U.S. FOOD & DRUG ADMINISTRATION
Human Foods Program

Susan Cho, PhD
AceOne RS, Inc.
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Re: GRAS Notice No. GRN 001301

Dear Dr. Cho:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 001301. We received the notice that you submitted on behalf of NovoSana (Taicang) Co., Ltd. (NovoSana) on August 12, 2025, and filed it on February 3, 2026. NovoSana submitted amendments to the notice on January 8, 2026, May 16, 2026, June 13, 2026, July 22, 2026, and July 28, 2026, containing additional information on the manufacturing process, production organism, specifications, intended uses, estimated dietary exposure, and safety narrative.

The subject of the notice is algal oil (≥45% docosahexaenoic acid from *Schizochytrium* sp. GDMCC 70108 (algal oil (≥45% DHA)) for use as an ingredient in the same food categories as those listed in 21 CFR 184.1472(a)(3) (Menhaden oil) at use levels that are no more than 22% of the levels specified for menhaden oil in that regulation, excluding use in products under the jurisdiction of the United States Department of Agriculture (USDA). NovoSana states that algal oil (≥45% DHA) will be used as the sole added source of DHA in any given food category, and if algal oil (≥45% DHA) is blended with a source of eicosapentaenoic acid (EPA), the total dietary exposure will be no more than 1.5 g of DHA/person(p)/d and no more than 3.0 g/p/d of DHA and EPA combined. NovoSana also intends to use algal oil (≥45% DHA) as an ingredient in cow milk-, goat milk, soy-, and partially hydrolyzed milk-based, non-exempt infant formula for term infants and in 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 arachidonic acid (ARA) at a ratio ranging from 1:1 to 1:2 DHA to ARA. The notice informs us of NovoSana's view that these uses of algal oil (≥45% DHA) are GRAS through scientific procedures.

Our use of the term, "algal oil (≥45% 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 (≥45% DHA)."

NovoSana states that algal oil (≥45% DHA) is a yellow oil composed predominantly of triglycerides (>98%), with minor amounts of diglycerides and monoglycerides. Algal oil (≥45% DHA) contains on average, as a percent of total fat, 50% DHA (22:6 n-3), 19% palmitic acid (16:0), 13% n-6 docosapentaenoic (DPA; 22:5 n-6), 2% oleic (18:1 n-9), 4% linoleic (18:2 n-6), 1% stearic (18:0), and 1% margaric (17:0) acids. Low levels (<1%) of other fatty acids, including dihomo-gamma-linolenic acid (18:3 n-6), EPA (20:5 n-3), and ARA (20:4 n-6), are also present. Expressed on an area percent basis, these fatty acids are within limits specified in the Food Chemicals Codex (FCC) monograph (updated in FCC 13, 2024)[1] for *Schizochytrium* sp. oil. NovoSana also provides data on the sterol composition of algal oil (≥45% DHA) and identifies the major sterols as known components of *Schizochytrium* sp. algal oils consumed in the human diet.

NovoSana describes the production organism used in the manufacturing process for algal oil (≥45% DHA). The production organism, *Schizochytrium* sp. GDMCC 70108, is non-pathogenic and non-toxigenic and is deposited in the Guangdong Microbiological Culture Collection Center (GDMCC) under the deposition number GDMCC 70108. NovoSana states that the identity of the production organism was confirmed using 18S rRNA sequencing.

NovoSana describes the method of manufacture for algal oil (≥45% DHA) produced via fermentation of a pure culture of *Schizochytrium* sp. GDMCC 70108 under controlled conditions. Following fermentation, the algal biomass is steam sterilized and agitated to lyse the cells. The crude algal oil is then separated from the biomass by centrifugation. The crude oil is stored in stainless steel tanks under nitrogen until it is refined using standard procedures including caustic refining, water washing, winterization, bleaching, and vacuum deodorization. The resulting algal oil (≥45% DHA) is treated with antioxidants (mixed natural tocopherols, ascorbic acid), filtered, and packaged in nitrogen-flushed containers. NovoSana states that algal oil (≥45% DHA) is produced in accordance with current good manufacturing practices (cGMP) and that all processing aids, components, and food contact materials are food-grade and comply with applicable U.S. regulations, are GRAS for their intended use, or are the subject of an effective food contact notification.

NovoSana provides specifications for algal oil (≥45% DHA) that include limits for fatty acids expressed on a weight percent (g/100g) of total fat basis: DHA (≥45%), n-6 DPA (≤16.5%), ARA (≤1.3%), EPA (≤2%), acid value (≤0.8 mg potassium hydroxide/g), free fatty acids (≤0.4%), peroxide value (≤5 milliequivalents/kg), *p*-anisidine value (≤20), total oxidation value (≤20), trans fatty acids (≤1%), unsaponifiable matter (≤2%), moisture and volatile matter (≤0.1%), total arsenic (≤0.1 mg/kg), cadmium (≤0.1

[1] NovoSana cites the fatty acid limits associated with "acceptance criteria 1" limits in the FCC 13, supplement 2 (2024). FDA notes that these levels remain unchanged in the current FCC 15 (2026) monograph.

mg/kg), mercury (≤0.1 mg/kg), lead (≤0.1 mg/kg), and microorganisms, including *Escherichia coli* (not detected (ND) in 25 g), *Cronobacter* sp. (ND in 10 g), Enterobacteriaceae (ND in 10 g), *Listeria* spp. (ND in 25 g), and *Salmonella* serovars (ND in 25 g), as well as cereulide (<0.05 µg/kg). NovoSana provides the results from three non-consecutive batches to demonstrate that the algal oil (≥45% DHA) can be produced to meet the stated specifications. NovoSana states that algal oil (≥45% DHA) is stable for 24 months at room temperature (≤ 25 °C).

NovoSana discusses the dietary exposure to DHA from algal oil (≥45% DHA) based on the food categories in 21 CFR 184.1472(a)(3), excluding food categories 21 CFR 170.3(n) (11) egg products, (13) fish products, (29) meat products (29), and (34) poultry products, and the use levels in each category calculated for a content of 45% DHA in algal oil. The maximum use levels are adjusted to 22% of those indicated for menhaden oil so that the resulting dietary exposure to DHA will not exceed 1.5 g/p/d, the amount corresponding to approximately 50% of the total estimated dietary exposure to DHA plus EPA from menhaden oil. NovoSana states that the intended uses of algal oil (≥45% DHA) are substitutional for other DHA-containing oils currently used in foods; therefore, the cumulative dietary exposure to DHA is not expected to change.

NovoSana estimates the dietary exposure to algal oil (≥45% DHA) from the intended use of up to 0.5% (w/w) of total fat as DHA and assuming 50% of calories in term infant formula are provided by fat (9 kcal/g). Using the highest reported 90th percentile energy intakes for infants (140 kcal/kg body weight (bw)/d for formula-fed infants 14-27 days old) reported in Fomon et al. (1993)[2], NovoSana estimates the dietary exposure to DHA for term infants to be up to 39 mg DHA/kg body weight (bw)/day (approximately 156 mg/person (p)/d for a 4-kg infant) at the 90th percentile. The corresponding estimate of algal oil (≥45% DHA) is 87 mg/kg bw/d (approximately 350 mg/p/d for a 4-kg infant).

NovoSana presents an upper estimate of dietary exposure for pre-term infants based on a reference value in Koletzko et al., 2014[3] for the upper level of recommended caloric requirements (range of 110-130 kcal/kg bw/d) for pre-term infants, an assumed fat content of 6 g per 100 kcal (or 54% of kcals as fat) in pre-term infant formula, and an intended maximum use level of 0.5% of total fat as DHA from algal oil (≥45% DHA). Using these assumptions, NovoSana estimates the upper limit of dietary exposure to be 39 mg/kg bw/d DHA[4] (approximately 97.5 mg/p/d for a 2.5-kg infant) for low birth weight and/or pre-term infants.

NovoSana discusses data and information to support the safe use of algal oil (≥45% DHA). NovoSana incorporates into the notice safety data and information from various

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[2] Fomon S.J. (1993) "Energy", in *Nutrition of Normal Infants*. Mosby, St. Louis, pp. 103-120.
[3] Koletzko, B., Poindexter, B, and Uauy, R. (2014) "Recommended nutrient intake levels for stable, fully enterally fed very low birth weight infants." in *Nutritional Care of Preterm Infants: Scientific Basis and Practical Guidelines*, Koletzko et al., (eds), Series: World Rev Nutr Diet, Vol. 110, Karger, Basel, pp. 297-99.
[4] In amendments to GRN 001301, NovoSana's estimates of dietary exposure for preterm infants assume 60% of kcals as fat, corresponding to estimates of dietary exposure of 43 mg/kg bw/d for preterm infants.

GRNs for long-chain polyunsaturated fatty acid-containing oils[5] and states that an updated literature search conducted through April 2026 did not identify any newly published studies inconsistent with previous safety determinations for DHA-rich algal oils.

NovoSana asserts that algal oil (≥45% DHA) is substantially chemically equivalent to other DHA-rich algal oils that are the subjects of previously submitted GRAS notices receiving No Questions Letters, including those derived from *Schizochytrium* sp., such as the subject of GRN 000677, and compares fatty acid and sterol profiles among these ingredients in support of this statement. NovoSana notes that fatty acid levels, other than DHA, and sterol levels either approximate or are less than those of other DHA-rich algal oils listed on the GRAS inventory. On this basis, NovoSana incorporates into the notice published genotoxicity, acute, sub-chronic, and developmental and reproductive toxicity studies previously reviewed in various GRNs for DHA-containing oils derived from other microorganisms such as *Aurantiochytrium* sp. and other strains of *Schizochytrium* sp. NovoSana concludes that DHA-containing oils derived from *Schizochytrium* sp. show no evidence of genotoxicity or general toxicity. NovoSana also addresses the safety of both the saponifiable and non-saponifiable fractions of the article of commerce, including squalene, sterol, and carotenoid components, by reference to background dietary levels and consistency with FCC specifications.

NovoSana reports human studies on DHA and DHA-rich oils discussed in prior notices to support the safe use of algal oil (≥45% DHA) in term infants (GRNs 000731, 000776, and 001008), pre-term infants (GRNs 000326, 000379, 000553, and 000677), and children and adults (GRNs 000836, 000934, and 001008). Based on these evaluations, NovoSana concludes that *Schizochytrium* sp.-derived DHA-containing oils are well tolerated in term and pre-term infants, children, and adults.

Based on the totality of the data and information, NovoSana concludes that algal oil (≥45% DHA) is GRAS for its intended uses.

Standards of Identity

In the notice, NovoSana states its intention to use algal oil (≥45% DHA) 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 products may be used in a standardized food only if it is permitted by the applicable standard of identity.

[5] Long-chain polyunsaturated fatty acid-containing oils were the subjects of GRNs 000137, 000326, 000379, 000553, 000677, 000731, 000776, 000836, 000934, and 001008. We evaluated these notices and responded in letters dated February 12, 2004, October 24, 2010, November 8, 2011, June 19, 2015, May 2, 2017, April 6, 2018, October 26, 2018, September 3, 2019, July 20, 2021, and February 25, 2022, respectively, stating that we had no questions at that time regarding the notifiers' GRAS conclusions. These letters are available on our GRAS Notice inventory at https://www.cfsanappsexternal.fda.gov/scripts/fdcc/?set=GRASNotices.

Potential Labeling Issues

Under section 403(a) of the Federal Food, Drug, and Cosmetic Act (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 (≥45% 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.

Potential Requirement for a Color Additive Petition

There is no GRAS provision for color additives. In the notice, NovoSana describes algal oil (≥45% DHA) as a yellow oil. As such, the use of algal oil (≥45% DHA) in food products may constitute a color additive use under section 201(t)(1) of the 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 001301 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 OPMAS.

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 NovoSana's GRAS notice does not alleviate the responsibility of any infant formula manufacturer that intends to market an infant formula containing algal oil (≥45% 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 NovoSana's notice concluding that algal oil (≥45% 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 (≥45% DHA). Accordingly, our response should not be construed to be a statement that foods containing algal oil (≥45% DHA), if introduced or delivered for introduction into interstate commerce, would not violate section 301(ll).

Conclusions

Based on the information that NovoSana provided, as well as other information available to FDA, we have no questions at this time regarding NovoSana's conclusion that algal oil (≥45% DHA) is GRAS under its intended conditions of use. This letter is not an affirmation that algal oil (≥45% 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 GRN 001301 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

SUSAN J. CARLSON -S

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