because foods with added phytosterols were considered "a substance that does not have a history of safe use as a food." Health Canada has received several novel food submissions for a range of foods with added phytosterols. The Food

Directorate (FD) has conducted the safety assessments according to its *Guidelines for the Safety Assessment of Novel Foods*. These Guidelines are based upon internationally accepted principles for establishing the safety of novel foods. The following summarizes the major elements of the assessment:

Toxicological Assessment

The toxicological assessment considered data from reports of adverse effects of excessive plant sterol accumulation in humans, data from experimental animals, and well-documented and well-conducted human safety trials. In the toxicological assessment, critical consideration was given to the adverse effects observed in individuals with excessive plasma plant sterol concentrations (e.g. decreased red blood cell and platelet counts, increased serum alanine aminotransferase and aspartate aminotransferase activity, increased total serum bilirubin) because these effects would suggest the potential of plant sterols to interfere with the biological role of cholesterol (e.g. structure of cell membranes, and the production of bile acids, steroid hormones, and vitamin D).

The available human trials that sufficiently reported haematology and clinical chemistry parameters provided evidence of a lack of adverse effects at doses as high as 6.6 g of free phytosterols/day for 12 weeks and 8.8 g of free phytostanols/day for 10 weeks. However, there is uncertainty regarding the potential for adverse effects with the consumption of levels higher than 3 g of free phytosterols per day for an extended period of time, specifically for a subset of the population who hyperabsorb phytosterols from the diet. This subset cannot self-identify and therefore cannot know to avoid use of foods with added phytosterols. An upper limit of 3 g of free phytosterols per day provides a conservative approach which mitigates the potential for adverse effects from increased phytosterol consumption by those individuals who hyperabsorb plant sterols.

Based on its review of the available evidence, therefore, the Food Directorate has concluded that 3 g per day for adults and 1 g per day for children should be used as reference safe intakes.

The FD has no safety concerns regarding the consumption of plant sterol fortified products by the targeted population, (i.e. hypercholesterolemic adults who wish to lower their cholesterol levels), at levels lower than the reference safe intakes. In addition, there are no safety concerns for the general population, including hyperabsorbers, children, and pregnant women, who may unintentionally consume plant sterol fortified food products.

Nutritional Assessment

A potential nutritional safety issue raised in the literature is the lowering of serum carotenoids after consumption of phytosterols, particularly provitamin ß-carotene.

Carotenoids are important to humans in mainly two aspects: their provitamin A activity and their antioxidant capacity. If consumed regularly in excessive amounts, it has been suggested that phytosterols may decrease serum ß-carotene. However, serum concentration of ß-carotene is highly variable and the variability can be attributed to a variety of life-style and physiological factors. According to the Institute of Medicine (2000), serum concentration of ß-carotene ranges from 2.2 to 122.7 g/dL. In addition, the published studies overall demonstrate that at the consumption level of 3 g of phytosterols per day, there is no significant effect on serum levels of ß-carotene, or the effect disappears when the change in ß-carotene levels is adjusted for the change in serum total cholesterol level. Therefore, it is concluded that the consumption of plant sterols up to the reference safe intake of 3 g per day is nutritionally safe for the general population with respect to ß-carotene.

Dietary Exposure:

Modelling studies were conducted by Health Canada to determine the appropriate food categories and level of addition of phytosterols in order to help ensure that potential exposure to the addition of phytosterols to foods would be below the safe reference levels in the general population, including children. In the modelling studies, various scenarios were examined using a broad range of foods and levels of addition, including those proposed by petitioners and those approved in other jurisdictions. The distribution of potential intakes across the population relative to the reference safe intake was used to determine the appropriate food categories and level of addition of phytosterols. The studies estimated potential exposure by age and sex in the population including non-target populations, particularly children. The findings of the simulation studies suggested that the addition of phytosterols at up to 1 g (free phytosterols) per serving and per reference amount to unstandardized spreads, mayonnaise, margarine, calorie-reduced margarine, salad dressing and unstandardized salad dressings, yogurt and yogurt drinks and vegetable and fruit juices would not result in over exposure in the non-target population. Post-market studies conducted in Europe also support that over consumption of phytosterols, even in the target population, is very unlikely.

Labelling:

Health Canada and the Canadian Food Inspection Agency (CFIA) share responsibility in regard to labelling requirements for food. Health Canada is responsible for policy and standard setting for matters related to health and safety under the FDR, whereas CFIA is responsible for enforcement of the Regulations. CFIA also administers and enforces those aspects of the *Food and Drugs Act and Regulations* and the *Consumer Packaging and Labelling Act and Regulations* to ensure that labelling is understandable, truthful and not misleading.

Phytosterols are not nutrients and under nutrition labelling regulations, the amount of phytosterols may not be included in the Nutrition Facts table (NFT). The total phytosterol content may be declared elsewhere on the label in g per serving, rounded to the nearest multiple of 0.1 g.

It is recognized that the food industry would like to include a health claim on the label to position their products in the marketplace for consumers who wish to use a dietary approach to lower blood cholesterol. For guidance on acceptable health claims please see *Summary of Assessment - Plant Sterols and Blood Cholesterol Lowering*. For additional information please consult: *Plant Sterols (phytosterols)*.

Conclusion:

In light of these conclusions, manufacturers of the following types of foods containing added phytosterols at a maximum level of 1 g (free phytosterols) per serving and per reference amount are invited to file notifications of their intention to sell these foods as novel foods:

> unstandardized spreads, mayonnaise, margarine, calorie-reduced margarine, salad dressing and unstandardized salad dressings, yogurt and yogurt drinks, and vegetable and fruit juices.

Petitioners are asked to notify the Food Directorate of each new product with added plant sterols by sending a letter or e-mail to the address below indicating the type of product, the level of addition of phytosterols, the name of the product, and the name and address of the manufacturer. In these cases, a record will be made of the intention to sell and a letter of no objection will be sent back to the petitioner, once it is confirmed that the product intended for sale fits the conditions of the current review of the use of phytosterols in food, as described in the current decision document. Petitioners who wish to market foods not appearing on the list, or foods containing levels greater than 1 g phytosterols/serving are required to notify Health Canada in accordance with Division 28 of the Food and Drug Regulations.

All notifications should be addressed to:

Submission Management and Information Unit
Food Directorate, Health Products and Food Branch
Health Canada, Postal Locator 2201C
251 Sir Frederick Banting Driveway
Ottawa, Ontario, Canada, K1A 0K9.

The e-mail address for the unit is: smiu-ugdi@hc-sc.gc.ca.