U.S. Food and Drug Administration

Food

Agency Response Letter GRAS Notice No. GRN 000229

CFSAN/Office of Food Additive Safety
February 18, 2008

George A. Burdock, Ph.D.
Burdock Group
801 N. Orange Ave. Suite 710
Orlando, FL 32801

Re: GRAS Notice No. GRN 000229

Dear Dr. Burdock:

The Food and Drug Administration (FDA) is responding to the notice, dated July 11, 2007, that you submitted on behalf of Bergstrom Nutrition 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); the GRAS proposal). FDA received the notice on July 17, 2007, filed it on July 25, 2007, and designated it as GRAS Notice No. GRN 000229.

The subject of the notice is methylsulfonylmethane (MSM). The notice informs FDA of the view of Bergstrom Nutrition that MSM is GRAS, through scientific procedures, for use as an ingredient in meal supplement and meal replacement foods, fruit smoothie-typ drinks, and fruit-flavored thirst quencher-type beverages at levels up to 4,000 milligrams per kilogram (mg/kg) and in food bars such as granola bars and energy-type bars at levels up to 30,000 mg/kg provided that food standards of identity do not preclude such use.

As part of its notice, Bergstrom Nutrition includes the report of a panel of individuals (Bergstrom Nutrition's GRAS panel) who evaluated the data and information that are the basis for Bergstrom Nutrition's GRAS determination. Bergstrom Nutrition considers the members of its GRAS panel to be qualified by scientific training and experience to evaluate the safety of substances added to food. Bergstrom Nutrition's GRAS panel evaluated the starting materials, method of manufacture, product specifications, supporting analytical data, intended use levels in specified foods, consumption estimates for all intended uses and estimates of dietary exposure, as well as published and unpublished studies. Based on this review, Bergstrom Nutrition's GRAS panel conclude that the intended uses of MSM are GRAS.

Bergstrom Nutrition provides information about the identity, composition, and method of manufacturer of MSM. MSM is a white, odorless, slightly bitter tasting crystalline substance; it is readily soluble in water. Bergstrom describes MSM as a metabolite of dimethyl sulfoxide (DMSO), which is also the starting material for the manufacture of MSM. To manufacture MSM, DMSO is treate with hydrogen peroxide, followed by a four-stage distillation purification process to remove impurities. After distillation, the molte product is processed into microprills (microspherical pellets of MSM) in a prilling chamber. Bergstrom Nutrition provides specifications for food-grade MSM, including specifications for lead, arsenic, aluminum, mercury, and cadmium.

Bergstrom Nutrition provides information about the intended use of, and estimates the daily intake of, MSM. Bergstrom intends MSM for use as an ingredient in various foods, noting that the use of MSM is self-limiting in foods due to its bitter taste at high levels. Bergstrom Nutrition notes that MSM is currently used as a dietary supplement (approximately 17 milligrams per kilogram body weight per day (mg/kg bw/d; based on a 60 kilogram person) and includes this intake in its estimate of the daily intake for MSM. The notifier estimates the daily intake for all uses (conventional food + dietary supplement) to be approximately 49 mg/kg bw/d and approximately 81 mg/kg bw/d at the mean and 90th percentile level of intake, respectively.

Bergstrom Nutrition discusses the metabolic fate of, and toxicology studies conducted on, MSM. MSM is rapidly absorbed, with a half-life of approximately 12 hours as calculated from published rat studies. Published studies have shown that MSM and its metabolites are excreted mainly via urine and, there is no accumulation of MSM by the body.

To support the safe use of MSM in foods, Bergstrom Nutrition summarizes several published toxicological studies conducted in rodents under acute, subacute, and subchronic periods of exposure via the oral route of administration. The notifier concurs with the published results that the no observed adverse effect level in rats consuming MSM for 90 days is 1500 mg/kg bw/d and that the no observed adverse effect level in a teratology study is 1000 mg/kg bw/d. Bergstrom Nutrition also describes a published study in which arthritic mice consumed 3.75 g/kg bw/d for 12 weeks in their drinking water, concurring with the study authors conclusions that there were no adverse effects in the mice. Bergstrom Nutrition describes several studies in humans that report

that MSM is well tolerated when consumed at levels up to 100 mg/kg bw/d.

Potential Labeling Issues

Under section 403(a) of the Federal Food, Drug, and Cosmetic Act (FFDCA), a food is misbranded if its labeling is false or misleading in any particular. Section 403(r) of the FFDCA lays out the statutory framework for a health claim. In describing the intended use of MSM and in describing the information that Bergstrom Nutrition relies on to conclude that MSM is GRAS under the conditions of its intended use, Bergstrom Nutrition raises a potential issue under these labeling provisions of the FFDCA. If products that contain MSM bear any claims on the label or in labeling, such claims are the purview of the Office of Nutrition, Labeling, and Dietary Supplements (ONLDS) in the Center for Food Safety and Applied Nutrition. The Office of Food Additive Safety neither consulted with ONLDS on this labeling issue nor evaluated the information in the notice to determine whether it would support any claims made about MSM on the label or in labeling.

Conclusions

Based on the information provided by Bergstrom Nutrition, as well as other information available to FDA, the agency has no questions at this time regarding Bergstrom Nutrition's conclusion that MSM is 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 MSM. As always, it is the continuing responsibility of Bergstrom Nutrition 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 responding to GRN 000229, as well as a copy of the information in this notice that conforms to the information in the proposed GRAS exemption claim (proposed 21 CFR 170.36(c)(1)), is available for public review and copying on the homepage of the Office of Food Additive Safety (on the Internet at http://www.cfsan.fda.gov/~lrd/foodadd.html).

Sincerely,
Laura M. Tarantino, Ph.D.
Director
Office of Food Additive Safety
Center for Food Safety and Applied Nutrition

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