

ADVISORY COMMITTEE ON NOVEL FOODS AND PROCESSES**ZEAXANTHIN****Issue**

Bioresco has provided a response to the concerns raised by the Committee at their September 2005 meeting, when they considered the initial opinion from the Dutch Competent Authority on this company's application for authorisation of zeaxanthin as a novel food ingredient. Members are asked if this response is satisfactory.

Background

1. Zeaxanthin is a fat-soluble xanthophyll pigment that is naturally present in some fruit, vegetables and flowers. Zeaxanthin and the closely related pigment lutein are the most common xanthophylls present naturally in food.
2. On 1 August 2005, the European Commission forwarded to Member States the Dutch Competent Authority (CA)'s initial opinion on the application made under Article 4(1) of Regulation (EC) No 258/97 submitted by Bioresco, on behalf of DSM Nutritional Products, for the authorisation of zeaxanthin as a novel food ingredient (NI).
3. The Committee considered the application and the Dutch initial opinion at their September 2005 meeting (ACNFP/73/4) and agreed with the conclusions of the Dutch CA that it was not possible to complete the safety assessment of zeaxanthin without a list of the proposed food uses. Members raised three further comments which are outlined in a letter sent to the Commission on 13 October 2005 (Appendix A), related to:
 - the stability of zeaxanthin in foodstuffs,
 - the absence of safety data on high level consumers such as elderly people, and
 - the need to evaluate the implication of the formation of "polarising structures" in the eyes of tested animals given high doses of zeaxanthin in relation to high level consumers.
4. Four other Member States (Austria, Germany, Greece and Portugal) provided comments on the Dutch initial opinion. The applicant has provided a response to answer all Member States' concerns (Appendices B and C). A summary of the comments received from all Member States can be found in tables 1 and 2 of Appendix B. However, in this paper, the Secretariat has focused on the responses to the UK concerns.

Applicant's response

(i) Stability of zeaxanthin in foodstuffs

Appendices B p.9-10 and D p.3-7 **CONFIDENTIAL**

5. The applicant has provided the following information to clarify the stability of the NI during the shelf-life of the food products to which it has been added:
 - Data provided in the original application dossier (section 3.5.4) shows that the NI used in the form of beadlets was stable in a biscuit during baking (15 min, 180°C),
 - Supplementary information was submitted to the Dutch CA to demonstrate the stability of the NI in foodstuffs (see Appendix D, section 1.3). This explains that the apparent degradation of up to 10% in model foods may be an artefact of the precision of the analytical method, which has a margin of error of 10% in formulated foods. The applicant reports that "The zeaxanthin values found are all within this margin of error and a time-related decrease in zeaxanthin is hardly apparent within the shelf-life of the product, except perhaps for zeaxanthin containing tablets". (Appendix D, page 6)
 - The applicant notes that that stability of the NI in different food products may vary with the composition of the individual food and its storage conditions. Through the use of Good Manufacturing Practice, food manufacturers would determine the shelf life of their products in order to avoid excessive degradation of the NI. (Appendix B, pages 9-10)

(ii) Absence of safety data on high level consumers such as elderly people

Appendix C **CONFIDENTIAL**

6. The applicant is unaware of a genetic, metabolic or medical condition that would lower the ADI of this substance below the 2 mg/kg bw/d proposed by JECFA or the upper end of the "Adequate Intake" range of 20 mg/person/d as proposed in their application dossier. It is a general principle that ADIs for food additives are set at a level that provides a suitable safety margin for all sections of the population (except young infants).
7. The applicant has concluded that the ADI of zeaxanthin (which is 6-fold higher than the proposed Adequate Intake) is extremely unlikely to be exceeded, even by subgroups of the population (e.g., elderly persons) who may consume zeaxanthin containing products more often than the average consumer.

(iii) Evaluate the implication of the formation of "polarising structures" in the eyes of tested animals given high doses of zeaxanthin in relation to high level consumers

Appendix B p.5-6 **CONFIDENTIAL**

8. The applicant notes the Committee's comment which relates to the study cited on pages 72-76 of the original dossier and repeats the point made in the dossier that since the incidence and severity of the polarising structures were not treatment or dose related, no toxicological significance was attributed to this observation.

Information on intended food uses and level of incorporation

Appendices B p.10-12 and D p.7-8 **CONFIDENTIAL**

9. The NI will be sold in two stable forms: as a powder preparation (“beadlets”) with either a modified starch or corn-starch base (5% zeaxanthin content) or as a corn oil suspension (20% zeaxanthin). The applicant will market this food ingredient for incorporation into food supplements, foods intended for a particular nutritional purpose (PARNUTS) and foods with added vitamins, minerals and/or other nutrients. The applicant has not provided a list of intended food uses and levels of incorporation, but highlights that the proposed food uses are similar to the uses of vitamins and minerals which can be added to foodstuffs without maximum limits of use expressed in mg/kg of food.
10. The applicant has proposed a range of ‘Adequate Intake’ for zeaxanthin of 2-20mg/day, and considers that intake above 20 mg/day results in little additional uptake of zeaxanthin and provides no additional benefit. This range is below the group ADI of 0-2 mg/kg bw allocated by JECFA for the combined intake of zeaxanthin and lutein at its 63rd meeting.
11. The applicant does not accept that estimation of the daily intake of a novel ingredient, based on proposed food uses and levels of incorporation, is a necessary part of the risk assessment. In their view, it is the objective of the risk assessors to determine whether intakes within the proposed range would cause a significant risk to human health, and it is for the risk managers to define measures that would prevent over-consumption of the NI. The applicant notes that EFSA has recently determined tolerable upper levels for vitamins and minerals based on the available safety data but detailed lists of food uses for these substances have not been established. The applicant is of the view that the same approach should be applied to zeaxanthin.

Committee Action Sought

12. The Committee is asked whether the applicant's response is sufficient to adequately address their earlier questions and concerns in relation to
 - (a) stability;
 - (b) intake by high level consumers;
 - (c) ocular effects;
 - (d) proposed food uses and levels of incorporation.

**Secretariat
March 2006**

Appendices attached

Appendix A: Letter to the Commission with the ACNFP's comments on the Dutch Competent Authority's Initial opinion

Appendix B: Applicant's response of 2nd February 2006 (**Confidential**)

Appendix C: Applicant's response of 20 February 2006 to the specific point relating to 'at risk groups' (**Confidential**)

Appendix D: Supplementary information for the evaluation of Zeaxanthin as a novel ingredient under Regulation (EC) 258/97. (**Confidential**)

ACNFP/76/2 Appendix A

ADVISORY COMMITTEE ON NOVEL FOODS AND PROCESSES

Letter to the Commission with the ACNFP's comments on the Dutch Competent Authority's Initial opinion.

**Secretariat
March 2006**

Mr A Klepsch
European Commission
DG-SANCO
Rue De La Loi 200
Brussels
Belgium B-1049

13 October 2005

Reference: NFU 518

Dear Mr Klepsch,

**Application under (EC) 258 / 97 for the novel food ingredient Zeaxanthin
(Bioresco, on behalf of DSM Nutritional Products)**

As the UK Competent Authority (CA), the Food Standards Agency has sought advice from the Advisory Committee on Novel Foods and Processes (ACNFP) on the initial assessment report prepared by the Dutch CA for the above product, at the Committee's meeting on 29 September 2005.

The UK agrees with the conclusions of the Dutch CA that an additional assessment of zeaxanthin is required because the applicant has not provided information on intended products and levels of incorporation. We would also like to highlight the following points for consideration in an additional assessment by EFSA:

1. Whilst the Committee noted that the stability data for zeaxanthin showed that it was stable in a range of food matrices, there was nevertheless measurable degradation during the shelf life of the products. Members suggested that the shelf life should be limited in order to avoid significant reduction in the quantity of zeaxanthin present in the consumed product.



2. Members noted that the applicant had not considered whether there were particular “at risk” groups of the population including those who, as a result of the perceived health benefits attributed to the consumption of this novel ingredient, could be particularly high consumers. Members highlighted elderly people as likely high level consumers and suggested that special consideration be given to this user group.
3. The Committee noted that the study cited on pages 72-76 of the dossier found no crystal formation in the eyes of animals given high doses of zeaxanthin, but it revealed unexpected findings described as “polarising structures”. The Committee requested that this issue be evaluated further to determine whether there are implications, especially for the high user group described in point 2.

In conclusion, the UK CA agrees with the initial assessment report from the Netherlands that the assessment cannot be completed without information relating to the intended uses and we ask that the points raised above be taken into account in the further assessment of this application.

Yours sincerely

[Sent by email]

Dr Sandy Lawrie
Novel Foods, Additives and Supplements Division