

EFSA ANNOUNCEMENT

E171 no longer considered safe food additive

- EFSA concluded that a concern for genotoxicity of TiO_2 particles cannot be ruled out.
- An Acceptable Daily Intake (ADI) cannot be established for E171.
- Raises concerns about cancer
- No effects on reproductive and developmental toxicity based on evidence submitted


safety assessment of titanium dioxide (E171)



safety assessment of the food additive titanium dioxide (E 171), for
revision in March 2020.

E171-no-longer-considered-safe-when-used-food-additive#faq—efsa-2021-safety

SCIENTIFIC OPINION



ADOPTED: 28 June 2016
doi: 10.2903/j.efsa.2016.4545

Re-evaluation of titanium dioxide (E 171) as a food additive

EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS)

Abstract

The present Opinion deals with the re-evaluation of the safety of titanium dioxide (TiO₂, E 171) when used as a food additive. From the available data on absorption, distribution and excretion, the EFSA Panel on Food Additives and Nutrient Sources added to Food concluded that the absorption of orally administered TiO₂ is extremely low and the low bioavailability of TiO₂ appears to be independent of particle size. The Panel concluded that the use of TiO₂ as a food additive does not raise a genotoxic concern. From a carcinogenicity study with TiO₂ in mice and in rats, the Panel chose the lowest no observed adverse effects levels (NOAEL) which was 2,250 mg TiO₂/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 TiO₂, the margins of safety (MoS) calculated from the NOAEL of 2,250 mg TiO₂/kg bw per day identified in the toxicological data available and exposure data obtained from the reported use/analytical levels of TiO₂ (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 (AGI).

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Keywords: titanium dioxide, E 171, anatase, rutile, food colour

EFSA 2016 opinion

“The use of TiO₂ as a food additive does not raise a genotoxic concern.”

SCIENTIFIC OPINION



ADOPTED: 26 June 2018
doi: 10.2903/j.efsa.2018.5366

Evaluation of four new studies on the potential toxicity of titanium dioxide used as a food additive (E 171)

EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS), Maged Younes, Peter Aggett, Fernando Aguilar, Riccardo Crebelli, Birgit Dusemund, Melika Filipic, Maria Jose Frutos, Pierre Galzer, David Gott, Ursula Gundert-Bremy, Gunter Georg Kuhnle, Claude Lambre, Jean-Charles Leblanc, Inger Therese Lillegaard, Peter Moldaers, Aljica Mortensen, Agneta Oskarsson, Ivan Stankovic, Ine Waalkens-Berendsen, Matthew Wright, Federica Lodi, Ana Maria Rincon, Camilla Sineralli and Rudolf Antonius Woutersen

Abstract

The European Commission requested EFSA to carry out a scientific evaluation on four studies on the potential toxicity of titanium dioxide (TiO₂) used as a food additive (E 171) and to indicate whether they would merit re-opening the existing opinion of EFSA on the safety of TiO₂ (E 171) as a food additive. The results of the Bettini et al. (2017) study did not provide enough justification for a new carcinogenicity study, but, should additional useful mechanistic information become available, this could be reconsidered in future. The new *in vitro* findings in the Proquin et al. (2017) study did not modify the conclusion on the genotoxicity of TiO₂ as stated in the previous EFSA opinion of 2016 on the safety of TiO₂ (E 171) as a food additive. The effects of engineered TiO₂ nanoparticles reported by the Guo et al. (2017) study were of uncertain biological significance and therefore of limited relevance for the risk assessment of the food additive TiO₂ (E 171). There was significant uncertainty in the risk assessment performed by Herings et al. (2016), which did not include a weight of evidence analysis of the whole database. The Panel considered that the four studies evaluated, highlighted some concerns but with uncertainties, therefore their relevance for the risk assessment was considered limited and further research would be needed to decrease the level of uncertainties. Overall, three of the studies, reporting that TiO₂ induced various effects in *in vitro* and *in vivo* models, may be useful for hazard identification of TiO₂. In the fourth study by Herings et al. (2016), numerous assumptions were made, which resulted in large uncertainty in their conclusion. Altogether, the Panel concluded that the outcome of the four studies did not merit re-opening the existing opinion of EFSA related to the safety of TiO₂ (E 171) as a food additive.

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EFSA 2018 opinion

“(…) did not modify the conclusion on the genotoxicity of TiO₂ as stated in the previous EFSA opinion of 2016”

STATEMENT



ADOPTED: 10 May 2019
doi: 10.2903/j.efsa.2019.5714

EFSA statement on the review of the risks related to the exposure to the food additive titanium dioxide (E 171) performed by the French Agency for Food, Environmental and Occupational Health and Safety (ANSES)

EFSA (European Food Safety Authority)

Abstract

On 15 April 2019, the French Agency for Food, Environmental and Occupational Health and Safety (ANSES) published an opinion on the risks related to the exposure to the food additive titanium dioxide (E 171) taking into account the most recent scientific studies available. Further to this publication, EFSA was requested by the European Commission to provide urgent scientific and technical assistance regarding the opinion issued by ANSES. In the ANSES opinion, 25 new relevant publications published between 2017 and 2019 were reviewed together with previous opinions by EFSA and ANSES and a systematic review on *in vitro* genotoxicity of nano titanium dioxide. In this statement, EFSA concludes that the ANSES opinion published in April 2019 does not identify any major new findings that would overturn the conclusions made in the previous two scientific opinions on the safety of titanium dioxide (E 171) as a food additive issued by the EFSA ANS Panel in 2016 and 2018. The ANSES opinion reiterates the previously identified uncertainties and data gaps, which are currently being addressed in the context of the follow-up activities originating from the previous EFSA evaluations and their recommendations. In addition to the aspects for which the follow-up work is currently ongoing, ANSES recommends further investigation of *in vivo* genotoxicity. EFSA considers this recommendation should be revisited once the ongoing work on the physico-chemical characterisation of the food additive titanium dioxide (E 171) is completed.

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Keywords: Titanium dioxide, E 171, food additive

Requestor: European Commission

EFSA may 2019 opinion

“ANSES recommends further investigation of *in vivo* genotoxicity. EFSA considers this recommendation should be revisited once the ongoing work on the physico-chemical characterisation of the food additive titanium dioxide (E 171) is completed”

STATEMENT



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Requestor: European Commission

EFSA june 2019 opinion

“In particular, the characterisation of titanium dioxide (E 171) does not provide a reason to revise the conclusion on genotoxicity of titanium dioxide (E 171) previously drawn by the ANS Panel. “

Safety assessment of titanium dioxide (E171) as a food additive

EFSA Panel on Food Additives and Flavourings (FAF),
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Abstract

The present opinion deals with an updated safety assessment of the food additive titanium dioxide (E 171) based on new relevant scientific evidence considered by the Panel to be reliable. Data obtained with TiO₂ nanoparticles (NPs) and data from an extended one-generation reproductive toxicity (EOGRT) study. Less than 50% of constituent particles by number in E 171 have an external dimension < 100 nm. In addition, the Panel noted that constituent particles amounted to less than 1% of particles by number. The Panel therefore considered that TiO₂ NPs < 30 nm were of limited relevance to the safety assessment of E 171. The Panel noted that although gastrointestinal absorption of TiO₂ particles is low, they may accumulate in the liver. Studies on general and organ toxicity did not indicate adverse effects with either E 171 up to 1,000 mg/kg body weight (bw) per day or with TiO₂ NPs (> 30 nm) up to the highest dose of 100 mg/kg bw per day. No effects on reproductive and developmental toxicity were observed. Observations of potential immunotoxicity and inflammation with E 171 and potential neurotoxicity with TiO₂ NPs, together with the potential induction of aberrant crypt foci with E 171, may indicate adverse effects. With respect to genotoxicity, the Panel concluded that TiO₂ particles have the potential to induce DNA strand breaks and chromosomal damage, but not gene mutations. No clear correlation was observed between the physico-chemical properties of TiO₂ particles and the outcome of *in vitro* or *in vivo* genotoxicity assays. A concern for genotoxicity of TiO₂ particles that may be present in E 171 could therefore not be ruled out. Several modes of action for the genotoxicity may be identified in parallel and the relative contributions of different molecular mechanisms elicited by TiO₂ particles are unknown. There was uncertainty as to whether a threshold mode of action could be identified. In the absence of a cut-off value for TiO₂ particle size with respect to genotoxicity could not be identified. In the absence of an appropriately designed study was available to investigate the potential carcinogenic effects of E 171. Based on all the evidence available, a concern for genotoxicity could not be ruled out. In the absence of any other safety concerns, the Panel concluded that E 171 can no longer be considered as safe for use as a food additive.

EFSA Panel on Food Additives and Flavourings (FAF), European Food Safety Authority. *EFSA Journal* published by John Wiley and Sons Ltd on behalf of the European Food Safety Authority.

Titanium dioxide, E 171, CAS No 13463-67-7

Basis of the EFSA opinion includes (page 46):

- New information regarding the constituent particle size distribution of E 171
- The updated EFSA Guidance on risk assessment of the application of nanoscience and nanotechnologies in the food and feed chain
- References from the previous ANS Panel opinion (2016)
- Data submitted in the context of the NANOGENOTOX project, 2013
- Publications reported in the OECD dossier (OECD, 2016) and documentation provided by interested business operators (IBOs)

MEDIA/POLITICAL REACTION

Political

- Commissioner for Health, Stella Kyriakides, [tweeted](#) that the Commission will ban the use of E171 in the EU and the discussions will start with the Member States this month.
- German Agriculture Minister Julia Klöckner said in a [statement](#) that she asked Commission to move forward with ban
- ANSES welcomed conclusions of EFSA – French Government still to react

Media/social media

- Story was reported by tier 1 EU media in major markets including the Guardian, El Pais, Zeit, Le Monde etc.
- Stories mostly relay EFSA conclusion and political reactions across Europe
- High volume of negative reactions on social with strong focus from NGOs to push for immediate political action

 **Stella Kyriakides**  @SKyriakidesEU · 22 t

Following @EFSA_EU's new scientific opinion on the food additive E171, we will propose to ban its use in the EU.



◆ Discussions with Member States will start this month.

◆ Our priority is the health of citizens and the safety of the food they eat.
[#EUFoodSafety](#)



7 58 74

 **Annika Bruna**  @Bruna_Annika · 1 t



Following the opinion delivered by the @EFSA_EU, the @EU_Commission must now ban the additive #E171 not only in foodstuffs but also in pharmaceutical and cosmetic products!

 Find my press release 

[id-france.eu/le-colorant-e1 ...](http://id-france.eu/le-colorant-e1...)

 **UFC-Que Choisir**  @UFCquechoisir · 49 min

L'@UFCquechoisir se félicite de cette proposition d'interdire le #DioxydeDeTitane dans les #aliments au sein de l'#UE. Mais quid de l'interdiction dans les #médicaments et les #cosmétiques ? Quand va-t-on s'occuper des autres #nanomatériaux (#silice, #argent, #carbone...)? #E171

 **Stella Kyriakides**  @SKyriakidesEU · 22 t

Following @EFSA_EU's new scientific opinion on the food additive E171, we will propose to ban its use in the EU.

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◆ Our priority is the health of citizens and the safety of the food they eat.
[#EUFoodSafety](#)

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WHAT NEXT

- The Commissioner will not backtrack after promising a ban of E171 in food on the record
- Given France and Germany support combined with a negative EFSA opinion, it is difficult to change the situation in SCOPAFF
- The ban would meet the European Parliament's request in its objection to the revised E171 specification last autumn
- New court judgement makes clear under the precautionary principle that measures may be taken without an exhaustive risk assessment
- See Case C-499/18 P, Bayer CropScience AG v. Commission

