Food

Agency Response Letter GRAS Notice No. GRN 000044

CFSAN/Office of Premarket Approval

November 22, 2000

Paula Karabell
GTC Nutrition Company
14252 W. 44th Ave., Unit F
Golden, CO, 80403

Re: GRAS Notice No. GRN 000044

Dear Ms. Karabell:

The Food and Drug Administration (FDA) is responding to the notice, dated May 1, 2000, that Environ Corporation submitted on your behalf 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 Office of Premarket Approval (OPA) received the notice on May 2, 2000 and designated it as GRAS Notice No. GRN 000044. In a letter of August 31, 2000, you informed FDA of the intent of GTC Nutrition Company (GTC Nutrition) to act as its own agent.

The subject of your notice is fructooligosaccharide. Your notice informs FDA of the view of GTC Nutrition that fructooligosaccharide is GRAS, through scientific procedures, for use as a bulking agent as listed in Table 1. Your notice includes the findings of a panel of individuals who evaluated the data and information that are the basis for GTC Nutrition's GRAS determination. GTC Nutrition considers these individuals to be qualified by scientific training and experience to evaluate the safety of substances added to food.

Table 1
Intended Use of Fructooligosaccharides

Food	Level of use
Acidophilis milk	2 per cent
Bars	4.6-13.6 per cent
Baby foods	0.1-3.6 per cent
Beverages	1.2 per cent
Biscuits	3.6 per cent
Cakes	1.6-3.6 per cent
Confectionery	5.0 per cent
Cookies	2.5-3.3 per cent
Crackers	1.7-3.3 per cent
Flavored and unflavored milks	0.4 per cent
Hard candy	6.7 per cent
Ice cream	1.5 per cent
Jams and jellies	0.9 per cent
Muffins	3.6 per cent
Ready-to-eat cereals	3.3-15.4 per cent
Sorbet and sherbet	1.4 per cent
Soup	0.4 per cent
Yogurt	1.3 per cent

Your notice describes published information pertaining to fructooligosaccharide's chemical identity and its natural occurrence. Fructooligosaccharide is a mixture composed of fructose (F) chains with a terminal glucose (G) unit. The number of fructose units varies from two to four. The first fructose unit that is attached to glucose is joined by an alpha 1-1' glycosidic linkage. The remaining fructose units are joined to the first fructose unit in a chain by beta 2-1 glycosidic linkages.

Because the combination of the terminal glucose and the first attached fructose is chemically identical to the moiety known as sucrose, another way to describe each oligosaccharide in the fructooligosaccharide mixture is as a terminal sucrose unit to which one to three additional fructose units are attached. In fact, the starting point in the manufacture of fructooligosaccharide is sucrose. Fructooligosaccharide is manufactured from sucrose syrup by the action of the fungal enzyme beta-fructofuranosidase. The enzyme acts as an invertase on sucrose, yielding fructose and glucose. The enzyme also acts as a fructosyltransferase between sucrose and a fructofuranosyl-sucrose molecule (i.e., a molecule comprised of fructose chains with a terminal glucose), yielding GF2, GF3, and GF4. Your notice includes published information pertaining to the source organism from which the beta-fructofuranosidase is derived. Your notice also provides information on specifications for fructooligosaccharide, including a lead specification of

less than 0.2 parts per million.

Fructooligosaccharide exists naturally in plants, and is consumed by humans as a component of the commonly consumed foods onions, bananas, lettuce, and wheat (in rough and bran forms). You estimate that background exposure to fructooligosaccharide from its consumption as a component of various foods ranges from approximately 145 to 250 milligrams per person per day at the 90th percentile consumption level. You also estimate that dietary exposure to fructooligosaccharide from its intended use as a bulking agent would range from approximately 3.1 to 12.8 grams per person per day at the 90th percentile consumption level.

Based on published studies, which were conducted with fructooligosaccharide or related oligosaccharides, you conclude that fructooligosaccharide is virtually unabsorbed and undigested by endogenous enzymes, although a very small amount is hydrolyzed by stomach acid and absorbed into the body as fructose and glucose. About 89 percent of the undigested fructooligosaccharide passes unchanged into the colon where it is fermented by microflora into gases and short-chain carboxylic acids (predominantly acetic acid, while propionic and butyric acids are generated in smaller amounts).

Your notice describes additional studies conducted with fructooligosaccharide. The published animal studies include acute studies in rats and mice, 6-week feeding studies in rats, a teratogenicity study in rats, and a chronic bioassay in rats. The animal studies also include an unpublished 90-day feeding study in rats. Additional published studies include mutagenicity studies, studies describing physiological or systemic effects of fructooligosaccharide, and human studies.

Labeling issues

Section 403(a) of the Federal Food, Drug, and Cosmetic Act (FFDCA) provides that 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 fructooligosaccharide and in describing the information that GTC Nutrition relies on to conclude that fructooligosaccharide is GRAS under the conditions of its intended use, GTC Nutrition raises a number of issues under these labeling provisions of the FFDCA. These issues include (1) physiological effects of fructooligosaccharide that GTC Nutrition views as "beneficial;" (2) the caloric value of fructooligosaccharide; and (3) the classification of fructooligosaccharide as "soluble" fiber. These issues are the purview of the Office of Nutritional Products, Labeling, and Dietary Supplements (ONPLDS) in the Center for Food Safety and Applied Nutrition (CFSAN). OPA neither consulted with ONPLDS on these labeling issues nor evaluated the information in your notice to determine whether it would support any claims made about fructooligosaccharide on the label or in labeling.

OPA did consult with ONPLDS regarding the common or usual name that you provided under proposed 21 CFR 170.36(c)(1)(ii) (i.e., "short-chain fructooligosaccharide"). ONPLDS advises that fructooligosaccharides vary in chain length from 2 to 10 monomers and are also referred to as oligofructose or fructosugar, and that the term "oligosaccharides" itself refers to short chain lengths with 2-10 monomers while longer chain lengths of above 10 monomers are referred to as "polysaccharides." Moreover, sugars composed of 2-5 monomers are associated with specific terms such as di-, tri-, tetra-, and penta-saccharides. ONPLDS found no literature reference that specifically defines or distinguishes fructooligosaccharides as short-chain, medium-chain, or long-chain. For these reasons, in this letter, OPA uses the term "fructooligosaccharide," rather than the term "short-chain fructooligosaccharide," to refer to the ingredient that is the subject of your notice. If you have any questions about the common or usual name that would be used to identify fructooligosaccharide in the ingredient statement of food products that would be marketed in the United States, OPA suggests that you contact the Division of Standards and Labeling Regulations, ONPLDS, CFSAN, HFS-820, 200 C Street S.W., Washington, DC 20204. You can reach this division by telephone at (202)205-4168.

Conclusions

Based on the information provided by GTC Nutrition, as well as other information available to FDA, the agency has no questions at this time regarding GTC Nutrition's conclusion that fructooligosaccharide 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 fructooligosaccharide. As always, it is the continuing responsibility of GTC 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, 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 OPA's homepage on the Internet (at http://vm.cfsan.fda.gov/~lrd/foodadd.html).

Sincerely,

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

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