



Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment

Interim position paper on titanium dioxide

Background

1. Titanium dioxide (TiO₂) is an inorganic compound which exists in nature in different crystalline forms - the anatase and rutile being the two most common.
2. Titanium dioxide is an authorised Food Additive (E171) in the EU in accordance with Annex II to Regulation (EC) No 1333/2008 in both anatase and rutile forms (Commission Regulation (EU) No 231/2012) and under GB Food Law (retained EU law Regulation No 1333/2008 on food additives). Titanium dioxide is used in food as a colour to make food more visually appealing, to give colour to food that would otherwise be colourless, or to restore the original appearance of food. It is also widely used in cosmetics and medicines (EFSA, 2016).
3. Titanium dioxide has been the subject of multiple safety evaluations; by the Scientific Committee on Food (SCF) in 1975 and 1977, and by the Joint FAO/WHO Expert Committee of Food Additives (JECFA) in 1969. In 1969, JECFA allocated an acceptable daily intake (ADI) 'not limited except for good manufacturing practice'. In 1975, the SCF did not establish an ADI for titanium dioxide, whereas in 1977, the SCF included titanium dioxide in the category 'colours for which an ADI was not established but which could be used in food'.

4. In 2016, the EFSA Food Additives and Flavourings panel (FAF) reviewed the safety of titanium dioxide. One of the largest uncertainties identified by the FAF Panel related to the composition of titanium dioxide. EFSA considered that E171 mainly consisted of micro-sized titanium dioxide particles, with a nano-sized (<100 nm) fraction less than 3.2% by mass. No limits for the particle size of E171 were set in the EU specifications (EFSA, 2021). Subsequently, in 2019, and following the evaluation of data submitted by interested operators, the EFSA Food Additives and Nutrients Sources added to Food (ANS) Panel recommended that “the EU specifications for E171 include the parameter of median minimum external dimension by particle number >100 nm (measured by electron microscopy), which is equivalent to less than 50% of constituent particles by number with a minimum external dimension <100 nm.”

5. On the basis of the data available, the ANS Panel concluded that the absorption and oral bioavailability of titanium dioxide was low and independent of size. With regards to genotoxicity, based on the available genotoxicity data and considering other absorption, distribution, metabolism and excretion parameters (ADME) the ANS Panel concluded that orally ingested titanium dioxide particles (micro- and nanosized) were unlikely to represent a genotoxic hazard *in vivo*. For the other endpoints, the ANS Panel identified a no-observed adverse effect level (NOAEL) of 2,250 mg/kg bw/d based on a carcinogenicity study in rats. Compared to the exposure based on reported use levels and analytical data, the use of E171 was not considered to be of concern.

6. The ANS Panel did not establish an ADI due to the lack of either an extended 90-day toxicity study or a multi-generation or an extended one generation reproduction toxicity study with E171. This was because possible adverse effects were identified in the reproductive system in some literature studies which used test substances that were non-food grade or which contained inadequately characterised nanomaterial. Overall, the ANS Panel concluded that once definitive and reliable data on the reproductive toxicity of E 171 were available, the full dataset would enable the ANS Panel to establish a health-based guidance value (ADI). They further recommended that as well as additional testing that would allow the ANS Panel to address the data gaps, such as a

multigeneration or extended one-generation reproduction toxicity study; the EU specifications for TiO₂ should include a characterisation of particle size distribution using appropriate statistical descriptors. The measuring methodology applied should comply with the EFSA Guidance document (EFSA Scientific Committee, [2011](#)). Additionally, the maximum limits for the impurities of the toxic elements (arsenic, lead, mercury and cadmium) in the EU specification for TiO₂ (E 171) should be revised in order to ensure that TiO₂ (E 171) as a food additive will not be a significant source of exposure to those toxic elements in foods.

7. In 2018 four additional studies were evaluated, including one *in vitro* genotoxicity study in two human colon cancer cell lines. The ANS Panel re-confirmed that E171 did not raise concerns with regard to *in vivo* genotoxicity (EFSA 2018a).

Other evaluations

8. Following a report by the French Authorities in 2016 and a proposal for evaluation of titanium dioxide, the Committee for Risk Assessment (RAC) of the European Chemicals Agency (ECHA) concluded in June 2017 that titanium dioxide met the criteria to be classified as a substance suspected of causing cancer (category 2) if inhaled. The main mechanism thought to explain the effects induced by titanium dioxide, in common with effects seen with other substances, was inflammation and an indirect genotoxic effect through production of reactive oxygen species (ROS) arising from the biopersistence and insolubility of all forms of titanium dioxide particles. However, a direct interaction with DNA could not be excluded, since titanium dioxide had been found in the cell nucleus in various *in vitro* and *in vivo* studies. This was in line with the International Agency for Research on Cancer (IARC) evaluation which concluded that in relation to exposure via inhalation “titanium dioxide is possible carcinogenic to humans (Group 2B) based on sufficient evidence in experimental animals and inadequate evidence from epidemiological studies.” (IARC 2009). However, the 2016 report by the French Authorities the Agency for Food, Environmental and Occupational

Health and Safety (ANSES) concluded that there was no carcinogenic concern after oral or dermal administration.

9. In 2018, the Dutch Office for Risk Assessment and Research held a workshop on the “potential health effects of the food additive titanium dioxide (E171)”, the results of which were published in 2019, where overall the need for further studies to further investigate the effects of titanium dioxide exposure—particularly for the endpoints of colon tumours and immunotoxicology based on the data gaps and study limitations of the available database at the time was highlighted. Furthermore the need to better characterise the composition of E171 was noted. In 2020, a review was published that summarised the outcomes of this workshop and additionally aimed to identify and evaluate recent toxicological studies on food-grade titanium dioxide and nano-sized titanium dioxide in *ex-vivo*, *in-vitro*, and *in-vivo* experiments along the gastrointestinal route, and to postulate an Adverse Outcome Pathway (AOP) following ingestion. Adverse effects were identified including the generation of ROS, alterations of the gut microbiota, persistent inflammation, and other effects on the immune system. It was noted that the findings were inconsistent between the different species and independent research groups. With regards to the animal studies that reported positive effects on precancerous lesions/tumour formation, it was noted that those were mainly used as research models and a proper investigation of a dose-response relationship was not performed. Based on the available information, it was not possible to carry out a risk assessment. When considering the mode of action, it was postulated that it was closely related to the ability of titanium dioxide to induce ROS formation and promote inflammation. The potential key events were considered to be persistent inflammation and ROS generation that can result in oxidative stress as well as persistent epithelial cell injury and potentially lead to DNA damage and exert a tumour-promoting effect of E171 seen in some of the studies. Finally, it was noted that it is generally assumed that the round and spherical crystal forms of TiO₂ contribute to the induction of adverse effects to a lower extent when ingested and similarly that titanium dioxide nanoparticles are suspected to induce more adverse effects than other particle sizes. However, a study by Proquin *et al.* (2017) was also mentioned that demonstrated that a

mixture of nano- and micro-sized TiO₂ particles, as present in E171, induce more adverse effects than the single fractions alone. The authors further expanded on possible interactions of E171 with its direct environment as well as other factors that could potentially affect agglomeration for example and discussed how these could directly affect the properties of titanium dioxide. Therefore, they considered that “it is important to carefully examine and analyze the physicochemical characteristics of TiO₂ particles in its vehicle, as well as in its surrounding matrix as their final milieu, to guarantee a profound assessment of potential adverse health effects of E171 and to adequately compare different studies in the process of risk assessment.” (Bischoff *et al.*,2020)

10. In their most recent evaluation, the EU Scientific Committee on Consumer Safety (SCCS) assessed titanium dioxide used in cosmetic products that lead to exposure by inhalation. With regards to mutagenicity and genotoxicity, the SCCS noted that in the 2010 evaluation, IARC concluded that most of the *in vitro* genotoxicity studies with titanium dioxide exposure were negative despite the high rate of false positives and that the EFSA FAF Panel in 2016 considered that the positive genotoxicity results may have been due to experimental conditions associated with the induction of oxidative stress. The SCCS also noted that studies showing a positive association between the so-called group of Poorly Soluble Low Toxicity (PSLT) particles exposure and genotoxicity are generally consistent with the mechanism that sub-toxic concentrations of PSLT particles can cause inflammation and oxidative stress, which may lead to mutations. Oxidative stress is considered the underlying mechanism of the proliferation and genotoxic responses to PSLT particles including titanium dioxide and thus there is a large body of evidence that titanium dioxide has no direct genotoxic potential. The SCCS was of the opinion that “The genotoxic effects of titanium dioxide most probably manifest through an indirect mechanism (oxidative stress), or secondary mechanisms (e.g. oxidative stress and inflammation caused by immune cells). The SCCS therefore considers it plausible that there is a practical threshold for this mode of action and therefore a risk assessment could be carried out for its use in cosmetic products.” They concluded that when used in cosmetic products, titanium dioxide does not pose a genotoxic risk (SCCS, 2020).

2021 Evaluation by EFSA (EFSA FAF Panel)

11. Following the review of titanium dioxide specifications in 2019, and based on the fraction of nanoparticles present in E171, the food additive falls under the scope of the EFSA guidance on nanotechnology which was revised in 2018 to include 'a material that is not engineered as nanomaterial but contains a fraction of particles, less than 50% in the number–size distribution, with one or more external dimensions in the size range 1–100 nm'. The proposed amendment to E171 specifications was therefore accompanied by a recommendation for re-assessment of toxicological data in line with the requirements of the 2018 EFSA guidance on nanotechnology (EFSA, 2018b).

12. The data evaluated was for the food additive titanium dioxide E171 as well as titanium dioxide other than E171 containing a fraction of nanoparticles <100 nm or nano titanium dioxide (TiO₂ NPs). The characterisation of E171 was previously evaluated by the Panel and it was concluded that, according to data received from interested business operators, less than 50% of constituent particles in E171 have a minimum external dimension below 100 nm by number. The Panel considered that studies performed with TiO₂ NPs that predominantly consist of particles smaller than 30 nm (e.g. P25) are of limited relevance to the safety assessment of E171, as the data available to EFSA showed that the percentage by number of constituent particles < 30 nm was in the order of 1% or less in samples of pristine E171 or in E171 extracted from foods analysed after dispersion. However toxicity studies performed with TiO₂ <30 nm have been considered for completeness of the database and may be relevant with respect to whether a minimum limit for particle size should be included in the EU specifications for E171.

Overall EFSA conclusions:

13. With regard to the genotoxicity studies, combining the available lines of evidence, the FAF 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 – such as crystalline form, size of constituent particles, shape and

agglomeration state – and the outcome of *in vitro* or *in vivo* genotoxicity assays” (*i.e* a cut-off value for TiO₂ particle size with respect to genotoxicity could not be identified). The Panel also concluded that “several modes of action (MOA) may operate in parallel and the relative contributions of the different molecular mechanisms resulting in the genotoxicity of TiO₂ particles are unknown. Based on the available data, no conclusion could be drawn as to whether the genotoxicity of TiO₂ particles is mediated by a mode (s) of action with a threshold(s)”. Therefore, the Panel concluded that a concern for genotoxicity of TiO₂ particles cannot be ruled out.

14. With regards to other endpoints the FAF Panel concluded “that the absorption of TiO₂ particles is low, however they can accumulate in the body due to their long half-life; studies on general and organ toxicity, including the newly performed EOGRT study with E171, did not indicate adverse effects up to a dose of 1,000 mg/kg bw per day. In addition, no effects were seen in literature studies employing TiO₂ NP > 30 nm up to the highest dose tested of 100 mg/kg bw per day. No effects on reproductive and developmental toxicity up to a dose of 1,000 mg/kg bw per day, the highest dose tested, were observed in the EOGRT study with E171. No other reliable studies were found in the literature addressing these effects with E171; some findings regarding immunotoxicity and inflammation with E171 as well as neurotoxicity with TiO₂ NPs may be indicative of adverse effects. They also considered that there are indications of the induction of aberrant crypt foci in the small intestine with E171 and that no studies appropriately designed and conducted to investigate the potential carcinogenicity of TiO₂ nanoparticles were available.”

15. Overall, on the basis of all currently available evidence along with all the uncertainties, in particular the fact that genotoxicity concern could not be ruled out, the FAF Panel concluded that E171 can no longer be considered as safe when used as a food additive.

16. The FAF Panel, after evaluating the scientific evidence available, has identified uncertainties related to the following points:

- The size distribution of the particles in marketed E171 that consumers are exposed to, related to the different types of E171, as presented in the EFSA FAF Panel (2019) opinion.
- The processes used by industry when using E171 in food and to what extent these processes may affect the degree of agglomeration and thus internal exposure.
- State of agglomeration i.e. presence of 'free' (non-agglomerated) particles of tested material in gastrointestinal tract (GIT) of the animals and its effect on absorption.
- Representativity of different tested materials used in toxicity and genotoxicity studies for the food additive E171 when used in food.
- Differences in the physico-chemical properties of the different tested materials and the extent of their impact on the observed results.
- Interference in the measurements of Ti/TiO₂ in blood, tissues or organs with the most widely used analytical technique, i.e. ICP-MS, and its impact on the reliability of tissue concentration data.
- Confidence in the limited kinetic data as the basis for estimating half-lives and accumulation and for assessment of internal exposure and, related to that, the extent of systemic availability.
- None of the rodent studies were sufficiently long to cover the time needed for reaching the steady state for accumulation and this impacted the interpretation of the study results.
- Relative contribution of different molecular mechanisms leading to the production of ROS resulting in the genotoxicity of TiO₂ (inflammation, interaction with mitochondria, intrinsic potential of TiO₂ to generate ROS).
- Several modes of action for the genotoxicity may operate in parallel. The relative contributions of different molecular mechanisms elicited by

TiO₂ particles are unknown; it is unclear if a threshold mode of action could be assumed.

- Nature of the interactions between DNA and TiO₂ particles leading to conformational changes in DNA (EFSA, 2021).

EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP)

17. Following the FAF Panel's evaluation of the safety of titanium dioxide, the FEEDAP endorsed the conclusion and considered that it also applied to titanium dioxide when used as a feed additive for all animal species (EFSA FEEDAP, 2021). It should be noted that the conclusions presented below are on the basis of the information provided to the FEEDAP Panel by the applicant for use of titanium dioxide in animal feed and they are independent of the information considered by the EFSA FAF Panel for the 2021 Opinion for the use of titanium dioxide as a food additive. The FEEDAP Panel concluded that the genotoxicity of titanium dioxide particles could not be ruled out and this raised potential concerns on safety for the target species (especially long living and reproductive animals). On this point the conclusion was made on the basis that no studies were submitted by the applicant to support the safety of titanium dioxide for the target species and considering that titanium dioxide is intended for use in all animal species, the fact that there were no specific studies available designed to assess the safety for the target species, that genotoxicity could not be ruled out.

18. Furthermore no conclusion could be reached for the safety of titanium dioxide for consumers or the environment. For consumers, this conclusion was based on the findings of the FAF Panel and also as there was no available information on potential exposure of consumers to titanium dioxide particles in food products from animals that were fed the additive. With regard to effects on the environment there was an absence of adequate data to allow evaluation of the safety of titanium dioxide particles.

19. For occupational users, no data were available to allow for evaluation of the effects of the additive on the skin and the eyes. It was concluded that inhalation of the dust represents a risk to the users, as titanium dioxide is potentially carcinogenic (based on the IARC and RAC classifications) if inhaled and that the dusting potential of the anatase form was very high (150 g/kg). The concern with respect to the genotoxicity of titanium dioxide particles could not be ruled out, which the Panel noted should be considered as an additional potential concern to users handling the additive (EFSA, 2021a).

FSA response

20. Following the publication of the EFSA Opinion on Titanium Dioxide, the FSA initiated their review on this publication. Identifying a number of concerns, it was decided that the Opinion should be referred to the UK's Scientific Advisory Committees for independent expert review. The Opinion was presented to the Committee on Mutagenicity of Chemicals in Food, Consumer Products and the Environment (COM) (MUT/2021/03) in June of 2021 and the COT (TOX/2021/36) in July of 2021.

21. Members of both Committees were asked to evaluate the EFSA Opinion and comment on whether they agreed with EFSA's conclusions and, if not, provide further guidance on the next steps that should be taken by the FSA.

COM Consideration

22. The paper presented to the COM summarised the EFSA evaluation and particularly focused on the endpoints relating to genotoxicity.

23. The COM questioned the quality of the dataset and robustness of some of the studies used by the EFSA panel to draw its conclusions and noted that the overall data considered by EFSA were heterogeneous (e.g. the range of particles evaluated was diverse, there were different types of experimental approach and assays used; different doses were used; some studies were published in obscure or non-genotoxicity journals and non-GLP studies were included, which all contributed to the difficulty in making comparisons and an overall evaluation).

Members were also concerned about the potential for publication bias in the studies evaluated by EFSA (i.e. where negative studies were less likely to be published). It was also noted that until relatively recently, the specification of E171 was poorly defined, which contributed to uncertainty in evaluation.

24. Regarding the mode of action for genotoxicity, the COM agreed that the evidence indicated an indirect interaction with DNA with a threshold for genotoxicity. Although some *in vitro* tests reported a positive result these appeared to mainly relate to nanoparticles with the micro-sized particles mainly giving negative results. The *in vivo* studies tended to be of better quality and negative. The relatively low nano-fraction in E171 (i.e. often less than 3.2%) and its low bioavailability, could be important factors when considering risk assessment.

25. In conclusion, Members considered that the evidence did not allow definitive conclusions to be drawn and therefore they did not agree with the overall EFSA conclusions on the genotoxicity of E171 Titanium dioxide. They considered that a more reliable and robust dataset would be required before any conclusions could be drawn on the on the mutagenicity of TiO₂ particles. Members noted that EFSA made no clear distinction between the genotoxicity of nano-sized and micro-sized titanium dioxide particles. EFSA seemed to have put a lot of emphasis on the evidence from studies investigating nano-sized particles when only a small fraction of E171 is made up of nanoparticles. The COM suggested that that if practicable, restricting the amount of nanoparticles in the specification for E171 might reduce any potential genotoxicity risk. Additionally, the COM considered that the wording of EFSA's conclusion was not helpful from a risk communication perspective. Due to the heterogenous data and equivocality of the evidence further refinement of the data evaluated may be needed before definitive conclusions on the genotoxicity and safety of titanium oxide could be made. Currently, the EFSA conclusions were not justifiable based on the available evidence and this may create unnecessary concern for the public.

26. Further information can be found in the COM minutes. The link to the finalised minutes will be provided as soon as the minutes are published on the COM website.

COT Consideration

27. As mentioned previously, the COT considered the EFSA Opinion on titanium dioxide at their July 2021 meeting. The Committee considered a summary of the EFSA opinion as well as the preliminary comments from the COM meeting. It should be noted that some of the COT Members were also Members of the EFSA Scientific Panels that reviewed the safety of titanium dioxide for the 2021 Opinion. They were available to answer COT Member's questions and offer clarifications on the EFSA Opinion, however they did not participate in the COT's discussion or conclusions.

28. The COT highlighted the COM's preliminary comments. In particular that the COM had questioned the quality of the data and noted the difficulties in evaluating it adequately from the description given in the opinion, and furthermore their concerns over the robustness of the data, the use of data from laboratories not proficient in genotoxicity studies in a regulatory context and the weight given to studies with low reliability scores. The lack of a good dataset and a well-defined test compound (due to the poorly defined specifications) were also considered as severe limitations. Additionally the COT noted that the COM considered an indirect, thresholded mode of action and that the positive effects were likely attributable to the nano-fraction.

29. The COT were in agreement with the COM's view and further noted the large discrepancy between the underlying dataset and the conclusions drawn by EFSA. They further highlighted the inconsistencies between the outcomes of the 2020 SCCS Opinion discussed in detail in paragraph 10, where it was determined that the genotoxic effects of titanium dioxide manifest either via a thresholded or secondary mechanism, and the outcomes of the 2021 EFSA evaluation, where the FAF Panel concluded that it was unclear if a threshold mode of action could be assumed.

30. Regarding the genotoxicity of the nanoparticles, the COT considered that this could either be a concentration effect leading to oxidative damage or a stress effect, however, it was unclear as the results in different cell lines were equivocal and inconsistent. It was also noted that in some tests titanium dioxide had shown less reactivity. Members were informed that EFSA considered that genotoxicity was most likely due to an indirect mode of action however it was difficult to determine a threshold due to the multiple pathways that might act in parallel and that the conclusion erred on the side of caution. It was also acknowledged that the greater the nanoparticle content present in the test material, the more likely that the outcome of the study was to be positive.

31. The COT also noted that in several parts of the Opinion, published papers were presented at face value, and there was no discussion of the results nor the overall Weight of Evidence to support the conclusions being made. They furthermore noted discrepancies and conflicts between the results of the studies reported and the overall conclusions. Overall, the COT considered that there appeared to be a lack of internal consistency and of objective weighing of all the evidence. While some of this might have been due to differences in the nature of the TiO₂ tested, this was not clear in the Opinion. Members also noted that it was difficult to draw any conclusions from the studies and a closer look in terms of material characterisation was needed in order to understand some of the effects reported. Members also considered that follow up was needed on the reproductive toxicity study as only the presence or absence of an effect was measured.

32. The large variation in the specifications of E171 was also discussed, based on the analytical data for pristine E171 that indicated that more than 50% of the constituents were in the nano-range (Appendix W) so the COT considered that more clarification was needed on the actual composition of E171. It was noted that the EFSA definition of nanomaterials lacked clarity with regard to materials that were not engineered as nanomaterials but contained particles in the nano range. The possibility and plausibility of removing the nano fraction from E171 in order to mitigate the risk was also discussed by the COT.

33. Members were informed that EFSA had indications that when used by industry, E171 was dispersed into nanoparticles by sonication and therefore also considered data on materials made solely of nanoparticles for the assessment. However, this was questioned by Members as it was noted that pure nano-titanium dioxide would lose its technical function in the food (as it would not provide colour) and would therefore not be of use.

34. It was observed that the percentage of absorption was reported to be higher in the 2021 opinion than in previous evaluation (EFSA, 2016), based on the same dataset. Members were advised that newer studies used in the previous evaluation were re-considered (evidence from deceased humans and indications that titanium dioxide could cross the placenta). The duration of the animal studies was not sufficient to evaluate at which levels steady state would be reached and therefore it was considered that absorption had previously been underestimated. Finally, the extended one generation reproductive toxicity (EOGRT) study provided indirect evidence for systemic exposure following administration of titanium dioxide.

35. The COT also questioned the conclusions with regards to the ability of TiO₂ to induce aberrant crypt foci. On this point of the Committee were advised that because of the above consideration by EFSA (paragraph 33), only one study that used sonication of the material was considered, as the material tested was undispersed in the other available studies.

36. The findings of the studies on neurotoxicity were considered inconsistent by the COT. It was noted that the EOGRT study did not report any effects and that most of the other studies on this endpoint were of nanomaterials. Members were advised that in the EFSA evaluation, the issue of the test material in the EOGRT not being dispersed was taken into consideration with regards to the conclusions on this endpoint. They considered that had it been dispersed and stabilised in the nano form, some effects could possibly have been observed. The COT, as previously, questioned the relevance of such dispersion to real world use. Members noted that the histopathology tests performed for the EOGRT study

were standard and were not sensitive enough in comparison to other studies on this endpoint that performed specific neuro-histopathology testing.

37. On balance, the Committee considered that the weight of evidence did not support the conclusions drawn by EFSA. The COT also agreed with the comments of the COM with regards to risk communication that “As it stands the conclusion is highly risk adverse based on the weak evidence available, and it might create unnecessary concern to the public.” They considered that care should be taken when expressing the conclusions as they might cause unnecessary concern and they were uncomfortable with EFSA’s binary communication on a dataset with a lot of uncertainties. The COT suggested that the COM should independently review the database on genotoxicity and apply the COM’s Guidance on determining thresholds. When considering whether they agreed with EFSA’s conclusion that no differentiation could be made with regards to size/form of titanium dioxide and different aspects of toxicity, the COT erred towards the view that nanoparticles were driving the toxicity. It was decided that an interim position paper, capturing the COT’s view and the proposed next steps should be published.

38. More information on the COT discussion can be found in the [Minutes of the July meeting](#).

Next Steps

39. Considering the outputs of the discussions from the COT and the COM, the FSA has decided to launch their own review of the safety of titanium dioxide as a food additive. In the following months the FSA Secretariat will be presenting the available database on the genotoxicity of titanium dioxide to the COM for their independent review as proposed by the COT. Furthermore, the rest of the database on the remaining endpoints will also be considered by the COT.

40. The FSA is also working with other interested government departments to co-ordinate the UK’s effort on the independent review of the safety of titanium dioxide.

COT position paper

January 2022

Abbreviations:

ADI – Acceptable Daily Intake

ADME – Absorption, Distribution, Metabolism, Excretion

ANSES – Agency for Food, Environmental and Occupational Health and Safety

AOP – Adverse Outcome Pathway

ECHA – European Chemicals Agency

EFSA – European Food Safety Authority

EOGRT – Extended one-generation reproduction toxicity

FAF – Panel on Food Additive and Flavourings

FEEDAP - Panel on Additives and Products or Substances used in Animal Feed

GIT – Gastrointestinal Tract

IARC – International Agency for Research on Cancer

JECFA – Joint FAO/WHO Expert Committee of Food Additives

NOAEL – No Observed Adverse Effect Level

PSLT – Poorly Soluble Low Toxicity

RAC – Committee for Risk Assessment

ROS – Reactive Oxygen Species

SCCS - Scientific Committee on Consumer Safety

SCF – Scientific Committee on Food

TiO₂ – Titanium Dioxide

TiO₂ NPs – Titanium Dioxide Nanoparticles

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