Call for scientific and technical data on the permitted food additive processed Eucheuma seaweed (E 407a)

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Deadline for step 1 (Registration of the contact details of business operators interested in submitting data): 30 November 2018

Deadline for step 2 (Confirmation of data submission, deadlines and milestones): 31 January 2019

Background

According to Article 32 of Regulation (EC) No 1333/2008[1], food additives permitted in the EU before 20 January 2009 should be subject to a new risk assessment by the European Food Safety Authority (EFSA). The programme for the re-evaluation of these permitted food additives has been set up by Commission Regulation (EU) No 257/2010[2].

So far EFSA has not identified a major safety concern (such as a proven carcinogenic or genotoxic activity) for any of the re-evaluated food additives. In fact, in most cases EFSA confirms the safety of those food additives at their currently reported uses and use levels. However, for some additives EFSA has identified issues that require a follow-up. Additional specific data is needed to address those issues.

The additives whose safety re-evaluation by EFSA was hindered by limited data availability, but which are not expected to pose an immediate food safety concern, are not going to be immediately removed from the Union list of permitted additives, or their uses and/or use levels revised. Instead, business operators are requested to indicate to the Commission their interest in the continuity of approval of the additive(s) under re-evaluation and in providing, by a certain deadline, the data needed by EFSA to complete its risk assessment. In general, new toxicological studies will be needed to generate these missing data.

Once EFSA has assessed the new data, the current authorisation of the additive(s) may be revised, if needed.

If business operators do not provide the requested data (by the predefined deadline) the present authorisation will be revised based on EFSA's current scientific opinion and the additive(s) may be removed from the Union list of permitted additives. The same applies if the new data submitted is not sufficient for EFSA to conclude the risk assessment, since there will be no successive requests for additional data.

Food additives for which EFSA has identified concerns in terms of exposure or specifications will be subject to the same follow-up approach, but EFSA's assessment of the new data may not always be needed.

The Commission will undertake that the time assigned for addressing issues identified by EFSA is as short as possible and dependent on the time needed to generate and assess the required new data.

[1] OJ L 354, 31.12.2008, p. 16.
[2] OJ L 80, 26.3.2010, p. 19.

EFSA's Scientific Opinion on the re-evaluation of carrageenan (E 407) and processed Eucheuma seaweed (E 407a) as food additives

EFSA's Panel on Food Additives and Nutrient Sources added to Food (ANS) delivered a scientific opinion re-evaluating the safety of carrageenan (E 407) and processed Eucheuma seaweed (E 407a) when used as food additives[3].

Because of the structural similarities, the Panel concluded that processed Eucheuma seaweed can be included in the evaluation of food-grade carrageenan.

In its evaluation of carrageenan (E 407) and processed Eucheuma seaweed (E 407a), the Panel noted that the ADME database was sufficient to conclude that carrageenan was not absorbed intact. In a subchronic toxicity study performed with carrageenan almost complying with the EU specification for E 407 in rats, the no-observed-adverse-effect level (NOAEL) was 3,400–3,900 mg/kg body weight (bw) per day, the highest dose tested. No adverse effects have been detected in chronic toxicity studies with carrageenan in rats up to 7,500 mg/kg bw per day, the highest dose tested. There was no concern with respect to the carcinogenicity of carrageenan. Carrageenan and processed Eucheuma seaweed did not raise a concern with respect to genotoxicity. The NOAEL of sodium and calcium carrageenan for prenatal developmental dietary toxicity studies were the highest dose tested. Furthermore, the Panel concluded that the safety of processed Eucheuma seaweed was sufficiently covered by the toxicological evaluation of carrageenan. Data were adequate for a refined exposure assessment for 41 out of 79 food categories.

However, the Panel noted uncertainties as regards the chemistry, the exposure assessment and biological and toxicological data. Overall, taking into account the lack of adequate data to address these uncertainties, the Panel concluded that the existing group acceptable daily intake (ADI) for carrageenan (E 407) and processed Eucheuma seaweed (E 407a) of 75 mg/kg bw per day should be considered temporary, while the database should be improved within 5 years after publication of this opinion

Overall purpose of this call for data

To give the opportunity to business operators to submit the scientific and technical data needed to address issues identified by EFSA in the re-evaluation of the safety of processed Eucheuma seaweed (E 407a) as a food additive. The data gaps identified by EFSA for carrageenan (E 407) are the subject of a call for data issued by EFSA on 10 October 2018, in the context of its upcoming risk assessment of carrageenan (E 407) for uses in food for young infants (see https://www.efsa.europa.eu/en/consultations/call/181010-0). Therefore, specific data requirements for all uses of carrageenan (E 407) are included in that call for data.

It should be noted that this call for data does not cover data on uses and use levels needed to address EFSA's recommendations about the definition of numerical maximum permitted levels for all food authorised uses, as well as the refining of the exposure assessment for E 407a. Those data will be the subject of a specific call for data.

Scientific and technical data required

The data required to address the various issues identified by EFSA in the re-evaluation of the safety of processed Eucheuma seaweed (E 407a) as a food additive are the following:

1. **Technical data**

- The characterisation of all commercial preparations marketed as food additive E 407(a) from five non- consecutive batches of each preparation, in relation to:

[3] https://www.efsa.europa.eu/en/efsajournal/pub/5238

- the characterisation of carrageenan (the weight ratio of the κ-, ι- and λ- carrageenan);
- the full molecular weight distribution. In addition, the weight- and number-average molecular weight range as calculated for each of the batches of processed Eucheuma seaweed (E 407a) should be provided;

- an interlaboratory validated analytical method to detect low molecular weight in commercial preparations of processed Eucheuma seaweed (E 407a) at the limit specified in the Commission Regulation (EU) No 231/2012 (5% for the fraction below 50 kDa);
- the stability of processed Eucheuma seaweed (E 407a) in food, addressing the usual variation of parameters (temperature, pH) relevant for the authorised food uses. In particular, information on possible degradation products under acidic conditions in relevant food products is needed; detailed analytical data on the stability of these food additives in different food matrices including those with low pH (e.g. FC 12.3), and taking into account the influence of heat during food processing and storage (FC 2.3, 4.2.2, 4.2.4.1, 11.2);
- analytical data on current levels of lead, mercury, cadmium and arsenic in commercial samples of the food additive 407a;
- the lowest technologically achievable level for lead, mercury, cadmium and arsenic in order to adequately define their maximum limits in the specifications for E 407a.

Specific data on the methods of analysis used for the generation of the technical data requested above. These include but are not limited to e.g. the principle of the method, the scope of the method (i.e. the range of sample types that the method is used for), the concentration units used to express the analytical result(s), validation of the method (in particular limit of detection (LOD) and (LOQ).

2. Biological and Toxicological data

Data are sought primarily for the different carrageenan preparations used as food additive, whereby specifications of test preparations should meet the EU specifications (Commission Regulation (EU) No 231/2012). The test preparations should be characterized with respect to the weight ratio of the κ-,ι- and λ- carrageenan and the full molecular weight distribution.

These data should address the uncertainties in the biological and toxicological data as identified by the ANS Panel:

- the lack of reliable comparative toxicokinetic and toxicological studies between the different types of carrageenan and their corresponding low molecular weight fractions;
- the theoretical possibility that limited degradation could occur under conditions representative of the in vivo situation;
- the conclusion on the other types of carrageenan that could be drawn for the observation of occult blood in faeces of rhesus monkeys dosed with a commercial carrageenan (κ/λ-carrageenan types at a ratio of 70:30 from *Chondrus crispus*);
- the limitations of the characterisation of the test material in most of the toxicological studies was limited;
- the lack of adequate toxicological studies performed with low weight-average molecular weight carrageenan (around 200 kDa), apart from one 90-day study (with an average molecular weight carrageenan in the range of 196–257 kDa, not specified if it was a number average or a weight-average);
- the testing of carrageenan preparations for chronic toxicity and reproductive and developmental toxicity. Tests were performed almost exclusively with κ/λ-carrageenan; almost no data on ι-carrageenan was available;
- the inadequate data on the possible relevance of carrageenan exposure for existing

inflammatory bowel diseases in humans;

- the unclear relevance for humans of observations in animal studies pointing to the induction of glucose intolerance and glucosuria by carrageenan;
- the possible role of sulfate and the interactions of the various forms of carrageenans with the gut microflora in some of the reported inflammatory effects of carrageenans.

It should be noted that for the toxicological evaluation of processed Eucheuma seaweed (E 407a) read across can be made from study results used in the toxicological evaluation of carrageenan (E 407).

EFSA's "Guidance for submission for food additive evaluations"[4] provides a description of the data requirements for the evaluation of the safety of a food additive and therefore it will be useful to clarify the nature of the data requested. Also EFSA's scientific report on "Indicative timelines for submitting additional or supplementary information to EFSA during the risk assessment process of regulated products"[5] could be useful.

Procedure of the call for data

Step 1: Registration of the contact details of business operators interested in submitting data

Business operators are requested to communicate to the Commission **by 30 November 2018** whether they are interested that processed Eucheuma seaweed (E 407a) remains permitted in the EU and therefore whether they are interested in providing the new data required. This communication should include the contact details of the business operator (name of business operator and postal address), as well as a clear indication of which of the requested data the business operator would be interested in providing. This communication should be submitted to the email address Sante-E2-Additives@ec.europa.eu.

Once the deadline for step 1 has elapsed, the Commission will make publicly available (on DG SANTE's website on food additives[6]) the list of business operators having expressed interest in submitting the data required. This aims at facilitating interactions among business operators and a possible coordinated action in the generation and submission of data.

Communication of interest to submit data would be considered as permission for the Commission to include the details of the party concerned in a list to be published online. In case a party objects to the online publication of its contact details, this should be mentioned on the first communication to the Commission.

Step 2: Confirmation of data submission, deadlines and milestones

Business operators are requested to confirm **by 31 January 2019** their intention to submit the new data required and to provide a list of the data they intend to submit, a timeline for submission of those data as well as a justification for that timeline. When appropriate, the timeline should be in line with EFSA's Scientific Report on "Indicative timelines for submitting additional or supplementary information to EFSA during the risk assessment process of regulated products". Business operators are also requested to provide a list of intermediate milestones of the data generation and when they will be achieved. This communication should be sent to the email address Sante-E2-Additives@ec.europa.eu.

[4] http://www.efsa.europa.eu/sites/default/files/scientific_output/files/main_documents/2760.pdf
[5] http://www.efsa.europa.eu/sites/default/files/scientific_output/files/main_documents/3553.pdf
[6] http://ec.europa.eu/food/safety/food_improvement_agents/additives/re-evaluation/index_en.htm

The Commission will acknowledge receipt of this confirmation of data submission and will confirm the proposed timetable for data submission as well as the defined milestones and their time scheduling. Business operators will be requested to keep the Commission informed of the timely achievement of these milestones.

After completion of this step (step 2), the data to be submitted and both deadlines and milestones will be published on the DG SANTE's website[7].

Submission of the required data

Business operators are requested to submit the above-indicated data by the agreed deadline in one paper and two electronic copies (standard physical medium such as CD, DVD or USB flash drive). Common electronic formats should be used (e.g. MS Office, Adobe Acrobat Reader) allowing content copying and printing (no content copy protection). The text of the files should be searchable using the search facilities of standard software packages. The submission should include a cover letter stating clearly in the subject line the food additive(s) to which it refers.

All data shall be submitted by registered post to the following contact address:

Bruno Gautrais, Head of Unit E2
European Commission
Directorate-General for Health and Food Safety
Directorate E – Food and feed safety, Innovation
Unit E2 – Food Processing Technologies and Novel Foods
B-1049 Brussels

Once the new data are received, they will be submitted to EFSA for evaluation and preparation of a scientific opinion, if appropriate.

Confidential data

Business operators have the right to request a confidential treatment of certain information. They shall indicate which data they wish to be treated as confidential and give verifiable justification for each part for which a confidential treatment is required following the provisions on confidentiality as laid down in Article 12 of Regulation (EC) No 1331/2008[8]. Furthermore, the business operator shall provide the Commission with two paper and electronic versions of the dossier, namely the complete dossier and a second version of the complete dossier without confidential information.

Possibility for EFSA to use the data for the safety assessment of the same substance under other legal or regulatory frameworks

In line with Union policy objectives on animal welfare and testing on vertebrates, EFSA aims to avoid the duplication of testing on vertebrates, and to achieve an optimal use of the relevant financial and human resources by the private sector. Therefore, in anticipation of cases where EFSA may be interested in using or reusing relevant information or data (i.e. technical, toxicological data) for the evaluation of the same substance under a different legal or regulatory framework from the one mentioned above, or for the evaluation of another substance under the same or different legal framework as above, please indicate explicitly in writing, whether by participating in the voluntary submission of relevant data or information, you also give EFSA the permission to use and/or reuse these data for other EFSA safety assessments, and/or for a data sharing exercise with third parties or other international bodies.

[7] https://ec.europa.eu/food/safety/food_improvement_agents/additives/re-evaluation_en
[8] OJ L 354, 31.12.2008, p. 1.