U.S. FOOD & DRUG ADMINISTRATION

Human Foods Program

Claire Kruger, Ph.D., DABT
Spherix Consulting Group, Inc.
751 Rockville Pike, Unit 30-B
Rockville, MD 20852

Re: GRAS Notice No. GRN 000934

Dear Dr. Kruger:

The Food and Drug Administration (FDA, we) completed our evaluation of the supplement to GRN 000934 that you submitted on behalf of CABIO Biotech (Wuhan) Co., Ltd. (CABIO). We received the supplement on September 27, 2024. The supplement addresses an additional use for the subject of GRN 000934. CABIO submitted clarifying information on June 16, 2025, and July 7, 2025.

We previously responded to GRN 000934 on July 20, 2021. We stated that we had no questions at that time regarding CABIO's conclusion that algal oil from *Schizochytrium* sp. strain CABIO-A-2 containing ≥35% docosahexaenoic acid algal oil (≥35% DHA is GRAS for use as an ingredient in the food categories listed in 21 CFR 184.1472(a)(3) Menhaden oil at levels up to 29% of the levels specified, excluding products under the U.S. Department of Agriculture's jurisdiction, and as the sole added source of DHA in any given food category so that the total dietary exposure to DHA will be no more than 1.5 g/person (p)/d. CABIO also intends to use algal oil ≥35% DHA) as an ingredient in cow milk- and soy-based, non-exempt infant formula for term infants at a maximum level of 0.5% (w/w) of total fat as DHA in combination with a safe and suitable source of arachidonic acid (ARA) at a ratio ranging from 1:1 to 1:2 DHA to ARA.

In the supplement dated September 27, 2024, CABIO informs us of its view that algal oil (≥35% DHA is GRAS, through scientific procedures, for use as an ingredient in cow milk- and soy-based, exempt infant formula for pre-term infants at a maximum level of 0.5% w/w of total fat as DHA in combination with a safe and suitable source of ARA at a ratio ranging from 1:1 to 1:2 DHA:ARA.

Our use of the term, "algal oil ≥35% DHA," in this letter is not our recommendation of that term as an appropriate common or usual name for declaring the substance 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 Nutrition Center of Excellence (NCE). The Office of Pre-Market Additive Safety (OPMAS) did not consult with ONFL regarding the appropriate common or usual name for "algal oil (≥35% DHA)."

In the supplement, CABIO provides information on the identity of algal oil (≥35% DHA and states that it is produced in the same way as described in GRN 000934. In the June 16, 2025, amendment, CABIO provides revised specifications for algal oil (≥35% DHA), which includes the contents expressed on a weight % basis for DHA (≥35.0%), docosapentaenoic acid ≤20% , eicosapentaenoic acid (≤3.0% , moisture (≤0.05% , unsaponifiable matter ≤3.5%), trans fatty acids (≤1.0%), and limits for residual hexane not detected with a limit of quantitation of 1 mg/kg), anisidine value ≤20 , total oxidation value (≤26 , acid value (≤0.5 mg KOH/g), peroxide value (≤5 meq/kg), total arsenic (≤0.1 mg/kg), cadmium (≤0.1 mg/kg), copper (≤0.05 mg/kg), iron (≤0.2 mg/kg), lead (≤0.1 mg/kg , mercury (≤0.04 mg/kg), and microorganisms, including *Salmonella* serovars (absent in 25 g), *Cronobacter sakazakii* (absent in 10 g), and *Listeria monocytogenes* (absent in 25 g). CABIO provides the results from three recent non-consecutive batch analyses to demonstrate that algal oil (≥35% DHA can be produced to meet the specifications.

In the supplement, CABIO estimates the dietary exposure to DHA from the expanded intended use. CABIO estimates the dietary exposure to DHA based on published estimates of the maximum daily energy requirements of low birth weight, very low birth weight, and extremely low birth weight pre-term infants and associated infant body weights, the maximum fat content of infant formula per 21 CFR 107.100 (6 g fat/100 kcal , and the maximum intended use level of algal oil (≥35% DHA). CABIO estimates the maximum dietary exposure to DHA to be 45 mg/kg body weight/d, which corresponds to 112.5 mg/p/d, 67.5 mg/p/d, and 45 mg/p/d for low birth weight, very low birth weight, and extremely low birth weight pre-term infants, respectively.

CABIO conducted an updated literature search through June 2025, and identified a new published toxicity study using a DHA oil from a different strain of Schizochytrium. This study describes a single dose acute toxicity test, a repeated dose sub-chronic oral toxicity study, and various *in vitro* and *ex vivo* genetic toxicity assays. CABIO also incorporated into the notice published clinical studies from prior notices (i.e., GRNs 000326, 000379, 000553, 000677, 000731, 000933, and 001008)[1] to support the safe use of algal oil from *Schizochytrium* sp. in pre-term infants. CABIO did not identify any data or information that would contradict its safety conclusion from GRN 000934.

Based on the totality of the data and information, CABIO concludes that algal oil (≥35% DHA) is GRAS for its intended use.

Potential Labeling Issues

[1] Various DHA and ARA oils were the subjects of GRNs 000326, 000379, 000553, 000677, 000731, 000933, and 001008. We evaluated these notices and responded in letters dated October 24, 2010, November 8, 2011, June 19, 2015, May 2, 2017, April 6, 2018, November 13, 2020, and February 25, 2022, respectively, stating that we had no questions at that time regarding the notifiers' GRAS conclusions.

Under section 403(a) of the Federal Food, Drug, & Cosmetic (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 algal oil (≥35% DHA 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 ONFL. OPMAS 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.

Intended Use in Infant Formulas

Under section 412 of the FD&C Act, a manufacturer of a new infant formula must make a submission to FDA providing required assurances about the formula at least 90 days before the formula is marketed. Our response to CABIO's GRAS notice does not alleviate the responsibility of any infant formula manufacturer that intends to market an infant formula containing algal oil (≥35% DHA) to make the submission required by section 412. Infant formulas are the purview of the Office of Critical Foods in NCE.

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 CABIO's supplement concluding that algal oil (≥35% DHA) 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 algal oil (≥35% DHA . Accordingly, our response should not be construed to be a statement that foods containing algal oil (≥35% DHA), if introduced or delivered for introduction into interstate commerce, would not violate section 301(ll).

Conclusions

Based on the information that CABIO provided, as well as other information available to FDA, we have no questions at this time regarding CABIO's conclusion that algal oil (≥35% DHA is GRAS under its intended conditions of use. This letter is not an affirmation that algal oil (≥35% DHA) 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 the supplement to GRN 000934 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

Susan J. Carlson -S

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