

## Call for scientific and technical data on the permitted food additive titanium dioxide (E 171)

**Published:** 30 January 2017

**Deadline for step 1 (Registration of the contact details of business operators interested in submitting data):** 2 March 2017

**Deadline for step 2 (Confirmation of data submission, deadlines and milestones):** 30 July 2017

### Background

According to Article 32 of Regulation (EC) No 1333/2008<sup>1</sup>, 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<sup>2</sup>.

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.

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<sup>1</sup> OJ L 354, 31.12.2008, p. 16.

<sup>2</sup> OJ L 80, 26.3.2010, p. 19.

## **EFSA's Scientific Opinion on the re-evaluation of titanium dioxide (E 171) as a food additive**

The EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS) recently delivered a scientific opinion re-evaluating the safety of titanium dioxide when used as a food additive (E 171)<sup>3</sup>. From the available data on absorption, distribution and excretion, the Panel concluded that the absorption of orally administered titanium dioxide is extremely low and the low bioavailability of titanium dioxide appears to be independent of particle size.

The Panel concluded that the use of titanium dioxide as a food additive does not raise a genotoxic concern. From a carcinogenicity study with titanium dioxide in mice and in rats, the Panel chose the lowest no observed adverse effects levels (NOAEL) which was 2,250 mg titanium dioxide/kg body weight (bw) per day for males from the rat study, the highest dose tested in this species and sex. The Panel noted that possible adverse effects in the reproductive system were identified in some studies conducted with material which was either non-food-grade or inadequately characterised nanomaterial (i.e. not E 171). There were no such indications in the available, albeit limited, database on reproductive endpoints for the food additive (E 171). The Panel was unable to reach a definitive conclusion on this endpoint due to the lack of an extended 90-day study or a multigeneration or extended-one generation reproduction toxicity study with the food additive (E 171). Therefore, the Panel did not establish an acceptable daily intake (ADI).

The Panel considered that, on the database currently available and the considerations on the absorption of titanium dioxide, the margins of safety (MoS) calculated from the NOAEL of 2,250 mg titanium dioxide /kg bw per day identified in the toxicological data available and exposure data obtained from the reported use/analytical levels of titanium dioxide (E 171) would not be of concern. The Panel concluded that once definitive and reliable data on the reproductive toxicity of E 171 were available, the full dataset would enable the Panel to establish a health-based guidance value (ADI).

The Panel noted that there are no set limits for the particle size of titanium dioxide in the EU specifications (Commission Regulation (EU) No 231/2012<sup>4</sup>), and therefore characterisation of the particle size in the food additive E 171 should be included among the specifications. The Panel also noted that, according to the EU specifications for E 171, impurities of the toxic elements arsenic, lead, mercury and cadmium are accepted up to concentrations of 1, 10, 1 and 1 mg/kg, respectively. Contamination at those levels could have a significant impact on the exposure to these metals, for which the intake is already close to the health-based guidance values established by EFSA.

### **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 titanium dioxide as a food additive (E 171).

### **Scientific and technical data required**

The data required to address the various issues identified by EFSA in the re-evaluation of the safety of titanium dioxide as a food additive (E 171) are the following:

- **Reproductive toxicity data:** In order to enable the EFSA Panel to establish a health-based guidance value (ADI) for the food additive titanium dioxide (E 171), additional reproductive toxicity testing needs to be performed, such as an extended 90-day study or a multigeneration or extended-one generation reproductive toxicity study, carried out according to the current OECD guidelines. Such studies should be performed with titanium

<sup>3</sup> <http://onlinelibrary.wiley.com/doi/10.2903/j.efsa.2016.4545/epdf>

<sup>4</sup> OJ L 83, 22.3.2012, p. 1.

dioxide (E 171) complying with the EU specifications and additionally including a characterisation of the particle size distribution of the test material.

- Data on particle size and particle size distribution for titanium dioxide (E 171): Because of their potential importance in toxicokinetics and toxicological effects, particle size and particle size distribution should be included in the EU specifications of titanium dioxide (E 171). The determination of particle size and particle size distribution should be performed using appropriate methodologies, and at least two independent methods, as presented in the EFSA's "Guidance on the risk assessment of the application of nanoscience and nanotechnologies in the food and feed chain"<sup>5</sup>. The characterisation of particle size distribution should include appropriate statistical descriptors (e.g. range, median, quartiles) as well as the percentage (in number and by mass) of particles in the nanoscale (particles with at least one dimension below 100 nm) present in titanium dioxide used as a food additive (E 171).
- Data on the lowest achievable limits for the impurities of toxic elements (arsenic, lead, mercury and cadmium) in titanium dioxide (E 171): the current maximum limits for those impurities in the EU specifications are too high and therefore should be revised to ensure that titanium dioxide as a food additive (E 171) will not be a significant source of exposure to those toxic elements in food.
- Data on the actual use of alumina (aluminium oxide) in titanium dioxide (E 171) formulations/lowest achievable limit for the use of alumina in those formulations: according to the current EU specifications for E 171, titanium dioxide may be coated with small amounts of alumina and/or silica to improve the technological properties of the product. A level of aluminium oxide of up to 2% is permitted. An actual presence of aluminium oxide at that level would make E 171 an important source of exposure to aluminium through food.

EFSA's "Guidance for submission for food additive evaluations"<sup>6</sup> 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"<sup>7</sup> could be useful.

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

## 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 2 March 2017** whether they are interested that titanium dioxide (E 171) remains 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](mailto: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<sup>8</sup>) the list of business operators having expressed

<sup>5</sup> <http://onlinelibrary.wiley.com/doi/10.2903/j.efsa.2011.2140/epdf>

<sup>6</sup> <http://onlinelibrary.wiley.com/doi/10.2903/j.efsa.2012.2760/epdf>

<sup>7</sup> <http://onlinelibrary.wiley.com/doi/10.2903/j.efsa.2014.3553/epdf>

<sup>8</sup> [http://ec.europa.eu/food/safety/food\\_improvement\\_agents/additives/re-evaluation/index\\_en.htm](http://ec.europa.eu/food/safety/food_improvement_agents/additives/re-evaluation/index_en.htm)

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 30 July 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](mailto: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 website<sup>9</sup>.

## **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 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

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<sup>9</sup> [http://ec.europa.eu/food/safety/food\\_improvement\\_agents/additives/re-evaluation\\_en](http://ec.europa.eu/food/safety/food_improvement_agents/additives/re-evaluation_en)

laid down in Article 12 of Regulation (EC) No 1331/2008<sup>10</sup>. 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.

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<sup>10</sup> OJ L 354, 31.12.2008, p. 1.