October 19, 2022

Office of Food Additive Safety (HFS-200)
Center for Food Safety and Applied Nutrition
Food and Drug Administration
5001 Campus Drive
College Park, MD 20740-3835

Subject: GRAS Notification – DHA Algal Oil

Dear Sir or Madam,

On behalf of Jiangsu Grand Xianle Pharmaceutical Co., Ltd., the law firm of Benjamin L. England & Associates (its agent) is submitting for FDA review, a copy of the GRAS notification as per FDA regulations at 21 CFR part 170, Subpart E.[1] The enclosed document provides notice of a claim that the food ingredient, DHA algal oil, as described in the enclosed notification, is exempt from the premarket approval requirement of the Federal Food, Drug, and Cosmetic Act because it has been determined to be generally recognized as safe (GRAS), based on scientific procedures, for addition to food.

If you have any question regarding the above, please do not hesitate to contact me at 410-220-2800 or blengland@englandlawgroup.com.

Sincerely,

Benjamin L. England, Esq.

[1] *See*, Appendix A – Authorization

GRAS Determination of DHA Algal Oil for Use in Foods

October 19, 2022

GRAS Determination of DHA Algal Oil for Use in Foods

SUBMITTED BY:

Jiangsu Grand Xianle Pharmaceutical Co., Ltd.
No.1 Zhongshan Seven Road
Coastal Industrial Park
Binhai 224555
Yancheng, Jiangsu, China

SUBMITTED TO:

U. S. Food and Drug Administration
Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
5100 Campus Drive
College Park, MD 20740-3835

CONTACT FOR TECHNICAL OR OTHER INFORMATION

Benjamin L. England, *Esq.*
Benjamin L. England & Associates
810 Landmark Drive, Suite 126
Glen Burnie, MD 21061

October 19, 2022

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I. § 170.22f Part 1, GRAS Notice: Signed Statements and Certifications

1) GRAS Submission

Jiangsu Grand Xianle Pharmaceutical Co., Ltd., (Sponsor) through its agents, Benjamin L. England & Associates, hereby notifies the U.S. Food and Drug Administration (FDA) of the determination of a Generally Recognized as Safe (GRAS) notice for the use of docosahexaenoic acid (DHA) – rich algal oil in foods, in accordance with Subpart E of 21 CFR § 170.

2) Name and Address

Jiangsu Grand Xianle Pharmaceutical Co., Ltd.
No.1 Zhongshan Seven Road
Coastal Industrial Park
Binhai 224555
Yancheng, Jiangsu, China

3) Name of Notified Substance

The substance that is the subject of our GRAS petition is a semi-refined oil (commonly referred to as semi-refined DHA algae sourced oil, DHA algal oil, DHA-rich algal oil, omega- 3-rich algal oil, omega-3 algal oil, and algal oil) that is sourced oil from *Schizochytrium*.[2]

4) Intended Use in Food

The DHA algal oil is intended for use as a direct food ingredient in foods in accordance with current good manufacturing practices (cGMP).

5) Statutory Basis for GRAS Determination

The Sponsor, through its agents, Benjamin L. England & Associates, LLC, hereby notifies FDA of the submission of a GRAS notice for DHA algal oil, meeting the specifications described herein, which has been determined to be GRAS through scientific procedures in accordance with 21 C.F.R. §§ 170.30(a) and (b).

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[2] The microalgal family *Thraustochytriaceae* has historically comprised seven genera: (1) *Japanochytrium*, (2) *Schizochytrium*, (3) *Ulkenia*, (4) *Althornia*, (5) *Diplophrys*, (6) *Aplanochytrium*, and (7) *Thraustochytrium*, collectively referred to as "thraustochytrids." The genera *Thraustochytrium*, *Schizochytrium*, and *Ulkenia* comprise marine protists commonly found in marine and estuarine environments. Thus, the Schizochytrium genus is part of the taxonomic *Thraustochytriaceae.* The taxonomic classification within the *Thrausochytrid*s has evolved over the years, in particular following the taxonomic rearrangement of the *Schizochytrium* genus which resulted in the erection of two new genera (*Oblongichytrium* and *Aurantiochytrium*) and an amended description of the genus Schizochytrium. See, Yokoyama R, Honda D. 2007. Taxonomic rearrangement of the genus *Schizochitrium sensu lato* based on morphology, chemotaxonomic characteristics, and l8S rRNA gene phylogeny (*Thraustochytriaceae*, *Labynthulomycete*s): emendation for *Schizochitrium* and erection of *Aurantiochytrium* and *Oblongichytrium* gen. nov. Mycoscience 48:199-211. The strain has been purified and isolated when the library was established. The strain identification test report uses 18sDNA gene sequence alignment analysis, which can only be identified to the genus level. This strain is Schizochytrium sp. See, APPENDIX B - Schizochytrium Strain of Algae Identification Report.

6) Premarket Approval Statement

The Sponsor further asserts that the use of the DHA algal oil, as described below, is exempt from pre-market approval requirements of the Federal Food, Drug, and Cosmetic Act, based on its conclusion that the substance is GRAS under the conditions of its intended use.

7) Availability of Information

The data and information that serve as the basis for this GRAS determination, as well as any information that has become available since the GRAS determination, will be sent on request, or are available for the FDA's review and copying during customary business hours from Benjamin L. England & Associates. Please contact Benjamin L. England, *Esq*. for all technical or regulatory information.

8) Data and Information Confidentiality Statement

None of the data and information in the GRAS notice are exempt from disclosure under the Freedom of Information Act.[3]

9) GRAS Certification

To the best of our knowledge, the GRAS determination is a complete, representative, and balanced review. Sponsor is not aware of any information that would be inconsistent with a finding that the proposed use of the DHA-rich algal oil in foods, meeting appropriate specifications, and used according to cGMP, is GRAS. Recent reviews of the scientific literature revealed no potential adverse health concerns.

10) Name/Position of Notifier

[redacted]

10/19/2022

Benjamin L. England, *Esq.* Date
Benjamin L. England & Associates
Agent for Jiangsu Grand Xianle Pharmaceutical Co., Ltd.

11) FSIS Statement

The data and information in the GRAS notice can be shared with the Food Safety Inspection Service (FSIS) of the U.S. Department of Agriculture (USDA).

[3] *See*, 5 U.S.C. 552.

II. § 170.230 Part 2, Identity, Method of Manufacture, Specifications, and Physical or Technical Effect

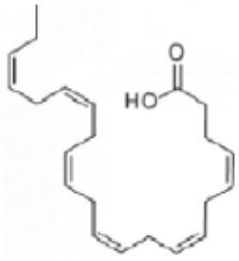
1) Identity

The Product is a light yellow to orange oily liquid with a unique odor that is extracted and refined from the wild-type heterotrophic microalgae *Schizochytrium* sp.[4] It is a mixture of triglycerides containing mostly polyunsaturated fatty acids in which the predominant fatty acid (>35%) is DHA.

2) Empirical Formula and Chemical Structure of DHA

The empirical formula for DHA is $C_{22}H_{32}O_2$. The systematic name is docosahexaenoic acid, often written as 22:6n-3 where the numbers indicate the number of carbon atoms in the molecule (22), the number of double bonds (6), and the number of carbon atoms from the methyl terminus to the first double bond (3). The molecular weight of DHA is 328.5 g/mol. The structural formula for DHA is represented below in Figure 1.

Figure 1 DHA Structural Formula Diagram



3) Common or Chemical Names

The preparation under consideration is referred to as DHA algal oil, DHA-rich algal oil, omega-3-rich algal oil, omega-3 algal oil, and algal oil. The CAS No. is 6217-54-5; glycerides, Cl 4-C22 and Cl 6-C22 unsaturated.

4) Characterization of Strain

Schizochytrium sp. are part of the human food chain, and they are consumed as a function of eating mussels and clams, as well as other marine organisms in general.[5] The *Schizochytrium* strain is naturally occurring and not a product of genetic engineering.

5) Manufacturing Process

The following image depicts the processes used to manufacture the crude algal oil and then refine the DHA algal oil isolated from the fermentation process. The processes employed to refine the oil are similar to those used in the refining of vegetable oils. In order to manufacture the Product,

[4] *See*, Appendix B - Schizochytrium Strain of Algae Identification Report.
[5] Hammond BG, Mayhew DA, Kier LO, Mast RW, Sander WJ. 2002. Safety assessment of DHA-rich microalgae from Schizochitrium sp. Regul Toxicol Pharmacol 35:255-265.

a pure culture of *Aurantiochytrium* is fermented under controlled axenic conditions in a medium that consists primarily of dextrose, soy peptone, yeast extract, ammonium sulfate, and sodium chloride.

Following fermentation, the algal cell walls are enzymatically disrupted after a pH adjustment using sodium hydroxide to release the intracellular oil. The crude oil layer is separated from the fermentation biomass by centrifugation and then treated with antioxidants as necessary. The oil can then undergo an optional fractionation/winterization step in which the oil is cooled and centrifuged. The oil may also be further treated with citric or phosphoric acid and refined using water degumming. The oil is then bleached and deodorized. Antioxidants can be added as necessary and sunflower or low erucic acid rapeseed oil can be added to the refined oil to standardize the DHA content. All reagents and processing aids used in the manufacture of algal oil 35% DHA) are food grade and the ingredient is manufactured in accordance with current good manufacturing practices.

The Product specifications include a minimum content of DHA (35%) and limits for acid value ≤ 1.0mg (KOH)/g), trans fatty acids (1.0%), moisture (0.1%), unsaponifiable matter 4%), lead (< 0.1 mg/kg), arsenic (<0.1 mg/kg), mercury (<0.1 mg/kg), insoluble impurities (≤0.2%), residual solvents (≤2mg/kg), PoV (≤2.5mmol/kg), and Aflatoxin B1 (≤5.0 μ g/kg).[6] The Sponsor has provided Certificates of Analysis which show that its manufacturing methods conform to these specifications.[7]

The following image depicts the processes used to manufacture the crude algal oil and then refine the DHA algal oil isolated from the fermentation process. The processes employed to refine the oil are similar to those used in the refining of vegetable oils.

[6] *See*, APPENDIX C – Specifications for Finished DHA.
[7] *See*, APPENDIX D – COA of DHA Powder and Specifications.

Figure 2 Manufacturing Process for DHA Oil

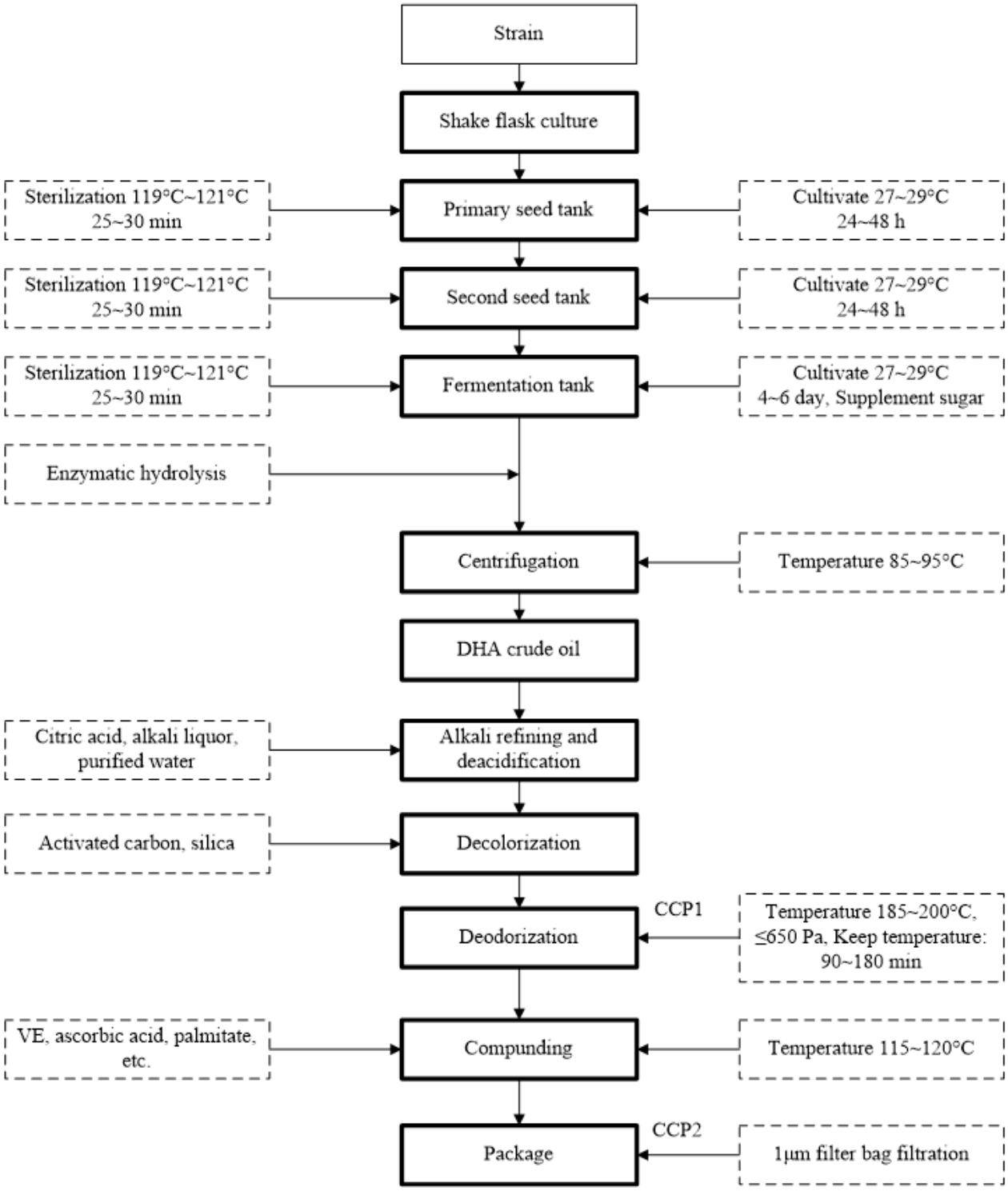
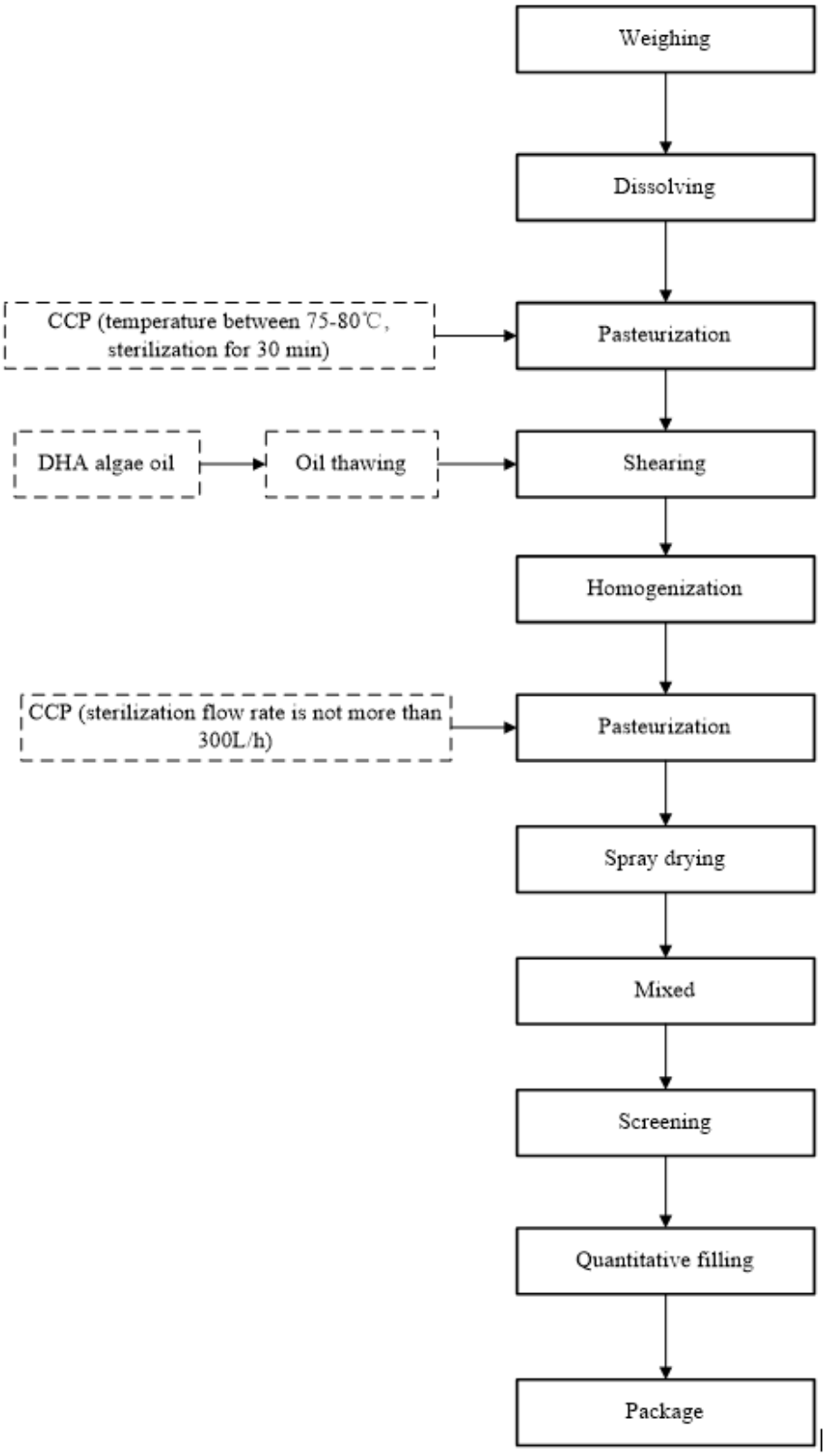


Figure 3 Manufacturing Process for DHA Powder



An oil rich in polyunsaturated fatty acids is produced by a heterotrophic fermentation process with a single-cell marine microalgae of the genus *Schizochytrium*. The fermentation process uses a medium containing carbon and nitrogen sources, bulk and trace mineral nutrients, and vitamins. The microorganism is maintained in a freezing tube and on nutrient agar plates before production. Following inoculation of the microorganism into a shake flask, the cultivation process is scaled up through multiple stages of transfers, and finally into the production fermentation vessel. All vessels, pipelines, and fermentation media are put through a rigorous, timed, and controlled sterilization process prior to the transfer of the microorganism. The fermentation is carried out under axenic conditions.

During the fermentation process, more sterile carbon substrate (e.g., dextrose syrup) is added to the fermenter to allow higher cell growth and more oil synthesis. Operating parameters such as temperature, pH, aeration, and agitation are controlled throughout the process to ensure that results, in terms of cell growth, oil synthesis, and the oil's fatty acid profile, are reproducible. The vessel is operated under positive pressure to prevent any contamination by foreign organisms. Table 1 below depicts the fermentation medium ingredients. P

Table 1 Fermentation Medium Ingredients

Ingredient	CFR Citation
Water	N/A
Dextrose	21 CFR § 184.1857, 184.1865, 184.1866
Soy peptone	21 CFR § 184.1553
Yeast extract	21 CFR § 184.1983
Ammonium sulfate	21 CFR § 184.1143
Monosodium glutamate (MSG)	21 CFR § 182.1500
Sodium chloride	21 CFR § 182.1
Magnesium sulfate heptahydrate	21 CFR § 184.1443
Potassium phosphate monobasic	21 CFR § 175.I05
Potassium phosphate dibasic	21 CFR § 182.6285
Ferric chloride	21 CFR § 184.1297
Calcium chloride	21 CFR § 184.1193
Trace Element Solution	
Copper sulfate	21 CFR § 184.1261
Sodium molybdate	Similar to ORN 384 (FDA no questions letter) (see ORN 553, 2014)
Zinc sulfate	21 CFR § 182.8997
Cobalt (II) chloride	N/A
Manganese chloride	21 CFR § 184.1446
Nickel sulfate	21 CFR§ 184.1537
Vitamins	
Vitamin B12	21 CFR § 184.1945
Biotin	21 CFR § 182.8159
Thiamine hydrochloride	21 CFR § 184.1875
Processing Aids	
Sodium hydroxide solution	21 CFR§ 184.1763
Ammonium hydroxide solution	21 CFR§ 184.1139
Defoaming agents	21 CFR § 173.340
Feeding Medium	
Dextrose syrup	21 CFR § 184.1865

Once fermentation is complete, the crude oil that accumulates intracellularly is recovered from the fermentation broth via an aqueous extraction process. To release the oil from the cells, the cell wall must be disrupted. In the cell-wall disruption process, the fermentation broth is pH-adjusted with sodium hydroxide and hydrolyzed enzymatically. As a result, no intact algae remain in the oil. The oil is then recovered from the hydrolyzed biomass. In the oil recovery process, the hydrolyzed biomass can be treated and centrifuged to yield the crude algal oil. At each step after cell-wall disruption, exposure to air is minimized. Antioxidants can be added as necessary.

The main purpose of deodorization is to remove compounds that cause off-flavors, but the process also removes free fatty acids, tocopherols, squalene, and sterols. In addition, other volatile contaminants that have undesired off-flavors are removed. The oil undergoes heat bleaching, where thermal destruction of flavor precursors and certain colored pigments, such as carotenoids, occurs. The oil becomes lighter in color. Deodorization is performed under vacuum to aid in stripping specific compounds, and it protects the oil from oxidation. Although nitrogen can be used as the stripping agent, superheated steam is frequently used.

The deodorization process is fully defined by temperature, time, pressure, and amount of stripping steam. Deodorization on a commercial scale is a multi-step process comprising de-aeration, multi-stage heating, deodorization-de-acidification, and multi-stage cooling of the oil. The oil after bleaching is de-aerated prior to being heated to deodorizing temperatures, to avoid oxidation and polymerization. De-aeration can be accomplished in a separate vessel connected to the vacuum system (around 50 mbar), or at an even lower pressure in the deodorizer. Sparge steam may be used to improve de-aeration.

Deodorization can be performed in a batch deodorizer, a semi-continuous system, or a continuous system. Stripping efficiency is superior in the continuous system, which has a column filled with structured packing with a high surface area. Counter-current contact of oil with the stripping steam over the structured packing provides efficient stripping with a short contact time. Various configurations of deodorizers can be used (horizontal or vertical vessels, tray-type, or packed columns). Antioxidants such as mixed tocopherols, ascorbyl palmitate, or other safe and suitable antioxidants are again added, as necessary. In addition, non-genetically modified organism (GMO) sunflower or rapeseed oil can be added as an option in order to standardize the oil for DHA content.

Reagents/processing aids that are employed in the extraction and refining process are listed in Table 2, below. The DHA-rich algal oil is manufactured in accordance with Hazard Analysis Critical Control Point (HACCP) and cGMP, including quality control (QC) checks at every stage of the production process. All the steps outlined in the above manufacturing process are conducted under conditions that minimize the risk of contamination by foreign materials.

Table 2 Regents/Processing Aids

Reagent/Processing Aid	CAS Number	CFR Citation
Phosphoric acid	7664-38-2	21 CFR § 182.1073
Citric acid	77-92-9	21 CFR § 184.1033
Clay (bleaching)	68515-07-1	21 CFR § 184.1155
Nitrogen	7727-37-9	21 CFR § 184.1540
Mixed tocopherols	1406-18-4	21 CFR § 182.3890; 21 CFR § 182.8890

Ascorbyl palmitate (optional)	137-66-6	21 CFR § 182.3149
Alcalase	9014-01-1	21 CFR § 184.1027
Sodium hydroxide	130-73-2	21 CFR § 184.1763
Sodium sulfate	7757-82-6	21 CFR § 186.1797
Filter aid	68855-54-9	21 CFR § 182.90
Rapeseed oil	8002-13-9	21 CFR § 184.1555
High-oleic sunflower oil	8001-21-6	GRAS per 21 CFR § 170.30
Rosemary extract (optional)	84604-14-8	GRAS per 21 CFR § 182.20

6) Product Specifications

The Product is intended for use as a direct food ingredient in foods, and to increase the dietary intake of the omega-3 fatty acid DHA. The approved use levels for menhaden fish oil are defined in 21 CFR § 184.1472, along with the proposed maximum use levels for the proposed DHA-algal oil. As noted for menhaden oil and other sources of DHA and/or EPA, FDA has determined that these oils may be used at a level that provides a total intake of DHA and/or EPA up to 3.0 grams per day. A review of previous GRAS notifications indicates that suppliers of DHA and EPA products, as well as their GRAS expert panels, have generally recommended a maximum limit of 1.5 grams of DHA or EPA per day when combined together. The maximum levels of use were designed to ensure that the combined daily intake of the two fatty acid components (i.e., EPA and DHA) would not exceed 3 grams per person per day. FDA has concurred with such an approach, providing "no questions" letters regarding such proposed food uses and associated intakes. In addition, the proposed food uses for this DHA-rich algal oil product are identical to the uses for other GRAS DHA and/or EPA products.

The fatty acid profile of this Schizochytrium sp. manufactured Mara DHA-algal oil is consistent across lots.[8] All of the fatty acids detected are well-known components of the human diet and found in both animal and vegetable food sources. This Schizochytrium sp. manufactured Mara DHA algal oil is comparable to that of several other DHA-algal oils, including the DHA-algal oil that was the subject of GRN 677.[9] When compared to the spectrum of available DHA oils from a variety of sources, including algae and fish, the fatty acid profile of this specific DHA algal oil is comparable to currently marketed DHA oil products. The residual solvent detected in DHA oil is n-hexane, and the residual solvent is not detected in DHA powder.[10]

Table 3 Specifications for DHA-algal oil from Schizochytrium

Items	Regulatory specifications	Method
Appearance	Light yellow to orange oily liquid with a unique odor of this product	Visual inspection Nose smell
Assay（Calculated as C22H32O2 triglycerides）	≥35.0%	GB 26400－2011
Unsaponifiable matter	≤4.0%	GB/T 5535.1
Moisture	≤0.1%	GB 5009.236
Insoluble impurities	≤0.2%	GB/T 15688
Residual solvents	≤2mg/kg	GB/T 5009.262

[8] *See*, Appendix E - Proximate Analysis of Three Non-Consecutive Lots.
[9] *Id.*
[10] *See*, Appendix F - Analytical results compared to a representative lot of GRN 677 Mara DHA-algal oil.

Acid value (calculated in KOH)	≤1.0mg (KOH)/g	GB 5009.229
PoV	≤2.5mmol/kg	GB 5009.227
Trans fatty acids	≤1.0%	GB 5413.36
*Aflatoxin B1	≤5.0μg/kg	GB/T 5009.22
*Total arsenic (calculated as As)	≤0.1 mg/kg	GB/T 5009.11
*Lead (Pb)	≤0.1 mg/kg	GB/T 5009.12

7) Stability Data

Stability testing (accelerated conditions) was conducted on three non-consecutive batches of DHA algal oil.[11] DHA algal oil is typically shipped and stored at 4°C, -4°, or frozen (-25°C). The results of the accelerated stability study demonstrate the stability of the product over an 8-week period.

III. § 170.235 Part 3, Dietary Exposure

The Product is intended for use as a direct food ingredient in foods, and to increase the dietary intake of the omega-3 fatty acid DHA. The approved use levels for menhaden fish oil are defined in 21 CFR § 184.1472, along with the proposed maximum use levels for the proposed DHA-algal oil. See Table 3 for approved use levels of DHA-oil compared to the proposed maximum level of use in the Sponsor's product.

Table 4 Approved use levels of DHA-oil compared to proposed maximum use levels of Sponsor's DHA algal oil in food

Category of Food	Maximum Approved level of DHA-oil in Food	Maximum Intended Use Level of DHA-oil in Food
Based goods, baking mixes	5.0%	1.0%
Cereals	4.0%	0.80
Cheese products	5.0%	1.0%
Chewing gum	3.0%	0.60
Condiments	5.0%	1.0%
Confections	5.0%	1.0%
Dairy product analogs	5.0%	1.0%
Egg products	5.0%	1.0%
Fats, oils	12.0%	2.4%
Fish products	5.0%	1.0%
Frozen dairy desserts	5.0%	1.0%
Gelatins, puddings	1.0%	.2%
Gravies, sauces	5.0%	1.0%
Hard candy	10.0%	2.0%
Jams, jellies	7.0%	1.4%
Meat products	5.0%	1.0%
Milk products	5.0%	1.0%
Nonalcoholic beverages	0.5%	.1%
Nut products	5.0%	1.0%

[11] *See*, Appendix E - Proximate analysis of three non-consecutive lots of DHA-algal oil produced using Schizochytrium, Appendix G - Accelerated stability study of DHA powder-6 months, and Appendix H - Long stability study of DHA oil-24 months.

Pastas	2.0%	.4%
Plan protein products	5.0%	1.0%
Poultry products	3.0%	.6%
Processed fruit juices	1.0%	.2%
Processed vegetable juices	2.0%	.2%
Snack foods	5.0%	1.0%
Soft candy	4.0%	.8%
Soup mixes	3.0%	.6%
Sugar substitutes	10.0%	2.0%
Sweet causes, toppings, syrups	5.0%	1.0%
White granulated sugar	4.0%	.8%

As noted for menhaden oil and other sources of DHA and/or EPA, FDA has determined that these oils may be used at a level that provides a total intake of DHA and/or EPA up to 3.0 grams per day. A review of previous GRAS notifications indicates that suppliers of DHA and EPA products, as well as their GRAS expert panels, have generally recommended a maximum limit of 1.5 grams of DHA or EPA per day when combined together. The maximum levels of use were designed to ensure that the combined daily intake of the two fatty acid components (i.e., EPA and DHA) would not exceed 3 grams per person per day. FDA has concurred with such an approach, providing "no questions" letters regarding such proposed food uses and associated intakes. In addition, the proposed food uses for this DHA-rich algal oil product are identical to the uses for other GRAS DHA and/or EPA products.

IV. § 170.240 Part 4, Self-Limiting Levels of Use

The use of DHA and DHA-algal oil and powder in foods is controlled as described in Part 3. Therefore, there are no self-limiting levels of use.

V. § 170.245 Part 5, Experience Based on Common Use in Food

The statutory basis of our conclusion of GRAS status in the notice is not based on common use in food.

VI. § 170.250 Part 6, GRAS Narrative

1) History of Use/Regulatory Approval of DHA-Algal Oil

DHA-rich oils from numerous sources including microalgae are considered GRAS for use in food for human consumption, including infant formula. Sources of the oils include *Schizochytrium* sp., *Ulkenia* sp. SAM2179, *Chlorella protothecoides* strain S106, and *Prototheca moriformis* strain S2532. ln addition, FDA has approved other sources of DHA for use in human food and infant formula, such as menhaden and fish oils.[12] DHA produced via fermentation employing various microalgae has been approved previously and sold for incorporation in food and infant formula. To date, algal oil produced from *Schizochytrium sp*. (DHA-S) has been approved for direct use in foods by the U.S. Food and Drug Administration (FDA), Health Canada, European Union, Food Standards Agency of Australia, China's Ministry of Health, and Brazil's National Health Surveillance Agency.

2) Safety

DHA is an important component of most cell membranes and tissues. DHA and DHA algal oils are currently marketed for use in food, dietary supplements, and infant formula for human consumption. The Product has a lipid (fatty acid) profile similar to that of currently marketed DHA from *Schizochytrium sp.*[13] Regulatory authorities have reviewed the safety of DHA and DHA-algal oils and found their use to be safe in human food, including infant formula. Numerous studies and publications support the safety of DHA and DHA-algal oils, including *in vitro* studies, *in vivo* animal studies, and clinical studies in humans. The most relevant studies on DHA include acute and sub-chronic toxicity, reproductive and developmental toxicity, mutagenicity and genotoxicity, chronic toxicity, and irritation/sensitization, along with clinical and epidemiological studies. The published data, as well as reviews conducted by regulatory authorities, support the conclusion that your DHA-rich algal oil produced using *Schizochytrium sp.* is safe for use in food.

3) Safety Data Summary

The available published scientific data on the safety of DHA from algae and other sources (e.g., fish oil), including *Schizochytrium sp*. algal sources, are extensive. The compositional profile of the DHA-rich algal oil ingredient presents no obvious safety concerns. The totality of published study data, as presented in previous GRNs reviewed by FDA support the safe use of DHA algal oil from *Schizochytrium sp.* in foods. Additionally, FDA has already reviewed numerous GRAS notifications for similar products and their use in foods and infant formulas and issued "letters of no objection." In addition, DHA products have been reviewed and approved around the world for addition to food, including infant formula, and for use as a dietary supplement.

DHA-rich oils from numerous sources, including microalgae, are considered GRAS for use in food for human consumption, including infant formula.[14] In addition, FDA has approved other DHA

[12] *See*, U.S. Food and Drug Administration. 2008. GRN242.
[13] *See*, U.S. Food and Drug Administration. 2017. GRN677.
[14] *See*, GRN1008, GRN041, GRN137, GRN319, GRN384, GRN553, GRN527, GRN677, GRN73, GRN732, GRN776, GRN777, GRN836, GRN843, GRN844, GRN963, GRN934, GRN933, GRN862, GRN844, GRN777, GRN776, GRN730, GRN326, GRN 913, and GRN94.

sources, such as menhaden and fish oils, for use in human food and/or infant formula. The safety of orally administered DHA from many different sources (e.g., fish oil), including previously submitted Schizochytrium sp., have been characterized extensively in the publicly available preclinical and clinical study literature. The compositional profile of the proposed DHA-rich algal oil from Schizochytrium sp. presents no obvious safety concerns. Finally, similar DHA products have been reviewed and approved around the world for addition to food and infant formula.

4) Basis for the GRAS Determination

According to federal law, in order to determine whether or not a substance can be considered GRAS, there must be:

> General recognition of safety… based only on the view of experts qualified by scientific training and experience to evaluate the safety of substances directly or indirectly added to food. The basis of such views may be… scientific procedures… General recognition of safety requires common knowledge about the substance throughout the scientific community knowledgeable about the safety of substances directly or indirectly added to food.
>
> General recognition of safety based upon scientific procedures shall require the same quantity and quality of scientific evidence as is required to obtain approval of a food additive regulation for the ingredient. General recognition of safety through scientific procedures shall ordinarily be based upon published studies, which may be corroborated by unpublished studies and other data and information.[15]

These criteria are applied in the analysis below to determine whether the use of DHA-rich algal oil in foods is GRAS based on scientific procedures. All data used in this GRAS determination are publicly available and generally known, and therefore meet the "general recognition" standard under the FD&C Act.

5) Safety Determination

DHA and DHA-algal oils are currently marketed for use in food for human consumption, including infant formula, as well as dietary supplements. The proposed DHA-algal oil and encapsulated powder from *Schizochytrium* has a composition and lipid (fatty acid and sterol) profile similar to that of currently approved/marketed DHA oils from *Schizochytrium* sp. T18 and other algal and marine sources.[16] Regulatory authorities have reviewed the extensive safety study database of DHA and DHA-algal and fish oils and found no issues of concern with respect to their use in human food, including infant formula. Numerous studies have been conducted and published in support of the safety evaluation of DHA and DHA-algal and fish oils, including *in vitro* studies and *in vivo* animal studies (i.e., acute and subchronic toxicity, reproductive and developmental toxicity, mutagenicity and genotoxicity, chronic toxicity, irritation/sensitization), as well as clinical studies in infants and adults.

[15] 21 CFR 170.30.
[16] *See*, Appendix F - Analytical results compared to a representative lot of GRN 677 Mara DHA-algal oil

DHA-rich oils from numerous sources, including microalgae, are considered GRAS for use in food for human consumption, including infant formula. FDA has responded that it has “no questions” regarding GRN862 for DHA-rich oil from microalgae. Sources of the DHA rich algal oils include *Schizochytrium* sp., *Crypthecodinium cohnii, Ulkenia* sp. SAM2179, *Chlorella protothecoides* strain S106, and *Protecheca moriformis* strain. In addition, FDA has approved other DHA sources, such as menhaden and fish oils, for use in human food and/or infant formula.

In Europe, DHA-rich oils from microalgal sources have been the subject of several authorization decisions and/or notifications under the EU Novel Food Regulation 258/97. A Novel Food Application was approved for the use of DSM's DHASCO-B from *Schizochytrium* sp. in conventional foods, infant formula and follow-up formula, and food supplements (DSM, 2013; EU, 2015). The first authorized use of DHA-rich oil from the thraustochytrid microalgae *Schizochytrium* sp. was for a range of foodstuffs, and they established a specification for the material. The second was for a DHA-rich oil derived from a second thraustochytrid microalgae, *Ulkenia* sp., based on its substantial equivalence with the oil from *Schizochytrium* sp. The other decisions authorized extensions to the approved food uses of the oils from *Ulkenia* sp. and *Schizochytrium* sp., respectively. An additional DHA-rich oil derived from the microalgae *Crypthecodinium cohnii* was already on the EU market before the Novel Food Regulation came into effect and was therefore legally and safely in use without the need for explicit approval. It should also be noted that in 2012 the UK Food Standards Agency concluded that T18 algal oil met the criteria for equivalence to the currently marketed DHA algal oils, as defined in Article 3(4) of regulation (EC) 258/97, and that the *Schizochytrium* strain used in the production of T18 oil was closely related to the organism used in the production of other *Schizochytrium* sp. DHA-rich algal oils (Food Standards Agency, 2012). To date, algal oil produced from Schizochytrium sp. has been approved for direct use in foods by the U.S. FDA, Health Canada, European Union, Food Standards Agency of Australia, China's Ministry of Health, and Brazil's National Health Surveillance Agency.

The safety of orally administered DHA from many different sources (e.g., fish oil), including Sponsor's proposed algal source and previously submitted *Schizochytrium* sp. T18, been characterized extensively in the publicly available preclinical and clinical study literature. The compositional profile of the proposed DHA-rich algal oil presents no obvious safety concerns. Finally, similar DHA products have been reviewed and approved around the world for addition to food and infant formula.

6) General Recognition of the Safety of DHA-Algal Oil

The intended use of a DHA-rich algal oil has been determined to be safe through scientific procedures as set forth in 21 CFR § 170.3(b), thus satisfying the “technical” element of the GRAS determination, and this conclusion is based on the following:

- There is common knowledge of a long history of human consumption of DHA from food and foods containing added DHA, from infant formula, and from other products such as dietary supplements.
- Literature searches did not identify safety/toxicity concerns related to any individual fatty acid or their ratios in the proposed DHA-algal oil.

- The proposed uses of the DHA-algal oil product from *Schizochytrium* sp. in food are identical to the approved uses for other GRAS DHA and/or EPA products. As with the use of menhaden oil, the maximum levels of use are designed to ensure that the combined daily intake of the two fatty acid components would not exceed 3 grams per person per day.

- DHA-rich oils from numerous sources, including microalgae, are considered GRAS for use in food for human consumption, including infant formula.

- Toxicity testing has been conducted with the similar products, including acute and sub-chronic toxicity studies, a battery of genotoxicity studies, and developmental and reproductive toxicity studies. In all of the studies, no evidence of toxicity was noted at the highest dose levels tested.

- The body of publicly available scientific literature on the consumption and safety of DHA and DHA-algal oil ingredients from both clinical studies in humans as well as animals is extensive and is sufficient to support the safety and GRAS status of the Product.

- Because this safety evaluation was based on generally available and widely accepted data and information, it also satisfies the so-called "common knowledge" element of a GRAS determination.

VII. § 170.250 Part 7, Supporting Data and Information

The following references are all generally available, unless otherwise noted.[17] Analytical COAs for DHA-algal oil and material safety data sheets are not generally available but are attached for reference.

[17] *See*, APPENDIX D – COA of DHA Powder and Specifications and Appendix I - MSDS of DHA oil.

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APPENDIX A – Authorization

CGE 远大健康 CGE HEALTH
江苏远大仙乐药业有限公司
Jiangsu Grand Xianle Pharmaceutical Co., Ltd.

No.1 Zhongshan Seven Road,
Coastal Industrial Park, Binhai 224555,
Yancheng, Jiangsu, China

Oct 19,2022

To Whom It May Concern:

RE: FDA matters

Please be advised that we have retained the Law Firm of Benjamin L. England & Associates, LLC and Consulting Firm of FDAImports.com LLC (the "Firms") to represent us before the Food and Drug Administration (FDA) respecting all issues related to the manufacture, distribution, exportation, and importation of FDA-regulated products. Various attorneys and consultants at Firms will be primarily handling such matters for us.

This letter authorizes you to discuss our FDA related issues, filings, and records with Mr. Benjamin England (blengland@englandlawgroup.com) or any of the attorneys or consultants at the Firms.

The telephone number for the Firms is (410)-220-2800 (FAX: 443-583-1464). If you have any questions regarding this authorization, please do not hesitate to contact me at +8613517274195.

Sincerely,

Liu sha
Quality Director
Jiangsu Grand Xianle Pharmaceutical Co., Ltd.

APPENDIX B - Schizochytrium Strain of Algae Identification Report.

CICC®

国家菌种资源库

检 测 报 告

Test Report

报告编号：19-157-738-699S

Report No. Jiangsu Grand Xianle Pharmaceutical Co., Ltd.

委托单位：江苏远大仙乐药业有限公司

Client Schizochytrium

样品名称：裂殖壶菌

Sample Fungus identification test

检测内容：真菌鉴定检测

Testing Items

中国工业微生物菌种保藏管理中心

China Center of Industrial Culture Collection

声　明

Statement

1. 报告为计算机打印，涂改无效。

   The printed report shall become invalid if altered.

2. 报告未经批准人签字无效。

   The report shall be invalid without signature of approver.

3. 报告未加盖本中心检测章无效。

   The report shall be invalid without CICC testing stamp.

4. 未经本中心主任书面批准，部分复制本报告无效。

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5. 本报告只对送检样品负责。

   The report only applies to the submitted sample.

6. 对本报告若有异议，请在收到报告之日起 15 日内向本中心提出，逾期不予受理。

   Any objection must be submitted within 15 days from the date of receiving the test report, and the overdue request will not be processed.

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   The sample source is provided by the applicant and CICC is not responsible for its authenticity.

中国工业微生物菌种保藏管理中心

China Center of Industrial Culture Collection (CICC)

地址：北京市朝阳区酒仙桥中路 24 号院 6 号楼

Address: Building 6, No.24 Yard, Jiuxianqiao Middle Road Chaoyang District, Beijing, China.

邮编 Zip：100015　　电话 Tel：010-53218302

传真 Fax：010-53218307　　E-mail：tech@china-cicc.org

www.china-cicc.org

检测报告

Test Report

编号№: 19-157-738-699S 号

样品名称 (Sample Name)	裂殖壶菌 Schizochytrium	样品状态 (Sample Status)	斜面培养物 Inclined culture
样品批次 (Sample Lot)	LSX190502	样品来源 (Sample Source)	/
委托单位名称 (Client)	Jiangsu Grand Xianle Pharmaceutical Co., Ltd.		
委托单位地址 (Address)	江苏盐城滨海沿海工业园中山七路 1 号 No. 1 Zhongshan Seven Road, Coastal Industrial Park, Economic Development Zone, Binhai County, Yancheng City, Jiangsu Province, China		
接收日期 (Receiving Date)	2019 年 05 月 22 日 May 22th, 2019	完成日期 (Reporting Date)	2019 年 06 月 18 日 June 18th, 2019
检测方法 (Method)	FMIC-QO01-003 真菌多相鉴定检测方法；QO-03-02 微生物菌种分子生物学鉴定操作规程 FMIC-QO01-003 Multiple identification and detection methods for fungi；QO-03-02 Operating Procedures for Molecular Biology Identification of Microbial Strains		
检测结果 (Conclusion)	破囊壶菌属 *Aurantiochytrium sp.*		
备注 (Remark)	"*Aurantiochytrium limacinum*"同物异名："蛞蝓裂殖壶菌*Schizochytrium limacinum*"。 "*Aurantiochytrium mangrovei*"同物异名："红树林裂殖壶菌*Schizochytrium mangrovei*"。 参考文献：Yokoyama R, Honda D. Taxonomic rearrangement of the genus *Schizochytrium* sensu lato based on morphology, chemotaxonomic characteristics, and 18S rRNA gene phylogeny (*Thraustochytriaceae*, *Labyrinthulomycetes*): emendation for *Schizochytrium* and erection of *Aurantiochytrium* and *Oblongichytrium* gen. nov.[J]. Mycoscience, 2007, 48(4): 199-211.		
编制人 (Reporter)	Zhang Tianci	审核人 (Checker)	Xiang Feirong
批准人 (Approver)		签发日期 (Issuing Date)	2022.06.28

检测报告

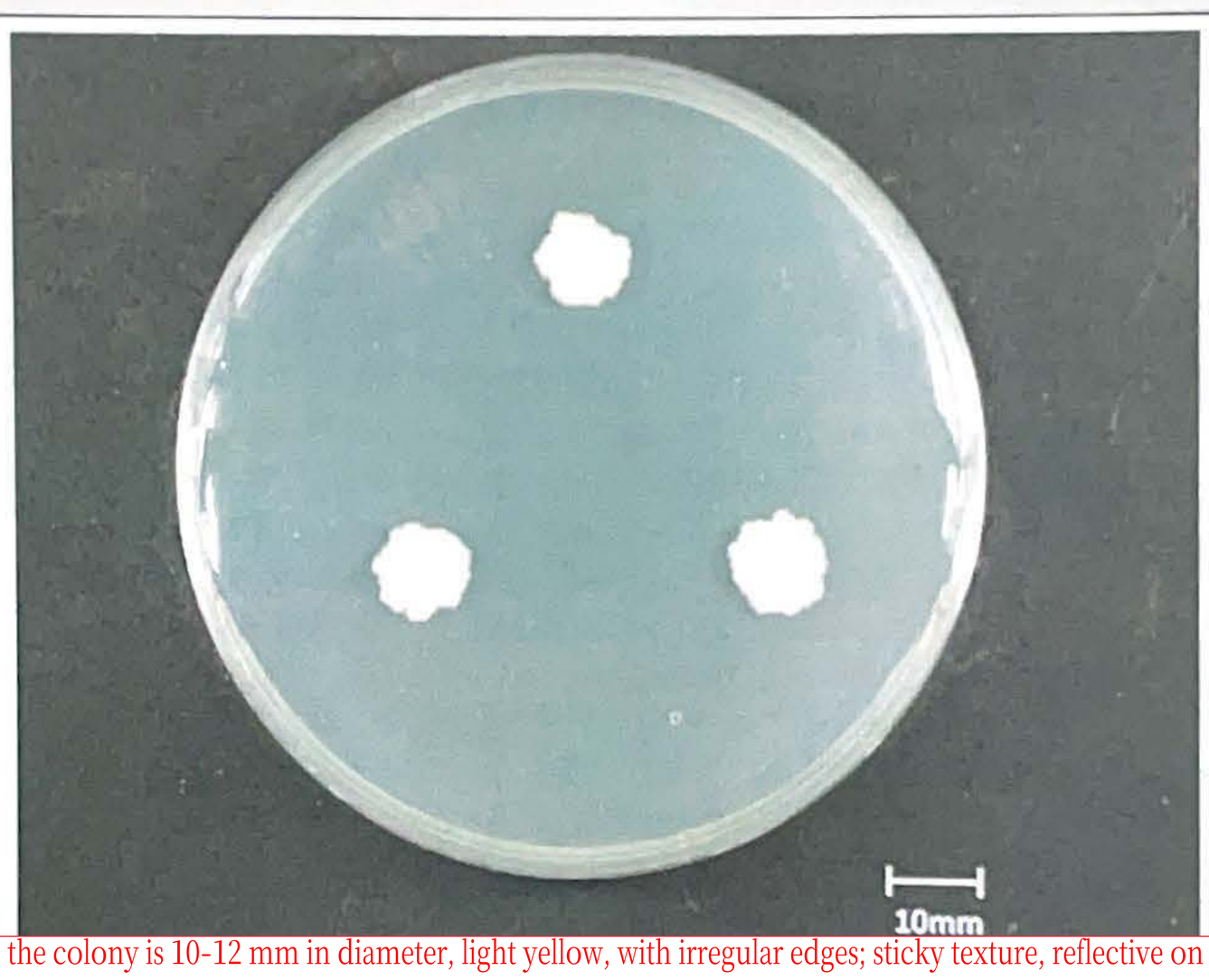
Test Report

编号№: 19-157-738-699S 号

形态特征 （Morphological Characteristic）

宏观形态

Macroscopic form



Cultured on a medium at 28 ° C for 14 days, the colony is 10-12 mm in diameter, light yellow, with irregular edges; sticky texture, reflective on the surface; light yellow on the reverse side; no soluble pigments are produced.

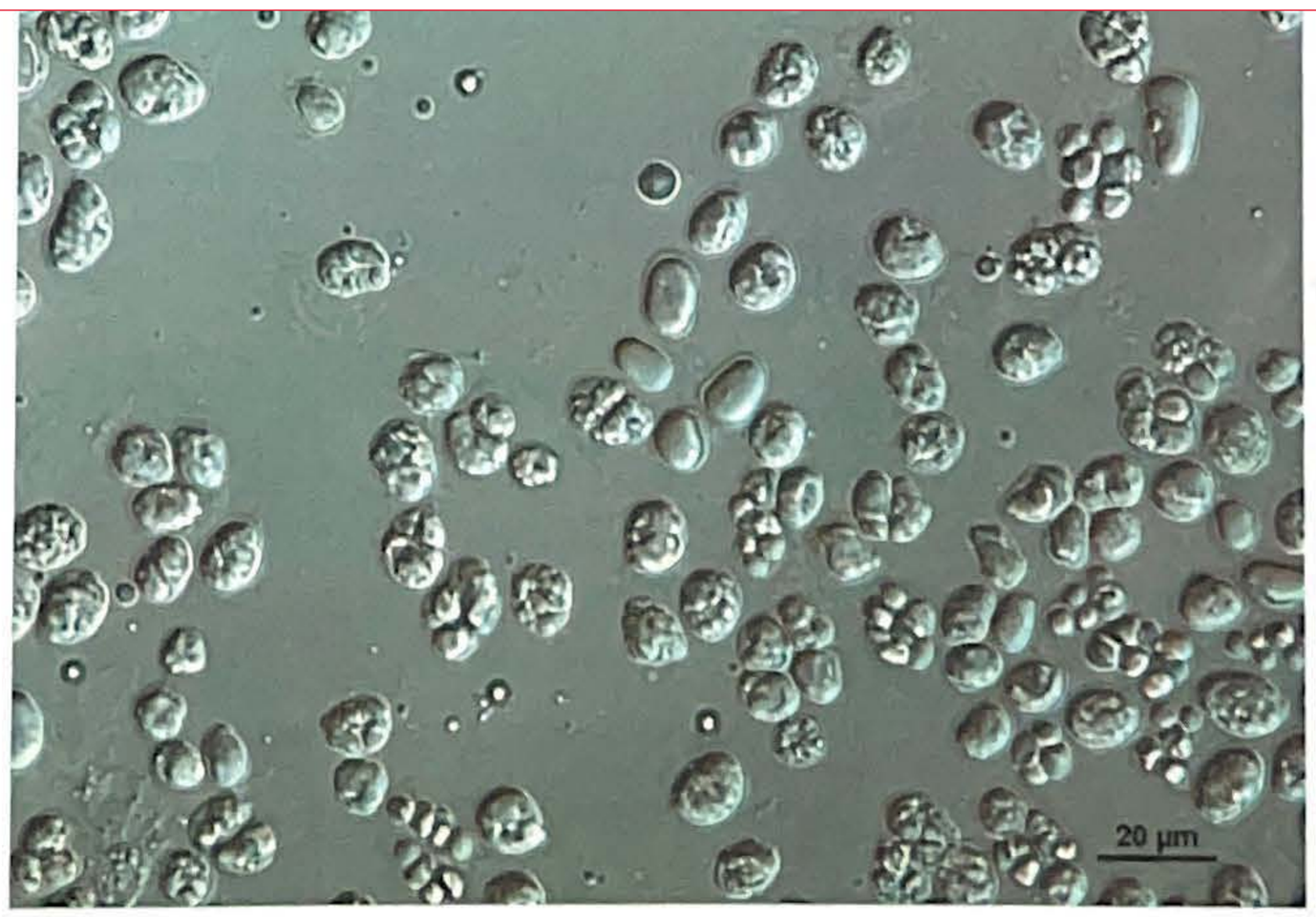
在培养基上，28℃培养 14 天，菌落直径 10-12 mm，浅黄色，边缘不整齐；质地粘稠，表面反光；反面浅黄色；无可溶性色素产生。

培养基配方：葡萄糖 30g/L，酵母浸粉 4g/L，氯化钠 13g/L，硫酸镁 4g/L，氯化钙 0.8g/L，氯化钾 0.4g/L，水 1L，pH6.0。(琼脂粉 15~20g/L 固体培养基)。

Medium formula: glucose 30g, yeast extract powder 4g/L, sodium chloride 13g/L, sulfuric acid 4g/L, calcium chloride 0.8g/L, chlorinated bait 0.4g/L, water 1L, pH 6. 0. (Agar powder 15-20g/L solid medium).

微观形态

Microscopic morphology



细胞椭圆形、卵圆形或近球形，长轴直径 5-16 μm，以分裂方式增殖，单个细胞可连续分裂为多个子细胞。

The cells are elliptical, oval or nearly spherical, with a major axis diameter of 5-16 μ m. They proliferate in a divisional manner, and a single cell can continuously divide into multiple daughter cells.

检测报告

Test Report

编号№: 19-157-738-699S 号

DNA 序列分析 (DNA sequences analysis)

区段

18S rDNA 基因序列 18S rDNA gene sequence

DNA segment

Sequence comparison

信息

S

in

```
1       GCCAGCTGGC GAAAGGGGGA TGTGCTGCAA GGCGATTAAG TTGGGTAACG CCAGGGTTTT
61      CCCAGTCACG ACGTTGTAAA ACGACGGCCA GTGAATTCGA GCTCGGTACC CGGGGATCCT
121     CTAGAGATTG TAGTCATATG CTTGTCTCAA AGATTAAGCC ATGCATGTGT AAGTATAAGC
181     GATTGTACTG TGAGACTGCG AACGGCTCAT TATATCAGTA ATAATTTCTT CGGTAGTTTC
241     TTTTATATGG ATACCTGCAG TAATTCTGGA AATAATACAT GCTGTAAGAG CCCTGTATGG
301     GGCTGCACTT ATTAGATTGA AGCCGATTTT ATTGGTGAAT CATGATAATT GAGCAGATTG
        TCGATGAAT CGTTTGAGTT TCTGCCCCAT CAGTTGTCGA CGGTAGCGTA
        TGACTATAA CGGGTGACGG AGAGTTAGGG CTCGACTCCG GAGAGGGAGC
        CTACCATAT CCAAGGATAG CAGCAGGCGC GTAAATTACC CACTGTGGAC
        GTGACGAGA AATATCGATG CGAAGCGTGT ATGCGTTTTG CTATCGGAAT
        AAAACCCTC ATCGAGGATC AACTGGAGGG CAAGTCTGGT GCCAGCAGCC
        AGCTCCAGA AGCATATGCT AAAGTTGTTG CAGTTAAAAA GCTCGTAGTT
        ATGGGCGAC CGGTGCTTTC CCTGAATGGG GATTGATTGT CTGCGTTGCC
        CTTCTTTTC TTTATTGATG AGAAATCTTT CACTGTAATC AAAGCAGAGT
        GTCGTATGA CCGGTATGTT TATTATGGGA TGATAAGATA GGACTTGGGT
        GGTTTGCAC GCCTGAGTAA TGGTTAATAG GAACAGTTGG GGGTATTCGT
961     ATTTAGGAGC TAGAGGTGAA ATTCTTGGAT TTCCGAAAGA CGAACTAGAG CGAAGGCATT
1021    TACCAAGCAT GTTTTCATTA ATCAAGAACG AAAGTCTGGG GATCGAAGAT GATTAGATAC
1081    CATCGTAGTC TAGACCGTAA ACGATGCCGA CTTGCGATTG TTGGGTGCTT TTTTCTATGG
1141    GCCTCAGCAG CAGCACATGA GAAATCAAAG TCTTTGGGTT CCGGGGGGAG TATGGTCGCA
1201    AGGCTGAAAC TTAAAGGAAT TGACGGAAGG GCACCACCAG GAGTGGAGCC TGCGGCTTAA
1261    TTTGACTCAA CACGGGAAAA CTTACCAGGT CCAGACATAG GTAGGATTGA CAGATTGAGA
1321    GCTCTTTCAT GATTCTATGG GTGGTGGTGC ATGGCCGTTC TTAGTTGGTG GAGTGATTTG
1381    TCTGGTTAAT TCCGTTAACG AACGAGACCT CGGCCTACTA AATAGTGCGT GGTATGGCAA
1441    CATAGTACGT TTTTACTTCT TAGAGGGACA TGTCCGGTTT ACGGGCAGGA AGTTCGAGGC
1501    AATAACAGGT CTGTGATGCC CTTAGATGTT CTGGGCCGCA CGCGCGCTAC ACTGATGGGT
1561    TCATCGGGTT TTAATTCTAT TTTATTGGAA TTGAGTGCTT GGTCGGAAGG CCTGGCTAAT
1621    CCTTGGAACG CTCATCGTGC TGGGGCTAGA TTTTTGCAAT TATTAATCTC CAACGAGGAA
1681    TTCCTAGTAA ACGCAAGTCA TCAGCTTGCA TTGAATACGT CCCTGCCCTT TGTACACACC
1741    GCCCGTCGCA CCTACCGATT GAACGGTCCG ATGAAACCAT GGGATGTTTG TGTTTGGATT
1801    AATTTTTGGA CATAGGCAGA ACTCGGGTGA ATCTTGTTGT TTAGAGGAAG GTGAAGTCGT
1861    AACAAGGTTT TCGTAGGTGA ACCTGCGGAA ATCGTCGA
```

序列比对

Alignment：裂殖壶菌 Schizochytrium

Se

99.8%	*Aurantiochytrium limacinum* NIBH SR21^T clone:2 (AB810939)
99.6%	*Aurantiochytrium limacinum* NIBH SR21^T clone:1 (AB810938)
99.6%	*Aurantiochytrium limacinum* NIBH SR21^T clone:3 (AB810940)
99.5%	*Aurantiochytrium mangrovei* RCC893 (DQ367049)
99.4%	*Aurantiochytrium limacinum* ATCC MYA-1381^T (AB973564)
98.4%	*Aurantiochytrium limacinum* NIBH SR21^T (AB022107)
92.8%	*Aurantiochytrium* sp. FJN-10 (AY773276)
92.4%	*Aurantiochytrium* sp. SEK 209 (AB290574)

检测报告

Test Report

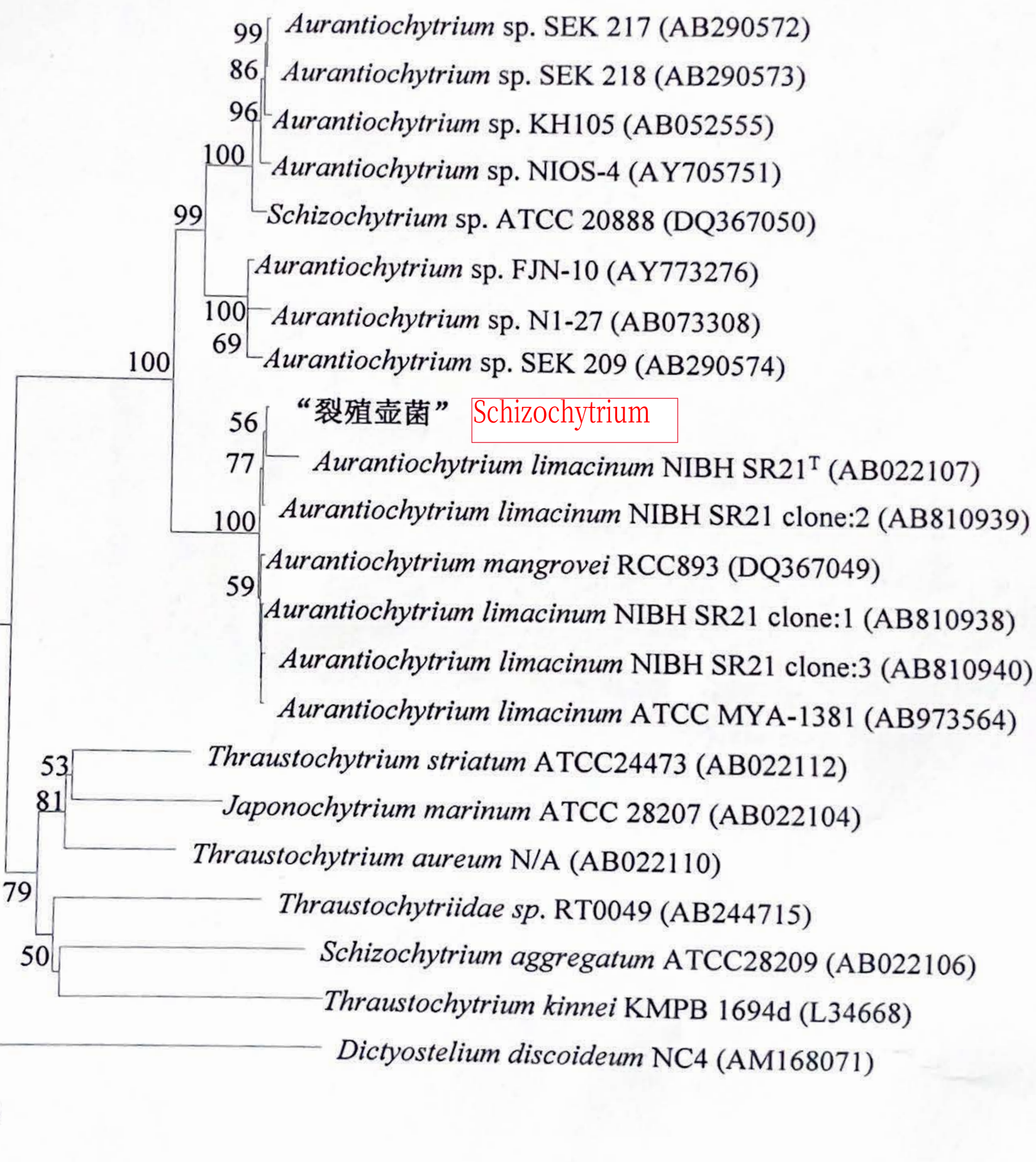
编号№: 19-157-738-699S 号

系统发育学分析

Phylogenetic analysis

菌株“裂殖壶菌”与相关种的 18S rDNA 序列系统发育树：

Phylogenetic tree of 188 rDNA sequence of strain "Schizochytrium" and related species



采用 MEGA5.0 软件，邻位连接法显示菌株“裂殖壶菌”与相关种的 18S rDNA 基因序列系统发育树，进行 1000 次的相似度重复计算，图中发育树节点只显示 Bootstrap 值大于 50%数值，上标“T”代表模式菌株。

Using the team GAS.O software, the ortho-join method was used to display the phylogenetic tree of the 18S rDNA gene sequence of the strain "Schizochytrium" and related species, and the similarity repetition calculation was performed 1000 times. The development tree node in the figure only shows that the Bootstrap value is greater than 50%, and the superscript "T" represents the model strain.

APPENDIX C – Specifications for Finished DHA

江苏远大仙乐药业有限公司

Jiangsu Grand Xianle Pharmaceutical Co., Ltd.

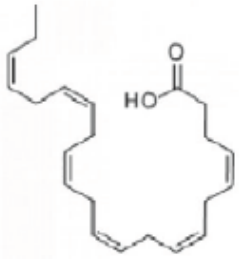
1. General Information

1.1 Chemical name：二十二碳六烯酸（DHA）油脂

1.2 English name：Docosahexaenoic Acid (DHA) Oil

1.3 Molecular formula：$C_{22}H_{32}O_2$ Molecular weight：328.5

1.4 Structural formula：



1.5 CAS：6217-54-5

1.6 Material code：s002

2. Content

2.1 The basis of the specifications: National Food Safety Standard-Food Additives: Docosahexaenoic Acid Grease (Fermentation Method) GB26400-2011.

2.2 Specifications

Items	Regulatory specifications	Method
Appearance	Light yellow to orange oily liquid with a unique odor of this product	Visual inspection Nose smell
Assay（Calculated as $C_{22}H_{32}O_2$ triglycerides）	≥35.0%	GB 26400－2011
Unsaponifiable matter	≤4.0%	GB/T 5535.1
Moisture	≤0.1%	GB 5009.236
Insoluble impurities	≤0.2%	GB/T 15688
Residual solvents	≤2mg/kg	GB/T 5009.262
Acid value (calculated in KOH)	≤1.0mg (KOH)/g	GB 5009.229

PoV	≤2.5mmol/kg	GB 5009.227
Trans fatty acids	≤1.0%	GB 5413.36
*Aflatoxin B1	≤5.0μg/kg	GB/T 5009.22
*Total arsenic (calculated as As)	≤0.1 mg/kg	GB/T 5009.11
*Lead (Pb)	≤0.1 mg/kg	GB/T 5009.12

DHA Quality standard

Test Item		Specification
Appearance	Color	White or light yellow dry powder
	Taste And Odor	With inherent smell and taste of this product, no special odor
	Organizational status	With no adhesion, agglomeration, good fluidity
	Dispersibility	Dissolve evenly in water at 25℃-45℃by stirringgently
	Impurity	No foreign impurities visible to the naked eye
DHA（as TG）/（g/100g）		Marked value 80%-125%
Peroxide Value/（meq/kg）		≤5.0
Surface Oil/（g/100g）		≤2.0
Ash/（g/100g）		≤5.0
Moisture/（g/100g）		≤5.0
Acid value（Fet meter，KOH）/（mg/g）		≤1.0
Nitrate（in $NaNO_3$）/（mg/kg）		≤50
Nitrite（in $NaNO_2$）/（mg/kg）		≤2.0
Trans fatty acids /（%）		≤1.0
Aerobic plate count（CFU/g）		≤1000
Yeast and Molds（CFU/g）		≤25
Coliforms（MPN/g）		＜0.3
Staphylococcus aureus /25g		No Detected
Salmonella /25g		No Detected
Enterobacter sakazakii/333g		No Detected
Lead（as Pb）/（mg/kg）		≤0.1
Total Arsenic（as As）/（mg/kg）		≤0.1
Total mercury（as Hg）/（mg/kg）		≤0.02
Cadmium（as Cd）/（mg/kg）		≤0.1
Aflatoxin M1/（μg/kg）		≤0.3
Aflatoxin B1/（μg/kg）		≤0.3

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Zhejiang Grand Biotech Co., Ltd.

检 验 报 告 单
Certificate of Analysis

检验单号/Analysis No.:2106-1 QC103/02

名称 Product	二十二碳六烯酸粉 Docosahexaenoic Acid (DHA) Powder		
批号 Batch No.	DP10PR2106001	批产量 Delivered Quantity	254.40kg
生产日期 Mfg. Date	2021-06-14	检验日期 Analysis Date	2021-06-14
有效期至 Expiry Date	2023-06-13	报告日期 Report Date	2021-06-25
检验依据 Reference	企业标准 In-house specification		

检验项目/Test Item	标准规定/ Specification	检验结果/Results
感官 Appearance	呈均匀一致白色或淡黄色粉末，具有本产品固有的气味和滋味，无特殊的异味，不应有腐败及霉变现象,干燥粉末状，无粘连、结块、潮解，有较好的流动性，25-45℃，能均匀地分散于蒸馏水中无肉眼可见的外来杂质 White or light yellow dry powder, with inherent smell and taste of this product, no special odor, with no adhesion, agglomeration, good fluidity, Dissolve evenly in water at 25℃-45℃by stirringgently, No foreign impurities visible to the naked eye.	符合 Conforms
DHA（以甘油三酯计）DHA（as TG）/（g/100g）	≥10.0	12.0
过氧化值 Peroxide Value/（meq/kg）	≤5.0	0.7
表面油 Surface Oil/（g/100g）	≤2.0	0.7
灰分 Ash/（g/100g）	≤5.0	3.14
水分 Moisture/（g/100g）	≤5.0	2.2
酸价（以脂肪计） Acid value（Fet meter，KOH）/（mg/g）	≤1.0	0.2
硝酸盐（以 $NaNO_3$ 计）Nitrate（in $NaNO_3$）/（mg/kg）	≤50	未检出 Not Detected
亚硝酸盐（以 $NaNO_2$ 计）Nitrite（in $NaNO_2$）/（mg/kg）	≤2.0	未检出 Not Detected
反式脂肪酸 Trans fatty acids /（%）	≤1.0	0.1
菌落总数 Aerobic plate count（CFU/g）	≤1000	<10
霉菌和酵母菌 Yeast and Molds（CFU/g）	≤25	<10
大肠菌群 Coliforms（MPN/g）	<0.3	<0.3
金黄色葡萄球菌 Staphylococcus aureus /25g	不得检出 No Detected	未检出 Not Detected
沙门氏菌 Salmonella /25g	不得检出 No Detected	未检出 Not Detected
阪崎肠杆菌 Enterobacter sakazakii/333g	不得检出 No Detected	未检出 Not Detected
铅 Lead（as Pb）/（mg /kg）	≤0.1	未检出 Not Detected
总砷 Total Arsenic（as As）/（mg /kg）	≤0.1	未检出 Not Detected
总汞（以 Hg 计）Total mercury（as Hg）/（mg /kg）	≤0.02	未检出 Not Detected
镉（以 Cd 计） Cadmium（as Cd）/（mg /kg）	≤0.1	未检出 Not Detected
黄曲霉毒素 M1 Aflatoxin M1/（μg/kg）	≤0.3	未检出 Not Detected
黄曲霉毒素 B1 Aflatoxin B1/（μg/kg）	≤0.3	未检出 Not Detected
结论 Conclusions:	本品按企业标准检验，结果符合要求 Meet the requirements of In-house specification	

QC Signature / Date 2021-08-20 Reviewer Signature / Date 2021-08-20 QC Director Signature / Date 2021-08-20

质检专用章 仅供产品检测使用，其他无效

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Zhejiang Grand Biotech Co., Ltd.

检 验 报 告 单
Certificate of Analysis

检验单号/Analysis No.:2106-1 QC103/02

名称 Product	二十二碳六烯酸粉 Docosahexaenoic Acid (DHA) Powder		
批号 Batch No.	DP10MT2106001	批产量 Delivered Quantity	175.10kg
生产日期 Mfg. Date	2021-06-13	检验日期 Analysis Date	2021-06-14
有效期至 Expiry Date	2023-06-12	报告日期 Report Date	2021-06-25
检验依据 Reference	企业标准 In-house specification		

检验项目/Test Item	标准规定/ Specification	检验结果/Results
感官 Appearance	呈均匀一致白色或淡黄色粉末，具有本产品固有的气味和滋味，无特殊的异味，不应有腐败及霉变现象,干燥粉末状，无粘连、结块、潮解，有较好的流动性，25-45℃，能均匀地分散于蒸馏水中无肉眼可见的外来杂质 White or light yellow dry powder, with inherent smell and taste of this product, no special odor, with no adhesion, agglomeration, good fluidity, Dissolve evenly in water at 25℃-45℃by stirringgently, No foreign impurities visible to the naked eye.	符合 Conforms
DHA（以甘油三酯计）DHA（as TG）/（g/100g）	≥10.0	12.1
过氧化值 Peroxide Value/（meq/kg）	≤5.0	0.8
表面油 Surface Oil/（g/100g）	≤2.0	0.7
灰分 Ash/（g/100g）	≤5.0	2.38
水分 Moisture/（g/100g）	≤5.0	1.8
酸价（以脂肪计） Acid value（Fet meter，KOH）/（mg/g）	≤1.0	0.1
硝酸盐（以 $NaNO_3$ 计）Nitrate（in $NaNO_3$）/（mg/kg）	≤50	未检出 Not Detected
亚硝酸盐（以 $NaNO_2$ 计）Nitrite（in $NaNO_2$）/（mg/kg）	≤2.0	未检出 Not Detected
反式脂肪酸 Trans fatty acids /（%）	≤1.0	0.1
菌落总数 Aerobic plate count（CFU/g）	≤1000	<10
霉菌和酵母菌 Yeast and Molds（CFU/g）	≤25	<10
大肠菌群 Coliforms（MPN/g）	<0.3	<0.3
金黄色葡萄球菌 Staphylococcus aureus /25g	不得检出 No Detected	未检出 Not Detected
沙门氏菌 Salmonella /25g	不得检出 No Detected	未检出 Not Detected
阪崎肠杆菌 Enterobacter sakazakii/333g	不得检出 No Detected	未检出 Not Detected
铅 Lead（as Pb）/（mg /kg）	≤0.1	未检出 Not Detected
总砷 Total Arsenic（as As）/（mg /kg）	≤0.1	未检出 Not Detected
总汞（以 Hg 计）Total mercury（as Hg）/（mg /kg）	≤0.02	未检出 Not Detected
镉（以 Cd 计） Cadmium（as Cd）/（mg /kg）	≤0.1	未检出 Not Detected
黄曲霉毒素 M1 Aflatoxin M1/（μg/kg）	≤0.3	未检出 Not Detected
黄曲霉毒素 B1 Aflatoxin B1/（μg/kg）	≤0.3	未检出 Not Detected
结论 Conclusions:	本品按企业标准检验，结果符合要求 Meet the requirements of In-house specification	

QC Signature / Date 2021-08-20 Reviewer Signature / Date 2021-08-20 QC Director Signature / Date 2021-08-20

质检专用章 仅供产品检测使用，其他无效

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检 验 报 告 单
Certificate of Analysis

检验单号/Analysis No.:2107-1 QC103/02

名称 Product	二十二碳六烯酸粉 Docosahexaenoic Acid (DHA) Powder		
批号 Batch No.	DP10ST2107001	批产量 Delivered Quantity	38.20kg
生产日期 Mfg. Date	2021-07-07	检验日期 Analysis Date	2021-07-07
有效期至 Expiry Date	2023-07-06	报告日期 Report Date	2021-07-19
检验依据 Reference	企业标准 In-house specification		

检验项目/Test Item	标准规定/ Specification	检验结果/Results
感官 Appearance	呈均匀一致白色或淡黄色粉末，具有本产品固有的气味和滋味，无特殊的异味，不应有腐败及霉变现象,干燥粉末状，无粘连、结块、潮解，有较好的流动性，25-45℃，能均匀地分散于蒸馏水中无肉眼可见的外来杂质 White or light yellow dry powder, with inherent smell and taste of this product, no special odor, with no adhesion, agglomeration, good fluidity, Dissolve evenly in water at 25℃-45℃by stirringgently, No foreign impurities visible to the naked eye.	符合 Conforms
DHA（以甘油三酯计）DHA（as TG）/（g/100g）	≥10.0	12.2
过氧化值 Peroxide Value/（meq/kg）	≤5.0	0.4
表面油 Surface Oil/（g/100g）	≤2.0	0.4
灰分 Ash/（g/100g）	≤5.0	1.99
水分 Moisture/（g/100g）	≤5.0	2.9
酸价（以脂肪计） Acid value（Fet meter，KOH）/（mg/g）	≤1.0	0.3
硝酸盐（以 $NaNO_3$ 计）Nitrate（in $NaNO_3$）/（mg/kg）	≤50	未检出 Not Detected
亚硝酸盐（以 $NaNO_2$ 计）Nitrite（in $NaNO_2$）/（mg/kg）	≤2.0	未检出 Not Detected
反式脂肪酸 Trans fatty acids /（%）	≤1.0	0.1
菌落总数 Aerobic plate count（CFU/g）	≤1000	<10
霉菌和酵母菌 Yeast and Molds（CFU/g）	≤25	<10
大肠菌群 Coliforms（MPN/g）	<0.3	<0.3
金黄色葡萄球菌 Staphylococcus aureus /25g	不得检出 No Detected	未检出 Not Detected
沙门氏菌 Salmonella /25g	不得检出 No Detected	未检出 Not Detected
阪崎肠杆菌 Enterobacter sakazakii/333g	不得检出 No Detected	未检出 Not Detected
铅 Lead（as Pb）/（mg /kg）	≤0.1	未检出 Not Detected
总砷 Total Arsenic（as As）/（mg /kg）	≤0.1	未检出 Not Detected
总汞（以 Hg 计）Total mercury（as Hg）/（mg /kg）	≤0.02	未检出 Not Detected
镉（以 Cd 计） Cadmium（as Cd）/（mg /kg）	≤0.1	未检出 Not Detected
黄曲霉毒素 M1 Aflatoxin M1/（μg/kg）	≤0.3	未检出 Not Detected
黄曲霉毒素 B1 Aflatoxin B1/（μg/kg）	≤0.3	未检出 Not Detected
结论 Conclusions:	本品按企业标准检验，结果符合要求 Meet the requirements of In-house specification	

QC Signature / Date 2021-08-20 Reviewer Signature / Date 2021-08-20 QC Director Signature / Date 2021-08-20

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Zhejiang Grand Biotech Co., Ltd.

检 验 报 告 单
Certificate of Analysis

检验单号/Analysis No.:2106-1 QC103/02

名称 Product	二十二碳六烯酸粉 Docosahexaenoic Acid (DHA) Powder		
批号 Batch No.	DP10ST2106001	批产量 Delivered Quantity	198.00kg
生产日期 Mfg. Date	2021-06-13	检验日期 Analysis Date	2021-06-14
有效期至 Expiry Date	2023-06-12	报告日期 Report Date	2021-07-16
检验依据 Reference	企业标准 In-house specification		

检验项目/Test Item	标准规定/ Specification	检验结果/Results
感官 Appearance	呈均匀一致白色或淡黄色粉末，具有本产品固有的气味和滋味，无特殊的异味，不应有腐败及霉变现象,干燥粉末状，无粘连、结块、潮解，有较好的流动性，25-45℃，能均匀地分散于蒸馏水中无肉眼可见的外来杂质 White or light yellow dry powder, with inherent smell and taste of this product, no special odor, with no adhesion, agglomeration, good fluidity, Dissolve evenly in water at 25℃-45℃by stirringgently, No foreign impurities visible to the naked eye.	符合 Conforms
DHA（以甘油三酯计）DHA（as TG）/（g/100g）	≥10.0	11.1
过氧化值 Peroxide Value/（meq/kg）	≤5.0	0.6
表面油 Surface Oil/（g/100g）	≤2.0	0.4
灰分 Ash/（g/100g）	≤5.0	1.77
水分 Moisture/（g/100g）	≤5.0	3.9
酸价（以脂肪计） Acid value（Fet meter，KOH）/（mg/g）	≤1.0	0.2
硝酸盐（以 $NaNO_3$ 计）Nitrate（in $NaNO_3$）/（mg/kg）	≤50	未检出 Not Detected
亚硝酸盐（以 $NaNO_2$ 计）Nitrite（in $NaNO_2$）/（mg/kg）	≤2.0	未检出 Not Detected
反式脂肪酸 Trans fatty acids /（%）	≤1.0	0.1
菌落总数 Aerobic plate count（CFU/g）	≤1000	<10
霉菌和酵母菌 Yeast and Molds（CFU/g）	≤25	<10
大肠菌群 Coliforms（MPN/g）	<0.3	<0.3
金黄色葡萄球菌 Staphylococcus aureus /25g	不得检出 No Detected	未检出 Not Detected
沙门氏菌 Salmonella /25g	不得检出 No Detected	未检出 Not Detected
阪崎肠杆菌 Enterobacter sakazakii/333g	不得检出 No Detected	未检出 Not Detected
铅 Lead（as Pb）/（mg /kg）	≤0.1	未检出 Not Detected
总砷 Total Arsenic（as As）/（mg /kg）	≤0.1	未检出 Not Detected
总汞（以 Hg 计）Total mercury（as Hg）/（mg /kg）	≤0.02	未检出 Not Detected
镉（以 Cd 计） Cadmium（as Cd）/（mg /kg）	≤0.1	未检出 Not Detected
黄曲霉毒素 M1 Aflatoxin M1/（μg/kg）	≤0.3	未检出 Not Detected
黄曲霉毒素 B1 Aflatoxin B1/（μg/kg）	≤0.3	未检出 Not Detected
结论 Conclusions:	本品按企业标准检验，结果符合要求 Meet the requirements of In-house specification	

QC Signature / Date 2021-08-20 Reviewer Signature / Date 2021-08-20 QC Director Signature / Date 2021-08-20

质检专用章 仅供产品检测使用，其他无效

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APPENDIX E - Proximate analysis of three non-consecutive lots of DHA-algal oil produced using Schizochytrium

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CGE HEALTHCARE

江苏远大仙乐药业有限公司
Jiangsu Grand Xianle pharmaceutical Co. , Ltd

质检专用章

Certificate of Analysis

Test NO：2204-8

Serial NO：QC/R909/2

Name of Product	DHA Oil	Code	DMY
Batch Number	DMY2203503	Test Date	2022.04.20
Quantity	1900.00kg	Report Date	2022.08.10
Manufacturing Date	2022.04.04	Expiry Date	2024.04.03
Standards	QA/ST269/3		
Items	**Specifications**		**Results**
Character	This product shall be light yellow to orange with liquid, No visible large impurities, allowing a small amount of impurities precipitation, allowing a slight odor, no other taste.		Complies
Docosahexaenoic Acid content	≥30.0%		43.40%
Acid value（KOH）	≤10 mg/g		3.18mg/g
Peroxide value	≤5.0mmol/kg		0.34mmol/kg
Insoluble impurities	≤0.50%		0.23%
Unsaponifiable matter	≤4.0%		1.28%
Anisidine value	≤15AV		2.92AV
Moisture and Volatiles	≤0.50%		0.42%
Trans Fatty Acids	≤1.0%		0.02%
Solvent residue	≤10mg/kg		Not detected
Conclusion	The product meets the requirements of QA/ST269/3		

Reported by: [redacted]　　QC Reviewed by: [redacted]　　QA Reviewed by: [redacted]

Date: 2022.08.10　　Date: 2022.08.10　　Date: 2022.08.10

Address: No.1 Zhongshan Seven Road, Coastal Industry Park, Economic Development Zone, Binhai County, Yancheng City, Jiangsu Province, P.R. of China, 224555
Tel: 86-515-68988210　　Fax: 86-515-68988212

CGE 远大健康 CGE HEALTHCARE

江苏远大仙乐药业有限公司

Jiangsu Grand Xianle pharmaceutical Co. , Ltd

质检专用章 仅供产品检测使用，其他无效

Certificate of Analysis

Test NO：2204-5

Serial NO：QC/R909/2

Name of Product	DHA Oil	Code	DMY
Batch Number	DMY2203501	Test Date	2022.04.08
Quantity	1900.00kg	Report Date	2022.08.10
Manufacturing Date	2022.03.29	Expiry Date	2024.03.28
Standards	QA/ST269/3		
Items	**Specifications**		**Results**
Character	This product shall be light yellow to orange with liquid, No visible large impurities, allowing a small amount of impurities precipitation, allowing a slight odor, no other taste.		Complies
Docosahexaenoic Acid content	≥30.0%		51.99%
Acid value（KOH）	≤10 mg/g		2.14mg/g
Peroxide value	≤5.0mmol/kg		0.32mmol/kg
Insoluble impurities	≤0.50%		0.27%
Unsaponifiable matter	≤4.0%		1.56%
Anisidine value	≤15AV		2.27AV
Moisture and Volatiles	≤0.50%		0.21%
Trans Fatty Acids	≤1.0%		Not detected
Solvent residue	≤10mg/kg		Not detected
Conclusion	The product meets the requirements of QA/ST269/3		

Reported by: [redacted]

Date: 2022.08.10

QC Reviewed by: [redacted]

Date: 2022.08.10

QA Reviewed by: [redacted]

Date: 2022.08.10

Address: No.1 Zhongshan Seven Road, Coastal Industry Park, Economic Development Zone, Binhai County, Yancheng City, Jiangsu Province, P.R. of China, 224555
Tel: 86-515-68988210 Fax: 86-515-68988212

CGE 远大健康
CGE HEALTHCARE

江苏远大仙乐药业有限公司
Jiangsu Grand Xianle pharmaceutical Co. , Ltd

质检专用章

Certificate of Analysis

Test NO：2106-3　　Serial NO：QC/R909/2

Name of Product	DHA Oil	Code	DMY
Batch Number	DMY210604	Test Date	2021.07.01
Quantity	1330.00kg	Report Date	2022.08.10
Manufacturing Date	2021.06.26	Expiry Date	2023.06.25
Standards	QA/ST269/3		
Items	**Specifications**		**Results**
Character	This product shall be light yellow to orange with liquid, No visible large impurities, allowing a small amount of impurities precipitation, allowing a slight odor, no other taste.		Complies
Docosahexaenoic Acid content	≥30.0%		55.34%
Acid value（KOH）	≤10 mg/g		0.74mg/g
Peroxide value	≤5.0mmol/kg		0.79mmol/kg
Insoluble impurities	≤0.50%		0.08%
Unsaponifiable matter	≤4.0%		1.62%
Anisidine value	≤15AV		0.39AV
Moisture and Volatiles	≤0.50%		0.21%
Trans Fatty Acids	≤1.0%		0.57%
Solvent residue	≤10mg/kg		Not detected
Conclusion	The product meets the requirements of QA/ST269/3		

Reported by:　　QC Reviewed by:　　QA Reviewed by:

Date: 2022.08.10　　Date: 2022.08.10　　Date: 2022.08.10

Address: No.1 Zhongshan Seven Road, Coastal Industry Park, Economic Development Zone, Binhai County, Yancheng City, Jiangsu Province, P.R. of China, 224555
Tel: 86-515-68988210　　Fax: 86-515-68988212

APPENDIX F - Analytical results compared to a representative lot of GRN 677 Mara DHA-algal oil

Parameter	Batch number								
	Mara DHA oil						Jiangsu Grand xianle DHAl oil		
	16039	16040	16041	N-2-006-C	N-2-008-C	N-2-010-C	DMY210604	DMY2203501	DMY2203503
Acid value,(mg KOH/g)	0.05	0.06	0.05	0.06	0.06	0.06	0.74	2.14	3.18
Peroxide value，(meq/kg)	1.0	1.0	1.3	1.06	＜0.1	＜0.1	1.58	0.64	0.68
Moisture，%	＜0.01	＜0.01	＜0.01	＜0.05	＜0.05	＜0.05	0.21	0.21	0.42
Unsaponifiables%	0.3	0.4	0.3	2.97	2.43	2.50	1.62	1.56	1.28
Trans-Fatty Acids%	0.2	0.2	0.2	＜0.05	＜0.05	＜0.05	0.57	Not detected	0.02
DHA(%Relative)	37.1	42.5	42.0	40.5	39.6	39.6	55.34	51.99	43.40
Arsenic(mg/kg)	＜0.1	＜0.1	＜0.1	＜0.01	＜0.01	＜0.01	＜0.005	＜0.01	＜0.01
Copper(mg/kg)	＜0.1	＜0.1	＜0.1	0.08	0.02	0.03	N/A	N/A	N/A
Iron(mg/kg)	0.15	＜0.1	＜0.1	＜0.02	＜0.02	＜0.02	N/A	N/A	N/A
Mercury(mg/kg)	＜0.005	＜0.005	＜0.005	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01
Lead(mg/kg)	＜0.05	＜0.05	＜0.05	＜0.01	＜0.01	＜0.01	＜0.05	＜0.05	＜0.05

APPENDIX G - Accelerated stability study of DHA powder-6 months

DP7PR2104001（Conditions of accelerated stability study : 40℃±2℃、75%±5%）															
Storage time (months)	Appearance	Assay g/100g	Peroxide value meq/kg	surface oil g/100g	Grayscale g/100g	Water g/100g	Acid value mgKOH/g	Trans fatty acid %	Total number of colonies CFU/g	Mold and Yeast CFU/g	Coliforms MPN/g	Staphylococcus aureus /25g	Salmonella bacteria /25g	Enterobacter sakazakii /333g	Commissioned inspection
	Conform	≥7.0	≤5.0	≤2.0	≤5.0	≤5.0	≤1.0	≤1.0	≤1000	≤25	＜0.3	Not Detected	Not Detected	Not Detected	Conform
0	Conform	7.8	2.0	0.4	3.14	3.1	0.1	0.1	＜10	＜10	＜0.3	Not Detected	Not Detected	Not Detected	Conform
1	Conform	7.9	2.2	0.4	/	2.6	0.2	/	＜10	＜10	＜0.3	Not Detected	Not Detected	Not Detected	/
2	Conform	7.6	3.0	0.4	/	3.1	0.2	/	＜10	＜10	＜0.3	Not Detected	Not Detected	Not Detected	/
3	Conform	7.5	3.7	0.4	/	3.1	0.3	/	＜10	＜10	＜0.3	Not Detected	Not Detected	Not Detected	/
6	Conform	7.8	2.8	0.4	3.42	3.3	0.2	0.1	＜10	＜10	＜0.3	Not Detected	Not Detected	Not Detected	/

DP10MT2106001（Conditions of accelerated stability study : 40℃±2℃、75%±5%）															
Storage time (months)	Appearance	Assay g/100g	Peroxide value meq/kg	surface oil g/100g	Grayscale g/100g	Water g/100g	Acid value mgKOH/g	Trans fatty acid %	Total number of colonies CFU/g	Mold and Yeast CFU/g	Coliforms MPN/g	Staphylococcus aureus /25g	Salmonella bacteria /25g	Enterobacter sakazakii /333g	Commissioned inspection
	Conform	≥10.0	≤5.0	≤2.0	≤5.0	≤5.0	≤1.0	≤1.0	≤1000	≤25	＜0.3	Not Detected	Not Detected	Not Detected	Conform
0	Conform	12.1	0.8	0.7	2.38	1.8	0.1	0.1	＜10	＜10	＜0.3	Not Detected	Not Detected	Not Detected	Conform
1	Conform	12.1	2.1	0.8	/	1.9	0.2	0.1	＜10	＜10	＜0.3	Not Detected	Not Detected	Not Detected	/
2	Conform	12.2	1.7	0.6	/	2.6	0.2	0.1	＜10	＜10	＜0.3	Not Detected	Not Detected	Not Detected	/
3	Conform	12.2	1.2	0.6	/	2.6	0.2	0.2	＜10	＜10	＜0.3	Not Detected	Not Detected	Not Detected	/
6	Conform	12.4	1.0	0.6	2.57	2.6	0.2	0.1	＜10	＜10	＜0.3	Not Detected	Not Detected	Not Detected	/

DP10PR2106001（Conditions of accelerated stability study : 40℃±2℃、75%±5%）															
Storage time (months)	Appearance	Assay g/100g	Peroxide value meq/kg	surface oil g/100g	Grayscale g/100g	Water g/100g	Acid value mgKOH/g	Trans fatty acid %	Total number of colonies CFU/g	Mold and Yeast CFU/g	Coliforms MPN/g	Staphylococcus aureus /25g	Salmonella bacteria /25g	Enterobacter sakazakii /333g	Commissioned inspection
	Conform	≥10.0	≤5.0	≤2.0	≤5.0	≤5.0	≤1.0	≤1.0	≤1000	≤25	＜0.3	Not Detected	Not Detected	Not Detected	Conform
0	Conform	12.0	0.7	0.7	3.14	2.2	0.2	0.1	＜10	＜10	＜0.3	Not Detected	Not Detected	Not Detected	Conform
1	Conform	12.1	1.6	0.6	/	1.8	0.3	0.1	＜10	＜10	＜0.3	Not Detected	Not Detected	Not Detected	/
2	Conform	12.4	1.9	0.7		2.4	0.2	0.1	＜10	＜10	＜0.3	Not Detected	Not Detected	Not Detected	/
3	Conform	12.3	1.1	0.6	/	2.2	0.2	0.1	＜10	10	＜0.3	Not Detected	Not Detected	Not Detected	/
6	Conform	12.4	1.4	0.6	3.18	2.3	0.2	0.1	＜10	10	＜0.3	Not Detected	Not Detected	Not Detected	/

DP10ST2107001（Conditions of accelerated stability study : 40℃±2℃、75%±5%）															
Storage time (months)	Appearance	Assay g/100g	Peroxide value meq/kg	surface oil g/100g	Grayscale g/100g	Water g/100g	Acid value mgKOH/g	Trans fatty acid %	Total number of colonies CFU/g	Mold and Yeast CFU/g	Coliforms MPN/g	Staphylococcus aureus /25g	Salmonella bacteria /25g	Enterobacter sakazakii /333g	Commissioned inspection
	Conform	≥10.0	≤5.0	≤2.0	≤5.0	≤5.0	≤1.0	≤1.0	≤1000	≤25	＜0.3	Not Detected	Not Detected	Not Detected	Conform
0	Conform	12.2	0.4	0.4	1.99	2.9	0.3	0.1	＜10	＜10	＜0.3	Not Detected	Not Detected	Not Detected	Conform
1	Conform	11.9	1.2	0.4	/	3.0	0.4	0.1	＜10	＜10	＜0.3	Not Detected	Not Detected	Not Detected	/
2	Conform	11.8	1.3	0.4	/	3.1	0.3	0.1	＜10	＜10	＜0.3	Not Detected	Not Detected	Not Detected	/
3	Conform	11.6	1.8	0.4	/	3.1	0.4	0.1	＜10	＜10	＜0.3	Not Detected	Not Detected	Not Detected	/
6	Conform	12.1	1.4	0.4	2.01	3.3	0.4	0.1	＜10	＜10	＜0.3	Not Detected	Not Detected	Not Detected	/

APPENDIX H - Long stability study of DHA oil-24 months

Summary of Stability Data for DHA Oil

Test conditions:Frozen(-18℃~-13℃）								
Batch number：DMY190801		Manufacturing Date：2019.08.30				Specification：QA/ST269/1		
Item	Specification	0-month	3-month	6-month	9-month	12-month	18-month	24-month
Character	This product shall be light yellow to orange with oily liquid.No visible large impurities, allowing a small amount of impurities precipitation, allowing a slight oder, no other taste.	Conforms	Conforms	Conforms	Conforms	Conforms	Conforms	Conforms
Acid value	≤10mg（KOH）/g	1.10	1.15	1.20	1.18	1.18	1.20	1.76
Peroxide value	≤5.0mmol/kg	0.73	0.70	0.64	1.38	2.94	2.96	2.98
DHA Content	≥30.0%	39.80	40.25	40.23	40.48	39.70	39.04	37.99
Conclusions		Conforms	Conforms	Conforms	Conforms	Conforms	Conforms	Conforms
Batch number：DMY190802		Manufacturing Date：2019.09.04				Specification：QA/ST269/1		
Item	Specification	0-month	3-month	6-month	9-month	12-month	18-month	24-month

Character	This product shall be light yellow to orange with oily liquid.No visible large impurities, allowing a small amount of impurities precipitation, allowing a slight oder, no other taste.	Conforms	Conforms	Conforms	Conforms	Conforms	Conforms	Conforms
Acid value	≤10mg（KOH）/g	2.82	2.78	2.83	2.85	2.88	3.11	4.40
Peroxide value	≤5.0mmol/kg	1.03	1.05	1.08	1.13	1.26	2.22	2.26
DHA Content	≥30.0%	41.10	41.39	40.94	40.97	41.00	41.01	40.97
Conclusions		Conforms	Conforms	Conforms	Conforms	Conforms	Conforms	Conforms
Batch number：DMY190901			Manufacturing Date：2019.09.10				Specification：QA/ST269/1	
Item	Specification	0-month	3-month	6-month	9-month	12-month	18-month	24-month
Character	This product shall be light yellow to orange with oily liquid.No visible large impurities, allowing a small amount of impurities precipitation, allowing a slight oder, no other	Conforms	Conforms	Conforms	Conforms	Conforms	Conforms	Conforms

	taste.							
Acid value	≤10mg（KOH）/g	1.69	1.57	1.60	1.65	1.63	1.66	1.91
Peroxide value	≤5.0mmol/kg	0.83	0.79	0.78	1.21	1.83	2.15	2.44
DHA Content	≥30.0%	44.76	44.69	44.22	43.83	43.95	44.33	44.30
Conclusions		Conforms	Conforms	Conforms	Conforms	Conforms	Conforms	Conforms

Summary: According to the long-term(-18℃~-13℃) stability study data of the three batches DMY190801, DMY190802 and DMY190901 within 24 months , the Character, Acid value, Peroxide value and Content of DHA Oil have met the requirements, indicating that the product quality can remain relatively stable within 24 months under the test conditions.

APPENDIX I - MSDS of DHA oil

MATERIAL SAFETY DATA SHEET

Transportation Emergency: 86-0515-68988210

1. Product and Company Identification

Product Name	**Algae DHA Oil**
Product Number	
Chemical Formula	**$C_{22}H_{32}O_2$**
CAS No.	**6217-54-5**
Company	Jiangsu Grand Xianle Pharmaceutical Co., Ltd
Address	No.1 Zhongshan Seven Road, Coastal Industry Park, Economic Development Zone, Binhai County, Yancheng City, Jiangsu Province, 224555, China
Telephone	+86 515 68988210
Fax	+86 515 68988212

2. Composition Information on Ingredients

Hazardous Ingredients Docosahexaenoic acid oil

3. Hazard Identification

Irritant

Avoid prolonged exposure

Do Not breathe vapor

Use caution when handling

Exposure to any chemical should be limited

To the best of our knowledge, the health hazards of this product have not been fully investigated.

This product is provided solely for the purposed of research and development.

4. First Aid Measures

Eye Contact: Check for and remove any contact lenses. Immediately flush eyes with clean, running water for at least 15 minutes while keeping eyes open. Cool water may be used. Seek medical attention.

Skin Contact: In case of contact, immediately flush skin with plenty of water. Wash with a disinfectant soap and cover the irritated skin with an emollient. Remove contaminated clothing and shoes. Wash clothing and clean shoes before reuse. Get medical attention.

Inhalation: Remove to fresh air. If not breathing, give artificial respiration. If breathing is difficult, give oxygen. Get medical attention.

Ingestion: Do NOT induce vomiting unless directed to do so by medical personnel. Seek medical attention.

5. Fire-Fighting Mearsures

Extinguishing media:

Carbon dioxide, dry chemical powder, alcohol or polymer foam.

Special fire fighting procedures

Wear self-contained breathing apparatus and protective clothing to prevent contact with skin and eyes.

Unusual fire and explosion hazards/ decomposition of product

Emits toxic fumes under fire conditions.

6. Accidental Release Measures

Steps to be taken if material is spilled or otherwise released into the environment

Wear Appropriate respirator, impervious boots and heavy rubber (or otherwise impervious) gloves. Scoop up solid material or absorb liquid material and place into appropriate container. Ventilate area and wash affected spill area after pickup is complete. Wash skin immediately with plenty of water. Place solid or absorbed material into containers and close for disposal.

7. Handling and Storage

Do not breath dust or vapor.
Have safety shower and eye wash available.
Do not get in eyes, on skin or on clothing.
Keep container tightly closed.
Store in a cool, dry, well-ventilated place.
Ensure adequate ventilation during use.
Use only in a chemical fume hood.

8. Exposure Controls/Personal Protection

Wear Protective safety goggles.
Wear chemical-resistant gloves.
Wear protective clothing and chemical resistant boots.
Ensure ventilation during use.
After contact with skin, wash immediately

9. Physical and Chemical Properties

Molecular Weight: 328.5g/mole

Boiling Point: 446.7±24 ºC at 760mmHg

Melting Point: -44 ºC

Flash Points: 343 ºC (Closed cup)

10. Stability and Reactivity

Incompatibilities: Strong oxidizing agents
Strong acid and bases

Hazard Decomposition Products

Carbon: carbon monoxide

carbon dioxide

11. Toxicological Information

Acute effect:

Irritant

May be harmful by ingestion and inhalation.

Material is irritating to mucous membranes and upper respiratory tract.

To the best of our knowledge, the toxicological properties of this product have not been fully investigated or determined.

12. Ecological Information

Mobility: Data not known

Persistence and degradability: No data available

Cumulative potential: No data available

Other adverse effects: no data available

13. Disposal Considerations

Absent other actions demanded by federal or local regulations - Dissolve or mix the material with a combustible solvent and burn in a regulated, chemical incinerator equipped with after burner and scrubber.

Observe all federal, state and local laws.

14. Transport Information

Shipping Name: Classed non-hazardous for shipment

15. Regulatory Information

Adhere to all Federal, State and local regulations.

16. Other Information

The information contained herein is accurate to the best of our knowledge, but is not meant to be complete and is included only as a guide. The end user is responsible for any damage resulting from handing or from contact with this product.

Form Approved: OMB No. 0910-0342; Expiration Date: 07/31/2022
(See last page for OMB Statement)

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

GENERALLY RECOGNIZED AS SAFE *(GRAS)* NOTICE (Subpart E of Part 170)

FDA USE ONLY

GRN NUMBER	DATE OF RECEIPT
001128	Oct 19, 2022
ESTIMATED DAILY INTAKE	INTENDED USE FOR INTERNET
NAME FOR INTERNET	
KEYWORDS	

Transmit completed form and attachments electronically via the Electronic Submission Gateway *(see Instructions)*; OR Transmit completed form and attachments in paper format or on physical media to: Office of Food Additive Safety *(HFS-200)*, Center for Food Safety and Applied Nutrition, Food and Drug Administration,5001 Campus Drive, College Park, MD 20740-3835.

SECTION A – INTRODUCTORY INFORMATION ABOUT THE SUBMISSION

1. Type of Submission *(Check one)*

☒ New ☐ Amendment to GRN No._____ ☐ Supplement to GRN No. _____

2. ☒ All electronic files included in this submission have been checked and found to be virus free. *(Check box to verify)*

3 Most recent presubmission meeting *(if any)* with FDA on the subject substance *(yyyy/mm/dd):* _____

4 For Amendments or Supplements: Is your amendment or supplement submitted in response to a communication from FDA? *(Check one)* ☐ Yes ☐ No If yes, enter the date of communication _____

SECTION B – INFORMATION ABOUT THE NOTIFIER

1a. Notifier

Name of Contact Person	Position or Title
NA	NA

Organization *(if applicable)*
Jiangsu Grand Xianle Pharmaceutical Co. Ltd.

Mailing Address *(number and street)*
No.1 Zhongshan Seven Road Coastal Industrial Park

City	State or Province	Zip Code/Postal Code	Country
Yancheng	Jiangsu		China

Telephone Number	Fax Number	E-Mail Address
410-220-2800		javanderiet@englandlawgroup.com

1b. Agent or Attorney *(if applicable)*

Name of Contact Person	Position or Title
Joshua Van De Riet	Associate Attorney

Organization *(if applicable)*
Benjamin L. England & Associates

Mailing Address *(number and street)*
810 Landmark Drive Suite 126

City	State or Province	Zip Code/Postal Code	Country
Glen Burnie	Maryland	21061	United States of America

Telephone Number	Fax Number	E-Mail Address
410-220-2800		javanderiet@englandlawgroup.com

SECTION C – GENERAL ADMINISTRATIVE INFORMATION

1. Name of notified substance, using an appropriately descriptive term

The substance that is the subject of our GRAS petition is a semi-refined oil (commonly referred to as semi-refined DHA algae sourced o

2. Submission Format: *(Check appropriate box(es))*

☒ Electronic Submission Gateway ☐ Electronic

☐ Paper

If applicable give number and type of physical media

_____

3. For paper submissions only:

Number of volumes _____

Total number of pages _____

4. Does this submission incorporate any information in CFSAN's files? *(Check one)*

☐ Yes *(Proceed to Item 5)* ☒ No *(Proceed to Item 6)*

5. The submission incorporates information from a previous submission to FDA as indicated below *(Check all that apply)*

☐ a) GRAS Notice No. GRN _____

☐ b) GRAS Affirmation Petition No. GRP _____

☐ c) Food Additive Petition No. FAP _____

☐ d) Food Master File No. FMF _____

☐ e) Other or Additional *(describe or enter information as above)* _____

6. Statutory basis for conclusions of GRAS status *(Check one)*

☒ Scientific procedures *(21 CFR 170.30(a) and (b))* ☐ Experience

7. Does the submission (including information that you are incorporating) contain information that you view as trade secret or as confidential commercial or financial information? (see 21 CFR 170.225(c)(8))

☒ Yes *(Proceed to Item 8*

☐ No *(Proceed to Section D)*

8. Have you designated information in your submission that you view as trade secret or as confidential commercial or financial information *(Check all that apply)*

☐ Yes, information is designated at the place where it occurs in the submission

☒ No

9. Have you attached a redacted copy of some or all of the submission? *(Check one)*

☐ Yes, a redacted copy of the complete submission

☐ Yes, a redacted copy of part(s) of the submission

☒ No

SECTION D – INTENDED USE

1. Describe the intended conditions of use of the notified substance, including the foods in which the substance will be used, the levels of use in such foods, and the purposes for which the substance will be used, including, when appropriate, a description of a subpopulation expected to consume the notified substance.

The DHA algal oil is intended for use as a direct food ingredient in foods in accordance with current good manufacturing practices (cGMP).

2. Does the intended use of the notified substance include any use in product(s) subject to regulation by the Food Safety and Inspection Service (FSIS) of the U.S. Department of Agriculture?

(Check one)

☐ Yes ☒ No

3. If your submission contains trade secrets, do you authorize FDA to provide this information to the Food Safety and Inspection Service of the U.S. Department of Agriculture?

(Check one)

☐ Yes ☐

SECTION E – PARTS 2 -7 OF YOUR GRAS NOTICE

(check list to help ensure your submission is complete – PART 1 is addressed in other sections of this form)

☒ PART 2 of a GRAS notice: Identity, method of manufacture, specifications, and physical or technical effect (170.230).

☒ PART 3 of a GRAS notice: Dietary exposure (170.235).

☒ PART 4 of a GRAS notice: Self-limiting levels of use (170.240).

☒ PART 5 of a GRAS notice: Experience based on common use in foods before 1958 (170.245).

☒ PART 6 of a GRAS notice: Narrative (170.250).

☒ PART 7 of a GRAS notice: List of supporting data and information in your GRAS notice (170.255)

Other Information

Did you include any other information that you want FDA to consider in evaluating your GRAS notice?

☒ Yes ☐ No

Did you include this other information in the list of attachments?

☒ Yes ☐ No

SECTION F – SIGNATURE AND CERTIFICATION STATEMENTS

1. The undersigned is informing FDA that Benjamin L. England, Esq.
(name of notifier)

has concluded that the intended use*(s)* of semi-refined oil (commonly referred to as semi-refined DHA algae sourced oil, DHA algal oil,
(name of notified substance)

described on this form, as discussed in the attached notice, is (are) not subject to the premarket approval requirements of the Federal Food, Drug, and Cosmetic Act based on your conclusion that the substance is generally recognized as safe recognized as safe under the conditions of its intended use in accordance with § 170.30.

2. Benjamin L. England, Esq. agrees to make the data and information that are the basis for the conclusion of GRAS status available to FDA if FDA asks to see them; agrees to allow FDA to review and copy these data and information during customary business hours at the following location if FDA asks to do so; agrees to send these data and information to FDA if FDA asks to do so.
(name of notifier)

810 Landmark Drive, Suite 126, Glen Burnie, Maryland 21061
(address of notifier or other location)

The notifying party certifies that this GRAS notice is a complete, representative, and balanced submission that includes unfavorable, as well as favorable information, pertinent to the evaluation of the safety and GRAS status of the use of the substance.The notifying party certifies that the information provided herein is accurate and complete to the best or his/her knowledge. Any knowing and willful misinterpretation is subject to criminal penalty pursuant to 18 U.S.C. 1001.

3. Signature of Responsible Official, Agent, or Attorney	Printed Name and Title	Date (mm/dd/yyyy)
	Benjamin L. England, Esq.	10/18/2022

SECTION G – LIST OF ATTACHMENTS

List your attached files or documents containing your submission, forms, amendments or supplements, and other pertinent information. Clearly identify the attachment with appropriate descriptive file names (or titles for paper documents), preferably as suggested in the guidance associated with this form. Number your attachments consecutively. When submitting paper documents, enter the inclusive page numbers of each portion of the document below.

Attachment Number	Attachment Name	Folder Location (select from menu) (Page Number(s) for paper Copy Only)
	Form3667.pdf	Administrative
	JiangsuGrandXianlePharmaceuticalGRASPetitionPartOne.pdf	Administrative
	JiangsuGrandXianlePharmaceuticalGRASPetitionPartTwo.pdf	Administrative