COMMITTEE PAPER FOR DISCUSSION **ACNFP/129/03**
ADVISORY COMMITTEE FOR NOVEL FOODS AND PROCESSES

DHA RICH ALGAL OIL FROM SCHIZOCHYTRIUM SPECIES T18

Issue

The Committee reviewed this application at the meetings in November 2016 and February and April 2017. When the application was last considered further information was requested by the Committee on which to base their assessment. Members are invited to consider the response from the applicant and whether it recommends authorisation of the extension of use of the product.

Background

1. The substantial equivalence of the Mara Renewables DHA oil also known as T18 was assessed and authorised by the Irish competent authority for the existing authorised uses of this form of algal oil (DHA –S).

2. An application has now been submitted to the UK by the company, for an extension of use authorisation of its DHA rich algal oil in the EU. The applicant proposes to incorporate the DHA rich oil into additional product categories namely fruit and vegetable purees, infant formula, other foods for special groups and baby foods.

3. At last meeting the Committee requested further information in a number of areas

    a) Specifications and the nutritional information on the novel food and

    b) Toxicology

4. A letter outlining the request for further information from the discussion at the February meeting is provided in **Annex A**. The applicant has now provided a response to the Committee's questions (**Annex B)**. A draft opinion has been prepared for discussion if the Committee considers it is appropriate in **Annex C**. Particular aspects where the Secretariat would welcome further input from the Committee are highlighted in the text. To assist in the Committee's consideration a summary of the issues considered to date are provided in **Annex D**.

a) Specification and nutritional content of the novel food

5. The Committee at the previous meeting had considered the information supplied by the applicant comparing the composition of the novel ingredient to other authorised DHA rich oils. The Committee commented that the fatty acid

profile for DHA-B, the existing authorised algal DHA oil, for use in infant formula was more nutritionally beneficial for the target age group than the novel ingredient. As this is the ingredient most likely to be replaced as a result of the extension of use, concerns were raised that this could nutritionally disadvantageous. The applicant was asked to comment on this.

6. In their response the applicant explains that their application is in part so that the novel ingredient can be used to meet new requirements for inclusion of DHA in infant formulas at up to 50mg/100kcal under Regulation 127/2016 EU. The applicant suggests that the most common form of DHA added to infant formula currently are fish oils and oil from *Crypthecodium cohni*, with only some use of DHA-B. A comparison of the fatty acid content of the different oils is reproduced below.

Fatty Acid Content % Relative (% w/w Total FA)	**T18**		**DHA-S FOR REFERENCE ONLY[1]**		**DHA-B FOR REFERENCE ONLY[1]**		**DHASCO FOR REFERENCE ONLY**		**Tuna[2]**
	Lowest of 6 batches	**Highest of 6 batches**	**Lowest of 5 batches**	**Highest of 5 batches**	**Lowest of 3 batches**	**Highest of 3 batches**	**Lowest of 4 batches**	**Highest of 4 batches**	**Reference values**
C12:0 Lauric	0.74	1.01	0.42	0.44	N/A	N/A	5.09	7.16	N/A
C14:0 Myristic	9.00	13.65	9.92	11.83	1.05	1.31	15.43	17.52	3
C15:0 Pentadecanoic	0.42	0.68	N/A	N/A	0.23	0.25	N/A	N/A	N/A
C16:0 Palmitic	21.46	29.45	24.11	27.02	13.15	14.03	12.92	14.97	22
C16:1 Palmitoleic	2.09	6.16	0.86	3.42	N/A	N/A	1.23	1.62	3
C17:0 Margaric	<0.10	0.15	N/A	N/A	ND	ND	N/A	N/A	
C18:0 Stearic	0.77	0.85	0.42	0.54	1.64	1.73	0.36	0.64	6
C18:1 Oleic + C18:1 cis-vaccenic	1.81	8.06	tr	1.43	24.89	28.41	13.32	17.69	21
C18:2 Linoleic	<0.10	0.78	N/A	N/A	2.02	2.16	0.31	0.74	1
C18:3 Linolenic	0.13	0.42	N/A	N/A	N/A	N/A	N/A	N/A	1
C18:4 Octadecatetraenoic	0.20	0.32	tr	0.92	N/A	N/A	N/A	N/A	1.9
C20:3 Eicosatrienoic + C20:4(n-7) Eicosatetraenoic	<0.10	0.15	2.12	2.74	N/A	N/A	N/A	N/A	N/A
C20:4(n-6) Arachidonic	0.63	0.76	0.76	1.20	0.63	0.7	N/A	N/A	2
C20:4(n-3) Eicosatetraenoic	N/A	N/A	0.84	0.97	N/A	N/A	N/A	N/A	N/A
C20:5 Eicosapentaenoic	0.90	1.59	1.98	3.59	5.94	6.14	N/A	N/A	6
C22:5 Docosapentaenoic	7.21	8.38	12.72	15.92	2.27	2.67	N/A	N/A	2
C22:6 Docosahexaenoic	37.10	42.47	35.02	40.35	41.48	44.62	41.85	44.78	22
C24:1 Nervonic	<0.10	0.95	N/A	N/A	N/A	N/A	N/A	N/A	N/A

tr = present but below the lowest calibration curve concentration (4 mg/g oil) and therefore not quantified, N/A = not available; ND = not detected

1Corrected to % total FA

2Handbook of Lipid Research

7. The applicant comments that in the case of infant formula the regulations in this area set specific requirements for the fatty acid profile which all formulas are required to meet. They suggest that this in practice means that the DHA ingredient will mainly contribute to the DHA content of the infant formula and the wider profile will be managed to meet regulatory standards. On this basis

they believe that use of their source of DHA the novel ingredient would not be nutritionally disadvantageous as the product's fatty acid profile, as consumed would not be negatively impacted by use of an alternative DHA source.

b) Toxicological information on the novel food

8. Previously the Committee has requested further information on the margin of safety between the NOAEL and the anticipated intake of the novel ingredient as a result of extending the food categories. Following discussion at the last meeting further clarification was sought on the NOAEL selection and whether exposure by infants from breast milk has been taken into account in the exposure assessment.

9. The applicant in their response has summarised the toxicological studies to date. They note that there was a lower NOAEL identified in the reproductive study, but explain that this was because this was the highest dose tested in that study. The NOAEL from the 90 day study of 3305 and 3679 mg/kg bw/day in males and females respectively was selected. The applicant argues this selection is supported by the further toxicological study that looked at animals across their lifecycle and included exposure across generations. They argue that as no evidence of toxicity is seen in this more robust study the NOAEL selection is appropriate and the novel ingredient is safe for the uses proposed.

10. The applicant has also confirmed that the exposure assessments provided previously include potential exposure through breast milk. They note that for this assessment, exposure from both sources will not be cumulative as the infant would be exposed either to breastmilk or infant formula limited by its calorific intake. The margin of exposure calculations provided previously is included in Annex E.

COMMITTEE ACTION REQUIRED

a) The Committee is asked whether the response from the applicant is sufficient to address the questions raised to date.

b) If not, the Committee is asked to indicate what feedback should be given to the applicant.

Secretariat
June 2017

Annexes attached:

Annex A - Letter providing feedback to the applicant from the April meeting of the ACNFP.

Annex B - The applicant's response to the request for further information.

Annex C – Draft opinion for the Committees input.

Annex D – Summary of issues raised in the assessment to date and the applicant's responses.

Annex E – Margin of Exposure Calculations in the applicant's response presented to the April meeting

Annex D - Summary of Committee's consideration to date:

Issue Raised	Applicants response	Committee's response from the minutes of the discussion
Specification of the novel food		
• The Committee were keen to understand how the novel ingredient's composition compares to other authorised DHA rich oils in order to understand if it would be nutritionally disadvantageous. • The Committee also requested information on the anti-oxidants listed as ingredients to the novel product.	• In their response the applicant has provided composition information, based on multiple batches, compared to the other authorised DHA rich oils. This includes the DHA -S to which the product has gained a substantial equivalence authorisation. This is subject to further discussion in the paper above. • Information has been provided on the antioxidants that are commonly used as ingredients in the oil.	Discussion ongoing
Production process and level of undesirable substance		
• The Committee had sought a further explanation from the applicant on the choice of algal toxins for analysis in their dossier. Of interest was whether the selection was a function of the production process and whether regular testing once in full production was planned to manage any risk of algal toxin production. • Questions were also raised on how it would be ensured that the system would not be contaminated with other microorganisms.	The applicant's response comments 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. The applicant therefore considers that it is unnecessary to undertake regular testing for the presence of microalgal toxins. An explanation of the microbial controls used in the system was provided by the applicant.	The information provided on the algal toxins produced during the production process was considered and it was suggested that this was not a risk. The Committee was content with the information supplied by the applicant on the production process and HACCP plans to manage the risks of microbial contamination.
Nutritional information on the novel food		
The Committee requested a comparison of the novel ingredient's composition compared to that of oils currently used in infant formulas as a source of DHA.	In their response the applicant has compared the fatty acid composition of the novel ingredient to both the authorised DHA rich oil that can be used in infant formulas (DHA-B) and Tuna oil an alternative source of DHA in this food category. Further information on this is provided in the paper above.	Consideration ongoing in light of further data on the composition.
Toxicology		

Margin of safety assessment The applicant was asked to provide an assessment of the Margin of Safety between the intakes calculated and the NOAEL's seen in the toxicological studies The Committee questioned the choice of NOAEL and whether infant exposure via breast milk had been considered in the exposure assessment	In response they have highlighted that the safety of microalgae oils has been demonstrated by a number of studies and that their novel ingredient is similar in composition to those already marketed. For this novel ingredient toxicological testing suggested a NOAEL at the highest dose tested, 5% of the diet, in a 90 day study of 3305 and 3679 mg/kg bw/day in males and females respectively. The consumption levels seen in the intake assessment vary between population groups between 8-60mg/kg bw/day which is 55-413 times lower than the NOAEL. The applicant therefore argues that the use of the oil is safe. Further information on this point is outlined in the paper above.	Consideration ongoing
Long term exposure Members noted that the longest toxicological study undertaken on the novel food has been 3 months in duration. It was recognised that infants, could have life-long exposure to the novel ingredient from the range of permitted uses. The applicant was asked to comment on the safety of long term use of the novel ingredient.	The applicant argues that DHA rich oils have been used safely in infant formula since the 1990's and the safety of this type of oil is well established. The same uses as currently sought were evaluated for other DHA rich oils and felt to be sufficient to support safety. The applicant has commented that for the highest intakes to be maintained over the longer term, infants would need to consume the ingredient at the maximum level of addition, which it is argued is overly conservative.	Conclusion not made but no further questions have been raised on this topic.
Level of silicon in the novel product 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 level of silicon in the novel ingredient was reported to be 51-110mg/kg. The applicant has calculated potential exposure for infants based on consuming 400mg DHA oil per day the daily exposure to silicon would be approximately 0.011mg/day; 15,636-18,727 times lower than seen in the case study described in Nishizono et al 2004 where there were detrimental health effects from high levels of silicon in the diet. On this basis the applicant does not consider that the level of silicon is a health concern.	The Committee accepted the information from the applicant that the level of silicon in the product as consumed was unlikely to be a safety concern.