

ADVISORY COMMITTEE FOR NOVEL FOODS AND PROCESSES**ASTAXANTHIN EXTRACT FROM *Haematococcus pluvialis*****Issue**

The Committee is asked to consider the information provided for Astaxanthin - rich carotenoid oleoresin (Zanthin®) extracted from the algae *Haematococcus pluvialis*, using super critical carbon dioxide (CO₂) extraction. The manufacturer of this product, U.S. Nutra, requests the scientific opinion of the UK Competent Authority (CA) indicating that their extracted product should be considered substantially equivalent to *H. pluvialis* astaxanthin-rich algal meal, currently on the market in the EU.

Background

1. Astaxanthin is a carotenoid which is found in *Haematococcus pluvialis*. This microalgae is part of the diet of fish or crustaceans (e.g. salmon, shrimps) and is responsible of the pink coloration in their flesh, through the ingestion of astaxanthin.
2. The algae *H. pluvialis* is currently sold to European consumers in the form of a dried meal. A Swedish company, AstaCarotene¹, has been selling capsules containing dried *H. pluvialis* algae (Astaxin), since at least 1995.
3. US Nutra has applied to the UK CA for an opinion on the equivalence of its algal extract with Astacarotene's algal meal, under Article 3(4) of EC Regulation 258/97 (Dossier in Annex A).
4. Regulation (EC) 258/97 makes provision for novel foods or ingredients that are substantially equivalent to an existing product to be placed on the market once the applicant has notified the Commission. In all cases to date, the Commission has required that the applicant first obtain an opinion on equivalence from a Member State. US Nutra are requesting such an opinion from the UK CA.
5. According to Article 3(4) of (EC) 258/97, the notification procedure applies to "foods or food ingredients ...which on the basis of the scientific evidence available and generally recognised or on the basis of an opinion delivered by one of the competent bodies ... are substantially equivalent to existing foods or food ingredients as regards their:

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

- composition,
- nutritional value,
- metabolism,
- intended use and
- level of undesirable substances contained therein”.

Evaluation

6. Composition²

- 6.1. 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. US Nutra has included information on the sale of *H. pluvialis* algal meal prior to 1997 in the EU (Annex A, appendix 13). The Secretariat has advised the applicant that this approach is consistent with the criteria mentioned in paragraph 5 above, provided that 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.
- 6.2. **Astaxanthin-rich carotenoid oleoresin** - US Nutra produce their extract (referred to in the application as an oleoresin) from a dry *H.pluvialis* algae biomass, using supercritical CO₂ extraction (Annex A, appendix 8). This extract is composed of 89.2% fatty acids and 10.2% carotenoids of which 99% is astaxanthin (Annex A, p.5, tables 3 & 4 and appendix 1). Batch to batch consistency is shown by analysis of 3 additional batches (appendix 10 of Annex A).
- 6.3. **Comparison between the extract and the raw material (*H. pluvialis* from ALGATECHNOLOGIES, Israel)** - In appendix 2 of the dossier, 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 algal meal and the extract. The carotenoid content is increased 2.5-fold, due to the absence of algal biomass in the extract (Annex A, p.7). The applicant is of the view that the slight change in isomeric ratio of the extract compared to the dried algae (Annex A, appendix 2) does not present any safety concerns and does not have any toxicological significance (Annex A, appendix 16).
- 6.4. **Comparison of US Nutra raw material (*H. pluvialis* from ALGATECHNOLOGIES, Israel) and Astacarotene algal meal (Sweden)** - The lipid and carotenoid levels found typically in *H. pluvialis* algal meal used for the production of the extract are respectively of 20-30% and 2-4% (Annex A, appendix 8). The total astaxanthin level in the dried *H. pluvialis* biomass used by ALGATECHNOLOGIES (3.4%-3.9% for 3 samples) is similar to that found in Astacarotene (>3.4%) although this comparison is based on the

² Analytical protocols used by US Nutra for the measurement of astaxanthin and carotenoids levels of *H.pluvialis* algae meal and Zanthin can be found in Annex A, appendix 3.

commercial specification of the latter product rather than analysis of the actual product (Annex A, p.10, appendices 6&7 for ALGAtotechnologies, appendix 12 for Astacarotene). The applicant has been asked to provide analytical data on the EU product and these will be provided to the Committee at or before its meeting.

6.5. The applicant has also provided 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 (Annex A, appendix 17). The applicant has also commented on the sources of the algal meal used by the Swedish manufacturer (Annex A, section 2.3.2 & confidential information in appendix 18) and has reported that the origin of *H. pluvialis* does not affect significantly the distribution of trans/cis isomers ratios of astaxanthin (Annex A-5, table 2).

7. Algal culture

7.1. The algae *H. pluvialis* used by US Nutra are cultivated by ALGAtotechnologies (Israel) in a solar powered photobioreactor in a closed strictly controlled system and (confidential information in Annex A, appendix 4). Other suppliers are known to produce the algal meal using an indoor pond system, and possibly using different production strains.

7.2. Given these variations, the expert opinion provided in appendix 17 of the dossier notes that “astaxanthin derived from *H. pluvialis* would be substantially equivalent regardless of the strain used to produce it, provided the production methods used were very similar in most regards”. Appendix 19 of the dossier (confidential information) provides a comparison of the production methods used by Algatechnologies (Israel) and Astacarotene (Sweden) and concludes that they are very similar for both sources of *H. pluvialis*. This is further supported by two experts' opinions in Annex A, appendix 20 (confidential information).

8. Nutritional value

8.1. US Nutra has provided a limited amount of relevant nutritional data for its extract (Annex A –14). 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 would be expected.

9. Intended use

9.1. 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 equivalent to the astaxanthin level found in algal meal dietary supplements currently sold on the EU market.

9.2. No decrease in astaxanthin content was found in capsules containing US Nutra oleoresin, over a period of 8 and 14 months (Annex A, appendix 11). Further data are provided in appendix 11a, showing stability of astaxanthin extract at elevated temperatures in a "beadlet" formulation.

10. Level of undesirable substances

10.1. No pesticide or heavy metal contamination has been detected in US Nutra oleoresin, at the limits of detection of the methods used. (Annex A, appendix 9).

10.2. US Nutra has also provided 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* was also reported in the same US Nutra oleoresin sample.

11. Additional information

11.1. An eight week trial looking at the immune boosting effect of oleoresin has shown that US Nutra's oleoresin had no deleterious effect on the human immune system (Annex A, appendix 15).

Committee action required

12. The Committee is asked if it has any objections or comments to raise and whether it is content to agree the substantial equivalence of US Nutra astaxanthin-rich extract derived from *H. pluvialis* to the existing dried algal meal of from *H. pluvialis* marketed in the EU, in accordance with Article 3(4) of regulation (EC) 258/97.

13. If not, the Committee is asked what additional information the applicant could supply in order to demonstrate equivalence.

**Secretariat
February 2004**

Annexes attached:

Annex A – Application dossier from US Nutra
(Note: Appendices 4,5,8 and 18-20 contain confidential information related to manufacturing processes and commercial transactions)

Available on request:

Appendix 13 to the dossier (documentation, largely in Swedish, showing the use of algal meal as a dietary supplement prior to 1997)