U.S. FOOD & DRUG ADMINISTRATION

Human Foods Program

Katherine Niederberger, Ph.D.
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UNITED KINGDOM

Re: GRAS Notice No. GRN 001313

Dear Dr. Niederberger:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 001313. We received the notice that you submitted on behalf of Huve Nutraceuticals Ltd. (HuveNutra) on November 17, 2025, and filed it on March 12, 2026. HuveNutra submitted amendments to the notice on May 20, 2026, June 22, 2026, and July 14, 2026, that clarified the manufacturing, specifications, dietary exposure, and aspects of the safety narrative.

The subject of the notice is algal oil (≥35% docosahexaenoic acid) from *Aurantiochytrium limacinum* CCAP A2[1] (algal oil (≥35% DHA)) for use as an ingredient in the same food categories listed in 21 CFR 184.1472(a)(3) (Menhaden oil) at levels that are not more than 20% of those specified for menhaden oil in that regulation, excluding use in products under the U.S. Department of Agriculture's jurisdiction. HuveNutra states that if algal oil (≥35% DHA) is blended with another source of DHA or eicosapentaenoic acid (EPA), the total dietary exposure will be no more than 1.5 g DHA/person (p)/d and no more than 3.0 g/p/d of DHA and EPA combined. HuveNutra also intends to use algal oil (≥35% DHA) as an ingredient in cow milk-, goat milk-, and soy-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 2:1 ARA to DHA. The notice informs us of HuveNutra's view that these uses of algal oil (≥35% DHA) are GRAS through scientific procedures.

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

[1] HuveNutra states that *A. limacinum* was previously classified as *Schizochytrium limacinum* and the strain was deposited in the Culture Collection of Algae and Protozoa (CCAP) as *S. limacinum* A2.

(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)."

HuveNutra provides information about the identity and composition of algal oil (≥35% DHA), which is described as a pale yellow to light orange liquid produced from the microalgae *A. limacinum* CCAP A2. Algal oil (≥35% DHA) contains triglycerides composed, on average as a percent of total fatty acids, of 39% DHA (22:6 n-3), 43% palmitic acid (16:0), 7% n-6 docosapentaenoic acid (DPA; 22:5 n-6), 3% myristic acid (14:0), 2% pentadecanoic acid (15:0), and 1% stearic acid (18:0). Low levels (<1%) of other fatty acids, including dihomo-gamma-linolenic acid (DGLA; 20:3 n-6) EPA (20:5 n-3), and ARA (20:4 n-6), are also present. Expressed on an area % basis, levels of DHA, DPA, DGLA, EPA, and ARA are within limits specified in the Food Chemicals Codex (FCC) monograph (updated in FCC, 13, 2024)[2] for *Schizochytrium* sp. oil.

HuveNutra describes the *A. limacinum* CCAP A2 production organism used in the manufacture of algal oil (≥35% DHA) as non-pathogenic and non-toxigenic. HuveNutra confirmed the strain identity through phylogenetic analysis and whole genome sequencing.

HuveNutra describes the method of manufacture for algal oil (≥35% DHA). Crude algal oil is obtained from a culture of *A. limacinum* CCAP A2 grown under controlled conditions in a medium composed of yeast extract, glucose, peptones, and minerals. Following fermentation, the *A. limacinum* CCAP A2 cells are enzymatically disrupted using a food-grade protease enzyme to release the oil. The crude algal oil is separated from the biomass and then neutralized with sodium hydroxide. The enzyme is deactivated and removed by subsequent oil refining processes. The oil is washed, winterized with use of a cellulose-based filtration aid, filtered, bleached using activated bentonite, and deodorized. HuveNutra states that mixed tocopherols are then added to stabilize the oil before packaging under nitrogen. HuveNutra states that algal oil (≥35% DHA) is produced in accordance with current good manufacturing practices 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.

HuveNutra provides specifications for algal oil (≥35% DHA) that include, on a weight % basis, content of DHA (35-50%) and limits for DPA (≤10%), acid value (≤0.5 mg potassium hydroxide/g), peroxide value (≤5.0 milliequivalents/kg), anisidine value (<20), unsaponifiable matter (≤4.5%), moisture and volatiles (≤0.05%), *trans* fatty acids (≤1%), free fatty acids (≤0.4%), arsenic (≤0.1 mg/kg), cadmium (≤0.1 mg/kg), lead (≤0.05 mg/kg), mercury (≤0.1 mg/kg), cereulide (<0.1 µg/kg), and microorganisms, including *Cronobacter* sp. (negative in 10 g), *Salmonella* serovars (negative in 25 g), and *Listeria monocytogenes* (not detected in 25 g). HuveNutra provides the results of three non-consecutive batch analyses to demonstrate that algal oil (≥35% DHA) can be

[2] HuveNutra cites the fatty acid limits associated with "acceptance criteria II" in the FCC 13, supplement 2 (2024). We note that these levels remain unchanged in the current FCC 15 (2026) monograph.

produced to meet these specifications. HuveNutra states that algal oil (≥35% DHA) is stable for 2 years at 5 °C and 25 °C and 60% relative humidity.

HuveNutra discusses the dietary exposure to DHA from algal oil (≥35% DHA) based on the food categories in 21 CFR 184.1472(a)(3), excluding food categories in 21 CFR 170.3(n) (11) egg products, (13) fish products, (29) meat products (29), and (34) poultry products, and use levels calculated for a content of 50% DHA in algal oil. The maximum use levels are adjusted to 20% of those indicated for menhaden oil in each food category 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. HuveNutra states that the intended uses of algal oil (≥35% DHA) are substitutional for other DHA-containing oils currently used in foods; therefore, the cumulative dietary exposure to DHA is not expected to change.

HuveNutra estimates the dietary exposure to DHA from the use of algal oil (≥35% DHA) in infant formula for term infants. Based on the assumptions that infants consume 100 to 120 kcal/kg body weight (bw)/d,[3] of which ~50% is fat, HuveNutra estimates term infants consume approximately 5.5 to 6.7 g fat/kg bw/d. Assuming a maximum use level of 0.5% total fat as DHA, HuveNutra estimates the dietary exposure to DHA for infants to be 27 to 33 mg/kg bw/d. Using published values from Fomon (1993) for the 90th percentile caloric intakes of male and female formula-fed term infants up to 6 months of age and assuming a fat content of 6 g/100 kcal for term infant formula and 0.5% of fat as DHA, HuveNutra estimates dietary exposure to DHA for term infants at the 90th percentile to be between 30 and 40 mg/kg bw/d. At the highest caloric intakes on a bw basis (~140 kcal/kg bw/d) observed for male infants 14-27 days old, and using the median value (4.0 kg) for bw in this population, the corresponding estimate of dietary exposure to DHA at the 90th percentile is 170 mg/p/d.

HuveNutra provides an upper estimate of dietary exposure for pre-term infants based on the following assumptions: a maximum daily caloric requirement of 150 kcal/kg bw/d[4] for pre-term infants, a fat content of 6 g/100 kcal in formula, and 0.5% of fat as DHA. HuveNutra estimates the upper limit of dietary exposure to DHA for low birth weight and/or pre-term infants to be 45 mg/kg bw/d or 112.5 mg/p/d (assuming a bw of 2.5 kg).

HuveNutra discusses data and information supporting the safety of algal oil (≥35% DHA) from prior GRNs for similar substances and from an updated literature search conducted through April 2026. HuveNutra states that algal oil (≥35% DHA) has

[3] HuveNutra cites data from Fomon (1993) that support mean caloric intakes of approximately 100-120 kcal/kg bw/d for term infants up to 83 days of age. For infants between 84 and 105 days of age, reported mean caloric intakes were slightly lower (91-96 kcal/kg bw/d).

[4] HuveNutra cites the American Academy of Pediatrics (AAP), Committee on Nutrition (1985) for the maximum value of 150 kcal/kg bw/d for pre-term infants. However, we note that the 150 kcal/kg bw/d value is the upper level for the range of caloric requirements (110-150 kcal/kg) indicated in the 1977 statement from the AAP Committee on Nutrition in *Pediatrics*, volume 60, pp. 519-530. In the 1985 AAP statement, estimated caloric requirement in a "typical growing premature infant" is given as 120 kcal/kg bw/d. For a formula with a caloric density of 81 kcals/100 mL, the corresponding volume of formula is 150 mL/kg bw/d.

quantitatively and qualitatively similar specifications, fatty acid profile, and sterol profile as compared to other DHA-rich algal oils previously concluded to be GRAS (i.e., GRNs 000137, 000553, 000677, 000731, 000732, 000776, 000777, 000836, 000843, 000844, 000913, 000933, 000934, 001008, and 001236).[5]

HuveNutra incorporates into the notice published safety data and information, including metabolic fate, genotoxicity, mutagenicity, acute, subchronic, developmental and reproductive toxicity studies in mice, rats, and piglets, as well as clinical studies conducted with infants, children, and adults previously reviewed in GRNs 000137, 000379, 000553, 000677, 000731, 000732, 000776, 000934, and 001008. HuveNutra conducted an updated literature search that identified recent publications describing acute toxicity tests, repeat dose short-term and sub-chronic oral toxicity studies, and various *in vitro* and *in vivo* genetic toxicity assays for DHA-rich algal oils and *S. limacinum* biomass. HuveNutra did not identify any data or information that would contradict its safety conclusion for algal oil (≥35% DHA).

HuveNutra states that allergenicity to algal oil (≥35% DHA) is not expected due to a lack of reported allergic reactions, as well as the highly refined nature of the algal oil, and low protein content of the subject of GRN 001313, and that the raw materials are not allergens.

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

Standards of Identity

In the notice, HuveNutra states its intention to use algal oil (≥35% 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.

Potential Labeling Issues

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.

[5] Various DHA oils were the subjects of GRNs 000137, 000379, 000553, 000677, 000731, 000732, 000776, 000777, 000836, 000843, 000844, 000913, 000933, 000934, 001008, and 001236. We evaluated these notices and responded in letters dated February 12, 2004; November 8, 2011; June 19, 2015; May 2, 2017; April 6, 2018; April 6, 2018; October 26, 2018; October 26, 2018; September 3, 2019; October 18, 2019; October 18, 2019; November 10, 2020; November 13, 2020; July 20, 2021; February 25, 2022; June 10, 2025, stating that we had no questions at that time regarding the notifiers' GRAS conclusions.

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, HuveNutra describes algal oil (≥35% DHA) as a light yellow to orange liquid. As such, the use of algal oil (≥35% 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 001313 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 HuveNutra'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 HuveNutra's notice 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 HuveNutra provided, as well as other information available to FDA, we have no questions at this time regarding HuveNutra'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 GRN 001313 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

SUSAN J. CARLSON -S

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