

Titanium dioxide: Are there health risks?

Update of frequently asked questions to the BfR of 12 May 2021

Titanium dioxide (TiO₂) is currently authorised as the food additive E 171 and can be used as a white colour pigment in confectionery and coatings, e.g. in dragees and chewing gum. Under the nomenclature CI 77891, the substance is contained as a white pigment in cosmetic products such as toothpaste. Titanium dioxide is also used as a UV filter in sunscreens. The majority of titanium dioxide is used in technical applications, however, such as the manufacture of paints, varnish, paper and plastics.

Due to the diversity of applications, all important routes of absorption must be considered in the context of a health assessment of titanium dioxide: absorption via the skin (dermal), via the respiratory tract (inhalation) or via the digestive tract (oral).

The BfR has compiled frequently asked questions on the topic of titanium dioxide.

What is titanium dioxide and which products contain the substance?

Titanium dioxide (EC 236-675-5, CAS 13463-67-7) is produced in millions of tonnes worldwide. More than 1 million tonnes are produced annually in Europe. Almost 90 % of the titanium dioxide is used as white pigment in the manufacture of paints, varnish and printing inks, as well as plastics and paper, and a further 10 % for cosmetics, foods, feeds and pharmaceuticals, where above all the high luminosity and opacity of the white pigment are exploited.

As a food additive with the nomenclature E 171, titanium dioxide can be contained in confectionery and coatings among other things, e.g. in dragees and chewing gum. Under the nomenclature CI 77891, the substance is also used in cosmetic products such as toothpaste.

In what forms does titanium dioxide occur?

Titanium dioxide is used as a pigment or as a nanomaterial. Both forms are tasteless, odourless and insoluble.

According to an EU recommendation¹, a substance can be considered as nanomaterial if more than 50 % of the number of particles with a diameter of 1-100 nm (nanometres) contained therein are present in at least one spatial dimension. It does not matter here whether this quantity exists in the material intentionally or unintentionally. This recommendation has been taken into account when amending the annexes to the REACH Regulation, which came into force on 01.01.2020 and nanoforms of substances were defined.

Titanium dioxide in nanoform is mainly marketed commercially in two different crystalline forms (anatase or rutile). A material that has often been used as a test material above all in inhalation toxicity studies (designation "P25"), is an 80/20 mixture of anatase and rutile. Commercial nanoforms can also be surface treated. Often a passivating protective coating of the particle surface is applied onto the particles, for example.

¹ Commission recommendation of 18 October 2011 on the definition of nanomaterials (2011/696/EU). https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2011:275:0038:0040:en:PDF



Titanium dioxide, specifically produced in nanoform, is used in some consumer products. Above all the high UV filter effect, the transparent properties of nano-forms and advantages in processing are made use of here.

How can titanium dioxide be ingested?

Due to the wide variety of applications, all of the important intake routes have to be looked at within the scope of a health risk assessment of titanium dioxide: intake via the skin (dermal), respiratory tract (by inhalation) or digestive tract (oral). The oral intake may, for example, result from eating food containing the additive E 171. Titanium dioxide is not absorbed via the skin (dermal), when using skincare products.

The inhalation of fine particles and especially nanoparticles is generally regarded as critical to health, as studies with animals have shown that they can penetrate deep into the lungs and might cause chronic inflammations. In rats, the inhalation of extremely high titanium dioxide concentrations over a very long period of time (the entire lifespan of the animals) led to the formation of lung tumours. These studies form the basis of the now completed European classification process (see below). The uptake of titanium dioxide via the oral mucosa and/or digestive tract (oral) was taken into consideration in the assessment conducted by EFSA on the use of titanium dioxide as the food additive E 171 and as a component of food contact materials.

The uptake of titanium dioxide via tattoo inks constitutes a special case. Titanium dioxide is used in tattoo inks and permanent make-up as a white pigment or in combination with pigments to produce certain shades. The predominant crystal form used in tattoo inks is rutile.

Which legal regulations apply to the use of titanium dioxide in cosmetic products?

Where use in cosmetic products is concerned, titanium dioxide is included in two positive lists of the EU Cosmetics Regulation (EC) No 1223/2009 (EUCR), firstly in the list of colourants allowed in cosmetic products (Annex IV EUCR) and secondly in the list of authorised UV filters (Annex VI EUCR). Currently only specific forms of nanoscale and nonnanoscale titanium dioxide are allowed as UV filters in cosmetic products and listed in the current valid version of EUCR, which is updated regularly. The transparent appearance of the nanoform is an advantage when applied to the skin. The EC includes a substance in the positive lists of the EUCR after a safety assessment was performed by the EU Commission's Scientific Committee on Consumer Safety (SCCS). Use of nanoforms of titanium dioxide in sunscreens is not authorised in applications which can lead to exposure of the lungs through inhalation. However, as a result of CLP classification, a new risk assessment of titanium dioxide by the SCCS was necessary pursuant to Article 15 (1) of the Regulation on Cosmetic Products, which was published on 6.10.2020

(https://ec.europa.eu/health/sites/health/files/scientific_committees/consumer_safety/docs/sccs_o_238.pdf). Conclusions could only be drawn for one specific material. An amendment of the EUCR on the basis of this recommendation has not yet been made.



Which legal regulations apply to the use of titanium dioxide in materials without food contact?

No specific legal regulations regarding the use of titanium dioxide exist for materials without food contact, such as textiles and toys. There is a general requirement that the products must be safe and that they may not damage health.

Accordingly, it is prohibited in accordance with Art. 30 of the German Food and Feed Law (LFGB) to produce or treat commodities for others in such a way that they are capable of damaging health due to their composition, in particular through toxicologically effective substances or impurities when put to their intended or foreseeable use. The general safety requirements of the European toy directive 2009/48/EC apply to toys. According to this directive, toys, including the chemical substances they contain, may not endanger the safety of children when put to their intended or foreseeable use under consideration of the behaviour of children.

As a consequence of the CLP classification, the EU Commission has mandated the Scientific Committee on Health, Environment and Emerging Risks (SCHEER) on 20.11.2020 for the safety assessment of titanium dioxide in toys.²

Thanks to its favourable material properties (chemical and thermal stability, light fastness, high covering properties as white pigment), titanium dioxide is used in various materials which occur in consumer products. It is used as white pigment as well as a texturing component of colour pigments for paints and varnishes. It is also used for décors on paper and porcelain and for the pigmentation of textiles and leather. It finds use in plastics as a coating, dye or stabiliser (UV protection). Other examples of materials containing titanium dioxide are ceramics and glassware. A characteristic feature of these material applications is that the titanium dioxide is bound into a fixed matrix, thus limiting its release.

Which legal regulations apply to the use of titanium dioxide in food contact materials?

The European Framework Regulation (EC) No 1935/2004 "on materials and articles intended to come into contact with food" applies to all food contact materials. It stipulates that materials and articles are to be produced in compliance with good manufacturing practice so that under normal or foreseeable conditions of use they do not transfer their constituents to food in quantities which could

- a) endanger human health or
- b) bring about an unacceptable change in the composition of the food or
- c) bring about an impairment of the organoleptic properties thereof (flavour, taste etc.).

Article 5 of the above Regulation also stipulates the adoption of so-called "specific measures" for certain groups of materials and articles. In the course of a specific measure of this kind, Titanium dioxide was authorised for use in food contact materials made of plastic in line with Regulation (EU) No 10/2011. The use of titanium dioxide in "nano-structure" is prohibited in this context.

There are no regulations on European level covering other material groups relevant to titanium dioxide. Within the scope of the "BfR recommendations for food contact materials", titanium dioxide (in nanoform, not identical with E 171) is listed as a heat stabiliser (max. 3 %) in Recommendation XV "Silicone" (e.g. silicone baking moulds) (BfR, 2018). There is

² https://ec.europa.eu/health/sites/health/files/scientific_committees/scheer/docs/scheer_g_018.pdf



no transfer of titanium dioxide from the silicone to the food with a limit of detection of $1.8 \mu g/kg$ food.

Assessment of titanium dioxide as part of European chemicals assessment

Titanium dioxide is the subject of the European chemicals assessment. One of the processes is the so-called EU-wide harmonised classification, completed in February 2020. The second process is concerned with the evaluation of the substance titanium dioxide within the scope of the European Chemicals Regulation REACH. Both of these regulatory processes were initiated by France. Neither process distinguishes explicitly between conventional titanium dioxide (pigment) and titanium dioxide in nanoform. The scope of the applicable EU Regulations comprises all forms of titanium dioxide.

1) Harmonised classification in line with the CLP Regulation (Regulation (EC) No 1272/2008)

Chemicals with particularly dangerous substance properties (e.g. mutagenic, carcinogenic or damaging to reproduction) are classified throughout the EU in accordance with Regulation (EC) No 1272/2008 on classification, labelling and packaging ("CLP Regulation"). This is a harmonised legal categorisation which is legally binding for manufacturers, importers and users of the substance as such, and which also applies to the substance when used in mixtures if general or, where available, specific concentration limits are exceeded.

A harmonised CLP classification is unbiased as to the application, i.e. it can be made for all chemicals present in the EU market and, if not restricted, it includes all forms of a substance. References to the classification are made in various legal standards and the existence of a harmonised CLP classification, especially the higher hazard categories, sometimes has drastic legal consequences and triggers various risk mitigation measures in other legal areas outside chemicals law (e.g. product law, cosmetics-, toys-, waste law).

Titanium dioxide has now completed the classification process in line with the CLP Regulation. The trigger was a proposal submitted by France in 2015. The Risk Assessment Committee (RAC) at the European Chemicals Agency (ECHA) concluded in 2017 that titanium dioxide is presumably carcinogenic to humans when inhaled (Category 2, H351 i). A possible health hazard is seen above all in the inhalation of dusts. The process was subject to discussions. The EU Commission completed classification and labelling in October 2019, according to which titanium dioxide [in powder form with at least 1 % of particles with aerodynamic diameter ≤ 10 μm] may be carcinogenic if inhaled. The proposed classification of titanium dioxide was finalised on 18 February 2020 as part of the 14th ATP (Adaption to technical progress) and shall be made mandatory as of 09 September 2021. The corresponding Delegated Regulation (EU) No 2020/217 was published in the Official Journal of the European Union in February 2020³. Furthermore, provisions were made for the labelling of certain mixtures containing titanium dioxide. The national helpdesk REACH-CLP-Biocide has published guidance on the application of the harmonised classification at https://www.reach-clp-biozid-

helpdesk.de/SharedDocs/Publikationen/EN/CLP/BAuA/Kompakt_CLP_How_to_apply_the_h armonised classification of titanium dioxide.html.

³ https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=uriserv:OJ.L_.2020.044.01.0001.01.ENG&toc=OJ:L:2020:044:TOC



2) Substance evaluation within the scope of the REACH Regulation

The substance evaluation in line with the REACH Regulation (EC 1907/2006) serves to verify an initial suspicion regarding the risk a substance poses to health or the environment and to request from the manufacturer or importer of the substance relevant but missing information for the assessment of a risk, and if necessary determine what action has to be taken to minimise it. The initiative for a substance evaluation usually lies with the authorities in each EU Member State.

Which legal regulations apply to the use of titanium dioxide as a food additive?

Regulation (EC) No. 1333/2008 applies to the use of titanium dioxide as a food additive. According to this regulation, the use of titanium dioxide (E 171) is currently permitted in several food categories, whereby the quantum satis principle⁴ mostly applies as the maximum quantity. The purity requirements and specifications are regulated in Regulation (EU) No. 231/2012. The authorisation is based on health assessments by the Scientific Committee on Food (SCF) of the EU Commission, which was responsible for this until 2003, and the European Food Safety Authority (EFSA), which has been responsible since then.

The EFSA evaluation published on 6 May 2021 is expected to form the basis for a decision by the risk management institutions (EU Commission, Member States and EU Parliament) on whether TiO₂ can continue to be approved as a food additive in the EU.

Is titanium dioxide authorised as a feed additive?

Titanium dioxide is authorised as a feed additive for all animal species (except dogs and cats) under Directive 70/524/EEC, but only if by-products of the food industry or other starting materials have been used in the manufacture of feed to which e.g. titanium dioxide has been added as an additive for identification in food. In feed for dogs and cats, titanium dioxide can be used as a colourant without these restrictions.

For all feed additives authorised under Directive 70/524/EEC, a new application for reevaluation of the existing authorisation had to be submitted under Regulation (EC) No 1831/2003. No final decision has yet been taken on such an application and thus on the further prolongation of the current authorisation of titanium dioxide as a feed additive.

How is the health risk of titanium dioxide as food additive E 171 assessed?

In May 2021, the European Food Safety Authority (EFSA) re-evaluated possible health risks associated with the use of titanium dioxide as a food additive (E 171) based on all currently available relevant scientific evidence and published the result on 6 May 2021. In addition to a new animal study investigating possible reproductive toxic effects, a total of almost 12,000 publications were considered. The re-evaluation also focused on concerns regarding possible genotoxic effects of titanium dioxide (genotoxicity). Following a systematic methodology, more than 200 publications were identified and evaluated in which possible genotoxic effects of titanium dioxide were investigated. After evaluation of the available data, the concern regarding possible genotoxic effects of titanium dioxide could not be ruled out. Therefore, and due to numerous scientific uncertainties, the EFSA experts came to the

⁴ According to the terminology of Regulation (EC) No 1333/2008 "Quantum satis" means: "No maximum numerical level is specified and substances shall be used in accordance with good manufacturing practice, at a level not higher than is necessary to achieve the intended purpose and provided the consumer is not misled.""



conclusion that the use of titanium dioxide as a food additive can no longer be considered as safe. No acceptable daily intake was derived.

The EFSA assessment is expected to form the basis for a decision by the risk management institutions (EU Commission, Member States and EU Parliament) on whether TiO₂ can continue to be authorised as a food additive in the EU.

Are adverse health effects to be expected for consumers when used as a food additive (E 171)?

EFSA concluded in May 2021 that studies on general and organ toxicity do not indicate any adverse effects. In animal studies, no adverse effects on fertility and offspring development have been observed. In an older study with rats and mice, no carcinogenic effects were observed after oral exposure to titanium dioxide, which was not characterised in terms of the particle size (NCI, 1979). No suitable study is available on the carcinogenic potential of titanium dioxide nanoparticles after oral exposure. EFSA's experts concluded that although titanium dioxide is absorbed from the gastrointestinal tract only at very low levels, it takes a long time to be excreted from the body and has the potential to accumulate in tissues.

After the evaluation of the available data, the suspicion of a genotoxic effect of titanium dioxide particles could not be refuted. According to EFSA, there are uncertainties, especially with regard to the molecular mechanism of the genotoxic effects. Furthermore, according to EFSA, the evaluated data do not point to a clear correlation between certain properties of titanium dioxide (nano-) particles, such as the size and nature of the particles, and the outcome of the genotoxicity studies. For this reason and due to numerous scientific uncertainties, the experts of the EFSA came to the conclusion that the use of titanium dioxide as a food additive can no longer be considered as safe. No acceptable daily intake level was derived.

EFSA's assessment is based on animal studies and mechanistic studies. Human studies and targeted epidemiological studies on possible health effects are currently not available.

In principle, many foods contain ingredients with a genotoxic potential. These are very often of natural origin and therefore unavoidable in the daily diet. For some genotoxic substances in food there are findings on adverse health effects in humans. In the case of titanium dioxide, this correlation has not yet been investigated in human studies. However, particular health requirements are placed on food additives. These are strictly tested and regulated.

Consumers who do not want to eat foods containing certain additives can avoid them. This is because the use of food additives is subject to labelling, i.e. they must be declared in the list of ingredients in packaged foods.

On which studies is the assessment of the European Food Safety Authority (EFSA) based?

The findings are based on a review of almost 12,000 publications. Following a systematic methodology, more than 200 publications were identified and evaluated in which possible mutagenic effects of titanium dioxide were investigated. For the assessment, the experts used, among others, the guidance document "Guidance on the risk assessment of the application of nanoscience and nanotechnologies in the food and feed chain" published by EFSA in 2018 (available at:

https://efsa.onlinelibrary.wiley.com/doi/abs/10.2903/j.efsa.2011.2140) of the EFSA Scientific Committee.



Are adverse health effects to be expected for consumers when using cosmetic products?

Titanium dioxide is not absorbed dermally, i.e. through the skin, via skin care products. According to the current state of knowledge, the Scientific Committee on Consumer Safety (SCCS), in the context of a statement on nanoparticles in sunscreens, considered absorption via the skin not to pose any risk of adverse effects after application on healthy, intact or sunburned skin. The inhalation of titanium dioxide nanoparticles, which results in exposure of the consumer's lungs to TiO_2 nanoparticles, has been assessed by the SCCS as a health concern (SCCS/1516/13; SCCS/1583/17 5). Therefore, titanium dioxide (nano) in applications that may lead to exposure of the end user's lungs through inhalation has been banned in the EU Cosmetics Regulation. There are currently no indications that the use of TiO_2 in cosmetic products does cause adverse health effects if the legal requirements are complied with.

The BfR currently has no data on the contents and specifications of titanium dioxide in toothpaste. A titanium dioxide pigment called CI 77891 is used in toothpaste. BfR is not able to assess whether the EFSA assessment on E 171 is transferable to this pigment. BfR has recommended to the competent risk management authorities to mandate the Scientific Committee on Consumer Safety (SCCS) with a risk assessment.

Are adverse health effects for consumers to be expected from the use of titanium dioxide in food contact materials?

Prior to the inclusion of titanium dioxide in BfR Recommendation XV (silicones), the BfR conducted a health assessment of the intended use on the basis of submitted analytical data and the evaluation by EFSA (EFSA, 2016; EFSA, 2018). Overall, the BfR came to the conclusion that the use of titanium dioxide (not identical to E 171) in food contact materials made of silicone, as stated in BfR Recommendation XV, does not pose a health risk (BfR, 2018). This conclusion is based, on the one hand, on the results of analytical studies that no release of titanium dioxide from the silicone into food takes place (at a very low detection limit 1.8 µg/kg food). On the other hand, the titanium dioxide applied for use in silicone was assessed as non-carcinogenic after oral intake (BfR, 2018). A study of the "National Cancer Institute" (NCI) of the "U.S. Department of Health and Human Services" on rats and mice was considered to be a key study, in which no differences to the control group in the type and number of tumour-like and non-tumour-like tissue damage were found up to the highest administered dose (50 g/kg feed, equivalent to about 2250 mg/kg body weight/day) (NCI, 1979). There is no new relevant study according to the EFSA assessment published on 6 May 2021.

When titanium dioxide is used in plastic food contact materials according to Regulation (EU) No 10/2011, the titanium dioxide is incorporated into the polymer matrix as a solid, similar as in the case of silicone. The experimental data available on some selected materials as well as modelling studies (EFSA 2019b) concluded that, as with silicone, a release of titanium dioxide from the plastic into the food does not occur or occurs to a very low extent. Accordingly, a health risk is very unlikely.

http://publications.europa.eu/resource/cellar/b635a200-38cd-11e9-8d04-01aa75ed71a1.0001.01/DOC_1

⁵ https://ec.europa.eu/health/sites/health/files/scientific_committees/consumer_safety/docs/sccs_o_136.pdf



Are adverse health effects to be expected for consumers from the use in tattoo inks?

So far, there are no known adverse health effects associated with exposure to TiO₂-containing pigments in tattoo inks. Questions and answers specifically on tattoo inks can be found in the BfR FAQ of 16 September 2019.

What does the Delegated Regulation (EU) No 2020/217 mean for health risk assessments of the use of titanium dioxide in consumer products?

The EU Commission completed classification and labelling in October 2019, according to which titanium dioxide [in powder form with at least 1 % of particles with aerodynamic diameter ≤ 10 µm] may be carcinogenic if inhaled. The corresponding Delegated Regulation (EU) No 2020/217 was published in the Official Journal of the European Union in February 2020 andtitanium dioxide was included in Annex VI of CLP Regulation (14th adaptation to technical progress (ATP) as presumably carcinogenic to humans when inhaled (Category 2, H351 i), valid from 09.09.2021).

This decision is based on a scientific opinion from the RAC dated 14 September 2017 which proposed classifying titanium dioxide as carcinogen category 2 by inhalation. In this case, as is listed in the recitals of Regulation (EU) No 2020/217, the titanium dioxide-induced lung carcinogenicity is associated with inhalation of respirable (titanium dioxide) particles, retention and poor solubility of the particles in the lung. This is also known from other particles.

What is the future of titanium dioxide as a food additive?

The evaluations of the European Food Safety Authority usually form the basis for risk management decisions of EU Commission, Member States and EU Parliament respectively, on the authorisation and use of the evaluated food additives.

Further information on the subject from the BfR website:

BfR questions and answers on nanotechnology of 28 August 2012 https://www.bfr.bund.de/cm/349/questions-and-answers-on-nanotechnology.pdf

FAQ on tattoo inks of 16 September 2019 https://www.bfr.bund.de/en/faq_about_tattoo_inks-201880.html

Questions and Answers on the Risk Assessment of Cosmetic Products of 3 March 2014 https://www.bfr.bund.de/cm/349/questions-and-answers-on-the-risk-assessment-of-cosmetic-products.pdf

Assessment of potential cancer risk of nanomaterials and nanoparticles released from products, Joint Opinion 005/2011 of the BfR and UBA of 15 April 2010 https://www.bfr.bund.de/cm/349/assessment_of_potential_cancer_risk_of_nanomaterials_and_nanoparticles_released_from_products.pdf

Sunscreen: According to the current state of knowledge zinc oxide as a UV filter is safe, BfR Opinion No. 037/2010 of 18 June 2010

https://www.bfr.bund.de/cm/349/sunscreen_according_to_the_current_state_of_knowledge_zinc_oxide_as_uv_filter_is_safe.pdf



References

ANSES (2019): Additif alimentaire E 171: l'Anses réitère ses recommandations pour la sécurité des consommateurs, Journal officiel de la République Française du 25 avril 2019, https://www.anses.fr/fr/content/additif-alimentaire-e171-l%E2%80%99anses-r%C3%A9it%C3%A8re-ses-recommandations-pour-la-s%C3%A9curit%C3%A9-des

ANSES (2019): AVIS de l'Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail relatif aux risques liés à l'ingestion de l'additif alimentaire E 171. Saisine n° 2019-SA-0036. Maisons-Alfort, le 12 avril 2019. https://www.anses.fr/fr/system/files/ERCA2019SA0036.pdf

Bettini S, Boutet-Robinet E, Cartier C, Coméra C, Gaultier E, Dupuy J, et al. (2017): Food-grade TiO2 impairs intestinal and systemic immune homeostasis, initiates preneoplastic lesions and promotes aberrant crypt development in the rat colon. Scientific Reports; 7:40373, doi: 10.1038/srep40373.

BfR (2018): 21. Sitzung der BfR-Kommission für Bedarfsgegenstände - Protokoll vom 7. November 2018. http://m.bfr-meal-studie.de/cm/343/21-sitzung-der-bfr-kommission-fuer-bedarfsgegenstaende.pdf

BfR (2011): Assessment of potential cancer risk of nanomaterials and nanoparticles released from products, Joint Opinion 005/2011 of the BfR and UBA of 15 April 2010 https://www.bfr.bund.de/cm/349/assessment of potential cancer risk of nanomaterials and nanoparticles released from products.pdf

BfR (2010): Sunscreen: According to the current state of knowledge zinc oxide as a UV filter is safe, BfR Opinion No. 037/2010 of 18 June 2010 https://www.bfr.bund.de/cm/349/sunscreen according to the current state of knowledge zinc oxide as uv filter is safe.pdf

Donner E.M., Myhre A., Brown S.C., Boatman R., and Warheit D.B. (2016): In vivo micronucleus studies with 6 titanium dioxide materials (3 pigment-grade & 3 nanoscale) in orally-exposed rats. Regulatory Toxicology and Pharmacology 74, 64-74. doi: https://doi.org/10.1016/j.yrtph.2015.11.003

ECHA (2017): https://echa.europa.eu/-/titanium-dioxide-proposed-to-be-classified-as-suspected-of-causing-cancer-when-inhaled

EFSA ANS Panel (EFSA Panel on Food Additives and Nutrient Sources added to Food) (2016): Scientific Opinion on the re-evaluation of titanium dioxide (E 171) as a food additive. EFSA Journal;14(9):4545, 83 pp. doi:10.2903/j.efsa.2016.4545, https://www.efsa.europa.eu/de/efsajournal/pub/4545

EFSA ANS Panel (EFSA Panel on Food Additives and Nutrient Sources added to Food) (2018): Evaluation of four new studies on the potential toxicity of titanium dioxide used as a food additive (E 171). EFSA Journal; 16(7):5366, doi: 10.2903/j.efsa.2018.5366 https://www.efsa.europa.eu/en/efsajournal/pub/5366

EFSA (2019): EFSA statement on the review on 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 Journal 2019; 17 (6): 5714, 11 pp. doi:10.2903/j.efsa.2019.5714, https://www.efsa.europa.eu/en/efsajournal/pub/5714

EFSA FAF Panel (EFSA Panel on Food Additives and Flavourings) (2019a) Scientific opinion on the proposed amendment of the EU specifications for titanium dioxide (E 171) with respect to the inclusion of additional parameters related to its particle size distribution. EFSA Journal 2019;17(7):5760, 23 pp.

https://www.efsa.europa.eu/de/efsajournal/pub/5760

EFSA Panel on Food Contact Materials, Enzymes and Processing Aids (CEP) (2019b) Safety assessment of the substance, titanium dioxide surface treated with fluoride-modified alumina, for use in food contact materials. EFSA Journal 2019;17(6):5737, 11 pp. doi: 10.2903/j.efsa.2019.5737, https://www.efsa.europa.eu/de/efsajournal/pub/5760

EFSA FAF Panel (EFSA Panel on Food Additives and Flavourings) (2021): Safety assessment of titanium dioxide (E171) as a food additive, EFSA Journal 2021;19(5):6585, https://www.efsa.europa.eu/en/efsajournal/pub/6585

EU-Kommission (2020): 14. ATP (Delegierte Verordnung (EU) 2020/217) zur CLP-Verordnung ((EG)1272/2008). Amtsblatt der Europäischen Union 2020, L44/14. https://eur-lex.europa.eu/legal-content/DE/TXT/PDF/?uri=CELEX:32020R0217&from=DE

EU-Kommission (2020): Scientific Committee on Consumer Safety. Request for a scientific opinion on Titanium dioxide used in cosmetic products.

https://ec.europa.eu/health/sites/health/files/scientific_committees/consumer_safety/docs/sccs2016_q_043.pdf

EU-Kommission (2018): Verordnung (EU) 2018/1881 der Kommission. Amtsblatt der Europäischen Union 2018, L 308/1.

https://eur-lex.europa.eu/legal-content/DE/TXT/PDF/?uri=CELEX:32018R1881&from=EN

EU-Kommission (2011): Empfehlung der Kommission vom 18. Oktober 2011 zur Definition von Nanomaterialien (2011/696/EU). https://eur-lex.europa.eu/legal-content/DE/TXT/PDF/?uri=CELEX:32011H0696&from=DE

Guo Z, Martucci N, Moreno-Olivas F, Tako E and Mahler G (2017): Titanium dioxide nanoparticle ingestion alters nutrient absorption in an in vitro model of the small intestine. NanoImpact, 5, 70-82, doi: 10.1016/j.impact.2017.01.002.

Heringa MB, Geraets L, vanEijkeren JCH, Vandebriel RJ, deJong W and Oomen AG (2016): Risk assessment of titanium dioxide nanoparticles via oral exposure, including toxicokinetic considerations. Nanotoxicology, 10, doi: 10.1080/17435390.2016.1238113

IARC (International Agency for Research on Cancer) (2010): "Carbon black, titanium dioxide, and talc," in IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, vol. 93, International Agency for Research France,

https://monographs.iarc.fr/wp-content/uploads/2018/06/mono93.pdf

Kreyling WG, Holzwarth U, Haberl N, et al. (2017): Quantitative biokinetics of titanium dioxide nanoparticles after intratracheal instillation in rats: Part 3. Nanotoxicology, Published online 03 April 2017, http://dx.doi.org/10.1080/17435390.2017.1306894



Louro H., Tavares A., Vital N., Costa P.M., Alverca E., Zwart E., Jong W.H., Fessard V., Lavinha J., and Silva M.J. (2014): Integrated approach to the in vivo genotoxic effects of a titanium dioxide nanomaterial using LacZ plasmid-based transgenic mice. Environmental and Molecular Mutagenesis 55 (6), 500-509. doi:10.1002/em.21864

Ministère de l'Economie et des Finances (2019): Arrêté du 17 avril 2019 portant sur la suspension de la mise en marché des denrées contenant l'additif E 171 (dioxyde de titane - TiO2), https://www.legifrance.gouv.fr/jo_pdf.do?id=JORFTEXT000038410047

National Institute for Occupational Safety and Health (2011): Current Intelligence Bulletin 63: Occupational Exposure to Titanium Dioxide, April, https://www.cdc.gov/niosh/docs/2011-160/pdf

NCI (1979): BIOASSAY OF TITANIUM DIOXIDE FOR POSSIBLE CARCINOGENICITY. National Cancer Institute. Carcinogenesis. Technical Report Series 97 (NCI-CG-TR-97). https://ntp.niehs.nih.gov/ntp/htdocs/lt_rpts/tr097.pdf

Proquin H, Rodriguez-Ibarra C, Moonen CG, Urrutia-Ortega IM, Briede JJ, de Kok TM, van Loveren H and Chirino Y (2017): Titanium dioxide food additive (E 171) induces ROS formation and genotoxicity: contribution of micro and nano-sized fractions. Mutagenesis, 32, 139-149, doi:10.1093/mutage/gew051

Ruiz PA, Morón B, Becker HM, Lang S, Atrott K, Spalinger MR, et al. (2016): Titanium dioxide nanoparticles exacerbate DSS-induced colitis: Role of the NLRP3 inflammasome. Gut. doi:10.1136/gutjnl-2015-310297

Weir, A., Westerhoff, P., Fabricius, L., Hristovski, K. & von Goetz, N. (2012): Titanium Dioxide Nanoparticles in Food and Personal Care Products. Environ Sci Technol 46, 2242-2250, doi:10.1021/es204168d

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