Timothy S. Murbach, ND, DABT
AIBMR Life Sciences, Inc.
2800 East Madison, Suite 202
Seattle, WA 98112

Re: GRAS Notice No. GRN 000773

Dear Dr. Murbach:

The purpose of this letter is to correct our response letter to GRN 000773, dated February 22, 2019, by revising the name of the notifier in paragraph one and amending details in paragraph seven.

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 000773. We received the notice you submitted on behalf of Triton Algae Innovations (Triton) on March 26, 2018, and filed it on April 25, 2018. Triton submitted an amendment to the notice on June 22, 2018, containing additional safety information.

The subject of the notice is dried biomass of *Chlamydomonas reinhardtii* strain THN 6 (dried *C. reinhardtii*) for use as a source of protein in foods[1] at levels equivalent to those currently consumed, replacing other dietary proteins. The notice informs us of Triton's view that this use of dried *C. reinhardtii* is GRAS through scientific procedures.

Triton describes dried *C. reinhardtii* as a green powder. Triton states that *C. reinhardtii* is a single-celled green alga. Triton notes that it is a wild-type isolate acquired from the Chlamydomonas Resource Center at the University of Minnesota and has not been genetically engineered. Triton states that identification was confirmed to the strain level based on DNA sequencing.

Triton describes the manufacture of dried *C. reinhardtii*. The strain is fermented under pH- and temperature-controlled aseptic conditions. After fermentation, the cells are collected by centrifugation and spray-dried. Triton states that the dried *C. reinhardtii* does not contain any allergens. Triton states that all materials used in the manufacturing process are food-grade and meet appropriate regulations.

Triton provides specifications for dried *C. reinhardtii* that include moisture (≤10%), protein (30-70%), and limits for microorganisms including total aerobic microbes (≤

[1] Triton states that dried *C. reinhardtii* is not intended for use in: 1) foods for which standards of identity exist, 2) infant formulas, or 3) foods regulated by the U.S. Department of Agriculture.

1000 colony forming units/g) and Salmonella (absent in 25 g sample). Triton provides the results of a single batch analysis to demonstrate manufacturing can meet the specifications.

Triton estimates the dietary exposure to dried *C. reinhardtii*. Triton intends to use dried *C. reinhardtii* as a source of protein in foods at levels currently consumed. Based on complete dietary protein replacement for the U.S. population (ages 2 and older), and the protein specification (30-70%) Triton estimates the 90th percentile dietary exposure to be approximately 3 to 7 g/kg bodyweight (bw)/day (d) respectively. Triton states that this is a conservative assumption and calculates a dietary exposure of approximately 0.3-0.7 g/kg bw/d assuming that 10% of total protein will be replaced.

Triton relies on published and unpublished safety information relevant to the safety of dried *C. reinhardtii*. Triton describes published information identifying the composition of dried *C. reinhardtii* as primarily protein, fiber, fat, vitamins, minerals, and chlorophyll, with no bioactive or toxic compounds. Triton states that dried *C. reinhardtii* will be digested and metabolized like plant-derived food, as the macronutrient and micronutrient components are common to plants. Triton discusses the results of published toxicology studies; a 28-day oral toxicity study in rats did not result in toxicity at the highest dose tested (4 g/kg bw/d). Published mutagenicity and genotoxicity studies were negative. The notifier also discusses results of an unpublished growth study in piglets, which did not show any adverse effects on growth following consumption of a diet containing 0.33% dried *C. reinhardtii* (approximately 27 g/kg bw/d).

Triton states that *C. reinhardtii* strain THN6 is non-pathogenic and non-toxigenic. Triton states that there is no evidence of pathogenicity or toxigenicity in any members of its class Chlorophyceae in the published literature. Triton discusses the published genome sequence of *C. reinhardtii* and cites its use as a model laboratory organism with an extensive history of scientific study.

Triton states that there are no published reports of allergenicity to *C. reinhardtii*. Triton corroborates this with a discussion of an unpublished digestibility study, which showed that *C. reinhardtii* THN6 proteins were rapidly digested and therefore the likelihood of allergenic potential is low

Based on the totality of the data and information described above, Triton concludes that dried *C. reinhardtii* is GRAS for its intended use in food.

Potential Requirement for a Color Additive Petition

There is no GRAS provision for color additives. In the notice, Triton describes dried *C. reinhardtii* as green. As such, the use of dried *C. reinhardtii* in food products may constitute a color additive use under section 201(t)(1) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) and FDA's implementing regulations in 21 CFR Part 70. Under section 201(t)(1) and 21 CFR 70.3(f), a color additive is a material that is a dye, pigment, or other substance made by a synthetic process or similar artifice, or is

extracted, isolated, or otherwise derived from a vegetable, animal, mineral, or other source. Under 21 CFR 70.3(g), a material that otherwise meets the definition of a color additive can be exempt from that definition if it is used (or is intended to be used) solely for a purpose or purposes other than coloring. Our response to GRN 000773 is not an approval for use as a color additive nor is it a finding of the Secretary of the Department of Health and Human Services within the meaning of section 721(b)(4) of the FD&C Act. Questions about color additives should be directed to the Division of Petition Review in the Office of Food Additive Safety.

Section 301(ll) of the FD&C Act

Section 301(ll) of the FD&C Act prohibits the introduction or delivery for introduction into interstate commerce of any food that contains a drug approved under section 505 of the FD&C Act, a biological product licensed under section 351 of the Public Health Service Act, or a drug or a biological product for which substantial clinical investigations have been instituted and their existence made public, unless one of the exemptions in section 301(ll)(1)-(4) applies. In our evaluation of Triton's notice concluding that dried *C. reinhardtii* is GRAS under its intended conditions of use, we did not consider whether section 301(ll) or any of its exemptions apply to foods containing dried *C. reinhardtii*. Accordingly, our response should not be construed to be a statement that foods containing dried *C. reinhardtii*, if introduced or delivered for introduction into interstate commerce, would not violate section 301(ll).

Conclusions

Based on the information that Triton provided, as well as other information available to FDA, we have no questions at this time regarding Triton's conclusion that dried *C. reinhardtii* is GRAS under its intended conditions of use. This letter is not an affirmation that dried *C. reinhardtii* is GRAS under 21 CFR 170.35. Unless noted above, our review did not address other provisions of the FD&C Act. Food ingredient manufacturers and food producers are responsible for ensuring that marketed products are safe and compliant with all applicable legal and regulatory requirements.

In accordance with 21 CFR 170.275(b)(2), the text of this letter responding to GRN 000773 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

Michael A. Adams -S

Digitally signed by Michael A. Adams -S
Date: 2019.03.13 10:09:57 -04'00'

Dennis M. Keefe, Ph.D.
Director
Office of Food Additive Safety
Center for Food Safety
and Applied Nutrition