

Call for scientific and technical data on the permitted food additives sulphur dioxide (E 220), sodium sulphite (E 221), sodium bisulphite (E 222), sodium metabisulphite (E 223), potassium metabisulphite (E 224), calcium sulphite (E 226), calcium bisulphite (E 227) and potassium bisulphite (E 228)

Published: 10 October 2016

Deadline for step 1 (Registration of the contact details of business operators interested in submitting data): 10 November 2016

Deadline for step 2 (Confirmation of data submission, deadlines and milestones): 10 April 2017

Background

According to Article 32 of Regulation (EC) No 1333/2008¹, 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 257/2010².

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 sulphur dioxide (E 220), sodium sulphite (E 221), sodium bisulphite (E 222), sodium metabisulphite (E 223), potassium metabisulphite (E 224), calcium sulphite (E 226), calcium bisulphite (E 227) and potassium bisulphite (E 228) as food additives

The EFSA's Panel on Food Additives and Nutrient Sources added to Food (ANS) recently delivered a scientific opinion³ re-evaluating sulphur dioxide (E 220), sodium sulphite (E 221), sodium bisulphite (E 222), sodium metabisulphite (E 223), potassium metabisulphite (E 224), calcium sulphite (E 226), calcium bisulphite (E 227) and potassium bisulphite (E 228) when used as food additives.

The Panel noted that the overall available database on sulphites and their reaction products with food components was limited and that this database did not indicate any concern for genotoxicity nor reported effects in chronic, carcinogenicity and reprotoxicity studies after oral exposure in the diet, by gavage, or in the drinking water. A no-observed-adverse-effect-level (NOAEL) of 70 mg SO₂ equivalent/kg bw/day was identified from a long-term toxicity study in rats. Although the majority of the available toxicological studies were performed using sodium or potassium metabisulphite, because exposure is predominantly to the sulphite ion irrespective of its source, read across of these data to other sulphites and sulphur dioxide was considered to be feasible. However, studies showed that an alternative pathway of the metabolism of sulphites exists, so that intermediate formation of sulphur trioxide radicals may occur. The Panel noted the absence of specific absorption, distribution, metabolism and excretion (ADME) studies measuring reaction products from the different sulphites. Furthermore, the Panel noted that it was not possible to ascertain the relative contribution of the differing pathways of sulphite metabolism at realistic levels.

The panel indicates that the group ADI (acceptable daily intake) allocated by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) and the Scientific Committee on Food (SCF) of 0–0.7 mg SO₂ equivalent/kg bw/day, based on a NOAEL in both the pigs and rats studies, was on the assumption that they can result from all sulphiting substances. Based on the common exposure to sulphite ions, it was considered that extrapolation between studies using various sulphite sources was possible.

The Panel noted that there are data suggesting that the critical effects of sulphites (and particularly sulphur dioxide) are site of contact effects. However, it was not possible to ascertain whether there were no systemic effects. Improving the toxicological database might result in either an increase or a decrease in the group ADI, depending on, for example, the effects detected, the identified point of departure and the use of chemical specific rather than default uncertainty factors.

The Panel concluded that the current group ADI of 0.7 mg SO₂ equivalent/kg bw/day (derived using a default uncertainty factor of 100) would remain adequate but should be considered temporary whilst the database was improved.

Regarding the exposure to sulphur dioxide–sulphites the Panel concluded this was:

- above the group ADI of 0.7 SO₂ equivalent/mg kg bw/day in all population groups at both the mean and the high level in the brand-loyal scenario, and at the high level in the non-brand-loyal scenario, when calculated in the refined exposure scenario considering only direct addition of sulphur dioxide–sulphites to food;
- above the group ADI in all populations at the high level for the non-brand loyal scenario in the refined exposure scenario considering additional exposure taking into account the available analytical data for food categories which may contain sulphur dioxide–sulphites due to carry-over and for food categories for which the direct addition of sulphur dioxide–sulphites (E 220–228) is not authorised and whose presence cannot be explained via carry-over.

³ <http://www.efsa.europa.eu/en/efsajournal/pub/4438>

The main food categories (FC) contributing to the exposure for the different types of consumers in the different scenarios are:

Infants and toddlers

- FC 04.2.6: 'Processed potato products, not dehydrated'
- FC 04.2.1: 'Dried fruit and vegetables'
- FC 08: 'Meat, only chicken meat'

Children and adolescents

- FC 04.2.1: 'Dried fruit and vegetables'
- FC 14.1.2: 'Fruit juices as defined by Directive 2001/112/EC and vegetable juices'
- FC 14.1.4: 'Flavoured drinks'
- FC 08: 'Meat, only chicken meat'

Adults and elderly

- FC 08.2: 'Meat preparations as defined by Regulation (EC) No 853/2004'
- FC 14.2.2: 'Wine and other products defined by Regulation (EC) No 1234/2007, and alcohol free counterparts'

The panel also observed that there are numerous reports of sensitivity/intolerance reactions in humans exposed to sulphited solid foods and beverages.

The Panel recommended that the database and the temporary group ADI should be re-evaluated. Additional studies performed according to recent internationally recognised Organisation for Economic Co-operation and Development (OECD) guidelines would allow more adequate risk assessment of the sulphites that are used as food additives. The Panel noted that those studies could require 5 years for completion.

In particular, absorption, distribution, metabolism and excretion (ADME) data for all the sulphites are needed, including identification of their forms and reaction products when they are used to treat beverages and solid foods. Depending on the outcome of these ADME studies, additional toxicity studies may be required. Moreover, the Panel considers that mode of action analysis should be conducted when the knowledge permits.

The panel also indicated that studies on the origin and mechanisms (forms of sulphites involved) of the reactions of individuals who are sensitive or intolerant to sulphites should be conducted.

The Panel recommended that the labelling 'contains sulphites' should provide information on the amount of SO₂ equivalent present in solid foods and beverages.

In addition, the Panel recommended that the maximum limits for the impurities of toxic elements (arsenic, lead and mercury) in the EU specifications for sulphur dioxide–sulphites (E 220–228) should be revised in order to ensure that those food additives will not be a significant source of exposure to these toxic elements in food.

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 sulphur dioxide–sulphites (E 220–228) as food additives.

Scientific and technical data required

The data required to address the various issues identified by EFSA in the re-evaluation of the safety of sulphur dioxide (E 220), sodium sulphite (E 221), sodium bisulphite (E 222), sodium metabisulphite (E 223), potassium metabisulphite (E 224), calcium sulphite (E 226), calcium bisulphite (E 227) and potassium bisulphite (E 228) as food additives are the following:

- Data on absorption, distribution, metabolism and excretion (ADME) for all the sulphites, including identification of their forms and reaction products, when they are used to treat beverages and solid foods: sound scientific data are needed to support a read-across among sulphites and consequently the establishment of a group ADI. Therefore the metabolic pathway for all the sulphites needs to be investigated and the reaction products of all sulphites in the different food matrices need to be identified, to ensure that the reaction products are independent from the sulphite used.
- Data on the mode of action of sulphur dioxide–sulphites (E 220–228): A mode of action analysis should be conducted. A good understanding of the mode of action of sulphites/their reaction products might support read-across among sulphites, and therefore it could avoid conducting additional toxicological studies for each individual sulphite.
- Data on the lowest achievable limits for the impurities of toxic elements (lead, mercury and arsenic) for sulphur dioxide–sulphites (E 220–228): the current maximum limits for those impurities in the EU specifications are too high and therefore should be revised to ensure that food additives will not be a significant source of exposure to those toxic elements in food.
- Data relevant for addressing the estimated exceedance of the ADI of sulphur dioxide–sulphites (E 220–228): EFSA concluded that the anticipated exposure estimates of sulphur dioxide–sulphites exceeded the current group ADI in most population groups, regardless of the exposure scenario and concentration data used in the assessment. These conclusions of EFSA demonstrate the need for a more refined exposure assessment and/or the need to review the currently authorised maximum levels. Food Business Operators, in particular those linked to the foods/food categories identified as main contributors to the exposure to sulphur dioxide–sulphites, are requested to provide feedback on the exposure assessment, and they should therefore, if interested in submitting feedback and/or data, register via step 1 of the procedure of the call for data explained below. A template for submission of data as regards use levels will be made available at a later stage.

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 could be useful to clarify the nature of the data requested above. 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.

All studies should be performed according to recent internationally recognised guidelines of the Organisation for Economic Co-operation and Development (OECD).

After evaluation of the ADME and mode of action data received, EFSA will determine whether new toxicological studies may be required, such as those described in EFSA's "Guidance for submission for food additive evaluations". If additional data from follow-up toxicological studies is needed, a new call for those data will be published. After the evaluation by EFSA of those new data, an additional call for data may be needed. Overall, it is considered that the process of acquisition of the needed new toxicological data on sulphites should not take more than 5 years from the publication of this call. After that time EFSA will carry out a re-evaluation of the database on sulphites and consequently of the currently temporary group ADI.

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

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 10 November 2016** whether they are interested that sulphur dioxide (E 220), sodium sulphite (E 221), sodium bisulphite (E 222), sodium metabisulphite (E 223), potassium metabisulphite (E 224), calcium sulphite (E 226), calcium bisulphite (E 227) and potassium bisulphite (E 228) remain permitted in the EU and therefore whether they are interested in providing the new data required. This communication should include full contact details of the business operator (name of business operator, name of contact person, postal address, telephone number and email 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 additives⁶) 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 10 April 2017** 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.

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 website⁷.

It should be noted that the submission of feedback and/or data on the exposure assessment will not be part of the step 2 of the call. Consequently, the Food Business Operators which indicate in step 1 interest in submitting feedback and/or data on the exposure assessment will receive a template and instructions for feedback/data submission after the end of step 1.

Submission of the required data

⁶ http://ec.europa.eu/food/safety/food_improvement_agents/additives/re-evaluation/index_en.htm

⁷ http://ec.europa.eu/food/safety/food_improvement_agents/additives/re-evaluation/index_en.htm

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 or DVD). 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:

Maria Iglesia, 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 1331/2008⁸. 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.

⁸ OJ L 354, 31.12.2008, p. 1.