Safety Assessment: Change of conditions of use for the novel food, *Schizochytrium sp.* oil rich in DHA and EPA

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Summary

An application was submitted to the Food Standards Agency (FSA) and Food Standards Scotland (FSS) in January 2022 from DSM Nutritional Products, Switzerland ("the applicant"). The application is for the authorisation of the proposed extension of use of *Schizochytrium sp.* oil rich in DHA and EPA as a novel food in two additional food categories.

The novel food is an algal oil that is rich in docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), which is intended to be used as a food ingredient and as an ingredient in food supplements. The novel food is manufactured by heterotrophic fermentation of *Schizochytrium sp.* algae, which produce oils predominantly comprised of triglycerides (DHA and EPA).

Schizochytrium sp. oil rich in DHA and EPA (hereafter "DHA-O") is currently authorised as a novel food in the UK (assimilated Commission Implementing Regulation (EU) 2017/2470). This new application is an extension of the intended uses of DHA-O, seeking to use the novel food within two new food categories: meat analogues and fish analogues.

To support the FSA and FSS in their evaluation of the application, the Advisory Committee on Novel Foods and Processes (ACNFP) were asked to review the safety dossier and supplementary information provided by the applicant. Please note the Committee did not consider any potential health benefits or claims arising from consuming the food, as the focus of the novel food assessment is to ensure the extension of use of the food is safe, and not putting consumers at a nutritional disadvantage.

The FSA and FSS concluded that the applicant had provided sufficient information to assure the proposed extension of use for DHA-O, was safe under the proposed conditions of use. The anticipated intake levels and the proposed use in foods was not considered to be nutritionally disadvantageous.

The views of the ACNFP have been taken into account in the regulatory assessment which represents the opinion of the FSA and FSS.

1. Introduction

1. *Schizochytrium sp.* oil rich in DHA and EPA (DHA-O) is an authorised novel food in the EU and UK. It was originally authorised through an application from Martek, USA, in December 2010. The assessment was undertaken in the UK and the FSA's initial opinion concluded that *Schizochytrium sp.* oil rich in DHA and EPA meets the criteria for acceptance as a novel food (FSA, 2012), as defined in Article 3(1) of Regulation (EC) No 258/97 (now repealed).

2. The Commission forwarded the FSA's initial opinion report to all Member States in December 2012. No reasoned safety objections were presented by the Commission or the EU Member States, and the applicant's *Schizochytrium sp.* oil rich in DHA and EPA was considered to have complied with the criteria (FSA, 2012) laid down in Article 3(1) of Regulation No 258/97 (now repealed).

3. In 2013, the applicant requested an extension of use of DHA-O. The proposed change in conditions increased the maximum daily dose of DHA + EPA for food supplements – in the normal population - to 3,000 mg per day. In food supplements for pregnant and lactating women, the maximum daily dose increased up to 450 mg per day. Consequently, the ACNFP concluded that this did not pose any safety concerns. The result was the conditions of the authorisation regarding dosing were amended following review by the Member States and the European Commission. Upon the creation of the list of authorised novel foods the existing authorisation for *Schizochytrium sp.* oil rich in DHA and EPA was included.

4. The evaluation by the FSA and FSS assessed the food safety risks of the novel food and its production, in line with Article 7 of assimilated Commission Implementing Regulation (EU) 2017/2469. The basis and structure of the assessment was conducted using the assimilated regulatory framework and the technical guidance put in place by the European Food Safety Agency (EFSA) for full novel food applications (EFSA NDA Panel, 2021).

5. With thanks to the members of the ACNFP during the course of the assessment, which were; Dr Camilla Alexander White, Dr Anton Alldrick, Dr Kimon Andreas Karatzas, Alison Austin, Professor George Bassel, Dr Mark Berry, Dr Christine Bosch, Professor Dimitris Charalampopoulos, Dr Catharina Edwards, Professor Susan Fairweather-Tait, Professor Paul Frazer, Dr Hamid Ghoddusi, Professor Andy Greenfield, Professor Wendy Harwood, Professor Huw D Jones, Dr Ray Kemp, Dr Elizabeth Lund, Professor Harry J McArdle, Mrs Rebecca McKenzie, Professor Clare Mills, Dr Antonio Peña-Fernández, Dr Lesley Stanley, Professor Hans Verhagen, Dr Maureen Wakefield, and Professor Bruce Whitelaw.

6. A safety dossier submitted by the applicant was evaluated by the ACNFP at their 157th and 162nd meetings. Requests for further information were sent to the applicant after the 157th meeting. The applicant's response to the request for further information from the April 2023 meeting was further evaluated at the ACNFP meeting in September 2023.

7. The FSA and FSS concluded that the specified novel food is safe under the newly proposed uses, as an ingredient within meat and fish analogues. The additional uses were not considered to be nutritionally disadvantageous. It was noted that the addition of the novel food to the proposed food categories would allow some sub-populations, whose diets are deficient, to intake DHA and EPA at normal levels. Under the assumption that consumers of the novel food would not be intaking DHA and EPA elsewhere in the diet, there is not expected to be any additional exposure arising from the addition of the proposed food categories.

8. The views of the ACNFP have been considered in this safety assessment which represents the opinion of the FSA and FSS on the change in use for *Schizochytrium sp.* oil rich in DHA and EPA.

2. Assessment

2.1. Identity

9. The novel ingredient is an oil which is rich in docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), derived from the heterotrophically grown marine microalgae, *Schizochytrium sp*. otherwise known as DHA-O. This DHA and EPA rich oil from *Schizochytrium sp*. (hereafter referred to as 'DHA and EPA-rich oil' or 'DHA-O oil') has a fatty acid profile that more closely represents that of common sources of long-chain omega-3 oils which are present naturally in the human diet. The DHA and EPA-rich oil contains a minimum level of 22.5% DHA and a minimum level of 10% EPA as outlined in the original UK opinion by the ACNFP in 2012, on the extension of use of *Schizochytrium sp*. Oil known as DHA – O with the composition as described above.

10. The source of the oil is a strain of *Schizochytrium sp*. algae. The taxonomic ranking of the source microalgae is defined below:

    - Kingdom = *Chromista (Stramenopilia)*
    - Phylum = *Heterokonta*
    - Class = *Thaustochytridae*
    - Order = *Thaustochytriales*
    - Family = *Thaustochytridiaceae*
    - Genus = *Schizochytrium*
    - Species/Strain = DHA-O

11. There were no changes to the identity of the novel food from the initial authorisation for *Schizochytrium sp.* oil rich in DHA and EPA. Therefore, the safety of the novel food remains unchanged..

2.2. Production Process

12. DHA-O oil is produced via a self-contained fermentation process using an alga from the genus *Schizochytrium*. The algae are grown in a pure culture heterotrophic fed-batch fermentation process and recovered from the fermentation broth. The subsequent oil recovery stages may be applied to either the recovered, dried algae (following reconstitution in water) or the fermentation broth may be used directly in the oil recovery process, in which case a pasteurisation step may be employed. Antioxidants may be added to the fermentation broth to aid stability in processing.

13. Fresh *Schizochytrium sp.* broth or reconstituted dried algae (from *Schizochytrium sp.* fermentation) may be used in the process. The mixture is then heated and centrifuged to separate the oil from the aqueous phase. The oil phase is dried and stored for oil purification.

14. The crude oil is further refined into the finished product using process operations commonly employed in the vegetable oil industry. Approved antioxidants are added to the oil to provide stability. At this stage the DHA and EPA percentage may be standardised by the addition of food grade vegetable oil, for example high oleic sunflower oil.

15. There were no changes to the production process of the novel food from the initial authorisation for *Schizochytrium sp.* oil rich in DHA and EPA. Therefore, the safety of the novel food remains unchanged.

2.3. Specifications and Composition

16. Below are the specifications set out for *Schizochytrium sp.* oil rich in DHA and EPA in legislation, along with quality control analyses of three independent batches of product from the initial authorisation, to provide evidence of compliance to the specifications was provided in the original assessment. Analysis of three representative batches of the novel food was the standard required at the time of the assessment.

17. Table 1 shows the specification for DHA-O oil and the analytical results for three independent batches of the novel ingredient as provided in the original application in 2011.

Table 1: Compositional specification and analytical results for DHA-O oil

Test Parameter	Specification	Batch 1	Batch 2	Batch 3
Acid Value	≤0.5 mg KOH/g	0.4	0.2	0.5
Peroxide Value	≤5.0 meq/kg of oil	2.2	1.7	3.6
Moisture and Volatiles	≤0.05%	<0.01	0.01	<0.01
Unsaponifiable Content	≤4.5%	1.2	1.1	1.1
Trans-fatty Acids	≤1%	<0.05	<0.05	<0.05
DHA Content	≥22.5%	35.1	33.3	32.7
EPA Content	≥10%	15.9	14.9	17.7

18. Additional compositional analyses are provided, which cover the requirements of regulation 2015/2283 EU, as retained in UK law. Table 2 displays residual solvents, protein, and heavy metal composition of three independent batches of the novel ingredient. Table 3 displays the mean fatty acid profile of three batches of the novel ingredient. Table 4 displays the mean unsaponifiable composition of three batches of the novel ingredient.

Table 2: Residual solvents, protein, and heavy metal composition of three independent batches of DHA-O oil

Test Parameter	Batch 1	Batch 2	Batch 3
Residual Solvent – IPA (mg/kg)	<1.0	<1.0	<1.0
Protein by Kjeldahl (%N x 6.25)	<0.02	<0.02	<0.02
Arsenic (mg/kg)	<0.2	<0.2	<0.2
Copper (mg/kg)	<0.02	<0.02	<0.02
Iron (mg/kg)	0.02	0.02	0.02
Mercury (mg/kg)	<0.04	<0.04	<0.04
Lead (mg/kg)	<0.1	<0.1	<0.1

Table 3: Mean fatty acid composition of three independent batches of DHA-O oil

Fatty Acid	Content mg free fatty acids (% w/w oil)
14:0 Myristic	1.59
14:1 Myristoleic	0.00
15:0 Pentadecanoic	0.40
16:0 Palmitic	18.56
17:0 Heptadecanoic	0.08
18:0 Stearic	1.20
18:1 (n-9)* Oleic	3.90
18:1 (n-7)* cis-vaccenic	0.03
18:2 Linoleic	0.50
18:4 Ocadecatetraenoic	0.07
20:0 Eicosanoic	0.37
20:1 Eicosenoic acid	0.01
20:3 (n-6) Eicosatrienoic	0.04
20:4 (n-6) Arachidonic	1.37
20:3 (n-3) Eicosatrienoic	0.12
20:4 (n-3) Eicosatetraenoic	0.55
20:5 (n-3) Eicosapentaenoic	16.18
22:0 Docosanoic	0.17
22:1 (n-11) Cetoleic	0.07
22:4 (n-6) Docosatetraenoic	0.23
22:5 (n-6) Docosapentaenoic	1.27
22:5 (n-3) Docosapentaenoic	3.61
24:0 Tetracosanoic	0.11
22:6 (n-3) Docosahexaneoic	33.72
Minor Components (individual fatty acids <0.005mg FFA/g)	0.12
Total Fatty Acids	**84.27**

Table 4: Mean unsaponifiable content of three independent batches of DHA-O oil

Sterol	Content (% w/w oil)
Cholesterol	0.182
Cholestanol	0.000
Brassicasterol	0.008
24-Methylene cholesterol	0.006
Campesterol	0.005
Campestanol	0.000
Stigmasterol	0.505
Δ-7-Campesterol	0.002
Δ-5,23-stigmastadienol	0.003
Clerosterol	0.015
β-sitosterol	0.033
Sitostanol	0.001
Δ-5-avenasterol	0.008
Δ-5,24-stigmastadienol	0.003
Δ-7-stigmastenol	0.003
Δ-7-avenasterol	0.001
Total Sterols	**0.775**

19. Further to the routine compositional analyses performed, the product conforms with the levels laid down in regulation 2006/1881 as assimilated in UK law, which sets out the maximum levels for certain contaminants in foodstuffs. This confirms the absence of significant levels of : dioxins, polycyclic aromatic hydrocarbons, pesticides, acrylamide, algal toxins, and microorganisms.

2.4. Stability

20. The stability of the novel ingredient remains unchanged since the original extension of use authorisation for DHA-O oil. However, as this extension of use pertains to a change in use of the novel ingredient (addition of the novel ingredient to two new food categories; meat and fish analogues), a further consideration of stability under the newly proposed uses was made by the ACNFP. Further information and data on its stability within the new food matrices have since been provided by the applicant, which show that the novel food remains stable under the newly proposed uses: meat analogues and fish analogues.

21. In order for the product to remain safe under the proposed conditions of use, a consideration of the stability must be made for each intended food matrix before, during, and after any further processing. Based on the advice of the ACNFP, the FSA/FSS consider the stability of the proposed additional uses have been demonstrated.

2.5. History of Use

22. *Schizochytrium sp.* oil rich in DHA and EPA (DHA-O oil) is currently authorised as a novel food within the UK and EU. The original application for this form of DHA oil was received in April 2011 and subsequently authorised in 2012 under the Novel Food Regulation (EC) 258/97. The text relates to omega-3 fatty acids which have a demonstrated history of use and natural prevalence within the human diet.

2.6. Proposed Use, Use Levels, and Anticipated Intake

23. The extension of use for the novel ingredient will increase the number of permitted food categories by two, to include both meat and fish analogues. These additions enable food manufacturers to deliver doses of DHA and EPA that could be found naturally in fish and meat products, in the newly proposed food categories.

24. Table 5 shows the list of currently authorised food categories and their specified maximum use levels, along with the two newly proposed food categories and their proposed maximum use levels.

Table 5: Authorised and newly proposed food categories for the use of *Schizochytrium sp.* oil rich in DHA and EPA and their maximum use levels

Specified Food Category	Maximum combined use level of DHA and EPA
Food Supplements as defined in Directive 2002/46/EC for adult population excluding pregnant and lactating women	3,000 mg/day
Food Supplements as defined in Directive 2002/46/EC for pregnant and lactating women	450 mg/day
Foods for special medical purposes as defined in Regulation (EU) No 609/2013	In accordance with the particular nutritional requirements of the persons for whom the products are intended
Total diet replacement for weight control as defined in Regulation (EU) No 609/2013 and meal replacements for weight control	250 mg/meal
Milk-based drinks and similar products intended for young children	200 mg/100 g
Processed cereal based food and baby food for infants and young children as defined in Regulation (EU) No 609/2013	
Foods intended to meet the expenditure of intense muscular effort, especially for sportsmen	
Foods bearing statements on the absence or reduced presence of gluten in accordance with the requirements of Commission Implementing Regulation (EU) No 828/2014	
Bakery Products (Breads, Rolls and Sweet Biscuits)	200 mg/100 g
Breakfast Cereals	500 mg/100 g
Cooking Fats	360 mg/100 g
Dairy Analogues except drinks	600 mg/100 g for cheese; 200 mg/ 100 g for soy and imitation milk products (excluding drinks)
Dairy Products except milk-based drinks	600 mg/100 g for cheese; 200 mg/ 100 g for milk products (including milk, fromage frais and yoghurt products; excluding drinks)
Non-alcoholic Beverages (including dairy analogue and milk-based drinks)	80 mg/100 g
Cereal/Nutrition Bars	500 mg/100 g
Spreadable Fats and Dressings	600 mg/100 g
Newly Proposed Food Categories	
Fish analogues	**300 mg/100g**
Meat analogues	**300 mg/100g**

25. Estimates for the intakes of DHA and EPA combined from *Schizochytrium sp.* oil in EU Member States were conducted using the authorised and proposed food uses and use levels in combination with food consumption data from the European Food Safety Authority (EFSA) Comprehensive Food Consumption Database (hereafter referred to as the EFSA Comprehensive Database). The estimated intakes of DHA and EPA were calculated on a per person and per kilogram body weight basis and are reported for each age category for the countries examined. The calculations were based on databases including UK data and therefore were considered to appropriately estimate consumer exposure in the UK.

26. Table 6 reports the highest mean and highest high levels of DHA+EPA for each of the population groups covered. The table also compares the overall intakes of the existing authorisations with the overall intakes including the proposed extension, the last column showing the increase of intake in mg/day for both the mean and high values.

Table 6: Comparison of the estimated daily intake of DHA and EPA from *Schizochytrium sp.* Oil in different population groups from authorised and proposed food uses in the EU (EFSA Comprehensive Database, 2020)

Population Group (Age)	Number of Surveys	Authorised Food Uses		Authorised and Proposed Food Uses			
		Maximum Intakes of DHA and EPA (mg/day)		Maximum Intakes of DHA and EPA (mg/day)		Change (mg/day)	
		Mean	High Level	Mean	High Level	Mean	High Level
Infants (<11 months)	13 (11)	885	1523	886	1523	**+1**	**0**
Toddlers (12 to 15 months)	20 (17)	1135	2475	1142	2485	**+7**	**+10**
Other Children (3 to 9 years)	30 (30)	1495	2655	1515	2656	**+20**	**+1**
Adolescents (10 to 17 years)	30 (29)	1564	2165	1577	2175	**+13**	**+10**
Adults (18 to 64 years)	34 (34)	1698	3363	1707	3372	**+9**	**-9**
Pregnant and lactating women	7 (7)	1155	1960	1176	1981	**+21**	**+21**
Elderly (65 to 74 years)	24 (24)	1758	3373	1767	3382	**+9**	**+9**
Very Elderly (≥75 years)	17 (12)	1281	2208	1295	2220	**+14**	**+12**

27. Overall, the impact of including meat and fish analogues in the intake assessment of 'DHA and EPA from *Schizochytrium sp.* oil' is minimal/negligible for all target population groups (considering the general uncertainties related to the methodology itself). This reflects that consumers are unlikely to be eating meat and fish analogues as well as foods high in DHA and EPA in a single sitting. It is expected that therefore the new categories will not provide DHA and EPA at levels that would be considered a safety risk, nor allow for excessive consumption of DHA and EPA.

28. Queries were raised by the Committee in relation to the range of products subject to the new food categories. This provided a basis to establish if there could be nutritional disadvantage from consuming these products as a replacement for meat and fish. Further information was provided by the applicant which details examples of such products. It was explained that the proposed use is as an alternative to other sources in the diet and the nature of the products would suggest these are not consumed at the same eating occasion as an additional source of DHA and EPA. No safety concerns were raised to the addition of the novel food to the new food categories and the Committee does not consider there to be any nutritional disadvantage to consuming the novel food within the new food categories.

2.7. Absorption, Distribution, Metabolism, and Excretion (ADME)

29. There are no changes to the adsorption, distribution, metabolism, or excretion of the novel ingredient since the original authorisation for DHA-O oil. Previous conclusions remain appropriate for the extension of use and no further review of ADME was required.

2.8. Nutritional Information

30. No additional data was presented on the nutritional profile of the novel food and as such no review of nutritional information was provided. It was noted that there are specific groups of the population that do not consume fish and fish-derived products such as fish oil, or meat or meat derived products due to allergenicity or diet choices (such as in veganism or vegetarianism). The authorisation of 'DHA and EPA-rich oil' in these additional food categories was considered to provide alternative sources for these components of the diet for those consumers.

2.9. Toxicological Information

31. The toxicity of DHA and EPA-rich oils produced from different strains of *Schizochytrium sp.* has been extensively reviewed and investigated over the years. In all previous reviews and investigations, the competent authorities have concluded that there were no concerns with regards to genotoxicity and sub-chronic toxicity of the tested materials.

32. There are no changes to the toxicological profile of the novel ingredient since the original authorisation for DHA-O oil. A NOAEL was identified at 200g per person, per day of DHA-O or 100g per person, per day of DHA and EPA.

33. The original 2011 ACNFP opinion noted:

    "In addition to the toxicological studies carried out on DHA and EPA-rich oil, the applicant notes that its traditional counterpart, fish oil, is widely used both in food supplements and in fortified foods in the EU without restriction."

34. There have been no additional data produced since the previous application and the Committee considers the conclusions to remain relevant for the proposed extension of use.

2.10. Allergenicity

35. There have been no changes to the allergenicity of the novel food since its initial authorisation. Therefore, the Committee considers the initial conclusions on allergenicity to remain relevant for the proposed additional food categories.

3. Discussion

36. The extension of use for the novel ingredient will increase the number of permitted food categories by two, to include both meat and fish analogues. The overall purpose for these additions is to enable food manufacturers to deliver doses of DHA and EPA that could be found in fish and meat products and to meet the labelling requirements for “source” and “high” in Omega-3 fatty acids as specified within Commission Regulation (EU) No 116/2010 of 9 February 2010 amending Regulation (EC) No 1924/2006 of the European Parliament and of the Council with regard to the list of nutrition claims.

37. No changes were made, nor additional data supplied, on identity and characterisation, production process, composition or specification of the oil itself, nutritional profile, ADME, toxicological or allergenicity data since the original authorisation for this form of DHA oil in 2012. As such no review was made of these sections and the original conclusions made by the FSA and FSS were considered to apply to the extension of use.

    It is concluded that the specified novel food is safe under the newly proposed uses, as an ingredient within meat and fish analogues. The additional uses were not considered to be nutritionally disadvantageous, to significantly increase exposure to the novel food, or to pose any safety concerns under the proposed conditions of use.

4. Conclusions

38. The FSA and FSS have undertaken the assessment of *Schizochytrium sp.* oil rich in DHA and EPA and concluded that the novel food is safe under the changed conditions of use and does not pose a safety risk to human health. Assessment has also been made and the novel food under the proposed conditions of use is not likely to be nutritiously disadvantageous. These conclusions are based on the information in the applicant's dossier.

39. The FSA and FSS have considered the advice of the Advisory Committee on Novel Foods and Processes for this novel food in reaching their conclusion.

References

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Abbreviations

ACNFP	Advisory Committee on Novel Foods and Processes
ADME	Adsorption, Distribution, Metabolism, and Excretion
DHA	Docosahexaenoic Acid
DHA-O	Novel Production Strain of *Schizochytrium sp.* algae
EFSA	European Food Safety Authority
EPA	Eicosapentaenoic Acid
EU	European Union
FFA	Free Fatty Acids
FSA	Food Standards Agency
FSS	Food Standards Scotland
g	Grams
GB	Great Britain
kg	Kilograms
Ltd	Limited Company
mg	Milligrams