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Rue Froissart 36
1040 Brussels, Belgium

Concerns: **Classification of TiO_2 and mixtures containing TiO_2**

Agenda Point: **19**

Action Requested: **Written comments can be sent by 15 December 2017 to:**

GROW-CARACAL@ec.europa.eu,
ENV-CARACAL@ec.europa.eu,
An.Jamers@ec.europa.eu
Sylvain.Bintein@ec.europa.eu

CLASSIFICATION OF TiO_2 AND MIXTURES CONTAINING TiO_2

1. Background

On 14 September 2017, RAC adopted its Opinion proposing harmonised classification and labelling at EU level of Titanium dioxide (TiO2, EC Number: 236-675-5; CAS Number: 1346367-7). The RAC Opinion was transmitted to the Commission on 12 October 2017, for possible integration into Annex VI CLP.

RAC proposed classification as **category 2 carcinogen** including the **hazard statement H351** (inhalation), with the following "Note": **"If the substance is placed on the market as particles of the substance fulfilling the WHO fibre criteria or as particles with surface coating their hazardous properties must be evaluated in accordance with CLP Title II to assess whether a higher category (Carc. 1B or 1A) and/or additional routes of exposure (oral or dermal) should be applied."**

Compared to other classifications, the classification of TiO_2 has a number of particularities, which the Commission would like to discuss with CARACAL members and observers. At this stage, the Commission does not yet have concrete proposals on how to translate those particularities into a legal proposal. The objective of discussing the below issues is to get more insight into the views of CARACAL members and observers, in order to allow the Commission to reflect on whether and how those particularities could be taken into account in the harmonised classification of TiO_2.

The lead registrant dossier for the joint registration for titanium dioxide was opened for dossier evaluation and a final decision targeting non-compliances relating to substance identity information reporting was issued in 2014. The substance identity for registration was defined very broadly and covered all crystal phases in all possible forms and also hydroxides, metal titanates and doped TiO2's. The final decision included requests relating to the reporting of name & other identifiers, composition and analytical data with Annex VI.2 as the legal basis for the requests made. The lead registrant challenged the requests to report information on nanoforms, crystal phase and surface treated nanoforms. In 2017, the BoA took the decision pointing out that registrants are at liberty to give a broad definition of the substance which they intend to register. Therefore, the Board of Appeal considered that, in the absence of explicit requirement for information on nanomaterials in Annex VI of REACH, ECHA has no competence to request substance identity related information on nanomaterials. On that ground, the Board of Appeal annulled the decision but specified that if registrants give a broad definition of their substance, however, the hazards posed by all possible forms of the substance covered by the substance definition must be addressed by the toxicological and ecotoxicological information provided in the registration dossier.

2. Specific properties

- The mode of action cannot be considered "intrinsic toxicity" in a classical sense but is characterised as particle toxicity.

"The evidence outlined in the CLH report and in this opinion do not indicate substantial differences in the toxicity profile of the tested TiO_2 materials. Rat lung carcinogenicity of the two tested TiO_2 materials is characterised as "particle carcinogenicity"."[1]

"RAC acknowledges that the TiO_2 inhalation toxicity observed in rats is particle toxicity and accepts the general understanding that the development of rat lung tumours is mediated by the pathological consequences of a higher loading of macrophages with particles of rather low solubility. The deposited particles, but not solutes of TiO_2 molecules, can be assumed to be responsible for the observed toxicity. RAC acknowledges as well that the carcinogenicity profile described for TiO2 is not exclusively characteristic for TiO_2 but applies to the whole group of chemicals referred to as "poorly soluble low toxicity particles"."[2]

"*The CLP regulation requires a classification to be based on the intrinsic properties of substances. The CLP Guidance defines the intrinsic property of a substance as the basic properties of a substance as determined in standard tests or by other means designed to identify hazards. RAC considers the toxicity profile observed as a basic property of inhaled and respirable particles of TiO2. With reference to the CLP definition of intrinsic properties, RAC considers that the CLP regulation regards the properties of TiO2 or other substances which are PSLT particles as relevant for classification*"[3]

"RAC acknowledges that the mode of action for the rat lung carcinogenicity in rats can not be considered "intrinsic toxicity" in a classical sense: the deposited particles, but not solutes of TiO_2 molecules can be assumed to be responsible for the observed toxicity."[4]

- The lung carcinogenicity is specifically linked to the inhalation route.

"Generally, classification for carcinogenicity does not specify a route of exposure. However, the profile of lung carcinogenicity described for TiO_2 is specifically linked to the inhalation route of application. Currently, there is no experimental evidence for TiO_2 carcinogenicity for the oral or dermal route of application. TiO_2 lung carcinogenicity is associated with inhalation of respirable TiO_2 particles. Based on the data available today RAC considers it conclusively proven that no other route of exposure causes the carcinogenicity hazard. Correspondingly, RAC proposes to classify TiO_2 as a Category 2 carcinogen, with the hazard statement H351 (inhalation)."[5]

"The carcinogenicity profile observed thus is specifically related to exposure to respirable TiO_2 particles with different crystal structures and different primary particle sizes, but which do not possess WHO fibre characteristics or additional specific surface toxicity because of coating of the TiO_2 particles."[6]

[1] RAC opinion, p. 36 third paragraph – the Opinion can be found at https://echa.europa.eu/documents/10162/6cf0942a-6e18-5ce9-fc95-5cd7fd2fbdad
[2] Idem, P. 38 penultimate paragraph
[3] Idem, p. 38 last paragraph
[4] Idem, P. 40 fourth but last paragraph
[5] Idem, P. 40 third but last paragraph
[6] Idem, P. 40 last paragraph

- *Further considerations*

"In the context of a weight-of-evidence approach RAC recognises that the described experimental conditions for rat lung tumour development indicate that TiO_2 can be considered a relatively weak rat lung carcinogen."[7]

"In the opinion of RAC, the mode-of-action proposed for the rat is consistent with the assumption a practical threshold. Based on the experimental data available, rat lung tumours develop if exposure levels are associated with marked overloading of macrophages and chronic alveolar inflammation. The Guidance on the Application of the CLP Criteria (chapter 3.6.2.2.4) refers to such considerations and indicates that the assumption of a practical threshold can be viewed as decreasing the level of concern for human carcinogenicity."[8]

3. Questions raised

As correctly remarked by RAC, the CLP regulation does not exclude a health hazard classification triggered by physico-chemical characteristics of a chemical, and the Commission has no reasons to question the correctness of the proposed classification of TiO_2 if inhaled as small particles. Nevertheless, the proposed classification will also apply to other forms of TiO_2, on their own or in mixtures, for which there is no evidence of such health hazards.

- The proposed classification does not specifically refer to particles although the observed effects seem to be related to inhalable particles only[9]. Therefore, the classification would apply to all forms of TiO_2 and mixtures containing TiO_2, including larger particles/massive forms etc., as well as dispersions.

  In this context, for some of the classified mixtures such as paints containing TiO_2, pursuant to Annex I, section 1.3.4. (for mixtures containing polymers and mixtures containing elastomers), if they do not present a hazard to human health by inhalation, a derogation for *labelling* could be applied. Nevertheless, even if these considerations are accepted, there is a need to clarify borderline cases such as spraying applications for some mixtures like paints. In addition, such derogation would not apply to *classification*. Moreover, section 1.3.4 would not apply to mixtures containing TiO_2 but not containing polymers or elastomers.

  For the application of section 1.3.4, there is a need to demonstrate that there is no hazard to human health by inhalation. Other criteria such as the application of Article 12(b) could also be taken into account to not classify mixtures containing TiO_2, arguing that non-respirable particles do not lead to lung exposure and that therefore there is no bioavailability.

[7] Idem, P. 35 penultimate paragraph
[8] Idem, P. 36 second paragraph
[9] This is without prejudice to the issue of fibres and coated particles which are addressed in a footnote stating that for those particles a more severe classification may apply and also other exposure routes might be relevant.

Do CARACAL members and observers consider that the proposed classification of TiO_2 can be translated directly into Annex VI, or, taking into account the scientific evidence, is there a possibility for adaptations (e.g. through further footnotes to differentiate between particles that can be inhaled and larger particles/massive forms of TiO_2)?

What are the views of CARACAL members and observers on the application of derogations such as Article 12(b) or Annex I, section 1.3.4?

- There are also questions why only TiO_2 will be subject to harmonised classification whereas the effects seem to be common to poorly soluble low toxicity particles (PSLT) of different chemistries.

  Is it appropriate to limit harmonised classification to TiO_2? or would it not be preferable to also classify poorly soluble low toxicity particles (PSLT), or a well-defined group of PSLT, in the same way in a grouping approach?

4. Next steps

Member States are invited to consider the above questions and comment at the CARACAL meeting/provide written comments by 15 December 2017 to:
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