

Assessment on Astaxanthin-rich Oleoresin From *Haematococcus pluvialis* Algae Used as a Novel Food (RP2213)

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FSA Research and Evidence

AstaReal AB (“the applicant”) submitted a novel food (NF) application for the modification in condition of use of the NF Astaxanthin (ATX)-rich oleoresin from *Haematococcus pluvialis* algae to each nation of Great Britain in April 2024. The NF is produced from *Haematococcus pluvialis* algae and then dried and extracted into an oil containing ATX.

The NF was authorised in the EU (and GB) in 2006 following an opinion through the substantial equivalence process of Regulation (EC) 258/97 to *Haematococcus pluvialis* biomass containing astaxanthin, which has been marketed in the EU since 1995.

The NF is currently authorised for use as food supplements in the general population excluding infants, toddlers, children, and adolescents younger than 14 years.

This application seeks to modify the specification of the oleoresin NF for ATX monoesters, ATX diesters, the 9-cis ATX stereoisomer, and the minimum protein content. The current maximum authorised level of the novel food is 40–80 mg/day of oleoresin, resulting in ≤ 8 mg astaxanthin per day, which will remain unchanged.

In 2023, the European Food Safety Authority (EFSA) published a scientific opinion on the safety of the change to the conditions of use of the NF ingredient. The Food Standards Agency (FSA) and Food Standards Scotland (FSS) have reviewed the information available, including the EFSA opinion, and confirmed that the NF is safe under the proposed change to the conditions of use. The anticipated intake levels and use in food supplements were not considered to be nutritionally disadvantageous.

This safety assessment represents the opinion of the FSA and FSS.

This is a joint FSA and FSS publication.



1. Introduction

The novel food (NF), oleoresin from *Haematococcus (H.) pluvialis* containing astaxanthin (ATX), is a permitted novel food in assimilated Implementing Regulation 2017/2470. In accordance with assimilated Regulation (EU) 2015/2283 on novel foods, application RP2213 for the change in the conditions of use of astaxanthin-rich oleoresin as a novel food has been submitted for authorisation in each nation of Great Britain (GB).

Whilst it was a Member State of the EU, the UK accepted the risk assessments of the European Food Safety Authority (EFSA) in respect of authorisations for regulated food and feed products. Since the end of the transition period, the FSA and FSS have adopted equivalent technical guidance and quality assurance processes to be able to undertake GB risk assessments for regulated product applications.

To ensure our regulatory systems are risk proportionate, and resources are used effectively, the FSA and FSS have used the evidence submitted by the applicant and other information in the public domain, including the EFSA risk assessment opinion, to inform this safety assessment.

The FSA and FSS reviewers have evaluated the published EFSA risk assessment on the novel food and confirmed that this is appropriate for GB risk analysis. Consideration has been given to the processes undertaken to ensure the EFSA opinion is robust and whether there are any aspects that would require further review, such as specific issues for the countries of GB. The result of the assessment is that there is sufficient evidence of safety to conclude without requiring further risk assessment at this time.

This assessment represents the opinion of the FSA and FSS.

2. Details of other Regulators Opinions

The applicant, AstaReal AB (Sweden) is seeking a change in the authorised conditions of use for Astaxanthin (ATX)-rich oleoresin from *Haematococcus pluvialis* algae. The change sought is to the specification of the novel food to adjust the levels of specific ATX isomers, ATX esters, and protein levels in the novel food. The novel food is authorised for use in food supplements.

The NF was authorised in the EU (and UK) in 2006 following an opinion through the substantial equivalence process of Regulation (EC) 258/97 to *Haematococcus pluvialis* biomass containing astaxanthin, which has been marketed in the EU since 1995.

The NF is currently authorised for use as food supplements in the general population. A number of other applicants have used this process to legally place astaxanthin on the market until the authorisation became generic with the establishment of the list of authorised novel foods in 2017.

In September 2023, the safety of the change in specification of ATX-rich oleoresin from *Haematococcus pluvialis* algae, AstaReal AB (Sweden), was assessed by EFSA and received a positive opinion (EFSA NDA Panel et al., 2023). This opinion has been reviewed by the FSA and FSS risk assessors.

The FSA/FSS must consider safety in the context of the currently established ADI within GB. EFSA's conclusion on this specification change is based upon several additional scientific opinions which have taken place since EU-exit, and have not yet been considered by GB. The previous ADI for ATX was set as 0.034 mg ATX/kg bw per day (corresponding to 2.0 mg ATX per day for a 60 kg person) by the EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) in 2014 (EFSA FEEDAP Panel, 2014a). In 2019 the FEEDAP Panel used additional evidence to derive a new ADI of 0.2 mg ATX/kg bw by re-assessing the toxicological profile of ATX (EFSA FEEDAP Panel et al., 2019). In 2020, the EFSA Panel on Nutrition, Novel Foods and Food Allergens (NDA) adopted this updated ADI of 0.2 mg/kg bw/day ATX for food use (EFSA NDA Panel et al., 2020). The new combined exposure calculation by the EFSA NDA Panel found that for some groups (infants and adolescents below the age of 14) there is an exceedance of the ADI of 28-524%, with infants and toddlers showing greater exceedance. Therefore, the conditions under which the novel food may be used were also updated to exclude infants, toddlers, and adolescents younger than 14 years, and this was amended in the Annex to Implementing Regulation (EU) 2017/2470 (The European Commission, 2021). The updated ADI and the exclusion of adolescents under the age of 14 were considered during EFSA's evaluation of the specification change requested by the applicant.

The Panel concluded that an intake of 8 mg ATX per day from food supplements is safe for adults and adolescents over the age of 14 in combination with exposure to ATX from the background diet, as the exposure is below the ADI in these consumer groups. This does not change the maximum authorised levels of 8 mg/day ATX in accordance with Regulation (EU) 2015/2283.

2.1. Methodology applied in the EFSA Opinion

The EFSA Assessment was in accordance with the procedure as outlined in the EFSA scientific opinion 'Guidance on the preparation and presentation of an application for authorisation of a novel food in the context of Regulation (EU) 2015/2283 and Commission Implementing Regulation (EU) 2017/2469.

Under Article 3(4) of assimilated Commission Implementing Regulation (EU) 2017/2469, it may not be necessary for the applicant to provide all the data required under Article 5 of this Regulation when a novel food application seeks to modify the conditions of use, the specifications, additional specific labelling requirements or post-market monitoring requirements of an authorised novel food. Verifiable justification explaining that the intended changes do not affect the results of the existing safety assessment is provided by the applicant. Given that the novel food is the same as that reviewed in the previous assessment, this new safety assessment has focused on the impact of the intended changes of use to alter the specification for the astaxanthin esters and isomers.

Astaxanthin was authorised for sale in the EU and UK in 2006 following an opinion through the substantial equivalence process of Regulation (EC) 258/97. This resulted in the inclusion of oleoresin from *Haematococcus (H.) pluvialis* containing astaxanthin on the permitted list of novel foods in the EU and UK (assimilated Commission Implementing Regulation (EU) 2017/2470). As the identity of the novel food and its production process remain unchanged, the conclusions drawn from the original application regarding the identity of the novel food, the production process, stability, and allergenicity, would not be affected by the proposed change in condition of use. Therefore, this information was not provided or reviewed as part of the assessment.

The FSA and FSS agree with the view that the changes in the conditions of use do not alter the previous assessment of the novel food or the conclusion that no safety concerns have been identified. As such, the focus of this review has been the impact of the changes to the conditions of use to amend the specification of the novel food.

2.1.1. Identity of the novel food

The novel food is a red viscous oil (oleoresin) composed mainly of algae-derived fat, containing 2.9-11.1 % ATX (chemical name: 3S,3'S-dihydroxy- β , β -carotene-4,4'dione). The novel food is obtained via a supercritical carbon dioxide extract of spray-dried algal meal from *Haematococcus pluvialis* algae. The fatty acid profile for the novel food was previously identified and quantified (EFSA NDA Panel, 2014), and remains unchanged in this application.

The FSA and FSS agree with EFSA that the identity of the novel food has been appropriately characterised.

2.1.2. Production Process

No changes to the production process were noted by the applicant from the original authorisation. EFSA concluded that the data provided on the production process was sufficient, and as such did not give rise to any safety concerns or hazards for management. Upon review, the FSA and FSS agree with this decision. No concerns were raised on this section of the assessment.

2.1.3. Compositional information

The data on the composition of the novel food provided by the applicant focused on the changed specification parameters only, with comparisons made to the specification included in the novel foods register for Great Britain, and in the EU's Union list of novel foods. Certifications were provided to demonstrate that the contract laboratories were accredited to perform these analytical studies.

A total of five batches were used for analysis of nutritional composition ([Table 1](#)), including fat, protein, carbohydrate, fibre, and ash.

Table 1. Nutritional composition of the novel food from five batches

Component [g/100g]	Current specification (1)	Batch 1	Batch 2	Batch 3	Batch 4	Batch 5	Method
Fat	42.2 – 99	92.7	93.1	97.4	92.8	93.6	NMKL 160 mod.
Protein	0.3 – 4.4	0.30	< 0.30	< 0.30	< 0.30	< 0.30	NMKL 6
Carbohydrates	0 – 52.8	7.06	6.57	2.53	7.15	6.34	(EU) No 1169/2011
Fibre	< 1.0	< 1.0	< 1.0	< 1.0	< 1.0	< 1.0	AOAC 991.43 Mod.

Component [g/100g]	Current specification (1)	Batch 1	Batch 2	Batch 3	Batch 4	Batch 5	Method
Ash	0.0 – 4.2	0.10	< 0.10	< 0.10	< 0.10	< 0.10	NMKL 173

AOAC: Association of Official Analytical Collaboration; NMKL: Nordic-Baltic Committee on Food Analysis

(1) Novel foods register for Great Britain, retained Regulation (EU) 2017/2470.

The concentrations of fat, carbohydrate, fibre and ash in the analysed five batches are in line with the composition of the novel food stated in the retained Regulation (EU) 2017/2470. The concentration of protein deviates from the specification in four of the five batches. These were measured at <0.3 % instead of current minimum level of 0.3 %. The applicant's state the reason for this is due to improved purification of the NF during the processing stages. The applicants are therefore requesting to lower the specification limit of protein to 0.0 % instead of 0.3 %. The EFSA Panel noted that the specification for protein was identical to the product previously assessed by the NDA Panel in 2014, and there are no safety concerns identified with reducing the minimum specification for protein in the novel food (EFSA NDA Panel, 2014; EFSA NDA Panel et al., 2023). Upon review, the FSA and FSS agree that the compositional information for nutrition has not highlighted areas of concern, and that the change in specification for protein would not adversely affect the safety of the novel food.

For the composition of carotenoids, the applicant provided analysis of five batches from the US production site (Table 2), and five batches from the Swedish production site (Table 3). For batches from the US site, carotenoid content was determined using HPLC by Fuji Chemical, and the ester composition of ATX was determined by HPLC (Holtin et al., 2009). For batches from the Swedish site, carotenoid content and the ratio of ester composition of ATX was determined using an in-house HPLC method.

Table 2. Carotenoid content of the novel food for five batches from the US production site

Carotenoid as w/w % of the NF	Current specification (1) w/w % of the NF	Batch 1	Batch 2	Batch 3	Batch 4	Batch 5
Total ATX	2.9-11.1 %	10.30	10.50	10.40	10.40	10.51
9-cis-ATX (2)	0.3 – 17.3 %	13.00	13.52	12.71	10.55	9.28
13-cis-ATX (2)	0.2-7.0 %	5.77	5.81	5.65	6.05	5.39
ATX monoesters (3)	79.8-91.5 %	75.41	75.54	76.05	75.77	74.88
ATX diesters (3)	0.16-19.0 %	23.68	23.56	23.06	23.30	24.40
β-carotene	0.01-0.3 %	0.27	0.24	0.26	0.27	0.31
Lutein	0-1.8 %	0.43	0.44	0.43	0.38	0.50

Carotenoid as w/w % of the NF	Current specification (1) w/w % of the NF	Batch 1	Batch 2	Batch 3	Batch 4	Batch 5
Canthaxanthin	0-1.30 %	0.70	0.73	0.69	0.71	0.78

NF: Novel food; ATX: astaxanthin

(1) Novel foods register for Great Britain, retained Regulation (EU) 2017/2470.

(2) As a percentage of total ATX. Note that the major isomer does not form part of the specification, therefore 9-cis-ATX and 13-cis-ATX together do not total 100%.

(3) As a percentage of total ATX. Free ATX is a minor component in the NF.

Table 3. Carotenoid content of the novel food for five batches from the Swedish production site

Carotenoid as w/w % of the NF	Current specification (1) w/w % of the NF	Batch 1	Batch 2	Batch 3	Batch 4	Batch 5
Total ATX	2.9-11.1 %	10.78	10.78	10.87	10.85	10.77
9-cis-ATX (2)	0.3-17.3 %	22.90	24.86	25.81	26.73	25.05
13-cis-ATX (2)	0.2-7.0 %	3.17	2.98	3.05	2.79	2.90
ATX monoesters (3)	79.8-91.5 %	78.77	78.99	79.29	79.47	79.18
ATX diesters (3)	0.16-19.0 %	20.62	20.41	20.09	19.88	19.78
β-carotene	0.01-0.3 %	<0.1	<0.1	<0.1	<0.1	<0.1
Lutein	0-1.8 %	<0.1	<0.1	<0.1	<0.1	<0.1
Canthaxanthin	0-1.30 %	0.02	0.02	0.02	0.02	0.02
Total carotenoids	-	11.05	11.06	11.16	11.11	11.02

NF: Novel food; ATX: astaxanthin

(1) Novel foods register for Great Britain, retained Regulation (EU) 2017/2470.

(2) As a percentage of total ATX. Note that the major isomer does not form part of the specification, therefore 9-cis-ATX and 13-cis-ATX together do not total 100%.

(3) As a percentage of total ATX. Free ATX is a minor component in the NF.

The carotenoid composition for the five batches at the US site complies with the current specifications set in the NF Union list, with exception for the ATX monoesters which are below the minimum, and ATX diesters which are above the maximum. The Swedish site batches also vary in the same manner (below the minimum for ATX monoesters and over the maximum for ATX diesters), in addition to 9-cis-ATX exceeding the limits in the NF Union list specification. Applicants noted that they were unable to determine the specific cause for the difference between sites, but ATX esterification can be influenced by small differences in cultivation and processing including maturation, growth media composition, light, temperature, and solvents.

The applicant used historic data to determine the proposed specification change for the NF. The change in specification for the monoesters and diesters of ATX within the NF is based upon data from 77 historical batches produced between 2014–2021, analysed in-house using HPLC in Japan ([Table 4](#)).

Table 4. Esters of astaxanthin within the novel food for 77 batches produced between 2014-2021

Ester of ATX	Current specification (% of total ATX) (1)	Minimum (% of total ATX)	Average (% of total ATX)	Maximum (% of total ATX)
Monoesters	79.8 - 91.5	66.7	74.0	81.1
Diesters	0.16 - 19.0	13.6	25.0	32.5

ATX: Astaxanthin

(1) Novel foods register for Great Britain, retained Regulation (EU) 2017/2470.

The historical data in [Table 4](#) demonstrates that the diester ratio of ATX contents typically exceed the maximum specification limit currently set by the NF Union list for this product. The FSA and FSS agree with the conclusion that the specification limits have been exceeded for this product.

The change in specification for ATX isomers within the NF is based upon data from 10 historical batches from 2013-2021, analysed in-house using HPLC in Sweden ([Table 5](#)).

Table 5. Isomers of astaxanthin within the novel food for 10 batches produced in Sweden between 2013–2021

Isomer of ATX	Current specification (% of total ATX) (1)	Minimum (% of total ATX)	Average (% of total ATX)	Maximum (% of total ATX)
9-cis-ATX	0.3-17.3 %	9.7	21.5	29.4
13-cis-ATX	0.2-7.0 %	3.1	3.8	4.7

ATX: Astaxanthin

(1) Novel foods register for Great Britain, retained Regulation (EU) 2017/2470.

The historical data in [Table 5](#) demonstrates that the 9-cis ATX contents typically exceed the maximum specification limit currently set by the NF Union list for this product. EFSA concluded that this is likely due to an extended maturation phase during cultivation of the microalgae from 8 days to 11 days. Literature was provided by the applicant demonstrating that growth media composition, light supply and temperature have influence isomerisation of ATX from the predominant trans isomer, to 9-cis and 13-cis isomer (Gong et al., 2020; Viazau et al., 2021).

The EFSA Panel noted that the relative contents of 9-cis ATX and of ATX diesters exceeded the respective specification limits in the NF Union list established in 2017 in the majority of batches. The FSA and FSS agree with this conclusion and note the 2017 version of the specification currently forms the basis for the conditions of use in the UK.

In addition, the applicant also provided additional data for some parameters which remained unchanged versus the specification in the Union list of novel foods. These were: the microbiological criteria (including total aerobic bacteria, yeast and moulds, coliforms, *E. coli*, *Salmonella* and *Staphylococcus*), which complies with Regulation (EC) No 2073/2005 on microbiological criteria for foodstuffs; the composition of heavy metals (including arsenic, lead, cadmium, mercury), which complies with Regulation (EC) No 1881/2006 on setting maximum levels for certain contaminants in foodstuffs; and a fatty acid profile.

EFSA did not raise concerns with the change in composition demonstrated by the data provided. The FSA and FSS were satisfied that the composition of the NF remains unchanged for all parameters other than the four proposed for a change in levels, and the NF complies with the current specifications for these as set out in the Union List of Authorised Novel Foods under Commission Implementing Regulation (EU) 2017/2470. For the four parameters where a change is requested, the FSA and FSS were satisfied that the compositional data matched the proposed specification change.

2.1.4. Specification

The applicant seeks to lower the minimum specification limits in the NF for the protein content (from 0.3% to 0.0%) and for ATX monoesters (from 79.8% to 66.7%; [Table 6](#)). The applicant also proposes to increase the maximum specification limits for 9-cis-ATX (from 17.3% to 30.0%), and for ATX diesters (from 19.0% to 32.5%). All other parameters in the specification remain unchanged.

Table 6. Current specifications for the NF as set by the NF Union list and changes proposed by the applicant

Parameter	Current specification (1)	Applicant's proposed specification
Fat	42.2–99 g/100 g	–
Protein	0.3–4.4 g/100 g	≤ 4.4 g/100g
Carbohydrates	0–52.8 g/100 g	–
Fibre	< 1.0 g/100 g	–
Ash	0.0–4.2 g/100 g	–
Total Astaxanthin	2.9–11.1 %	–
9-cis-ATX (2)	0.3–17.3 %	0.3–30.0 %
13-cis-ATX (2)	0.2–7.0 %	–
ATX Monoesters (3)	79.8–91.5 %	66.7–91.5 %
ATX Diesters (3)	0.16–19.0 %	0.16–32.5 %
β-carotene	0.01–0.3 %	–
Lutein	0–1.8 %	–
Canthaxanthin	0–1.30 %	–

Parameter	Current specification (1)	Applicant's proposed specification
Total aerobic bacteria (plate count)	< 3,000 CFU/g	-
Yeast	< 100 CFU/g	-
Moulds	< 100 CFU/g	-
Coliforms	< 10 CFU/g	-
<i>E. coli</i>	Negative	-
<i>Salmonella</i>	Negative	-
<i>Staphylococcus</i>	Negative	-

NF: novel food; CFU: colony forming units; ATX: astaxanthin; “-” means unchanged

(1) Novel foods register for Great Britain, retained Regulation (EU) 2017/2470.

(2) As a percentage of total astaxanthin. Note that the major isomer does not form part of the specification, therefore 9-cis-ATX and 13-cis-ATX together do not total 100%.

(3) As a percentage of total ATX. Free ATX is a minor component in the NF.

EFSA did not raise concerns with the change in specification demonstrated by the data provided. The FSA/FSS agree that the compositional data supports the proposed change in specification, and indicates that the applicant is able to comply with the new specification during production. Potential toxicological concerns related to the change in specification are addressed in the Toxicology section.

2.1.5. History of Use

Haematococcus pluvialis is a unicellular microalga that occurs naturally in the food chain. *H. pluvialis* is consumed by zooplankton and crustaceans, which in turn are consumed by other aquatic animals including fish such as trout and salmon. ATX is synthesised naturally by *H. pluvialis*, and the consumption of ATX in *H. pluvialis* by salmonoids leads to the characteristic pink colour of the flesh. In the UK diet, ATX is almost exclusively consumed through seafood.

H. pluvialis containing ATX has been used in food supplements since authorisation in Sweden in 1995 for use in food supplements, prior to the first Novel Food Regulation (EC) No 258/97 coming into effect on the 15 May 1997. The application was for ATX produced from a powder of *H. pluvialis* for use in food supplements at a maximum intake of 4 mg/day. The application was submitted by the company “AstaCarotene AB”, presently known as “AstaReal AB”, which is also the applicant for the subject of this safety assessment.

Following the 1995 authorisation by the Swedish competent authority, 10 different applicants submitted 11 notifications for oleoresins containing ATX from *H. pluvialis* based on “substantial equivalence” (SE) to the 1995 ATX product, under Article 5 of Regulation (EU) No 258/1997. These supplements are approved for food use up to 40–80 mg/day of oleoresin a day, corresponding to 4- 8 mg/day ATX (0.06 mg/kg bw) ATX per day, as per

the 1995 authorisation. AstaReal AB submitted one of these notifications for SE for oleoresin from *H. pluvialis* containing approximately 10% ATX, and the NF was authorised in 2006. This product is the subject of this assessment for a change in conditions of use to amend the specification.

The applicant has previously sought this change in conditions of use to amend the specification in the EU. This received a positive EFSA opinion in 2023 (EFSA NDA Panel et al., 2023) and has formed evidence to inform this safety assessment.

The assessment for the change in specification by the EFSA NDA Panel also used safety considerations of ATX from the EFSA FEEDAP panel, which considered ATX for use in feed. ATX is registered as a feed additive for salmon and trout. The safety of ATX in various forms for use in feed has been assessed multiple times by the FEEDAP. The most recent assessment for ATX dimethyldisuccinate for use in feed derived a new acceptable daily intake (ADI) for ATX and ATX dimethyldisuccinate based upon updated toxicology data, which established a new ADI of 0.2 mg astaxanthin/kg body weight (bw) per day (EFSA FEEDAP Panel et al., 2019).

In 2020, the EFSA NDA Panel considered that the updated ADI for ATX of 0.2 mg/kg body weight (bw) per day derived by the EFSA FEEDAP Panel in 2019 also applies to ATX from *H. pluvialis* algae for use in food supplements (EFSA NDA Panel et al., 2020). The EFSA NDA Panel also calculated estimated exposures and determined that infants, toddlers, children, and adolescents younger than 14 years would exceed the ADI of 0.2 mg kg bw/day for ATX (381-524% exceedance for infants age 4 to <6 months, 309% for toddlers age 1 to <3 years, 123% for children age 3 to <10 years, and 28% for adolescents age 10 to <14 years). The conditions under which the novel food may be used was therefore amended to exclude these groups, and specific labelling requirements were added to the NF (The European Commission, 2021).

The EFSA Panel noted that the applicant's batch-data demonstrated that there has already been exposure to increased levels of 9-cis ATX and of ATX diesters from FS, as proposed by the applicant in the specification change from the NF. In addition, the NF is produced from the same dried biomass of *H. pluvialis* authorised in 1995. The Panel therefore considers that there is a history of use of the proposed higher levels of 9-cis ATX and ATX diester contents in food supplements.

2.1.6. Proposed Use and Intake

The proposed food categories are unchanged, and the novel food is intended for use as a food supplement. The proposed target population is the general population but excluding infants, toddlers, children, and adolescents younger than 14 years. Use levels remain as 40-80 mg/day of oleoresin, resulting in ≤ 8 mg astaxanthin per day.

During their reassessment of the safety of ATX for use in food supplements, an updated exposure assessment for ATX was performed by the NDA Panel in 2020. This included combined intake of ATX from supplements and from the diet (found in fish and crustaceans) (EFSA NDA Panel et al., 2020). No other sources outside of seafood were considered by EFSA as ATX is not obtained from the diet from any other sources. Combined exposure from the diet and food supplements was below the updated 0.2 mg/kg bw/day ADI for adults, and met the ADI for 14 to <18 year old adolescents. However, the ADI in children aged 10 to 14 years was exceeded by 28% and was exceeded in infants aged 4-6 months by up to 524%. The specification change request by the applicant for this opinion is proposing that the use does not include infant children or adolescents below the age of 14 years.

The FSA and FSS agree with EFSA that exposure should be updated on the Novel foods register to exclude infants, toddlers, children, and adolescents younger than 14 years, as combined exposure from the diet and the NF would place these groups over the ADI of ATX. The Panel noted that the ADI for adolescents aged 14 to < 18 years may be exceeded, as the combined exposure assessment placed this group at very close to the ADI (at 1% exceedance). However, there is low likelihood of harm as it is unlikely that this group would consume 8 mg ATX from food supplements in combination with high dietary background intake of ATX. The FSA and FSS therefore recommend an addition to the conditions of use under which the novel food may be used to exclude infants, toddlers, children, and adolescents younger than 14 years, and that the NF should require additional labelling to state that these groups should not consume the NF.

No additional safety concerns regarding proposed use or intake were identified by EFSA for the target populations for the specification change for this NF. The FSA and FSS agree with this conclusion.

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

As the ratio of ATX diesters was increased, the applicant provided literature on the bioavailability and absorption of ATX diesters versus ATX monoesters. The FSA/FSS considered the applicant's literature and conclusions drawn by EFSA. For absorption, ATX esters are hydrolysed to

free ATX, resulting in only free ATX forms being present in tissues upon uptake in both human (Coral-Hinojosa et al., 2004; Mercke Odeberg et al., 2003) and mice studies (Zhou et al., 2019). The Panel considered that the increase in diesters would not affect the safety of the NF. The FSA/FSS agree with this conclusion.

The applicant also provided literature on the bioavailability of 9-cis ATX, as the ratio of 9-cis ATX was increased. Although data was limited, from available *in vitro* studies and studies in rodents and humans the Panel determined that the 13-cis ATX is more bioavailable than the 9-cis ATX (Honda et al., 2021; Yang et al., 2017; Zhou et al., 2019).

As such, there is no increased risk from a higher ratio of 9-cis ATX versus 13-cis ATX regarding ADME.

The EFSA assessment did not raise any safety concerns for ADME, and the FSA and FSS agree that no safety concerns were raised for ADME of the novel food.

2.1.8. Nutritional Information

No nutritional information was provided. EFSA did not consider the nutrition for the novel food as the nutritional parameters were not changed from that assessed previously for this novel food (EFSA NDA Panel et al., 2023).

FSA and FSS agree that no nutritional considerations are required for the change in specification for the novel food, as nutrition is not anticipated to be altered from that previously assessed.

2.1.9. Toxicological Information

Toxicological information on the safety of ATX was not reviewed during the original authorisation in Sweden in 1996, nor in the subsequent substantial equivalence process. More recently, an ADI for ATX has been calculated and refined through consideration of toxicological data, and this forms the basis for reviewing the changes requested by the applicant to the change in use.

Toxicity studies were considered in 2014 by the EFSA FEEDAP Panel to derive the original ADI of ATX as 0.034 mg/kg bw (EFSA FEEDAP Panel, 2014a). In this opinion, adverse liver effects were observed during a one-year chronic toxicity study using rats, and a two-year carcinogenicity study using rats. The Panel determined that adverse liver effects may have been caused by recurrent cell damage due to a hepatotoxic effect of the test compound, and subsequent cellular repair may have resulted in the dose-related increase in hepatocellular adenomas in the female rats.

A NOAEL could not be identified from the carcinogenicity study with rats; therefore a conservative benchmark dose (BMD) approach was taken using the BMD lower confidence level (BMDL) of 10 as recommended by EFSA (EFSA, 2005). There was a large uncertainty in the range of BMDL₁₀ estimates calculated, and therefore the lowest was selected to derive the ADI of 0.034 mg ATX/kg bw per day.

Upon reassessment of the safety of ATX in feed in 2019, the BMDL₁₀ approach was reconsidered by the FEEDAP Panel (EFSA FEEDAP Panel et al., 2019). Due to the large uncertainty in the range of BMDL₁₀ estimates, the FEEDAP Panel determined that the use of the lowest observed adverse effect level (LOAEL) was more appropriate than BMDL₁₀. The LOAEL for the adverse effects observed during the carcinogenicity study in rats was 40 mg ATX/kg bw per day, and the Panel applied an uncertainty factor (UF) of 100, with an additional UF of 2 for use of a LOAEL to calculate a new ADI of 0.2 mg ATX/kg bw. The FEEDAP Panel considered an additional UF of 2 acceptable since the adverse hepatocellular changes observed in female rats were reversible, at the LOAEL and were not observed in male rats, mice, or dogs.

In 2020, the EFSA NDA Panel reviewed the updated ADI for ATX of 0.2 mg/kg body weight (bw) derived by the EFSA FEEDAP Panel in 2019, and determined that this also applies to ATX from *H. pluvialis* algae for use in food supplements (EFSA NDA Panel et al., 2020).

The FSA/FSS consider the use of the LOAEL to update the ADI for ATX appropriate, and agree that the newly derived ADI of 0.2 mg ATX/kg bw can be applied to ATX for use in food supplements. This replaces the ADI established by the FEEDAP Panel in 2014 of 0.034 mg/kg bw.

EFSA has previously noted that there is a lack of evidence on potential differences in toxicity between isomers of ATX, including 9- and 13-cis isomers (EFSA FEEDAP Panel, 2014b). Therefore, the Panel assumed all ATX isomers to be of equal toxicity, and concluded that there are no additional safety concerns regarding toxicity due to an increase in the 9-cis isomer proposed for the novel food. The FSA and FSS agree that it is appropriate to assume that the toxicity of the 9-cis and 13-cis ATX isomers are equal, and therefore there are no increased toxicology safety concerns due to an increase in 9-cis-ATX.

From reviewing the applicant's literature and EFSA's conclusions, the FSA/FSS considered that there are no toxicological concerns for the change in specification for the novel food. Therefore, the FSA/FSS conclude that there were no toxicological concerns raised for the NF regarding intended intake levels of total ATX.

2.1.10. Allergenicity

No allergenicity information was provided. EFSA did not consider the allergenicity for the novel food (EFSA NDA Panel et al., 2023). The FSA/FSS note that as protein is removed from the NF in the change of specification, any allergenicity concerns would potentially be reduced.

FSA and FSS agree that no allergenicity considerations are required for the change in specification for the novel food, as allergenicity is not anticipated to be altered.

Other Regulators Opinions and Conclusions

The FSA and FSS agree with the conclusions of the EFSA Panel that the change in specification for Astaxanthin-rich oleoresin from *Haematococcus pluvialis* algae as a food supplement is safe for the target population (≥ 14 years old) under the new specification. The changes would not be nutritionally disadvantageous.

3. Uncertainties and limitations

No specific uncertainties or limitations were flagged in the assessment by EFSA.

The FSA and FSS note that for the combined exposure calculation of ATX and the NF, data for ATX exposure from the diet was obtained from the EFSA Comprehensive European Food Consumption Database, utilising data from populations within the European Union. There are limitations to the applicability of this data directly to UK populations where intake of seafood in the background diet may vary. This is relevant for the adolescent group aged 14 to < 18 years, as EFSA's calculation resulted in an exposure of approximately 0.2 mg/kg bw per day (calculated as 0.202 mg/kg bw per day) which corresponds to marginally over the ADI of 0.2 mg/kg bw per day. For a UK population, exposure in these groups could vary and combined exposure may be marginally higher than the ADI. Therefore, due to the uncertainty around the exposure calculation and the combined exposure to ATX from the diet and NF being very close to the ADI in the 14 to < 18 years group, there is uncertainty over whether the ADI may be exceeded in this group. The Panel considered that there is low likelihood of harm as it is unlikely that this group would consume 8 mg ATX from food supplements in combination with high dietary background intake of ATX from seafood.

The Panel also noted that there is a lack of evidence on potential differences in toxicity between isomers of ATX and therefore assumed that all can be considered equal. There may be differences between the isomers which are unknown, such as in their bioavailability.

The European Commission has stated that evidence from the marketplace indicates that “although food supplements containing ≤ 8.0 mg astaxanthin are currently authorised for the general population, in practice they are not used by children and adolescents but are almost exclusively used by the adult population” (The European Commission, 2021). The FSA and FSS therefore conclude that although there is a limitation in the applicability of EFSA’s combined exposure assessment to UK adolescent populations, this is unlikely to pose a safety concern for consumers.

4. FSA & FSS conclusions for GB assessment

The application has been evaluated in line with 'Guidance on the preparation and presentation of an application for authorisation of a novel food in the context of assimilated Regulation (EU) 2015/2283 (EFSA NDA Panel, presentation of an application for authorisation of a novel food in the context of assimilated Regulation (EU) 2015/2283 (EFSA NDA Panel, 2016), and assimilated Commission Implementing Regulation (EU) 2017/2469, for purposes of the GB assessment.

The conclusions of the EFSA opinion for Astaxanthin-rich oleoresin from *Haematococcus pluvialis* algae (EFSA NDA Panel et al., 2023), which have been reviewed in detail by the FSA and FSS for the purposes of the GB assessment, are considered appropriate and consistent within the uncertainties and limitations identified by EFSA.

The applicant has not requested data protection for any studies under Article 26 of Regulation (EU) 2015/2283.

5. Outcome of the assessment

The FSA and FSS have reviewed the applicant’s dossier, supporting documentation, and most notably the EFSA opinion (EFSA NDA Panel et al., 2023), and consider that there is sufficient evidence to conclude the safety assessment of Astaxanthin-rich oleoresin from *Haematococcus pluvialis* algae without obtaining further information or conducting a further risk assessment.

The FSA and FSS conclude that the change in conditions of use to amend the specification for Astaxanthin-rich oleoresin from *Haematococcus pluvialis* algae is safe under the proposed conditions of use, with the change in the target population groups to adults and adolescents ≥ 14 years old. The previous assessment of this novel food demonstrated that anticipated intake levels and the proposed use in food supplements is not considered to be nutritionally disadvantageous.

In making this assessment, the FSA and FSS were able to rely on sufficient scientific evidence to make a conclusion on safety with no further questions to the applicant, and therefore no further risk assessment activities are necessary.

Sufficient evidence was available in the literature to give the FSA and FSS confidence about the safety of this novel food, for example, where other national food safety authorities had positively assessed the application using the same risk assessment guidance and core legal requirements which apply in GB.

The applicant provided sufficient relevant information as requested by the FSA and FSS.

The FSA and FSS review did not find any issues of divergence from the EFSA guidance (EFSA NDA Panel, 2016) or mutual approaches or new scientific issues for consideration.

There were no other specific issues that would require an assessment for the UK or the nations of the UK.

Abbreviations

Abbreviation	Definition
ADI	Acceptable daily intake
ATX	Astaxanthin
BMD	Benchmark dose
BMDL	Benchmark dose lower confidence level
EFSA	European Food Safety Authority
FEEDAP	Additives and Products or Substances used in Animal Feed
LOAEL	Lowest observed adverse effect level
LOD	Limit of Detection
NDA	Panel on Nutrition, Novel Foods and Food Allergens
NF	Novel Food
NOEL	No Observed Effect Level

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