



EUROPEAN COMMISSION  
DIRECTORATE-GENERAL FOR HEALTH AND FOOD SAFETY

Food and feed safety, innovation  
Director

Brussels, 22.03.2018  
SANTE.E2/AF7/km (2018) 1605112  
Ares (2018) 1583962

Dear Dr Url,

**Subject: Request for a scientific opinion from the European Food Safety Authority in relation to four new studies on the potential toxicity of titanium dioxide used as a food additive (E 171)**

It came to our attention that four scientific articles describing a potential adverse health effect of titanium dioxide used as a food additive (E 171) have been published between 2016 and 2017, after the adoption and publication of EFSA's scientific opinion on the re-evaluation of titanium dioxide as a food additive (E171) in 2016.

The European Commission would like to request EFSA to provide a scientific opinion on this matter, in accordance with Article 29(1)(a) of Regulation (EC) No 178/2002. In particular, EFSA is requested to carry out a scientific evaluation of the studies presented in those articles and to indicate whether they would merit re-opening the existing opinion of EFSA related to the safety of titanium dioxide (E 171) as a food additive.

Given the relevance of the issue at stake, we would be grateful if EFSA could provide the requested scientific opinion before the end of May 2018.

Please find in the annex the background and the terms of reference for this request.

My services remain at your disposal for further information. On this matter, you can contact Ms Andreia Alvarez Porto and Mr Guillermo Cardon, who are responsible for this dossier in Unit E2 Food Processing Technologies and Novel Foods, and Mr Luis Vivas Alegre, who is the relevant contact point in Unit D1, which is in charge of relations with EFSA. Their respective phone and e-mail addresses are indicated below.

Yours sincerely,

Sabine Jülicher

Dr Bernhard Url  
Executive Director  
European Food Safety Authority  
Via Carlo Magno 1/a  
43126 Parma  
ITALY

Annex: Request for a scientific opinion from the European Food Safety Authority in relation to four new studies on the potential toxicity of titanium dioxide used as a food additive (E 171)

Contact persons: *Ms A. Alvarez Porto (+32 2 295 09 84) [andrea.alvarez-porto@ec.europa.eu](mailto:andrea.alvarez-porto@ec.europa.eu)  
Mr G. Cardon (+32 2 295 68 20) [Guillermo.cardon@ec.europa.eu](mailto:Guillermo.cardon@ec.europa.eu)  
Mr L. Vivas Alegre (+32 2 229 32 37) [luis.vivas-alegre@ec.europa.eu](mailto:luis.vivas-alegre@ec.europa.eu)*

Cc: Ms L. Carrouée, Mr R. Reig Rodrigo, Mr T. Brégeon, Ms V. Benault, Mr B. Gautrais, Mr P. Bokor, Mr L. Vivas-Alegre, Ms K. De Rijck, Ms A. Alvarez-Porto, Mr G. Cardon, Mr J. Sochor, Ms M. Schulzova

**Request for a scientific opinion from the European Food Safety Authority in relation to four new studies on the potential toxicity of titanium dioxide used as a food additive (E 171)**

**Background information on the request**

The use of food additives is regulated under the European Parliament and Council Regulation (EC) No 1333/2008 on food additives<sup>1</sup>. Only food additives that are included in the Union list, in particular in Annex II to that regulation, may be placed on the market and used in foods under the conditions of use specified therein. Moreover, food additives shall comply with the specifications as referred to in Article 14 of that Regulation and laid down in Commission Regulation (EU) No 231/2012<sup>2</sup>.

Titanium dioxide is authorised for use as a food additive (food colour) in the Union. Since titanium dioxide (E 171) was permitted in the Union before 20 January 2009, it belongs to the group of food additives which are subject to a new risk assessment by the European Food Safety Authority (EFSA), according to Commission Regulation (EU) No 257/2010<sup>3</sup>, and in line with the provisions of Regulation (EC) No 1333/2008.

The re-evaluation of titanium dioxide as a food additive (E171) was completed by EFSA in June 2016 and a scientific opinion was published in September 2016<sup>4</sup>. In that opinion, EFSA concluded, on the basis of the available evidence, that titanium dioxide used as a food additive (E 171) does not raise a concern with respect to genotoxicity and that it is not carcinogenic after oral administration. However, several data gaps were also identified by EFSA in the opinion. These warranted a follow-up by the European Commission<sup>5</sup> and new scientific evidence is being generated by interested parties in order to address the uncertainties highlighted by EFSA in its scientific opinion.

Nevertheless, authorised food additives should be kept under continuous observation and must be re-evaluated whenever necessary in the light of changing conditions of use and new scientific information.

---

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

<sup>2</sup> OJ L 83, 22.3.2012, p. 1.

<sup>3</sup> OJ L 80, 26.3.2010, p. 19.

<sup>4</sup> <http://onlinelibrary.wiley.com/doi/10.2903/j.efsa.2016.4545/full>

<sup>5</sup> [https://ec.europa.eu/food/sites/food/files/safety/docs/fs-iron titanium dioxide-overview-deadlines-milestones-20170730.pdf](https://ec.europa.eu/food/sites/food/files/safety/docs/fs-iron_titanium_dioxide-overview-deadlines-milestones-20170730.pdf)

Four new scientific articles<sup>6,7,8,9</sup> describing a potential adverse health effect of titanium dioxide used as a food additive (E 171) have recently been published, after the adoption and publication of EFSA's scientific opinion on the re-evaluation of titanium dioxide as a food additive (E171) in 2016. Consequently, the European Commission has decided to consult EFSA on this matter.

### **Terms of reference for the request**

In accordance with Article 29(1)(a) of Regulation (EC) No 178/2002<sup>10</sup>, the European Commission requests the European Food Safety Authority (EFSA) to provide a scientific opinion in relation to four new studies on the potential toxicity of titanium dioxide used as a food additive (E 171). In particular, EFSA is requested to carry out a scientific evaluation of those studies and to indicate whether they would merit re-opening the existing opinion of EFSA related to the safety of titanium dioxide (E 171) as a food additive.

---

<sup>6</sup> Minne B. Heringa, Liesbeth Geraets, Jan C. H. van Eijkeren, Rob J. Vandebriel, Wim H. de Jong & Agnes G. Oomen, Risk assessment of titanium dioxide nanoparticles via oral exposure, including toxicokinetic considerations. *Nanotoxicology* Vol. 10, Iss. 10, 2016

<sup>7</sup> Bettini S., Boutet-Robinet E., Cartier C., Coméra C., Gaultier E., Dupuy J., Naud N., Taché S., Grysan P., Reguer S., Thieriet N., Réfrégiers M., Thiaudière D., Cravedi J.-P., Carrière M., Audinot J.-N., Pierre F.H., Guzylack-Piriou L., Houdeau E. (2017). Food-grade TiO<sub>2</sub> impairs intestinal and systemic immune homeostasis, initiates preneoplastic lesions and promotes aberrant crypt development in the rat colon. *Sci Rep.* 2017, 7:40373.

<sup>8</sup> Proquin H., Rodriguez-Ibarra C., Moonen C., Urrutia Ortega I., Briedé J., de Kok T., van Loveren H., Chirino Y. , Titanium dioxide food additive (E171) induces ROS formation and genotoxicity: contribution of micro and nano-sized fractions. *Mutagenesis*, Volume 32, Issue 1, 1 January 2017, Pages 139–149

<sup>9</sup> Guo Z., Martucci N., Moreno-Olivas F., Tako E., Mahler G., Titanium dioxide nanoparticle ingestion alters nutrient absorption in an in vitro model of the small intestine. *NanoImpact*, 5 : 70-82, janvier 2017

<sup>10</sup> OJ L 31, 1.2.2002, p. 1.