Call for data relevant to the safety assessment of Astaxanthin in the framework of Regulation 2283/2015

EFSA-Q-number:	**EFSA-Q-2018-00595**
Published:	**25/07/2018**
Deadline for registering interest for submission:	**20/09/2018**
Deadline for submission of data:	**20/12/2018**
Updated deadline for submission of data:	**15/02/2019**

Background

In 2014, the EFSA NDA Panel assessed the safety of the Novel Food (NF) astaxanthin-rich ingredient derived from microalgae *Haematococcus (H.) pluvialis* in the context of an application submitted under Regulation (EC) No 258/1997 (EFSA NDA Panel, 2014a)[1]. In that Opinion, the Panel noted that the proposed maximum daily intake of 4 mg (0.06 mg/kg bodyweight (bw) for an adult weighing 70 kg) exceeded the acceptable daily intake (ADI) for astaxanthin of 0.034 mg/kg bw per day (corresponding to approximately 2.4 mg for an adult person). This ADI was established by the EFSA FEEDAP Panel (2014b)[2] and was based on a benchmark dose (BMD) lower confidence limit for a 10 % extra risk ($BMDL_{10}$) calculated for the liver hypertrophy observed in female rats in a chronic toxicity/carcinogenicity study with synthetic astaxanthin and by applying an uncertainty factor of 100 to the $BMDL_{10}$ of 3.4 mg/kg bw. In this study statistically significant increased incidences of hepatocellular vacuolation, hepatocellular hypertrophy and multinuclear hepatocytes were observed in female rats at all tested dose levels (i.e. 40, 200 and 1,000 mg synthetic astaxanthin per kg bw). Also statistically significant increased incidences of hepatocellular adenomas in females were reported for the mid and high dose groups of female rats in this study. The absence of genotoxicity of astaxanthin was noted in both EFSA Opinions from 2014.

In a mandate dated 27/02/2018[3], the European Commission (EC) informed EFSA that under Commission Implementing Regulation (EU) 2017/2470 establishing the Union list[4] of authorised novel foods in accordance with Regulation (EU) 2015/2283[5], an astaxanthin-rich ingredient from *H. pluvialis* algae is authorised in food supplements at levels of up to 40-80 mg/day, which correspond to a maximum authorised level of 8 mg astaxanthin per day. The EC also informed that since 1995 when astaxanthin was granted authorisation in food supplements at the maximum level of 8 mg/day in

[1] https://www.efsa.europa.eu/it/efsajournal/pub/3757
[2] https://www.efsa.europa.eu/it/efsajournal/pub/3724
[3] http://registerofquestions.efsa.europa.eu/roqFrontend/questionLoader?question=EFSA-Q-2018-00247
[4] https://eur-lex.europa.eu/legal-content/EN/TXT/HTML/?uri=CELEX:32017R2470&from=EN
[5] https://eur-lex.europa.eu/legal-content/en/TXT/?uri=CELEX%3A32015R2283

Sweden, a number of notifications of astaxanthin pursuant to Article 5 of Regulation (EC) No 258/1997[6] on novel foods were sent to the EC.

In accordance with Article 29(1) of Regulation (EC) No 178/2002[7], the EC tasked EFSA to evaluate whether the safety of astaxanthin used as a NF in food supplements at maximum levels of 8 mg/day is still in accordance with the requirements of Regulation (EU) 2015/2283[8], taking into account the overall, cumulative intakes of astaxanthin from all sources, including from its approved uses in food supplements and in other foods. In doing so, EFSA should solicit and make use of the most recent toxicological and exposure evidence which may be available to business operators and in the public domain.

Overall objective

The purpose of this call for data is to provide the opportunity for stakeholders and other interested parties to submit studies (published, unpublished or newly generated) relevant for the evaluation of the safety of astaxanthin. In particular, EFSA seeks data which may be suitable to confirm or amend the ADI established by EFSA in 2014.

Deadline for submission of data and disclosure of contact details

Interested parties and stakeholders should provide **by the updated deadline of 15/02/2019** the information described below.

To assist our planning for assessment purpose, if you intend to supply information after **20/09/2018** please e-mail to **nda_callfordata@efsa.europa.eu** your intention to submit the requested information within the timeline specified above or any proposal for a new deadline providing justified reasons. Depending on the replies received the final deadline will be communicated to you through e-mail and by updating the current call.

Information not submitted within the final deadline will only exceptionally be considered and EFSA can decide to finalise its opinion solely on the basis of the information provided within the final deadline (20/12/2018).

In order to facilitate the collaboration of all interested parties to provide the data needed, we are seeking your consent to disclose your personal data (name, e-mail address and telephone number) to the other parties that have expressed an interest to provide the requested information. If you do not wish to make your contact details available, clearly indicate it in your first communication.

Information sought

EFSA kindly invites business operators and other interested parties (governments, interested organisations, universities, research institutions, and companies) to submit data concerning astaxanthin in relation to:

- its natural occurrence in foods other than food supplements;
- intake estimates (oral exposure) in humans;
- kinetic studies (absorption, distribution, metabolism, excretion) in rats and humans;
- mechanistic studies, in particular regarding hepatic adverse effects of astaxanthin;

[6] https://eur-lex.europa.eu/legal-content/EN/TXT/HTML/?uri=CELEX:31997R0258&from=EN
[7] https://eur-lex.europa.eu/legal-content/EN/TXT/HTML/?uri=CELEX:32002R0178&from=EN
[8] https://eur-lex.europa.eu/legal-content/EN/TXT/HTML/?uri=CELEX:32015R2283&from=EN

- animal toxicity studies, particularly chronic and carcinogenicity studies, human data, in particular studies which included liver-related endpoints (e.g. blood markers such as liver enzymes, bilirubin, total protein, albumin, triglycerides, cholesterol, urea nitrogen, activated partial thromboplastin and prothrombin times);
- other information which may be relevant to confirm or amend the acceptable daily intake (ADI) established by EFSA in 2014.

(Note: EFSA does not seek studies on supposed potential benefits of astaxanthin for health)

Confidentiality

In order to comply with its requirements for transparency as outlined in Article 38 of Regulation (EC) No 178/2002[9] as well as in Regulation (EU) No 2015/2283, EFSA has to disclose in its published scientific opinions data received/available which are considered essential for the scientific assessment, as well as background information supporting the relevant scientific reasoning. However, according to Article 39(1) of Regulation (EC) No 178/2002 EFSA may not divulge to third parties confidential information received for which confidential treatment has been requested, justified, and agreed, except for information which must be made public if circumstances so require, in order to protect public health, or whenever its conclusions highlight foreseeable adverse health effects. Furthermore, EFSA is subject to Regulation (EC) No 1049/2001 regarding public access to European Parliament, Council and Commission documents.[10]

Therefore, business operators or interested parties submitting relevant datasets in response to this call are requested to proactively clearly identify as part of their submission all parts or bits of information or data they consider as deserving confidential treatment. For each item for which a claim for confidential treatment is submitted, the concerned individual has to provide verifiable justification supporting each claim by indicating the reasons and circumstances proving why the disclosure of these elements would cause them financial harm.

Confidential status ensures that EFSA does not disclose to the public the information or dataset to which it is granted.

A decision is taken by EFSA on each confidentiality claim submitted by concerned individuals. Confidential status may be granted to information the disclosure of which might significantly harm the competitive position of business operators or other interested parties.

Interested business operators or other interested parties will be informed by EFSA about which information or data will be granted confidential treatment, and on the legal remedies available thereto should a decision rejecting their confidentiality claims be taken.

[9] Regulation (EC) No 178/2002 of the European Parliament and of the Council of 28 January 2002 laying down the general principles and requirements of food law, establishing the European Food Safety Authority and laying down procedures in matters of food safety, as last amended.

[10] Regulation (EC) No 1049/2001 of the European Parliament and of the Council of 30 May 2001 regarding public access to European Parliament, Council and Commission documents, OJ L 145, 31.5.2001, p. 43–48.

Submission of information

Interested business operators and/or interested parties should submit the information to EFSA in **electronic form** (searchable files, including PDFs) to **nda_callfordata@efsa.europa.eu** including the supporting documents listed below. Alternatively, the information can be provided using data storage devices such as memory sticks, CD-ROMs, DVDs, etc. to be sent to the address provided below.

In both cases, the information should be submitted together with the supporting documents listed below:

Mandatory

- cover letter stating:
  - the reference to the specific call for data (EFSA-Q-2018-00595);
  - the contact details[11] (name of contact person, name of company/organisation, e-mail address and telephone number) of the person responsible for the data submission and, if applicable, the list of interested business operators and/or interested parties represented and their contact details;
- statement of the legal representative of the submitter that they hold all the necessary rights to grant EFSA permission to use and, where appropriate, to disclose, the submitted information, data, document, paper or study for the purposes defined in this call. In case the submitter does not enjoy the necessary rights for these data or studies, they should share the contact details of the respective owner(s) of data and/or of the relevant intellectual property right, so that EFSA may seek their approval directly;

Optional

- separate folders with any relevant confidentiality claim they have on the submitted information or data. Information or data for which a confidentiality claim is submitted should be kept to a minimum, and shall be supported by verifiable evidence composed of precise and factual information or, ideally, documents proving that the disclosure of the information would result in concrete harm to the commercial or economic interest of the concerned individual, or would undermine the protection of privacy and the integrity of the concerned individual. Note that the information described in article 23(4) of the Novel Foods Regulation[12] cannot be claimed confidential;
- the consent that EFSA may share the data or information submitted with the European Commission/member states national authorities dealing with novel foods applications;
- the explicit and written decision of the data owner to donate the information or data to EFSA. By donating to EFSA the submitted information or data, the concerned operator or interested party waives any right on the relevant information or data.

[11] The interested parties shall notify EFSA of any change in the contact details by sending an e-mail to **nda_callfordata@efsa.europa.eu**

[12] https://eur-lex.europa.eu/legal-content/EN/TXT/HTML/?uri=CELEX:32015R2283&from=E

Contact details for submission of information/data

It is recommended that submissions are sent electronically to the following e-mail address: **nda_callfordata@efsa.europa.eu**

Please use the same e-mail address for enquiries and further clarifications.

Alternatively, submissions on data storage devices (e.g. CD, DVD, memory stick, etc.) may be sent to the following address:

European Food Safety Authority
Nutrition Unit
Via Carlo Magno 1/a
I-43126 Parma
Italy