Claire L. Kruger, Ph.D.
Spherix Consulting Group, Inc.
11821 Parklawn Drive
Suite 310
Rockville, MD 20852

Re: GRAS Notice No. GRN 000986

Dear Dr. Kruger:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 000986. We received the notice that you submitted on behalf of Chlorella Industries Co., Ltd. (CICL) on December 21, 2020 and filed it on April 20, 2021. CICL submitted an amendment to the notice on August 19, 2021, providing clarification on the intended uses, manufacturing process, analytical methods, specifications, genotypic and phenotypic characteristics of *Chlorella sorokiniana* strain NITE SD 00247 (*C. sorokiniana* NITE SD 00247), and additional safety information.

The subject of the notice is chlorella powder and chlorella micro powder for use as an ingredient at levels ranging from 5 to 10 mg/g in yeast breads, doughnuts, nutrition bars, protein and nutritional powders, pasta, and noodles. The notice informs us of CICL's view that these uses of chlorella powder and chlorella micro powder are GRAS through scientific procedures.

Our use of the terms, "chlorella powder" and "chlorella micro powder," in this letter is not our recommendation of these terms as appropriate common or usual names for declaring the substances in accordance with FDA's labeling requirements. Under 21 CFR 101.4, each ingredient must be declared by its common or usual name. In addition, 21 CFR 102.5 outlines general principles to use when establishing common or usual names for nonstandardized foods. Issues associated with labeling and the common or usual name of a food ingredient are under the purview of the Office of Nutrition and Food Labeling (ONFL) in the Center for Food Safety and Applied Nutrition (CFSAN). The Office of Food Additive Safety (OFAS) did not consult with ONFL regarding the appropriate common or usual name for "chlorella powder" or "chlorella micro powder."

CICL provides information on the identity and composition of chlorella powder and chlorella micro powder. CICL states that chlorella powder is the spray-dried whole-cell biomass of *C. sorokiniana* NITE SD 00247 that is further milled to produce chlorella micro powder. CICL states that the only difference between chlorella powder and chlorella micro powder is the particle size.

CICL describes the manufacturing process of chlorella powder and chlorella micro

powder from *C. sorokiniana* NITE SD 00247, a single-celled, non-pathogenic, and non-toxigenic strain of green algae that was originally isolated from a pond in Saga-ken, Japan. CICL states that *C. sorokiniana* NITE SD 00247 is deposited in the culture collection of the National Institute of Technology and Evaluation (NITE) in Tokyo, Japan. CICL explains that *C. sorokiniana* NITE SD 00247 is cultured and sequentially expanded in the following steps: slant culture, flask culture, jar culture, seed culture, tank culture, and outdoor pool culture. After the culture process is complete, the *C. sorokiniana* NITE SD 00247 biomass is filtered, washed, and concentrated. The resulting slurry is strained, cooled to 2-5˚C, subjected to heat sterilization, spray-dried, and packaged in food-grade aluminum laminate bags. The chlorella micro powder is produced by pulverizing the chlorella powder prior to packaging. CICL states that chlorella powder and chlorella micro powder are manufactured under current good manufacturing practices using food-grade materials. CICL further states that no components of the culture medium are allergens or are derived from allergenic sources.

CICL provides specifications for chlorella powder and chlorella micro powder including: particle size (≥ 95% through 200 mesh),[1] moisture (> 7.0%), ash (> 11.0%), chlorophyll (≥ 1.5%), chlorophyll b (detectable), vitamin B2 (≥ 4.0 mg/100 g), protein (≥ 55.0%), iron (40-100 mg/100 g), fat (≥ 8.8%), carbohydrates (≥ 7.0%), omega 3 fatty acids (≥ 1.00%), total pheophorbide (< 50 mg/100 g); heavy metals, including lead (< 1.0 mg/kg); and limits for microorganisms, including *Salmonella* serovars (absent in 10 g). CICL provides the results from analyses of three non-consecutive batches to demonstrate that chlorella powder and chlorella micro powder can be manufactured to meet the specifications. CICL provides stability studies and states that both chlorella powder and chlorella micro powder are stable for at least 4 years.

CICL states that chlorella powder and chlorella micro powder are not intended to be used in combination in the same food. CICL provides an estimate of dietary exposure to chlorella powder (including chlorella micro powder) based on food consumption data from the 2015-2016 National Health and Nutrition Examination Survey (NHANES). CICL estimates the mean and 90th percentile eaters-only dietary exposures to chlorella powder from the intended uses to be 522 mg/person (p)/d and 870 mg/p/d, respectively, for the U.S. population aged 2 years and older. CICL further states that chlorella powder and chlorella micro powder will be substitutional for other ingredients from *Chlorella* spp. that are on the market.

CICL discusses the safety of the dried biomass of *C. sorokiniana* NITE SD 00247. CICL describes the history of use of ingredients produced by *Chlorella* spp. in human food. CICL states that the principal constituents of chlorella powder and chlorella micro powder are representative of typical components of the human diet (i.e., protein, lipids, carbohydrates) and will exhibit absorption, distribution, metabolism, and excretion characteristics similar to that of other dietary plant and microalgae sources via established metabolic pathways.

CICL describes published toxicological studies in rats administered chlorella powder;

[1] This particle size specification only applies to chlorella micro powder.

these include acute, 28-day, and 90-day toxicity studies. CICL states that no chlorella powder-related adverse effects were observed at the highest tested dose levels of 5.94 g/kg body weight (bw)/d in male rats and 6.41 g/kg bw/d in female rats. CICL concludes that chlorella powder and chlorella micro powder are not genotoxic based on published *in vitro* studies. To further corroborate safety, CICL incorporates information cited in GRN 000384[2] and GRN 000469.[3] CICL conducted an updated literature search through August 2021 and did not identify any information that would contradict its GRAS conclusion. Based on the weight of evidence, CICL concludes that the dried biomass of *C. sorokiniana* NITE SD 00247 is not expected to elicit an oral allergenic response.

CICL includes the statement of a panel of individuals (CICL's GRAS panel). Based on its review, CICL's GRAS panel concludes that chlorella powder and chlorella micro powder are safe under the conditions of intended use.

Based on the totality of the data and information, CICL concludes that its chlorella powder and chlorella micro powder are GRAS for the intended use.

Potential Requirement for a Color Additive Petition

There is no GRAS provision for color additives. In the notice, CICL describes chlorella powder and chlorella micro powder as green. As such, the use of chlorella powder or chlorella micro powder in food products may constitute color additive uses 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 000986 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 Food Ingredients in OFAS.

Standards of Identity

In the notice, CICL states its intention to use chlorella powder and chlorella micro powder in several food categories, including foods for which standards of identity exist, located in Title 21 of the CFR. We note that an ingredient that is lawfully added to food

[2] The subject of GRN 000384 is algal oil derived from *Chlorella protothecoides* strain "S106". FDA evaluated this notice and responded in a letter dated June 13, 2012, stating that we had no questions at the time regarding the notifier's GRAS conclusion.

[3] The subject of GRN 000469 is *C. protothecoides* strain "S106" flour with 40-70% lipid. FDA evaluated this notice and responded in a letter dated June 7, 2013, stating that we had no questions at the time regarding the notifier's GRAS conclusion.

products may be used in a standardized food only if it is permitted by the applicable standard of identity.

Potential Labeling Issues

Under section 403(a) of the FD&C Act, a food is misbranded if its labeling is false or misleading in any way. Section 403(r) of the FD&C Act lays out the statutory framework for labeling claims characterizing a nutrient level in a food or the relationship of a nutrient to a disease or health-related condition (also referred to as nutrient content claims and health claims). If products containing chlorella powder or chlorella micro powder bear any nutrient content or health claims on the label or in labeling, such claims are subject to the applicable requirements and are under the purview of the ONFL in CFSAN. OFAS did not consult with ONFL on this issue or evaluate any information in terms of labeling claims. Questions related to food labeling should be directed to ONFL.

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 CICL's notice concluding that chlorella powder and chlorella micro powder are GRAS under the intended conditions of use, we did not consider whether section 301(ll) or any of its exemptions apply to foods containing chlorella powder or chlorella micro powder. Accordingly, our response should not be construed to be a statement that foods containing chlorella powder or chlorella micro powder, if introduced or delivered for introduction into interstate commerce, would not violate section 301(ll).

Conclusions

Based on the information that CICL provided, as well as other information available to FDA, we have no questions at this time regarding CICL's conclusion that chlorella powder and chlorella micro powder are GRAS under the intended conditions of use. This letter is not an affirmation that chlorella powder and chlorella micro powder are 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 000986 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

Susan J. Carlson -S

Digitally signed by Susan J. Carlson -S
Date: 2021.12.21 12:18:57 -05'00'

Susan Carlson, Ph.D.
Director
Division of Food Ingredients
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