

ADVISORY COMMITTEE ON NOVEL FOODS AND PROCESSES

REQUEST FOR AN ARTICLE 5 OPINION ON THE SUBSTANTIAL EQUIVALENCE OF ASTAXANTHIN-RICH CAROTENOID OLEORESIN EXTRACTED FROM *Haematococcus pluvialis*

Applicant	US Nutra
Responsible Person	Dr Tony Evans
Application	Substantial equivalence
EC guidelines category	2.2 (the source of the NF has no history of food use in the Community)

Introduction

1. A request was submitted by US Nutra to the UK Competent Authority for an opinion on the equivalence of their astaxanthin - rich carotenoid oleoresin extracted from the algae *Haematococcus pluvialis*, using super critical carbon dioxide (CO₂) extraction, compared with the existing *H. pluvialis* astaxanthin-rich algal meal.
2. Astaxanthin is a carotenoid found in the algae *Haematococcus pluvialis* and is responsible of the pink coloration in the flesh of fish or crustaceans (e.g. salmon, shrimps), through the ingestion of astaxanthin.
3. *H.pluvialis* meal rich in astaxanthin is currently available to European consumers. A Swedish company, AstaCarotene¹, has been selling capsules containing dried *H. pluvialis* algae (Astaxin), since at least 1995.
4. The request addresses substantial equivalence in accordance with the five criteria set out in Article 3(4) of regulation 258/97: composition, nutritional value, metabolism, intended use and level of undesirable substances contained therein.

Composition

5. The applicant is claiming equivalence to the algal meal product marketed by Astacarotene (Sweden). This claim is substantiated by comparing the composition of the extract with the algal meal raw material, which in turn is equivalent to the algal meal product currently available on the EU market.

¹ Astacarotene is now owned by Fuji Chemical Industries, Japan.

6. **US Nutra extract (astaxanthin-rich carotenoid oleoresin)** - US Nutra produces its extract from a dry *H.pluvialis* algal biomass, using supercritical CO₂ extraction. This extract is composed of 89.2% fatty acids and 10.2% carotenoids of which 99% is astaxanthin. The applicant also demonstrates batch to batch consistency through the analysis of 3 lots of oleoresin complex containing 10% of astaxanthin.
7. **Comparison between the US Nutra extract and the US Nutra raw material** - The lipid and carotenoid levels found in dried *H.pluvialis* and the extract derived from it are compared. All the fatty acids are found in similar proportion in the extract and the algal meal. The carotenoid content is increased 2.5-fold, due to the absence of algal biomass in the extract. Regarding the slight change in astaxanthin isomeric ratio of the extract compared to the dried algae, safety and toxicological studies have not revealed any toxicity issue with the consumption of astaxanthin. The applicant also carried out a literature survey which did not reveal any toxicity issue with the astaxanthin skeleton based compounds.
8. **Comparison of US Nutra raw material and *H.pluvialis* algal meal currently on the EU market** - The lipid and carotenoid levels found typically in *H. pluvialis* algal meal used for the production of the extract are 20-30% and 2-4% respectively. The total astaxanthin level in the dried *H. pluvialis* biomass used by ALGAtotechnologies (3.4%-3.9% for 3 samples) is similar to the commercial specification of the existing EU product, which is manufactured in Sweden. The applicant therefore carried out further analysis on both algal meals which show that US Nutra raw material and the algal meal currently on the market contain similar levels of total astaxanthin at respectively 3.2% and 2.3%, on average. The astaxanthin isomeric ratio differs between the two algal meals, but this difference does not present any safety concerns (see para. 7).
9. The algae used by US Nutra are cultivated by a supplier who uses solar powered photobioreactors in a closed, strictly controlled system. Other suppliers are known to produce the algal meal using an indoor pond system, using different production strains.
10. The applicant provides an expert opinion stating that the phytochemical content of different strains of *H. pluvialis* are likely to be the same, if the production processes are similar. A comparison of the production methods used by the company supplying US Nutra and by the current Swedish manufacturer shows that they are very similar. This is further supported by two experts' opinions. The applicant also comments on the sources of the algal meal used by the Swedish manufacturer and has reported that the origin of *H. pluvialis* does not affect significantly the distribution of trans/cis isomers ratios of astaxanthin.

Discussion: *The Committee was satisfied that the data comparing the US Nutra extract, the US Nutra raw material and the existing algal meal shows that they are similar in composition and that levels of astaxanthin and other carotenoids are comparable. The isomeric ratios differ between these three products but the Committee accepted the applicant's argument that this would not have any adverse effects.*

Nutritional value

11. US Nutra provided a limited amount of relevant nutritional data for its extract. This is supporting information only and is not of direct relevance to the request

for substantial equivalence. The claimed nutritional value of the product lies in its carotenoid content and given the close correspondence between the levels of carotenoids in the extract and in the existing algal meal, no differences in nutritional value are expected.

Discussion: *The documentation supplied by the applicant did not address any specific benefits associated with the consumption of astaxanthin, and the Committee noted that general comments made by the applicant on the nutritional benefits of consuming carotenoids might not apply to the product in question. For example, it has been shown that high level consumption of β -carotene in supplements can increase the risk of cancer for smokers and it was not known whether other carotenoids might have a similar effect.*

Intended use

12. US Nutra astaxanthin-rich carotenoid oleoresin will be sold to dietary supplement manufacturers who will then dilute the product in a suitable carrier (e.g. olive oil) to produce capsules containing up to 5 mg of astaxanthin. This is higher than the astaxanthin level found in the Astacarotene product currently sold on the EU market. The label of the product states that there is 4 mg of astaxanthin per capsule (recommended dose: 1 capsule/day) although the applicant's analyses performed on three gave an average astaxanthin content of only 2.8mg.

13. No decrease in astaxanthin content was found in capsules containing US Nutra oleoresin, over a period of 8 and 14 months. Further data are provided in the dossier showing stability of astaxanthin extract at elevated temperatures in a "beadlet" formulation.

Discussion: *The Committee did not raise any concerns over the intended use of the oleoresin, compared with the existing product. The Committee concluded however that the daily consumption of astaxanthin should not exceed current levels. In view of this, the Committee was of the opinion that companies wishing to sell capsules containing US Nutra astaxanthin oleoresin should limit the level of incorporation to 4 mg, in line with astaxanthin levels found in existing similar products.*

Level of undesirable substances

14. No pesticide or heavy metal contamination has been detected in US Nutra oleoresin, at the limits of detection of the methods used.

15. US Nutra also provides microbiological results obtained on their product in appendix 14 of Annex A. Each count of total viable bacteria, yeast, mould, *Staphylococcus* or *Pseudomonas* is less than 10 per gram. The absence of *Salmonella* and *E.coli* is also reported in the same US Nutra oleoresin sample.

Discussion: *The Committee was satisfied with the information supplied on the level of undesirable substances in the oleoresin.*

Additional information relevant to the application

16. An unpublished eight-week trial on 42 subjects looking at the effect of oleoresin has shown that US Nutra's oleoresin had no obvious adverse effects.

Discussion: The Committee acknowledged this study but felt that these data did not provide any relevant information for the safety assessment of the oleoresin.

Conclusion

17. The Committee is content that the applicant's approach to demonstrate the equivalence of the US Nutra extract with the existing *H.pluvialis* algal meal is consistent with the criteria set in Article 3(4) of the Novel Foods Regulation (EC) 258/97. The extract is shown to be a subset of the constituents of the existing product, and that the new and existing products are being used in the same way as dietary supplements in capsule form.

18. Therefore, the astaxanthin-rich carotenoid oleoresin produced by US Nutra can be considered substantially equivalent to the existing algal meal produced by Astacarotene.

19. The data provided by US Nutra on their product relate to *H.pluvialis* algal meal produced by a single supplier. The applicant noted that they might wish in future to manufacture the extract from algal meal obtained from other manufacturers, including those who supply products that are currently on the EU market. The Committee considered that the use of extracts from *H.pluvialis* algal meal produced by other manufacturers would be acceptable, provided that the production methods and the composition of the meal and the resulting extract were similar to those described in the dossier.

15 June 2004