

U. S. Food and Drug Administration
Center for Food Safety & Applied Nutrition
Office of Premarket Approval

Agency Response Letter GRAS Notice No. GRN 000048

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Washington, DC 20204

November 27, 2000

Steven D. McCurry, Ph.D.
Cargill Incorporated
15407 McGinty Road West, MS110
Wayzata, MN, 55391-2399

Re: GRAS Notice No. GRN 000048

Dear Dr. McCurry:

The Food and Drug Administration (FDA) is responding to the notice, dated June 1, 2000, that you submitted in accordance with the agency's proposed regulation, proposed 21 CFR 170.36 (62 FR 18938; April 17, 1997; Substances Generally Recognized as Safe (GRAS)). FDA received the notice on June 2, 2000 and designated it as GRAS Notice No. GRN 000048. In a letter of October 24, 2000, you provided additional clarifying information.

The subject of your notice is vegetable oil phytosterol esters. The notice informs FDA of the view of Cargill Incorporated (Cargill) that vegetable oil phytosterol esters are GRAS, through scientific procedures, for use as an ingredient in vegetable oil spreads, dressings for salads, bars, and yogurt.

The main sterol components of the ingredient vegetable oil phytosterol esters are beta-sitosterol, campesterol, and stigmasterol. These components of vegetable oil phytosterol esters already are present as ingredients in other vegetable oil based spreads, dressings for salads, bars, and yogurt that have a similar intended use. Your notice describes the manufacturing process for vegetable oil phytosterol esters, in which sterols are esterified with vegetable oil fatty acids. The sterols are mostly derived from soy. The fatty acids are derived from soy, canola, sunflower or other vegetable oils. After the esterification reaction, adsorbents are used to remove trace components and color bodies, and the ingredient is subjected to vacuum stripping and filtration. Your notice includes food grade specifications for vegetable oil phytosterol esters, including a specification for lead of less than 0.1 milligrams/kilogram.

Your notice describes a series of published studies conducted with free phytosterols, vegetable oil sterol esters, or plant stanol esters. In general, you rely on the similarity of vegetable oil phytosterol esters to the test articles in these published studies to determine that these studies establish the safety of vegetable oil phytosterol esters. Because evaluation that a use of a food ingredient is safe is a time-dependent judgment, you commit to notify the agency if additional relevant information (i.e., changes in exposure, adverse events, or new scientific data) becomes known with respect to the safety of vegetable oil phytosterol esters.

Cargill views the ingredient vegetable oil phytosterol esters as an additional ingredient choice for manufacturers of currently marketed products that contain an enhanced level of phytosterol esters. For this reason, Cargill considers that the marketing of its ingredient would not change the cumulative dietary intake of phytosterol esters compared to what already is marketed.

Your notice includes the findings of a panel of individuals (Cargill's GRAS panel) who evaluated the data and information that are the basis for Cargill's GRAS determination. Cargill considers the members of its GRAS panel to be qualified by scientific training and experience to evaluate the safety of substances added to food. The clarifying information that you provided in your letter of October 24, 2000, included an addendum to the report of this GRAS panel.

In its original report, Cargill's GRAS panel concludes that the composition of vegetable oil phytosterol esters is equivalent to that of another marketed ingredient (i.e., vegetable oil sterol esters, also known as plant sterol esters), which was the subject of a previous submission to FDA.⁽¹⁾ Cargill's GRAS panel reported that FDA had evaluated vegetable oil sterol esters for use in vegetable oil spreads, dressings for salads, bars, and yogurt. However, as you discussed by telephone in July, 2000, with Dr. Linda Kahl of the Office of Premarket Approval, FDA's evaluation of the intended use of vegetable oil sterol esters was limited to its use in vegetable oil spreads (Ref. 1). FDA's evaluation of the intended use of two related ingredients (i.e., plant stanol esters and tall oil phytosterols)⁽²⁾ likewise was limited to their use in spreads (Refs. 2 and 3). Thus, at the time that you submitted your GRAS notice, FDA had only evaluated dietary exposure to plant sterol and stanol esters from their consumption in spread. This consumption would be approximately 3 grams of plant sterols or plant stanols per person per day (which is equivalent to approximately 5 grams of plant sterol esters or plant stanol esters per person per day). At that time, FDA had not evaluated the implications, if any, of the cumulative dietary exposure to plant sterol esters or plant stanol esters as a result of their use in food products such as dressings for salads, bars, and yogurt.

Your October 24 letter acknowledges that FDA's previous evaluation of the use of plant sterols and stanols, in free or esterified form, was limited to the use of these ingredients in spreads. Your October 24 letter also discusses an interim final rule that FDA issued, after FDA received your notice, to authorize a health claim for plant sterol/stanol esters (65 FR 54685; September 8, 2000). FDA authorized this health claim for plant sterol esters when used in spreads and dressings for salads, and for plant stanol esters when used in spreads, dressings for salads, and snack bars. In this interim final rule, FDA acknowledged receipt and consideration of information regarding the use of plant sterol esters and plant stanol esters in a broader array of food categories than spread. FDA also concluded that the health claim petitioners had met the burden to demonstrate, to FDA's satisfaction, that the use of plant sterol esters and plant stanol esters in this broader array of food categories is safe and lawful. In your view, the interim final rule makes clear that the primary source of data and information that FDA relied on in reaching this conclusion was the data and information that FDA evaluated regarding the use of these ingredients in spreads. Likewise, Cargill's GRAS panel primarily relied on data and information that supported the use of these ingredients in spreads. Thus, it is Cargill's view that the original report of its GRAS panel is consistent with the views expressed by FDA in the interim final rule authorizing a health claim.

Based on the information provided by Cargill, as well as other information available to FDA, the agency has no questions at this time regarding Cargill's conclusion that vegetable oil phytosterol esters are GRAS under the intended conditions of use. The agency has not, however, made its own determination regarding the GRAS status of the subject use of vegetable oil phytosterol esters. As always, it is the continuing responsibility of Cargill to ensure that food ingredients that the firm markets are safe, and are otherwise in compliance with all applicable legal and regulatory requirements.

In accordance with proposed 21 CFR 170.36(f), a copy of the text of this letter, as well as a copy of the information in your notice that conforms to the information in proposed 21 CFR 170.36(c)(1), is available for public review and copying on the Office of Premarket Approval's homepage on the Internet (at <http://www.cfsan.fda.gov/~lrd/foodadd.html>).

Sincerely,
/s/
Alan M. Rulis, Ph.D.
Director
Office of Premarket
Approval
Center for Food Safety
and Applied Nutrition

References

1. Letter dated April 30, 1999, from Alan Rulis of FDA to Daniel R. Dwyer.
2. Letter dated May 17, 1999, from Alan Rulis of FDA to Vivian A. Chester and Edward B. Nelson.
3. Letter dated April 24, 2000, from Alan Rulis of FDA to Judith A. Weinstein.

(1) In a submission dated January 11, 1999, Lipton informed FDA of its view that vegetable oil sterol esters are GRAS for use in spreads at a level up to 20 per cent.

(2) In a submission dated February 18, 1999, McNeil Consumer Healthcare informed FDA of its view that plant stanol esters are GRAS for use in spreads at a level of 1.7 grams of plant stanol esters per serving of spread. In a GRAS Notice dated January 28, 2000 (GRN No. 000039), Novartis Consumer Health, Inc. informed FDA of its view that tall oil phytosterols are GRAS for use in spreads at a level of up to 12 percent.

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