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VCI

*VCI Statement:*

# On the Proposal for a Harmonised Classification of Titanium dioxide[1]

## Executive Summary

The French agency “Agence nationale de sécurité sanitaire de l’alimentation, de l’environnement et du travail” (ANSES) elaborated a so-called CLH report with a proposal for a harmonised classification and labelling of titanium dioxide as “*potentially carcinogenic to humans*” (category 1B) / “may cause cancer by inhalation” (H350i).

At the European level, this proposal is currently undergoing the discussion and decision-making procedure, as prescribed by the CLP Regulation.

**The proposed classification and labelling is inappropriate for the following reasons and would have serious and disproportionately negative impacts:**

### 1. No indications of problems from epidemiological studies and application practice

Titanium dioxide has been used safely for many decades. No increased incidence of lung cancer has been observed. In epidemiological studies no connection was found between exposure at the workplace and a cancer risk. This is also noted in the CLH report: *“Human data do not suggest an association between occupational exposure to $TiO_2$ and risk of cancer* […]” [CLH Report, page 8].

### 2. Animal studies cannot be transferred to humans

The classification proposal in the CLH report is based essentially on studies in rats exposed to extremely high concentrations of titanium dioxide dusts, which led to so-called “lung overload” effects.

However, all relevant guidance documents by ECHA, OECD and the ECETOC Report unanimously observe that the results from “lung overload” studies in rats should not be transferred to humans for several reasons. Therefore, a classification is neither justified nor appropriate from the toxicological perspective.

### 3. Existing legislation provides sufficient safety

The carcinogenic effect found exclusively in animal testing is based on particle-caused inflammatory processes in the lungs due to dust exposure by inhalation. However, this is not substance-specific for titanium dioxide but characteristic of a large number of dusts, irrespective of the underlying substance.

Exposure by inhalation to titanium dioxide can be expected primarily at the workplace. Consequently, relevant dust limit values are in place in several EU Member States. In Germany, there are additionally a number of provisions for further-going protection measures to minimise dust exposure. At the European level, dust exposure could be

[1] Working translation of the original German position paper

regulated in a binding and uniform manner in the directives on occupational health and safety. A classification of titanium dioxide is not necessary for this purpose.

## 4. Major and disproportionately negative impacts due to automatic reference to classification and labelling in existing legislation

In many sets of legislation – e.g. on industrial plant safety and environmental or consumer protection or special legislations on biocidal products or cosmetics – classification and labelling give rise to comprehensive obligations and bans or restrictions, automatically and without any further examination of whether the use of the substance really poses risks. For example, mixtures (like titanium-dioxide containing white wall paint) could be no longer placed on the market for private end consumers.

## 5. No suitable alternatives are available

Because of the outstanding properties of titanium dioxide regarding health, safety, environment and performance, no suitable alternatives are available. As the carcinogenic effect in animal testing is not substance-specific but characteristic of dusts, this can be expected to occur with all potential alternative substances too.

## 6. Considerable negative impacts in all industrial sectors

Because of its outstanding properties, titanium dioxide is an all-rounder raw material in almost all sectors of industry. This substance is widely used, mainly as white pigment and particularly in paints, coatings, plastics, textiles, foods and feedstuffs, in paper production as well as in pharmaceutical and cosmetic products. A classification as "*potentially carcinogenic to humans*" would have considerable negative impacts on entire value chains.

**Conclusion:** The submitted proposal for classification and labelling of titanium dioxide is inappropriate from the toxicological perspective. Therefore, no classification should be made. A classification would not contribute to improving the protection of health and environment, while it would have serious and disproportionately problematic effects in almost all legal fields.

In the future, additional risk and impact assessments should be carried out for all substances as soon as a harmonised classification of a substance is possibly upcoming. Where sufficient risk management is already in place in uses for consumers, for workers and environment, exemptions should be granted in accordance with proportionality. This would ensure that the legislations, which refer to classification and labelling, do not result in automatic and disproportionate restrictions or bans.

# Detailed Statement

## Content



## Background

The harmonised and thus legally binding classification of a substance according to the CLP Regulation (for carcinogenic, mutagenic and reproductive toxic substances and sensitising substances by inhalation) has far-reaching impacts on almost all uses of this substance.

Under the legal provisions on occupational health and safety and environmental and consumer protection or in special legislations on biocidal products or cosmetics, a classification usually gives rise to comprehensive obligations and bans or restrictions for certain uses and the placing on the market – automatically and without any further examination of whether the use of the substance poses risks.

A harmonised classification of titanium dioxide ($TiO_2$; EC 236-675-5; CAS 13463-67-7) is currently being discussed at the EU level.

The basis for discussion is a CLH report[2] submitted by France according to Article 37 of the CLP Regulation. This report was elaborated by the French agency "Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail" (ANSES).

The Agency arrives at the following recommendation in the CLH report:

> *„4.1.6 Conclusions on classification and labelling*
>
> *$TiO_2$ should be considered as being potentially carcinogenic to humans when inhaled and thus be classified Carc. Cat 1B – H350i* [may cause cancer by inhalation]*. This classification applied for both fine particles and nanomaterials of*

[2] CLH report: http://echa.europa.eu/documents/10162/594bf0e6-8789-4499-b9ba-59752f4eafab

*$TiO_2$ without being able of any distinction in terms of morphology, crystal phase, and surface treatment.“*

The European Chemicals Agency (ECHA) is holding a public consultation on the CLH report which runs to 15 July 2016.[3]

According to Article 37(4) CLP, the Committee for Risk Assessment (RAC) has 18 months to adopt an opinion. Next, the RAC opinion – with a proposal for harmonised classification and labelling – is forwarded to the European Commission. The Commission makes the final decision on harmonised classification and labelling within a delegated act which leads to the corresponding entry of the classification and labelling in Annex VI to the CLP Regulation.

## Toxicology

From the toxicological perspective, the proposal for a classification of titanium dioxide as carcinogenic category 1B – H 305i is neither justified nor appropriate for the following reasons:

- **No relevance of the toxicological findings regarding humans and no observations of problems in practice**

In the given case, the indications of a carcinogenic effect rely exclusively on animal testing. A potential connection between titanium dioxide exposure and lung cancer was examined in several epidemiological studies (case and cohort studies in workers in titanium dioxide production). All relevant studies did not find any connection between titanium dioxide exposure and lung tumours.

Also the submitted CLH report for titanium dioxide states in chapter 2.2 “Short summary of the scientific justification for the CLH Proposal” that nothing suggests increased cancer risks due to occupational exposure, which is relativized mentioning methodological limitations:

*“Human data do not suggest an association between occupational exposure to $TiO_2$ and risk for cancer. However, all these studies have methodological limitations and the level of exposure reported is debatable.”* [CLH Report page 8]

No indications of problems for humans are known in practice. We do not share the view that there are relevant methodological limitations.

This is also in line with the conclusions from the European Centre for Ecotoxicology

[3] ECHA internet page of the consultation: http://echa.europa.eu/harmonised-classification-and-labelling-consultation/-/substance-rev/13832/term

and Toxicology of Chemicals (ECETOC) in the Technical Report 122 „poorly soluble particles / Lung Overload“ (published 01/2014)[4] :

> “[…] *results from several extensive human epidemiology studies in titanium dioxide or carbon black exposed workers clearly have demonstrated that long-term occupational exposures to these particle-types do not cause lung cancer or non-cancerous diseases of the respiratory tract.”*
> [ECETOC TR 122, Chapter: Relevance of ‘lung overload’ for humans]

### No relevance of the mode of action “lung overload” for humans

The conclusions from the CLH Report regarding the classification of titanium dioxide are based exclusively on studies in rats exposed to extremely high concentrations of titanium dioxide that lead to so-called “lung overload” effects:

> *“In experimental animal studies, lung tumours were reported after inhalation or intra-tracheal administration of TiO2 (fine rutile, anatase/rutile P25 nano-TiO2 and nano-rutile) in rats in an overload context. Overload is defined by an impairment of normal pulmonary clearance due to high accumulation of particles. Although inter-species variability was found in particle retention, the overload concept is relevant for humans, and in particular for workers exposed to high dust concentrations.”* [CLH Report page 8]

By contrast, in chapter 3.9.2.5.3 of the ECHA Guidance Document on CLP[5] the “lung overload” is expressly mentioned as a mechanism of no relevance for humans, so that it should not be resorted to for classification:

> *“3.9.2.5.3. Mechanisms not relevant to humans (CLP Annex I, 3.9.2.8.1. (e))*
>
> *In general, valid data from animal experiments are considered relevant for humans and are used for hazard assessment/classification. However, it is acknowledged that there are cases where animal data are not relevant for humans and should not be used for that purpose. This is the case when there is clear evidence that a substance – induced effect is due to a species-specific mechanism which is not relevant for humans. Examples for such species differences are described in this section.*
>
> […]
>
> *Lung Overload*
>
> *The relevance of lung overload in animals to humans is currently not clear and is subject to continued scientific debate.”*
> [ECHA Guidance document, page 469/470].

[4] http://www.ecetoc.org/publication/tr-122-poorly-soluble-particles-lung-overload/

[5] https://echa.europa.eu/documents/10162/13562/clp_en.pdf

Moreover, the following is noted in Guidance document No. 116[6] of the Organisation for Economic Co-operation and Development (OECD) on the carrying out of carcinogenicity studies:

> *"3.2.3 The inhalation route of exposure*
>
> *135. For substances likely to accumulate in the lung over time due to poor solubility or other properties, the degree of lung-overload and delay in clearance needs to be estimated based on adequately designed pre-studies; ideally a 90-day study with postexposure periods long enough to encompass at least one elimination half-time. The use of concentrations exceeding an elimination half-time of approximately 1 year due to lung-overload at the end of study is discouraged."*

There is no doubt that the elimination half-time of titanium dioxide in the animal studies resorted to for classification is in a range which the OECD rejects for the carrying out of inhalation carcinogenicity studies.

A detailed description of the topic "Lung Overload" can be read in the above mentioned ECETOC Technical Report 122 "poorly soluble particles / Lung Overload":

> *"The synopsis of currently available scientific data on ‚lung overload' allows the Task Force to conclude that:*
>
> - *The rat represents a particularly sensitive model concerning the development of pulmonary non-neoplastic lesions and, moreover, a unique model with regard to lung neoplastic responses under conditions of lung overload.*
> - *Lung tumours have to be regarded the final phenotypic `adverse outcome` only in rats, whereas in other species non-neoplastic lesions seem to be the respective `adverse outcome`.*
> - *Humans are less sensitive to `lung overload` as epidemiological studies thus far have not been able to detect an association between occupational exposures to poorly soluble particles of low toxicity and an increased risk for lung cancer.*
>
> […]"

Relevance for humans is summed up as follows in the ECETOC Report:

> *"Therefore, it was noted that the findings in rats are not useful endpoints for human risk evaluations of poorly soluble particulate exposures. In contrast to the experience with rats, epidemiological findings in coal mine workers, a -well studied occupationally- exposed group of workers with routine "particle overload" in their lungs, clearly demonstrate a lack of lung cancer risk when correlated with exposures. In addition, results from several extensive human epidemiology studies in titanium dioxide or carbon black exposed workers clearly have demon-*

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6 http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=ENV/JM/MONO(2011)47&doclanguage=en

*strated that long-term occupational exposures to these particle-types do not cause lung cancer or non-cancerous diseases of the respiratory tract."*
[ECETOC TR 122, Chapter: Relevance of 'lung overload' for humans]

All relevant guidance documents by ECHA, OECD and the ECETOC report unanimously observe that the results from "lung overload" studies in rats should not be transferred to humans for several reasons.

As regards inhalation toxicity through insoluble, inert particles, the rat is a particular sensitive species compared with all other studied species: Up until now, evidence of tumours in the respiratory tract has been found only in rats with insoluble, inert particles. Other species – like mouse or hamster – did not develop lung tumours at comparable exposure.

Tumour formation in rats is essentially due to particle-induced inflammatory reactions, cell proliferations, secondary genotoxicity through reactive oxygen species and resulting hyperplasia. The above-described effects occur particularly in the overload range where particle clearance (clearance/elimination) by alveolar macrophages is massively disturbed. These effects have not been found at all or not to a comparable degree in other species at comparable dose and particle load.

For the above-expounded reasons, the findings in rats on inhalation toxicity of inert, poorly soluble particles cannot be transferred to humans or are not relevant for humans. Therefore, a classification is neither justified nor appropriate from the toxicological perspective

## Exposure to titanium dioxide dusts at the workplace

The exposure pathway in which titanium dioxide shows a carcinogenic effect exclusively in animal testing is solely exposure by inhalation to titanium dioxide dusts. The effect is not substance-specific and according to current understanding based primarily on particle-caused inflammatory processes in the lungs that, subsequently, can lead to tumour formation. Where titanium dioxide comes e.g. in the form of a suspension, the particle-caused inflammatory effects do not come about.

Exposure by inhalation to titanium dioxide dusts can be expected primarily at the workplace.

- In Germany, effects are covered by the general dust limit value

In Germany, dust exposure at the workplace is already covered by the general dust limit value (allgemeiner Staubgrenzwert/ASGW). Comparable values are in place in other European countries too. The applicable limit values can be taken from the

GESTIS database for international limit values under “Dust, respirable”.[7] Germany has the strictest limit value.

In Germany, a new health-based dust limit value of 1.25 mg/m$^3$ for the respirable fraction and 10 mg/m$^3$ for the inhalable fraction was laid down in 2014 and published in the technical rules for hazardous substances TRGS 900. For health-based workplace limit values, it is taken that no hazard to workers’ health needs to be assumed if workplace exposure is below the workplace limit value. This health-based workplace limit value is defined as the time-weighted average of an 8-hour shift.

The general dust limit value applies for poorly soluble or insoluble dusts which are not regulated elsewhere. The TRGS 900 comprises a non-exhaustive list of examples of substances for which the general dust limit value (ASGW) is applicable. This list includes titanium dioxide (TRGS 900, chapter 2.5, entry 12)[8]. Consequently, titanium dioxide falls in the scope of the general dust limit value.

In the justification for the general dust limit value under TRGS 900[9] it says that a limit value is derived on the basis of the end point “chronic inflammation”. The goal is to avoid chronic, particle-caused inflammatory processes in the lungs, which also prevents the herewith linked pathological changes, e.g. fibroses and the formation of lung tumours observed in animal testing in rats (“threshold-like mechanism of action”).

Compliance with the general dust limit value is mandatory. If existing protection measures are not sufficient for complying with the workplace limit value, additional protection measures including personal protective equipment (PPE) need to be taken. §9(3) of the German Dangerous Substances Ordinance (Gefahrstoffverordnung)[10] stipulates that – if a workplace limit value is exceeded – the employer shall immediately repeat the risk assessment under §6 and take additional protection measures, in order to comply with the workplace limit value. If the workplace limit value is not complied with irrespective of exhausting all technical and organizational protection measures,

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[7] http://limitvalue.ifa.dguv.de/WebForm_gw2.aspx;

[8] http://www.baua.de/cae/servlet/contentblob/666762/publicationFile/89125/TRGS-900.pdf

[9] http://www.baua.de/cae/servlet/contentblob/664342/publicationFile/47939/900-allgemeiner-%20staubgrenzwert.pdf

Original German text in the justification: *„Die Ableitung eines Grenzwertes wird auf Basis des Endpunkts chronische Entzündung durchgeführt. Ziel ist die Vermeidung von chronischen, partikelbedingten Entzündungsprozessen in der Lunge, womit auch gleichzeitig hieran gekoppelte pathologische Veränderungen, wie z. B. Fibrosen und die im Tierexperiment an Ratten beobachtete Entstehung von Lungentumoren verhindert werden („schwellenartiger“ Wirkmechanismus).“*

[10] Original text of §9(3) Gefahrstoffverordnung: *„Bei Überschreitung eines Arbeitsplatzgrenzwerts muss der Arbeitgeber unverzüglich die Gefährdungsbeurteilung nach § 6 erneut durchführen und geeignete zusätzliche Schutzmaßnahmen ergreifen, um den Arbeitsplatzgrenzwert einzuhalten. Wird trotz Ausschöpfung aller technischen und organisatorischen Schutzmaßnahmen der Arbeitsplatzgrenzwert nicht eingehalten, hat der Arbeitgeber unverzüglich persönliche Schutzausrüstung bereitzustellen. Dies gilt insbesondere für Abbruch-, Sanierungs- und Instandhaltungsarbeiten.“*

the employer shall immediately provide PPE. This applies, in particular, for demolition, rehabilitation and maintenance work.

Furthermore, the requirements to employers for activities with mineral dusts are concretized in the technical rules for hazardous substances TRGS 559 “Mineral dust”. Here, inter alia, provisions are laid down for how to carry out the risk assessment for exposure to mineral dusts, what protection measures to derive and how to proceed in prevention within occupational medicine.

Technical rules for hazardous substances concretize, within their fields of application, the requirements of the German Dangerous Substances Ordinance and the German Ordinance on Occupational Health Care (Verordnung zur arbeitsmedizinischen Vorsorge). Where compliance with TRGS is given, employers can assume that the relevant requirements of the above-mentioned ordinances are fulfilled. If the employer chooses a different solution, he/she needs to achieve at least the same level of occupational health and safety for workers.

Thus, in Germany a high level of protection is achieved for workers in activities with titanium dioxide dusts. A classification of titanium dioxide as carcinogenic category 1B would not have any influence on the achieved protection level – while causing more bureaucracy for employers: because e.g. formal updates of the risk assessment and of the operating instructions would become necessary for all activities, albeit without making any changes in protection measures.

- **Rules on workplace exposure should be regulated by way of the EU directives on occupational health and safety**

The European directives on the protection of the health and safety of workers from the risks related to chemical agents at work (Directive 98/24/EC[11]) and from the risks related to exposure to carcinogens or mutagens at work (Directive 2004/37/EC[12]) do not yet have any comparable equivalent to the general dust limit value (ASGW). However, Directive 2004/37/EU (carcinogens and mutagens directive) includes rules for the exposure to hardwood dusts which can be seen as a precedent:

- Annex I to the Directive classifies “work involving exposure to hardwood dusts” as carcinogenic.
- Annex III to the Directive lays down an occupational exposure limit value of currently 5 mg/m$^3$. Lowering this limit value to 3 mg/m$^3$ is planned within the revision of the carcinogens and mutagens directive.

Transposition into national law of the binding occupational exposure limit value (BOEL), as laid down in the carcinogens and mutagens directive, is mandatory for the

[11] http://eur-lex.europa.eu/legal-content/EN/TXT/?qid=1466000613102&uri=CELEX:31998L0024

[12] http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32004L0037&from=EN

EU Member States. Deviations from the EU limit value are possible only if they achieve a higher level of protection, i.e. if the national limit value is more stringent than the EU value. Furthermore, the measures for the protection from exposure to carcinogens, as prescribed in Directive 2004/37/EC, need to be taken. This includes, inter alia, examining for potential replacements of substances or processes, minimising exposure where replacing is not feasible, instruction of workers, use of suitable protection measures etc.

Such a course of action – i.e. classification of work exposing workers to titanium dioxide dusts in Annex I to the cancer directive and laying down a binding occupational exposure limit value (BOEL) in Annex III to the directive – are also thinkable for harmonising the protection of workers from exposure to titanium dioxide dusts and should be preferred. This procedure should be given preference over an unjustified classification and labelling of titanium dioxide.

## Automatic legal consequences of classification – in the case of titanium dioxide

In many legislations – e.g. on industrial plant safety, environmental and consumer protection or special legislations on biocidal products or cosmetics – classification and labelling give rise to comprehensive obligations and far-reaching bans and restrictions, automatically and without any further examination of whether the use of the substance really poses risks.

Some examples in the following:

### REACH restriction

The manufacture, placing on the market and use of substances that pose an unacceptable risk to human health or the environment are restricted under REACH, by way of Commission regulations. After inclusion of CMR substances in Annex VI to the CLP Regulation, the Commission regularly enacts restrictions for the use of these substances in consumer products. Points 28 to 30 in REACH Annex XVII regulate the restriction in consumer products of substances classified as carcinogenic, mutagenic or toxic to reproduction (categories 1A and 1B). As soon as a substance is included by way of a Commission regulation in one of the tables under these points, the substance cannot be used for final consumer uses or placed on the market any longer if a certain concentration limit is exceeded. This concentration limit can be determined either with the harmonised classification according to the CLP Regulation as a substance-specific concentration limit, or the concentration limit is generically 0.1 percent for substances classified as carcinogenic or muagenic cat. 1A or 1B and 0.3 percent for substances classified as toxic to reproduction cat. 1A or 1B. Usually, this limit reflects the value below which no hazard needs to be expected.

In practice, this means that consumer products (e.g. paints or coatings) would, inter alia, fall under the ban of the sale to the general public according to the REACH Regu-

lation (EC) No 1907/2006, Annex XVII, point 28 if a substance-specific concentration limit, that would remain to be determined for titanium dioxide, was exceeded.

### REACH authorisation

After undergoing the procedure given by the REACH legislation, substances classified as carcinogenic or mutagenic cat. 1A or 1B can be subjected to an authorisation requirement. In this event, after expiration of a transitional period a use of the substance remains possible only if the impacted company makes an application for authorisation of the respective use. Furthermore, authorisations are reviewed and can be withdrawn, so that the authorisation costs need to be incurred repeatedly and the companies do not have sufficient investment protection.

In practice, already the inclusion of a substance in the candidate list of substances subject to authorisation triggers reactions of customers: Especially companies which produce consumer products do not want to use such substances in the production chain, even if the substance is no longer present in the end product.

### German ordinance on the ban of chemicals (Chemikalien-Verbotsverordnung)

The “Chemikalien-Verbotsverordnung” regulates bans and restrictions for the placing on the market of dangerous substances, preparations and articles in Germany. Also, requirements for distribution are laid down on the basis of labelling.

Substances and mixtures that are classified as carcinogenic cat. 1A and 1B must not be distributed in self-service to private final consumers, as a matter of principle. The distribution e.g. of paints and coatings would be possible only with an identity verification, even though the use of the products does not involve any danger. Mail order distribution would be excluded generally. Acceptance of products by consumers would be no longer given.

### Waste law

Under European waste law, the classification of waste is oriented to the EU chemicals legislation. In 2014 the properties of waste which render it hazardous (so-called HP-criteria) were adapted to the GHS systematics. The HP-criteria lay down from when the property of hazardous waste is given. The fundamentals for waste classification are provided in the EU Waste Framework Directive (2008/98/EU) and in the European List of waste.

Where waste contains a substance known to be carcinogenic cat. 1A or 1B in a concentration of $\geq$ 0.1%, that waste needs to be classified as hazardous by HP 7. Consequently, with a classification of titanium dioxide as carcinogenic the above-mentioned limit values would apply, and waste would need to be classified as hazardous if the relevant thresholds are exceeded. This makes matters more difficult in several respects. For example, the control of waste (including “waste bureaucracy”) becomes

clearly more exacting. In Germany, the “Andienungspflichten” (obligation of waste disposal in certain facilities) and “Überlassungspflichten” (obligation to make waste available to certain legal entities) for hazardous waste of the German federal states apply. Licensing of installations becomes more demanding. Requirements to waste disposal increase.

### IED Directive and TA Luft (technical instruction for clean air)

The Industrial Emissions Directive (IED Directive) mainly focuses on preventing or reducing environmental pollution from industrial activities. Furthermore, emissions of substances classified as critical are regimented by a far-reaching substitution requirement and by very strict emission limit values, up to the implementation of substitution. This would apply for titanium dioxide too.

In item 5.2.2 of the German TA Luft, there is a direct link between the classification of this substance according to the CLP Regulation and emission limitation in waste air, this is not based on requirements under IED or other European provisions. In the individual case, this link can lead to disproportionate requirements in the retrofitting of industrial installations.

### Biocidal Product Regulation

Titanium dioxide is used as a constituent of biocidal products. Within the Biocidal Products Regulation, substances classified as carcinogenic 1A or 1B fall under the exclusion criteria. They can be approved only in exceptional cases. If the substance is approved, it is considered a candidate for substitution and can be authorised for no longer than 7 years. Extended labelling obligations apply for treated articles.

### Cosmetics Products Regulation

Cosmetic products are subject to the EU Cosmetics Products Regulation (Regulation [EC] No 1223/2009). Under this regulation, cosmetic products made available on the market must be safe for human health when used under normal or reasonably foreseeable conditions of use. The safety assessment, which is to be performed for each cosmetic product, demonstrates the safety of the individual product and gives special consideration to exposure.

As regards the use of titanium dioxide in cosmetic products, a possible classification of this substance as carcinogenic category 1B would lead to this important ingredient being banned and not being permitted for use any longer in the short term, irrespective of the existing express authorisation. This is because of a direct link between the cosmetics legislation and the chemicals legislation, regarding CMR substances in cosmetic products.

### Legal provisions on human and veterinary medicines and foods and feedstuffs

The use of titanium dioxide as a constituent of foods and feedstuffs or human and veterinary medicines does not substantially fall in the scope of the REACH and CLP regulations. However, the production of foods and feedstuffs and of human and veterinary medicines is subject to the legislations on occupational health and safety and environmental protection. In case of a classification of titanium dioxide as carcinogenic, the above-mentioned productions would be fully impacted by the previously expounded, tighter rules.

## Titanium dioxide: fields of application – use as an "allrounder" raw material

According to the European Chemicals Agency (ECHA), titanium dioxide is manufactured and/or imported in the European Economic Area in 1 000 000 - 10 000 000 tonnes per year.[13]

Titanium dioxide is an inorganic, crystalline, white solid; it is chemically and biologically inert. The substance is thermally stable, not combustible and nearly insoluble in water, in diluted acids and organic solvents. Titanium dioxide has extreme light fastness, a high refractive index and – at an optimal particle size distribution in the range of 0.2 - 0.35 µm – a very high light scattering capability. From the coloristic perspective it has, therefore, the highest opacity among all white pigments as well as an excellent brightening capacity vis-à-vis coloured media. Usually, other white pigments cannot achieve these outstanding properties. For this reason, no equivalent substitution is possible in many uses.

Its excellent properties make titanium dioxide an "allrounder" raw material in almost all sectors of industry. The substance is widely used, mainly as a white pigment and particularly in paints and coatings, polymers, textiles, foods and feedstuffs, in paper production, in pharmaceutical and cosmetic products and also in enamel and ceramics. Special forms of titanium dioxide serve as photocatalysts, e.g. in pollutant degradation. These uses are, firstly, in the industrial and professional sectors and, secondly, in the field of private final consumers. In the vast majority of uses, titanium dioxide is bound in a matrix (e.g. a polymer matrix) and thus not freely available.

Because of the outstanding properties of titanium dioxide regarding health, safety, environment and performance, there are no suitable alternatives. As the carcinogenic effect in animal testing is not substance-specific but characteristic of dusts, this can be expected to hold true for all potential alternative substances too.

Against this backdrop, a classification as "potentially carcinogenic to humans" would have considerable negative impacts on almost all value chains.

**A detailed overview of the uses of titanium dioxide is given in annex 1.**

[13] ECHA Substance Information: http://echa.europa.eu/de/substance-information/-/substanceinfo/100.033.327

## Conclusion/Proposals

From the toxicological perspective, the submitted proposal for classification and labelling of titanium dioxide is neither justified nor appropriate. Therefore, no classification should be made.

Already now, existing legislation provides adequate safety. A classification would not contribute to improving the protection of health and environment, while it would have serious and disproportionately problematic effects in almost all legal fields.

In many sets of legislation – e.g. on industrial plant safety and environmental or consumer protection or special legislations on biocidal products or cosmetics – classification and labelling trigger comprehensive obligations and bans or restrictions, automatically and without any further examination of whether the use of the substance really poses risks. For example, mixtures (like titanium dioxide-containing white wall paint) could be no longer placed on the market for private end consumers.

Because of the outstanding properties of titanium dioxide regarding health, safety, environment and performance, no suitable alternatives are available. Titanium dioxide already substitutes earlier used, e.g. heavy metal-containing, pigments. As the carcinogenic effect in animal testing is not substance-specific but characteristic of dusts, this can be expected to occur with all potential alternative substances too.

Because of its outstanding properties, titanium dioxide is an all-rounder raw material in almost all sectors of industry. This substance is widely used, mainly as white pigment and particularly in paints, coatings, plastics, textiles, foods and feedstuffs, in paper production as well as in pharmaceutical and cosmetic products. A classification as "*potentially carcinogenic to humans*" would have considerable negative impacts on entire value chains.

In the future, for all substances additional risk and impact assessments should be carried out as soon as a harmonised classification is possibly upcoming. Where sufficient risk management is already in place in uses for consumers, for workers and environment, exemptions should be granted – in accordance with proportionality – in or by those legislations that refer to the new harmonised classification. This would ensure that the legislations, which refer to classification and labelling, do not result in automatic and disproportionate restrictions or bans.

Manufacturers, importers and users should be actively involved in the examination of the risk and in impact assessments of classification proposals.

Classification decisions on substances with risk management in place should be suspended until legislations that refer to such classification are adapted accordingly.

# Annex I: Applications of titanium dioxide

Pigments, pigment preparations, ceramic colours and masterbatches

For pigments and pigment preparations titanium dioxide is by far the most prominent raw material. It is used as starting material for the synthesis of important inorganic coloured pigments. Here, titanium dioxide is fully converted during the production process. As a structure-giving component, titanium dioxide is the indispensable basis for the manufacture of these colour pigments.

Titanium dioxide is used as the most important white pigment, for example in

- both organic and inorganic pigments (including effect pigments/pearlescent pigments) as constituent and for finishing and coating
- Ceramic colours
- Pigment preparations (powder, liquid, paste)
- Masterbatches for subsequent colouring of polymers
- Artists' and school colours

Because of its excellent brightening capacity vis-à-vis coloured media, titanium dioxide is also used as a filler.

Depending on the uses, contents of titanium dioxide in pigment preparations range between 1% and nearly 100%, in ceramic colours between 5% and 60%, and in masterbatches between 0.1% and up to 80%.

Titanium dioxide is extremely light resistant which leads to the highest opacity of all white pigments. Because of this unique combination of substance attributes with excellent health, safety and environmental properties there are no adequate alternatives available.

Paints, coatings and printing inks

Titanium dioxide as a white pigment is the by far most important raw material for paints, coatings, printing inks and polymers.

Titanium dioxide is used in many fields of paints, coatings and printing inks. Here some examples:

- Dispersion paints and decorative paints
- Plaster and putty
- Anti-corrosion coatings
- Wood varnishes and paints
- Industrial coatings
- Automotive refinishing coatings

- Powder coatings
- Natural paints
- UV-resistant coatings
- Printing inks (flexo and gravure printing inks, screen printing inks, digital printing inks)

Depending on the formulation, the concentration of titanium dioxide (e.g. in dispersion and decorative paints) ranges, on average, from 15 – 35%, in plaster and putty up to 30%, in anti-corrosion coatings up to 20%, in automotive refinishing coatings 25%, in natural paints up to 40%, up to 50% in industrial coatings, up to 20% in wood paints, and up to 55% in printing inks.

Titanium dioxide is extremely lightfast, has a high refractive index and a very high light scattering capacity. From the coloristic perspective it has, therefore, the highest opacity among all white pigments as well as an excellent brightening capacity vis-à-vis coloured media. Furthermore, titanium dioxide is thermally stable, not combustible, nearly insoluble in water, and weather and UV resistant.

For paints, coatings and printing inks, there are hardly any alternatives to titanium dioxide. Other raw materials (e.g. calcium carbonate, zinc oxide and zinc sulphide) are usually of inferior quality regarding stability and opacity, brightness (gloss) and abrasion resistance. Often, replacement substances are critical in ecological and toxicological terms, especially if they contain heavy metals like e.g. lead carbonate. As the carcinogenic effect in animal testing is not substance-specific but characteristic of dusts and as dust exposure can be expected also in the processing of potential replacement substances, a substitution of substances would not change the given situation.

Production of construction chemicals

Titanium dioxide is an indispensable input in the formulation of construction chemicals. As good as all pigmented coverings, fillers, sealants and other visible surface coverings on construction elements contain titanium dioxide. Here some typical product types:

- Floor coverings for heavy duty industrial floors
- Surface protection systems for concrete components
- Pigmented mortar (e.g. jointing grouts)
- Coverings for multi-storey carparks
- Sealants for sanitary joints and façade elements
- Synthetic resin screeds

In the majority of uses, titanium dioxide in construction chemicals acts as white pigment. For special uses, partly the photocatalytic effect of titanium dioxide is used too.

Depending on the product and the field of application, the usual use concentrations range between 1% and 20%.

Moreover, manufacturers of construction chemicals use quasi exclusively titanium diox-

ide as white pigment. This is because no alternative inputs with comparable properties are known. The outstanding properties include, in particular, the high refractive index (high opacity) and the degree of whiteness of titanium dioxide. In the historical development, titanium dioxide has replaced other white pigments like “white lead” (lead carbonate) which – unlike titanium dioxide – needed to be seen as critical in toxicological terms.

Plastics manufacture

Main fields of use are coating materials like varnishes and paints, followed by plastics colouring and laminated paper. Titanium dioxide has prevailed as the leading white pigment. Its interaction with light is evident, firstly, as light scattering which leads to opacity or as absorption of the energy of UV light, in order to protect polymers from decomposition under UV light.

Titanium dioxide is used as white pigment or as light stabiliser in plastics. The photocatalytic property of titanium dioxide is used in some polymer products (e.g. self-cleaning plastic surfaces).

Cosmetic products

Titanium dioxide is an important constituent of formulations of a wide range of cosmetic products, like skin protection and skin care products, sunscreens, tooth pastes and decorative cosmetics. Titanium dioxide is used both in the classic pigment grain size (as white pigment) and as nano-material (UV filter). Titanium dioxide is expressly permitted as colour pigment and as UV filter under the EC Cosmetics Regulation (Regulation [EC] No 1223/2009; Annexes IV and VI). These approvals are based on comprehensive risk assessments by the competent, independent scientific EU committee SCCS (Scientific Committee on Consumer Safety). Recently, the nanoscale form of titanium dioxide has been assessed once more in all toxicological endpoints specifically for use as UV filter.[14] In any case, titanium dioxide is firmly bound in the cosmetic formulations – typically in emulsions –, so that particularly an exposure by inhalation is usually not relevant for cosmetic products.

Active principle and advantages of titanium dioxide as UV filter pigment: The particles form a protective film on the uppermost skin layer and scatter and absorb the UV rays of the sun. In this manner, the skin is protected against UV radiation and its harmful effects to health (sunburn, DNA damage, skin aging etc). Particularly good sunscreen effects can be achieved through the combination with other filter substances. Nanoscale titanium dioxide in sunscreen products is invisible to the human eye and leaves no whitish film on the skin, which motivates consumers for a more generous application. Another outstanding feature of titanium dioxide is an optimal skin tolerance – intolerances or allergic reactions to titanium dioxide are practically unknown.

[14] http://ec.europa.eu/health/scientific_committees/consumer_safety/docs/sccs_o_136.pd

Pharmaceutical industry

For many decades, titanium dioxide has been widely used by the pharmaceutical industry in the manufacture of medicines. No consequences to health, which would lead to expect a conclusion of a carcinogenic effect, have become known here.

Inter alia, titanium dioxide is used as a white colorant in film coatings of tablets, in dragées or capsule casings (solid pharmaceutical form). Titanium dioxide has also an important role in primary packaging which is in direct contact with the medicine, e.g. in order to make blisters film non-transparent for child-resistant packaging.

The quality of titanium dioxide used in medicines is monographed in the European Pharmacopoeia. Consequently, it is subject to strict requirements.

All constituents of medicines and packaging need to be described comprehensively in the marketing authorisation documentation. They are examined by the competent regulatory agency and approved by that agency for the respective medicine. Compliance with the quality criteria is monitored constantly by the competent national authorities in the EU Member States and by the European Medicines Agency (EMA).

Its toxicological safety for dermal or oral applications makes titanium dioxide an ideal and safe excipient for all of the above-mentioned, important uses.

If pharmaceutical industry were obliged to change the formulations of their medicines, a changeover - where this might be possible at all - to a replacement substance would have considerable impacts: because changes in their formulations would become necessary for thousands of medicines. That would bring the need for comprehensive studies of efficacy, safety and stability of the new formulations, involving much work and cost.

In each individual case, a testing of the stability of the newly changed formulations would then become necessary for formal reasons. As this excipient is use widely, such testing alone would necessitate an unprecedented flood of tests. Their organisational and financial challenges would exceed anything previously seen in this field – however, with no extra benefit for patients.

A classification as a carcinogenic substance would necessitate not only direct additional measures in occupational health and safety: Given the specific features of the pharmaceutical industry, in special cases even considerable investments can become necessary for a full separation of substance flows. In this regard, see EMA “Guideline on setting health based exposure limits for use in risk identification in the manufacture of different medicinal products in shared facilities”.

Substances and mixtures intended for final consumers, which come in the form of finished products and are

- medicines within the scope of application of Directive 2001/83/EC on the Community code relating to medicinal products for human use or
- veterinary medicines within the scope of application of Directive 2001/82/EC on the Community code relating to veterinary medicinal products

are fully exempted from the provisions of the CLP Regulation.

This means that they require neither classification, packaging and labelling nor notification for the Classification and Labelling Inventory.

However, where a manufacturer or importer supplies substances and mixtures (e.g. active pharmaceutical ingredients/APIs) or excipients which do not come as finished products, the manufacturer or importer is indeed under the obligation to classify, pack and label such substances and mixtures in accordance with the CLP Regulation.

Manufacturers of films and capsules need to fulfil these requirements too.

Furthermore, these substances need to be notified for the Classification and Labelling Inventory when they are placed on the market. That would concern titanium dioxide too.

It is true that medicines are exempted from many parts of the REACH and CLP regulations. All the same, it would be difficult to imagine – and could not be conveyed to patients – if a substance classified as carcinogenic were used as excipient in medicines.

Food and feed additives

Titanium dioxide is an authorised food additive/food colour (E 171) according to Regulation (EU) No 1333/2008 on food additives. Pursuant to the specifications, high purity requirements need to be fulfilled for this. As part of group II “Food colourants authorised at quantum satis” this principle (i.e. as much as needed) applies here.

Some examples are white coatings of confectionery products and other sweets (dragée coatings).

According to Regulation (EU) No 1831/2003, E 171 is permitted as an additive for animal feedstuffs.

Based on the authorisation as food additive (E 171), titanium dioxide is also used in the field of medicines/tablets as film coating or dragée coating.

To date, no cases of poisoning are known to have occurred through the intake of authorised food colours.

Textile and leather production

$TiO_2$ has an important role in textile and leather production. For example, it is used as:

- matting agent in man-made fibres, e.g. for white pigmentation of glass fibre nonwovens
- component of paints and coatings; e.g. for sun protection (black-out, dim-out) / roller & vertical blinds / decorative textile ceilings
- component of printing inks (e.g. inkjet, digital print) and in printing pastes for pigment print
- carrier material for biocides
- component for the pigmentation of leather

$TiO_2$ enables the most effective white pigmentation with the best possible opacity. This comes with an outstanding UV resistance. Given its high durability, it is a very sustainable product. At the current moment in time, this makes it a product without alternative for most applications. For a small number of applications and on a rather theoretical basis, there are alternatives like barium sulphate, zinc sulphide, calcium carbonate or aluminium silicates. However, they are less efficient in white pigmentation and, moreover, there can be undesirable side effects like decomposition due to temperature or chemicals. Furthermore, this involves higher input volumes and possibly also stricter safety measures in production.

Adhesives

As a constituent of adhesive formulations, titanium dioxide is widely used as white pigment in many different sectors – ranging from the construction sector and the paper and packaging industries to the construction of motorcars, railway vehicles, ships and airplanes, electrical and electronics, the dental sector and other industries.

Titanium dioxide is used predominantly in reactive adhesives which equally comprises polyaddition, polycondensation and polymerisation adhesives like polyurethanes, epoxides, silane modified polymers, acrylates and anaerobically curing adhesives. Alongside this, titanium dioxide is also used in pasty dispersion adhesives and in the widely available EVA- and PE-based, thermoplastic hotmelts.

Irrespective of the comparatively high price, adhesive manufacturers use almost exclusively titanium dioxide as white pigment in their formulations – because of its unexcelled good opacity and the high degree of whiteness. Given the good opacity, in most cases low quantities of titanium dioxide are sufficient to achieve the desired colour effect without a strong, undesirable viscosity increase. Calcium carbonate fillers can perform this task only partly, especially when it is about chalk or limestone and not about marble - because calcium carbonate fillers have a clearly lower colour strength and their own colour; they are primarily intended to adjust rheology and mechanical proper-

ties. Also coloured adhesives (e.g. light green adhesive to glue artificial lawn or red adhesive to glue tartan tracks) are, first of all, brightened with titanium dioxide and then coloured with the desired colour. Often, the use of titanium dioxide enables the use of coloured natural resins to which – in view of sustainability – it is gladly resorted. Without pigment, application would not be possible with a visible bond seam. Moreover, white pigments of lower opacity need to be used in larger quantities in adhesive formulations, leading to a lower polymer share. Usually, this changes the adhesive properties in a negative way – which can cause problems, especially in high-strength compounds. One example of this is the use of adhesives in dental restauration where no replacement substance is available for the above-mentioned reasons.

The above-named adhesives have been used for many decades. No impairments to health through or intolerances to titanium dioxide are known.

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- Registration no. in the EU Transparency Register: 15423437054-40
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