DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
College Park, MD 20740

Dr. John Dore
Cyanotech Corporation
73-4460 Queen Kaahumanu Hwy., # 102,
Kailua-Kona, HI 96740

OCT 6 2003

Re: GRAS Notice No. GRN 000127

Dear Dr. Dore:

The Food and Drug Administration (FDA) is responding to the notice, dated March 24, 2003, that you submitted as an agent, on behalf of Cyanotech Corporation and Earthrise Nutritionals, Inc. (the notifiers) 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 Food Additive Safety (OFAS) received the notice on March 28, 2003, filed it on April 10, 2003, and designated it as GRN 000127. The notice incorporates by reference a previous GRAS notice (GRN 000101).

The subject of the notice is the dried biomass of *Arthrospira platensis* (spirulina). The notice informs FDA of the view of the notifiers that spirulina is GRAS, through scientific procedures, for use as an ingredient in foods such as specialty food bars, powdered nutritional drink mixes, popcorn, and as a condiment in salads and pasta, at levels ranging from 0.5 to 3 grams per serving.

Spirulina is the common name of the notified substance and refers to the dried biomass of *A. platensis*, a filamentous cyanobacterium (oxygenic photosynthetic bacterium) found worldwide in fresh and marine waters. The notifiers cite several published references describing the taxonomy and general characteristics of the organism.

The notifiers describe the composition of spirulina. Spirulina consists of 53-62 percent protein, 17-25 percent carbohydrates, 4-6 percent lipids, 8-13 percent minerals, and 3-6 percent water. The notice also provides analyses of other components in spirulina, including certain minerals, fatty acids, vitamins, cis-beta-carotene, trans-beta-carotene, zeaxanthin, chlorophyll a, phycocyanin, and c-phycocyanin.

The notifiers manufacture spirulina in accordance with Current Good Manufacturing Practice (21 CFR 110) and applicable state statutes and regulations. The method of manufacture utilizes the "raceway" design for outdoor mass cultivation of photosynthetic microorganisms that was

developed in the 1950s and is used widely in the industry. *A. platensis* is grown in large, shallow man-made "ponds" that are lined with nylon scrim-reinforced polypropylene. The growth medium consists of water, sodium bicarbonate, nitrates, phosphates, sulfates, and trace minerals. The *A. platensis* culture is rinsed and concentrated on a series of stainless steel screens. The paste is then spray dried to remove the moisture, resulting in a free flowing fine powder. Samples of the powder are collected in sterilized bags for microbiological assays and other quality control assessments. The dried powder is vacuum-sealed in oxygen-barrier bags. The notifiers discuss the procedures they use to ensure that the culture is free of other cyanobacteria and algae, especially those that are capable of producing toxins.

The notifiers provide specifications for spirulina, which include specifications for protein, lead, minerals, moisture, beta-carotene, total carotenoids, c-phycocyanin, arsenic, cadmium, mercury, pesticides, rodent hairs, and insect fragments. The notifiers also established the following microbiological specifications: absence of *E. coli*, *Salmonella*, and *Staphylococcus aureus*, total aerobic bacteria of less than 200,000 colony forming units per gram (cfu/g), and total coliforms of less than 10 cfu/g.

The notifiers estimate that daily intake of spirulina would be six grams per day for a high-end consumer, three grams per day for a medium consumer, and 3-12 grams per month for a low-end consumer.

The notifiers discuss published animal studies relevant to the safety of spirulina. These include oral feeding studies in rats, pigs, mice, and hamsters. The notifiers report that no adverse effects were observed in the studies. The notifiers also describe several published human studies evaluating the potential for beneficial effects of spirulina and report no adverse side effects.

Potential requirement for a color additive petition

In their notice, the notifiers note that spirulina may impart color to food. As such, the use of spirulina in food products may constitute the use of a color additive under section 201(t)(1) of the Federal Food, Drug, and Cosmetic Act (FFDCA) and FDA's implementing regulations in 21 CFR Part 70. Under section 201(t)(1) and 21 CFR 70.3(f), the term color additive means a material that is a dye, pigment, or other substance made by a process of synthesis or similar artifice, or extracted, isolated, or otherwise derived from a vegetable, animal, mineral, or other source, and that is capable (alone or through reaction with another substance) of imparting color when added or applied to a food; except that such term does not include any material which the Secretary[1], by regulation, determines is used (or intended to be used) solely for a purpose or purposes other than coloring. Under 21 CFR 70.3(g), a material that otherwise meets the definition of color additive can be exempt from that definition on the basis that it is used or intended to be used solely for a purpose or purposes other than coloring, as long as the material is used in a way that any color imparted is clearly unimportant insofar as the appearance, value, marketability, or consumer acceptability is concerned. Given the construct of section 201(t)(1) of the FFDCA and 21 CFR 70.3(f) and (g), the use of a substance that is capable of imparting color may constitute use as a color additive in addition to use as a food additive or GRAS substance. For example, beta-carotene is both approved for use as a color additive (21 CFR 73.95) and

[1]The Secretary of the Department of Health and Human Services (DHHS).

affirmed as GRAS for use as a nutrient supplement (21 CFR 184.1245); in some food products, beta-carotene is used for both purposes. Importantly, if the use of spirulina constitutes use as a color additive within the meaning of section 201(t)(1) of the FFDCA and FDA's implementing regulations in 21 CFR 70.3(f) and (g), section 721(a) of the FFDCA requires premarket review and approval of that use by FDA. Under section 402(c) of the FFDCA, a food product that contains an unapproved color additive would be deemed adulterated[2].

The notifiers state that spirulina is not intended for use as a color additive and, thus, would be exempt from the definition of color additive under section 201(t) of the FFDCA and FDA's implementing regulations in 21 CFR 70.3(f) and (g). Importantly, FDA's response to GRN 000127 does not include any comment by FDA about the notifiers' view on this issue. If, after receipt of this letter, the notifiers have any specific questions about this issue, we recommend that they contact the Division of Petition Review (HFS-265), Office of Food Additive Safety, Center for Food Safety and Applied Nutrition, Food and Drug Administration, 5100 Paint Branch Parkway, College Park, MD 20740. You can reach this division by telephone at (202)418-3035.

Conclusions

Based on the information provided by Cyanotech Corporation and Earthrise Nutritionals, Inc., as well as other information available to FDA, the agency has no questions at this time regarding the notifiers' conclusion that spirulina 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 spirulina. As always, it is the continuing responsibility of the notifiers to ensure that food ingredients that the firms market are safe, and are otherwise in compliance with all applicable legal and regulatory requirements. In particular, we note that any use of spirulina that constitutes use as a color additive requires premarket review and approval by FDA.

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[2]We note that section 721(b)(4) of the FFDCA provides that a color additive shall be deemed to be safe and suitable for the purpose of listing under section 721(b) of the FFDCA while there is in effect a published finding of the Secretary declaring that the substance is exempt from the definition of "food additive" because of its being generally recognized by qualified experts as safe for its intended use as provided in section 201(s) of the FFDCA. Importantly, FDA's response to GRN 000127 does not constitute a "finding of the Secretary" within the meaning of section 721(b)(4) of the FFDCA.

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 the notice that conforms to the information in 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

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