TDMA
TITANIUM DIOXIDE MANUFACTURERS ASSOCIATION
for a brighter future

Agence nationale de sécurité sanitaire de l'alimentation,
de l'environnement et du travail (ANSES)
14 rue Pierre et Marie Curie
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By email: contribution-nanos@anses.fr

Brussels, 29 March 2019
Our reference: TDMA1020b

Re: Call for information on nanomaterials in food

Dear Sir/Madam,

We write to you on behalf of the Titanium Dioxide Manufacturers Association (TDMA) in response to your request for contributions on nanomaterials in food. TDMA have commissioned a toxicological summary and science report update which we have attached to this submission. We have also attached a report prepared for the European Food Safety Authority (EFSA) titled Data on Particle Size and Particle Size Distribution for Titanium Dioxide (E 171) in June 2018. Following a clarification call with EFSA, an update of this report is being prepared by TDMA for submission by the end of April 2019. We will forward a copy of the update to ANSES at the same time.

We would also like to draw your attention to the fact that the European Food Safety Authority (EFSA) has evaluated TiO_2 in two recent opinions. The first one (EFSA Journal 2016;14(9):4545) concluded that "on the database currently available and the considerations on the absorption of TiO2... and exposure data obtained from the reported use/analytical levels of TiO_2, E 171 would not be of concern." In the second, EFSA concluded that four published investigations that they were asked to look at do not merit reopening the evaluation. To address these various points, TDMA are undertaking a comprehensive science programme which is detailed in the attached report. Key points of this plan are detailed below.

Extended one-generation reproductive toxicity study (EOGRTS)

For setting an acceptable daily intake (ADI), more information on reproductive toxicity was recommended by EFSA and therefore TDMA commissioned an extended one generation reproduction toxicity study (EOGRTS). To address a specific concern that E 171 may cross the intestinal barrier and adversely impact the immune system, the EU Commission recommended to monitor markers of preneoplastic lesions,

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aberrant crypt foci, (ACF) in the planned EOGRT study. To address this request, TDMA reviewed the EOGRTS and increased the scope to include a total of 80 additional animals.

The first part, a palatability study has now been completed and the EOGRTS started in February 2019 with the final report expected to be completed by the end of July 2020.

Immunological assessment

A study run jointly by Michigan State University (MSU) and University of Nebraska Medical Center is also addressing the immunological concerns. This looks at the effects of administration of E 171 on the formation of aberrant crypt foci in the intestine and on dendritic and T Cell tissue distribution and function (spleen and Peyer's Patches) in male rats with and without pretreatment with 1,2-dimethylhydrazine. The 7-day pre-study of this investigation is complete and a copy of the poster presentation at the Society of Toxicology (SOT) 58th Annual Meeting in Baltimore on 10 – 14 March 2019 is attached.

The in-life phase of the main 100-day sub-chronic study is complete and is now under histological/immunological examination. It is planned to present this at the 45th Annual Summer Meeting of The Toxicology Forum in Alexandria, Virginia (Washington DC) on 8–10 July 2019. We will forward more information when it is available.

Particle size and specification

We note in the call for data that you have a very broad definition of nanomaterials with no threshold at 100nm, whereas the European Recommendation of 18 October 2011 on the definition of a nanomaterial, which now legally enforceable in the Commission Regulation (EC) No 1881-2018 amending REACH for nanoforms, includes a threshold at 50% by number. We believe all E 171 placed on the market, and certainty from TDMA members, has less than 50% by number smaller than 100nm as detailed in the particle size report. This dimension imparts the light scattering and surface opacity properties required for a white pigment. Nano sized TiO_2, with greater than 50% of particles less than 100nm, is transparent and therefore is not effective as a pigment.

As part of the EFSA review of the particle size and purity characteristics of E 171, the EU Commission plan to revise and narrow the definition of E 171. Only a very limited range of titanium dioxide pigment grades are placed on the market as E 171. Most published studies on titanium dioxide are on grades that are not identified, or if they are identified, not used for food and we believe this creates some confusion and anxiety related to E 171 in food.

We believe the planned revision of the specification of E 171 could help to address concerns about the safety of E 171.

As you can see, there is a large number of activities currently being undertaken related to the safety of titanium dioxide and we would urge that ANSES take all these points into consideration to avoid a premature assessment.

TDMA would welcome the opportunity to meet and explain in detail any of the points raised in this submission or any other points related to the safety of titanium dioxide.

Yours faithfully

Attachments

Annex I - Titanium Dioxide Toxicological Summary and Science Update Report, March 2019.

Annex II - Data on Particle Size and Particle Size Distribution for Titanium Dioxide (E171), June 2018.

Annex III – Blevins, L. et. al - Immunologic Assessment of Rats Fed E171, a Food Grade Titanium Dioxide (TiO_2), Containing Diet for 7 Days, March 2019.