German Federal Institute for Risk Assessment

FAQ

11 October 2024

Titanium dioxide – are there health risks?

→ Changes compared to the version of 12 May 2021: Following the cancellation of the authorisation of titanium dioxide as a food additive in 2022, the FAQs have been fundamentally revised.

Titanium dioxide (TiO_2) is produced worldwide on a scale of millions of tonnes. Most of the titanium dioxide produced is used in technical applications such as the production of colours, paints, paper and plastics. Under the designation CI 77891, the substance is contained as a white pigment in cosmetic products such as toothpaste. Titanium dioxide is also used as a filter to protect against ultraviolet radiation in sunscreens. Until 2022, titanium dioxide was also authorised as a food additive E 171. As concerns regarding a possible mutagenic effect could not be dispelled in the most recent risk assessment, the authorisation as a food additive was withdrawn in the EU on 7 February 2022.

In this document, frequently asked questions and answers on titanium dioxide and potential health risks have been compiled by the German Federal Institute for Risk Assessment.

Which products contain titanium dioxide?

Millions of tonnes of titanium dioxide (EC 236-675-5, CAS 13463-67-7) are produced worldwide every year. In Europe alone, this amounts to more than 1 million tonnes per year. By far the largest proportion is used as a white pigment for the production of varnish, paints and printing inks as well as plastics and paper, while a smaller proportion is used in cosmetic products and pharmaceuticals.

In Germany, the responsibility for the use of titanium dioxide in medicinal products lies with the Federal Institute for Drugs and Medical Devices (BfArM).

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.

The European Commission has issued a recommendation[1] on the question of what constitutes a nanomaterial. The first version of the recommendation was taken into account when adapting the annexes to the REACH Regulation (Regulation concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals), which came into force on 1 January 2020. This defines nanoforms of substances.

Titanium dioxide in nanoform is commercially available mostly in two different crystalline forms (anatase or rutile). One material that has often been used as a test material, particularly in inhalation toxicity studies (labelled "P25"), is an 80/20 mixture of anatase and rutile. Commercial nanoforms can also be surface-treated. For example, a passivating protective coating is often applied to the particle surface.

Titanium dioxide produced specifically in nanoform is used in some consumer-related products. The main benefits here are the high filter effect for protection against ultraviolet radiation, the translucency of the nanoforms and advantages in processing.

Selected questions and answers on nanomaterials can be found here.

How can titanium dioxide be ingested?

When assessing the health risks of a substance, all important routes of exposure must be considered, i.e. absorption via the skin (dermal), intake via the respiratory tract (inhalation) or via the digestive tract (oral).

In the case of titanium dioxide, the risk assessment considers the inhalation of fine titanium dioxide particles and nanoparticles in particular to be critical to health, because they penetrate deep into the lungs in animal studies and can cause chronic inflammation. In rats, the inhalation of extremely high concentrations of titanium dioxide over a very long period of time (over the entire lifetime of the animals) led to the formation of lung tumours. Whether these results are applicable to humans is currently the subject of scientific discussion (see below "Assessment of titanium dioxide in the context of the European chemicals regulations").

The oral intake of titanium dioxide was taken into account in the health risk assessment of titanium dioxide as food additive E 171 by the European Food Safety Authority (EFSA). The risk assessment was the basis for the EU-wide withdrawal of the authorisation in 2022. Corresponding data was also used for the assessment of titanium dioxide as a component of food contact materials.

According to the current state of knowledge, titanium dioxide is not absorbed through the skin, e.g. via skin care products.

The exposure to titanium dioxide via tattoo inks is a special case. Titanium dioxide is used in tattooing products and permanent make-up as a white pigment or mixed with pigments to create certain colour shades. Rutile is the predominantly used crystal form in tattooing products.

[1] https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A32022H0614%2801%29

Assessment of titanium dioxide in the context of the European chemicals regulations

Titanium dioxide was assessed as part of the European chemicals regulations. One of the processes provides for the so-called EU-wide harmonised classification according to Regulation (EC) No. 1272/2008 on classification, labelling and packaging ("CLP Regulation"), which was completed in February 2020. The second process deals with the substance evaluation of titanium dioxide as part of the European chemicals regulation REACH (Registration, Evaluation, Authorisation and Restriction of Chemicals; (EC) Nr. 1907/2006). Both regulatory processes were initiated by France. Neither process explicitly distinguishes between conventional titanium dioxide (pigment) and titanium dioxide in nanoform. Rather, the scope of the relevant EU regulations covers all forms of titanium dioxide.

1) Harmonised classification according to CLP Regulation (Regulation (EC) No 1272/2008)

Industrial chemicals with particularly hazardous properties (e.g. carcinogenic, mutagenic or toxic to reproduction) are classified throughout the EU in accordance with the CLP Regulation. This is a harmonised legal classification, which is legally binding in the European Economic Area for manufacturers, importers and users of the substance as such and for the substance in mixtures. If general or specific concentration limits of the harmonised classified substance (or harmonised classified substances) in mixtures are exceeded, these mixtures must be labelled in accordance with the legal classification(s).

A harmonised CLP classification is unrestricted, i.e. it can apply to all chemicals on the EU market and, unless specified otherwise, includes all forms of a substance. References to the classification are made in various legal standards; the existence of a harmonised CLP classification and in particular the higher classification categories (e.g. carcinogen category 1B, "may cause cancer") sometimes trigger drastic legal consequences and various risk reduction measures in other areas of law outside chemicals law (e.g. product, cosmetics, toy, waste law).

Titanium dioxide has undergone process of classification in accordance with the CLP Regulation because of possible hazards in terms of carcinogenicity after inhalation of the substance. This was triggered by a corresponding proposal submitted by France in 2015 and partially confirmed by the Committee for Risk Assessment (RAC) at the European Chemicals Agency (ECHA) in 2017. According to the RAC opinion[2], titanium dioxide is presumed to be carcinogenic to humans when inhaling dusts of the substance. Accordingly, in October 2019, the EU Commission decided on a classification and labelling according to which titanium dioxide [in powder form with at least 1% particles with an aerodynamic diameter ≤ 10 µm] is probably carcinogenic when inhaled (carcinogen category 2, H351i).

In February 2020, the proposed classification of titanium dioxide was adopted as part of the 14th ATP (Adaptation to technical progress) and the relevant Delegated Regulation (EU) No 2020/217 was published in the Official Journal of the EU[3]. The implementation of the classification thus became binding on 09/09/2021; guidance on the application of the harmonised classification is published at the national REACH-CLP Biocides Helpdesk. In 2020, however, the harmonised classification of titanium dioxide was challenged before the European Court of Justice by several industry representatives. In November 2022, the Court

[2] https://echa.europa.eu/documents/10162/682fac9f-5b01-86d3-2f70-3d40277a53c2
[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

ruled that the harmonised classification of titanium dioxide dusts as carcinogenic by inhalation must be annulled. The reasons for the cancellation of the harmonised classification can be viewed here: https://curia.europa.eu/juris/document/document.jsf?text=&docid=268096&pageIndex=0&doclang=EN&mode=lst&dir=&occ=first&part=1&cid=2303522.

In spring 2023, France and the European Commission lodged an appeal[4] against the judgement of the European Court of Justice. As a result, the classification remains valid for the time being. A hearing on the matter is scheduled to take place in 2024 and a final decision on the harmonised classification of titanium dioxide in powder form as an inhalation carcinogen is expected in 2025.

2) Substance evaluation under the REACH Regulation

The purpose of substance evaluation under the REACH Regulation (EC 1907/2006) is to check whether there is an initial suspicion that a substance poses a risk to health or the environment, to request information from the manufacturer or importer of the substance that is relevant but missing for the assessment of a risk and, if necessary, to determine the need for action to minimise the risk. The initiative for a substance assessment usually lies with the authorities of the EU member states.

In 2018, the French competent authority (ANSES) initiated a substance evaluation of the different forms of titanium dioxide because of ambiguity in the available data regarding the potential genotoxic properties of the different forms (including different nanoforms). The initial assessment revealed that relevant data for a final assessment of the potential genotoxicity of the different forms of titanium dioxide are missing and need to be provided by the REACH registrants of the substance. A corresponding study request[5] was sent to the registrants in July 2021. This data is expected to be received in 2024. Once the requested information has been received, an assessment of the new data will be carried out by France.

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

For use in cosmetic products, titanium dioxide is included in two positive lists of the EU Cosmetics Regulation (Regulation (EC) No. 1223/2009), namely in the list of dyes (Annex IV of the EU Cosmetics Regulation) and in the list of filters for protection against ultraviolet radiation (UV filters) (Annex VI of the EU Cosmetics Regulation).

Nanoscale and non-nanoscale titanium dioxide is used in UV filters. The transparent appearance of the nanoform is an advantage when applied to the skin. Currently, only certain nanoforms of titanium dioxide are listed as UV filters in the current version of the Cosmetics Regulation in Annex VI. The inclusion of a substance in the positive lists of the EU Cosmetics Regulation is based on a safety assessment of the substance by the Scientific Committee on Consumer Safety (SCCS) of the EU Commission. Titanium dioxide (nano) must

[4] https://curia.europa.eu/juris/document/document.jsf?text=&docid=272294&pageIndex=0&doclang=en&mode=lst&dir=&occ=first&part=1&cid=2301257 and https://curia.europa.eu/juris/document/document.jsf?text=&docid=272298&pageIndex=0&doclang=en&mode=req&dir=&occ=first&part=1&cid=2303529

[5] https://echa.europa.eu/documents/10162/b1dd5108-5268-c7fd-2d70-c2d29ef9251e

not be used in sunscreen sprays that contain particles that can be absorbed by inhalation via the lung epithelium because of their small size.

Titanium dioxide is also used as a pigment, e.g. in toothpaste. In accordance with a scientific recommendation[6] from the SCCS to the EU Commission, the committee will revisit this use as soon as the industry has submitted new data on the specification and toxicological profile of the titanium dioxide grades used in these products.

The titanium dioxide grades used as UV filters (see above) are different materials (particle sizes distribution, coating, etc.); these materials are not the subject of the reassessment.

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

Because of its favourable material properties (chemical and thermal stability, light resistance, high covering power as a white pigment), titanium dioxide is used in various materials that are found in consumer products. It is used as a white pigment and as a structuring component of colour pigments for paints and varnishes. It is used for decorations on paper and porcelain as well as for the pigmentation of textiles and leather. In plastics, it is used for coating, colouring and as a stabiliser (protection against ultraviolet radiation). Other examples of materials containing titanium dioxide are ceramics and glassware. These material applications are characterised by the fact that the titanium dioxide is bound in a solid matrix, which limits its release.

There are no specific legal regulations regarding the use of titanium dioxide for non-food contact materials and articles. However, all manufacturers are obliged to guarantee the safety of their products by the European General Product Safety Directive or by the regulation (EU) 2023/988 on general product safety, the latter of which will apply from 13 December 2024.

According to Section 30 of the German Food, Commodities and Feed Code (LFGB), it is prohibited to manufacture or modify commodities for others in such a way that when used as intended or foreseeable, they are likely to be harmful to health because of their material composition, in particular because of toxicologically active substances or impurities.

General safety requirements for toys are set by the European Toy Safety Directive 2009/48/EC apply. Accordingly, toys, including the chemical substances they contain, must not endanger safety when used as intended or in a foreseeable manner and taking into account the behaviour of children. As a result of the harmonised classification of titanium dioxide under the CLP Regulation, which also includes mixtures in powder form with a concentration of at least 1% titanium dioxide in particle form with an aerodynamic diameter of $\leq$ 10 µm, as probably carcinogenic (category 2) when inhaled, the EU Commission mandated the Scientific Committee on Health, Environmental and Emerging Risks (SCHEER) to evaluate titanium dioxide in toys on 20 November 2020. Substances and mixtures classified as probably carcinogenic (category 2) may only be used in toys up to a concentration of 1%. The SCHEER opinion identified uses with no or negligible risk with regard to fine and ultrafine titanium dioxide particles, taking into account various exposure

[6] https://health.ec.europa.eu/publications/scientific-advice-titanium-dioxide-tio2-casec-numbers-13463-67-7236-675-5-1317-70-0215-280-1-1317-80_en

scenarios. Possible exemptions are currently being discussed for these uses in the Toys Safety Directive.

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

The so-called 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 must be manufactured in accordance with good manufacturing practice so that under normal or foreseeable conditions of use, they do not transfer components to food in quantities that are able to:

- endanger human health or
- bring about an unacceptable change in the composition of the food or
- cause an impairment of the organoleptic properties of the food (odour, taste, etc.).

Article 5 of the aforementioned regulation also provides for the adoption of so-called "specific measures" for certain groups of materials and articles. As part of such a specific measure, titanium dioxide is authorised for use in plastic food contact materials in accordance with Regulation (EU) No 10/2011. Titanium dioxide is listed in this regulation as pure and surface-modified in various forms. Titanium dioxide of "nanostructure" may only be used in a specific surface-modified form for which it has been demonstrated in the authorisation application that no release of the titanium dioxide occurs.

There are no regulations on other material groups relevant to titanium dioxide at European level. As part of the "BfR recommendations on food contact materials"[7], titanium dioxide (in nanoform, not identical to the previously permitted food additive E 171) is listed in recommendation XV "Silicones" (e.g. silicone baking moulds) as a heat stabilising agent (maximum 3%) (BfR, 2018). There is no transfer of titanium dioxide from the silicone into food with a limit of detection of 1.8 micrograms (µg)/kilogram (kg) of food.

Why is titanium dioxide no longer authorised as a food additive in the EU?

Until 6 February 2022, titanium dioxide was authorised as food additive E 171 in the EU in accordance with Regulation (EC) No. 1333/2008. With the entry into force of Regulation (EU) 2022/63 on 7 February 2022, this authorisation was revoked. Transitional periods are also regulated in this regulation.

The decision was based on a re-evaluation of possible health risks associated with the use of E 171 by the European Food Safety Authority (EFSA). The result of this assessment was published on 6 May 2021. According to this, the suspicion of mutagenic effects (genotoxicity) of titanium dioxide could not be refuted and an acceptable daily intake (ADI) could not be derived by EFSA. Accordingly, EFSA no longer considered the use of E 171 as a food additive to be safe.

Based on EFSA's scientific opinion, the European Commission has issued a ban on the use of titanium dioxide as a food additive (E 171). The EU member states unanimously approved a corresponding proposal by the Commission in October 2021.

[7] https://empfehlungen.bfr.bund.de/

Is titanium dioxide authorised as a feed additive?

Its use as a feed additive was no longer authorised for safety reasons for all animal species by the Implementing Regulation (EU) 2021/2090 of the Commission of 25 November 2021. This implementing regulation stipulated that titanium dioxide was no longer authorised in the European Union as a feed additive and premixture, and that feeds produced with the additives or premixtures would be withdrawn from the market by 20 March 2022 and 20 June 2022 respectively.

Are adverse health effects to be expected for consumers from the use of titanium dioxide in cosmetic products?

There are currently no indications that the use of titanium dioxide in cosmetic products is harmful to the health of consumers if the legal requirements are complied with. Titanium dioxide is not absorbed dermally, i.e. through the skin, and consequently not by application of skin care products containing titanium dioxide. In several opinions on titanium dioxide nanoparticles in sunscreens the Scientific Committee on Consumer Safety (SCCS) has considered absorption via the skin of no concern according to the current state of knowledge when applied to both intact and sunburn-damaged skin. The inhalation of titanium dioxide nanoparticles, which results in exposure of the consumer's lungs to titanium dioxide nanoparticles, has been assessed by the SCCS as posing a health risk (SCCS/1516/13; SCCS/1583/17[8]). For this reason, titanium dioxide (nano) was banned in the EU Cosmetics Regulation in applications that could lead to exposure of the end user's lungs through inhalation.

The use of titanium dioxide in oral cosmetic products such as toothpaste will be re-evaluated by the SCCS[9] as soon as the industry has submitted new data on the specification and toxicological profile of the titanium dioxide grades used in these products.

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 carried out a health risk assessment of the planned use based on submitted analytical data and the assessment 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 specified in BfR Recommendation XV, does not pose a health risk (BfR, 2018). On the one hand, this is based on the result of analytical tests, according to which there is no transfer of titanium dioxide from the silicone into food (at a very low limit of detection of 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 conducted by the National Cancer Institute (NCI) of the U.S. Department of Health and Human Services on rats and mice was considered a key study in which no differences were found in the species and number of tumour-like and non-tumour-like tissue lesions compared to the control group up to the highest dose administered (50 g/kg food, equivalent to about

[8] http://publications.europa.eu/resource/cellar/b635a200-38cd-11e9-8d04-01aa75ed71a1.0001.01/DOC_1
[9] https://health.ec.europa.eu/publications/scientific-advice-titanium-dioxide-tio2-casec-numbers-13463-67-7236-675-5-1317-70-0215-280-1-1317-80_en

2250 mg/kg body weight/day) (NCI, 1979). According to the EFSA assessment published on 6 May 2021, there is no newer relevant study.

When using titanium dioxide in plastic food contact materials in accordance with Regulation (EU) No. 10/2011, titanium dioxide is incorporated into the polymer matrix as a solid, as with silicone. The experimental data available on some selected materials and modelling studies (EFSA 2019b) came to the result that, as with silicone, there is no or very little release of titanium dioxide from the plastic into the food. Any health risk is therefore very unlikely.

Are adverse health effects for consumers to be expected from the use of titanium dioxide in tattoo products?

To date, there are no known adverse health effects associated with exposure to titanium dioxide-containing pigments in tattoo products. Questions and answers specifically on tattoo products can be found in the BfR FAQs of 6 January 2022 and 12 October 2017.

Further information on the BfR website on the topic:

FAQ Nanomaterials: Tiny particles mediate manifold properties
https://www.bfr.bund.de/cm/349/nanomaterials-tiny-particles-mediate-manifold-properties.pdf

FAQ on tattoo inks
https://www.bfr.bund.de/cm/349/frequently-asked-questions-about-tattoo-inks.pdf

FAQ Cosmetic products – all ingredients must be tested
https://www.bfr.bund.de/cm/349/cosmetic-products-all-ingredients-must-be-tested.pdf

BfR opinion: Assessment of potential cancer risk of nanomaterials and nanoparticles released from products
https://www.bfr.bund.de/cm/349/assessment_of_potential_cancer_risk_of_nanomaterials_and_nanoparticles_released_from_products.pdf

BfR opinion: Sunscreen: According to the current state of knowledge zinc oxide as UV filter
is safe
https://www.bfr.bund.de/cm/349/sunscreen_according_to_the_current_state_of_knowledge_zinc_oxide_as_uv_filter_is_safe.pdf

About the BfR

The German Federal Institute for Risk Assessment (BfR) is a scientifically independent institution within the portfolio of the Federal Ministry of Food and Agriculture (BMEL) in Germany. The BfR advises the Federal Government and the States ('Laender') on questions of food, chemicals and product safety. The BfR conducts independent research on topics that are closely linked to its assessment tasks.

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