ADVISORY COMMITTEE ON NOVEL FOODS AND PROCESSES

OPINION ON AN APPLICATION UNDER THE NOVEL FOODS REGULATION FOR DHA RICH ALGAL OIL FROM SCHIZOCHYTRIUM SPECIES T18

Applicant: Mara Renewables Corporation

Responsible Person: Roberto Armenta

EC Classification: 2.1

Introduction

1. An application was submitted to the UK by Mara Renewables Corporation, for an extension of use authorisation of its DHA rich algal oil in the EU. The application was accepted by the UK Competent Authority in November 2016. A copy of the application was placed on the Agency's website for public consultation. Following clarifications from the Committee to the applicant the Committee have now been able to complete their assessment

2. There have been multiple authorisations since 2003 for oils from three strains of *Schizochytrium* microalgae species. The company already has a substantial equivalence authorisation to the DHA rich oil from *Schizochytrium* strain ATCC-20888 authorised in Commission Implementing Decision 2014/463/EU.

3. The applicant proposes to extend the use of this DHA rich oil from this strain of microalgae into additional product categories namely fruit and vegetable purees, and infant formula.

4. The application was prepared pursuant to Commission Recommendation (97/618/EC) of 29 July 1997 concerning the scientific aspects and presentation of information necessary to support applications for the placing on the market of novel foods and novel food ingredients. This microalgal DHA rich oil has been classified by the applicant as a complex novel food from non-GM source, the source of the novel food has a history of food use in the EU (class 2.1). The information presented in the dossier is structured accordingly and is considered below under these schemes.

I. Specification of the novel food

5. The applicant provided a detailed compositional analysis of six separate batches of the DHA rich oil (three in oil form and three in semi solid form). As the composition of the novel ingredient is primarily fat, assessment of 6 batches of oil has been made of its fatty acid and sterol composition. The applicant has assessed six batches against the specification of the oil and demonstrated that the manufacturing process produces a consistent product meeting the physical and chemical specifications for the product.

6. The applicant has also investigated the stability of their oil. A long term stability study of the DHA rich oil was undertaken which measured the levels of DHA, peroxide and anisidine at 7 and 12 months into the study. The product was frozen as this is the condition in which it is expected the product will be stored and shipped. The DHA levels remained within the specification for the product.

7. The applicant has also undertaken an assessment of the stability of the oil under accelerated conditions (25 degrees Celsius at 60% relative humidity). The level of DHA in the oil was measured at 4 weeks and 8 weeks into the experiment and the level of DHA remained stable.

***Discussion**: The Committee sought further information on the composition of the product in particular the antioxidants that were used in the production of the oil. The applicant confirmed that these were standard authorised additives used to stabilise oils. The Committee were content that this question had been addressed.*

It was noted that the levels of silicon in the mineral analysis of the novel ingredient were higher than the other minerals in the oil. The applicant was asked to comment on the silicon levels that the end user would experience in the final product and to compare this to the level of silicon from other dietary sources to understand if this would be of health concern. The applicant explained that the use level of the oil in the final product was low and so the level of silicon to which infants and young children would be exposed was unlikely to be a safety concern. This view was accepted by the Committee.

In light of the further information provided, the Committee were content the novel ingredient was appropriately characterised.

II. Effect of the production process applied to the novel food

8. The applicant has provided full details of the production process which is the same as for the product for which they have substantial equivalence. The process involves growing the microalgae using a closed fermentation process. The resulting cells are broken open using enzymes and then a series of established techniques for edible oils are used to recover and purify the oil.

9. The applicant has submitted evidence of analysis of the oil to show that toxins are not present in the final product. These analyses form part of the applicant's quality control analysis and the applicant indicates the presence of contaminants would be monitored regularly against the specification for the product.

***Discussion:** The Committee sought clarification on the choice of algal toxins to be tested in the dossier. It was explained that algal toxins have not been identified in the Thraustochytriaceae family to which Schizochytrium sp. belong. However, further testing of microalgae toxins from the wider kingdom of microalgae were undertaken to demonstrate that these were not produced in this production system. This satisfied the Committee that production of algal toxins was unlikely to be a safety concern.*

The Committee also requested further information on the steps taken by the applicant to ensure cross contamination with other microorganisms such as cyanobacteria was minimised. The applicant highlighted their HACCP based control systems that sought to minimise potential for cross contamination during inoculation and during production. Testing against the specification for three batches of the product was provided to verify the effectiveness of the controls. The dark conditions were suggested to minimise the growth of cyanobacteria. In light of the further information, the Committee were content that appropriate controls were in place that would manage the risk of microbial contamination during production.

III. History of the organism used as a source of the novel food

10. The applicant has provided information characterising the source organism – *Schizochytrium* sp. T18 and its relatedness to other *Schizochytrium* sp. used to produce authorised DHA rich, novel oils. An expert opinion is provided to substantiate the similarity between strain T18 and ATCC 2088 that was subject to the authorisation for the currently authorised uses.

Discussion: *The Committee did not raise any concerns relating to this section of the dossier.*

IX. Anticipated intake/extent of use of the novel food

11. The applicant intends to continue to incorporate the DHA rich oil into the uses outlined in the latest authorisation (2014/463/EU) as detailed in the table below, in addition to new uses in foods for infants and young children as well as fruit/vegetable puree. The intention is that the DHA rich oil replaces DHA from other sources. Some of the categories have been updated in light of the changes to the Parnuts legislation, now Foods for Special Groups. The full list of uses are outlined below:

Food category	**Maximum level of use expressed as DHA**	
Dairy products except milk-based drinks	200 mg/100 g; 600 mg/100 g in the case of cheese products	As permitted under 2014/463/EU
Dairy analogues except drinks	200 mg/100 g; 600 mg/100 g in the case of cheese analogues	As permitted under 2014/463/EU
Spreadable fat and dressings	600 mg/100 g	As permitted under 2014/463/EU
Breakfast cereals	500 mg/100 g	As permitted under 2014/463/EU
Food supplements	250 mg DHA per daily dose as recommended by the manufacturer for normal	As permitted under 2014/463/EU

	population 450 mg DHA per daily dose as recommended by the manufacturer for pregnant and lactating women	
Foods intended for use in energy-restricted diets for weight reduction (including foods intended for use in total diet replacement for weight control as defined in Regulation (EU) No 609/2013)	250 mg per meal replacement equivalent	As permitted under 2014/463/EU
Foods intended to meet the expenditure of intense muscular effort	200 mg/100 g	As permitted under 2014/463/EU
Foods bearing statements on the absence or reduced presence of gluten in accordance with the requirements of Commission Implementing Regulation (EU) No 828/2014	200 mg/100 g	As permitted under 2014/463/EU
Foods for special medical purposes as defined in Regulation (EU) No 609/2013	Used in accordance with Regulation (EU) 2016/128 (50 mg/100 kcal in the case of foods intended for infants)	As permitted under 2014/463/EU
Bakery products (breads and rolls), sweet biscuits	200 mg/100 g	As permitted under 2014/463/EU
Cereal bars	500 mg/100 g	As permitted under 2014/463/EU
Cooking fats	360 mg/100 g	As permitted under 2014/463/EU
Non-alcoholic beverages (including dairy analogue and milk-based drinks)	80 mg/100 ml	As permitted under 2014/463/EU
Infant formula and follow-on formula	Used in accordance with Regulation (EU) 2016/127	New Use
Processed cereal-based foods and baby foods for infants and young children, including those defined in Regulation (EU) No 609/2013	200 mg/100 g	As permitted under 2014/463/EU
Fruit/vegetable puree	100 mg/100 g	New Use

12. Using the European Food Safety Authority (EFSA) 'Food Additives Intake Model' (FAIM) tool, the applicant calculated the mean daily estimated intake of the DHA rich oils from the existing authorised uses and the new proposed uses. The applicant estimated the population average and high intake levels on a per body weight per day basis for all the affected population groups as detailed in the table below.

	Population Average Intake mg/kg bw/day	Total High level intake mg/kg bw/day
Infants		
Min	19.3	43.2
Max	49.7	191.0
Toddlers		
Min	28.9	42.4
Max	59.3	111.1
Other Children		
Min	16.8	28.7
Max	51.1	101.0
Adolescents		
Min	8.4	13.3
Max	26.0	47.8
Adults		
Min	7.8	14.3
Max	17.9	39.5
Elderly		
Min	8.5	11.2
Max	18.1	39.9
Very Elderly		
Min	8.8	10.2
Max	14.1	30.0

13. The applicant suggests that the values are conservative estimates as they assume that consumers are always eating a DHA containing product with DHA added at the maximum level. The dossier comments that the main contribution to the high intakes were fermented milk products such as yoghurts, porridge and flavoured milk. Limited information has been provided estimating consumption on a Member State basis. No information was presented specifically for the potential intake in the UK population.

14. The supplements intake was calculated separately due to the difficulties in incorporating these into the model. Based on the daily dose of 250-450 mg/day intakes of DHA are estimated to range from 4.2 mg/day bw/day for 60kg adults to 7.5 mg/kg bw/day for pregnant and lactating women. The applicant therefore suggests that supplements would provide a relatively low contribution to DHA intake.

***Discussion**: The Committee sought further information on the Margin of Exposure between the intake from both existing and proposed uses of the oil and the NOAEL identified in the toxicological studies described below. The applicant provided information indicating that the consumption levels for average consumers seen in the intake assessment vary between population groups between 7.8-59.3 mg/kg bw/day which is 56-424 times lower than the male NOAEL and 62-472 times lower than the female NOAEL. Infants and toddlers were identified as the highest consumers of products containing the oil.*

The Committee requested further information on the exposure of infants and young children to the novel ingredient through maternal consumption and breastfeeding. A further analysis was undertaken to verify the assumption that exposure through breastmilk and bottle feeding would be similar. This was confirmed with the exposure from breast milk of mothers supplementing with the novel ingredient calculated as being 35-44 mg/100ml compared to the level of the novel ingredient in infant formula as consumed of 35 mg/100ml. Slight adjustments to the intake levels for infants and toddlers were made in light of further consideration of the impact of exposure to the novel ingredient from breastfeeding. These were used as a basis for assessing if the Margins of Safety seen were sufficient to support the view that the novel ingredient would not be a safety concern.

The Committee also question whether consideration of the impact of life long exposure to the novel ingredient had been considered. The applicant explained that DHA rich oils have been used since the 1990s without adverse effect. The calculated exposure for the novel ingredient was conservative and it was unlikely that consumption of the oil would be at the high levels calculated for prolonged periods of time.

X. Information from previous human exposure to the novel food or its source

15. The applicant explained that DHA rich oils from the *Schizochytrium* species have been subject to a series of authorisations under the novel food regulation since 2003. DHA rich oils from *Schizochytrium* species have been used consistently in food in the EU since that time. The novel ingredient in this application has been subject to a substantial equivalence assessment and authorisation by the Irish Competent Authority, comparing it with previous DHA rich oils from other strains of *Schizochytrium* species.

***Discussion:** The Committee did not raise any concerns relating to this section of the dossier.*

XI. Nutritional information on the novel food

16. The applicant states that the proximate analysis has shown that their DHA oil has the same nutritional composition as the DHA it will replace. A full fatty acid analysis and sterol analysis on six batches has been provided. Further

information comparing the composition of two further DHA rich oils were provided for comparison.

Discussion: *The Committee sought further information on how the composition of the product compared to existing authorised DHA rich oils and in particular in relation to those ingredients used in infant formulas. This was to inform whether the product meets the criteria for novel foods not to be nutritionally disadvantageous compared to those it may replace.*

The applicant provided further detail on this point, comparing their product to other algal oils and other sources of DHA used in infant formula. Detailed information was provided on the requirements of the infant formula regulations in relation to the fatty acid composition of these products. It was recognised by the Committee that while individual oils used as sources of DHA in infant formulas may have different compositions, as infant formulas are blended to meet a nutritional profile and ensure compliance with regulatory standards, it was unlikely that consumers would be placed at a nutritional disadvantage.

XII. Microbiological information on the novel food

17. The applicant has outlined the HACCP controls in the production process used to minimise the potential for microbial growth. Microbial hazards such as mould, yeast and coliforms have been included in specification. The applicant has provided analysis of three batches of the final product to demonstrate the effectiveness of the controls and that the specification is met consistently.

Discussion*: The questions of the Committee in relation to this area were considered under the production process section.*

XIII. Toxicological information on the novel food

18. As an extension of use, the data used to support the existing use of the novel ingredient may have relevance to the assessment of the extension of use. The applicant highlights that while tolerable upper intakes have not been produced for EPA and DHA either individually or in combination, EFSA has made some assessment of whether the level of use proposed in previous applications would represent a safety concern. The applicant references EFSA's view that supplemental intakes of up to 5g/day for EPA and DHA combined and 1g/day for DHA alone would not raise safety concerns for the general population. The applicant also highlights the long history of use of DHA in the diet suggesting a degree of safety in its consumption.

19. Below are summarised the toxicological studies undertaken on the applicant's DHA rich oil provided by the applicant to support their application. The dossier provides further detail on the studies undertaken on the novel DHA ingredient.

Study type/author	**Results/observations**

Genotoxicity	
Microbial reverse mutation assay – Schmitt et al 2012a	Negative*[1]
Rat bone marrow micronucleus assay - Schmitt et al 2012a	Negative*
Chromosomal aberration assay in human peripheral blood lymphocytes - Schmitt et al 2012a	Negative*
Acute Toxicity	
Oral LD_{50} in female rats Schmitt et al 2012a	>5 g/kg bw
Subchronic Toxicity	
90-Day repeat dose oral toxicity study in rats - Schmitt et al 2012a	NOAEL: 3305 mg/kg bw/day in males 3679 mg/kg bw day in females
Reproductive / Developmental toxicity	
Development/maternal toxicity in rats (maternal exposure by gavage, once daily from days 6-19 of gestation); - Schmitt et al 2012b	NOAEL for maternal toxicity and embryo/foetal development: 2000 mg/kg
3-Month dietary toxicity study with an in utero exposure phase in rats - Schmitt et al 2012b	NOAEL for F0 males (pre-mating): 3421 mg/kg bw/day NOAEL F0 males (after mating): 2339 mg/kg bw/day NOAEL F0 females (pre-mating): 3558 mg/kg bw/day NOAEL F0 females (gestation): 3117 mg/kg bw/day NOAEL F0 females (lactation): 7464 mg/kg bw/day NOAEL F1 males: 3526 mg/kg bw/day NOAEL F1 females: 4138 mg/kg bw/day

Discussion*: In addition to the comments made in relation to the margin of exposure the Committee questioned the NOAEL selection. The applicant provided further information on the basis for their choice and how in their view this supported the view that the novel ingredient was safe. It was explained that the doses for the NOAELs in the studies were the highest dose in each case but in selecting the NOAEL consideration had been given to the methodology and the applicant considered the 90 day study to be most appropriate. In light of the further information the Committee were content that the NOAEL selection was appropriate.*

[1] *In these assays negative was considered to represent no increase in the factors associated with risks of genotoxicity

Allergenicity

20. The applicant stated that as highly refined oil the level of protein was below the limit of detection 0.15% and suggests that it is unlikely that allergens would be present.

Discussion: *The Committee did not raise any concerns relating to this section of the dossier.*

CONCLUSION

The ACNFP has completed its assessment of the extension of use for DHA rich oil from *Schizochytrium* sp. as a novel ingredient for use in food supplements.

The Committee requested further information from the applicant in several areas:

- The composition of the product.
- Microbiological controls and the potential for toxin production
- The nutritional value of the novel food compared to existing sources of DHA used in the proposed food categories.
- Several factors in the margin of exposure calculation including, NOAEL selection and whether the intake assessment has taken account of likely exposure of the novel ingredient in the new food categories.
- The potential impact of long term exposure to the novel ingredient.

After reviewing the applicant's responses to these issues, the Committee did not have any outstanding safety concerns. Based on the evidence provided the ACNFP therefore concluded that the extension of use for DHA rich oil from *Schizochytrium* sp. used as proposed by the applicant is unlikely to present a health risk to consumers. The Committee also considers that as proposed to be used the novel food would not be nutritionally disadvantageous.

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