~~Confidential~~

Helsinki, 19 April 2023

Addressees
Registrant of Titanium Dioxide - JS TDIC as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
11/03/2022

Registered substance subject to this decision ("the Substance")
Substance name: Titanium dioxide
EC number: 236-675-5

Registered form subject to this decision ("the Set of Nanoforms")
Name of set of similar nanoforms: [redacted]

Decision number: Please refer to the REACH-IT message which delivered this communication (in format CCH-D-XXXXXXXXXX-XX-XX/F)

DECISION ON A COMPLIANCE CHECK

Based on Article 41 of Regulation (EC) No 1907/2006 (REACH), ECHA requires that you submit the information needed to bring the registration of the "[redacted]" (hereafter, "the Set of Nanoforms") into compliance with the information requirements listed below by the deadline of ***26 February 2024***.

1. **Characterisation of the clearly defined boundaries of the set of nanoforms in accordance with the parameters set out in the points 2.4.2 to 2.4.5 of Annex VI**

2. **Justification demonstrating that a variation within the boundaries of the set of nanoforms does not affect the hazard assessment, exposure assessment and risk assessment of the similar nanoforms in the set**

In principle, each different nanoform covered by a registration must be reported and assessed individually. By derogation, it should be possible to group nanoforms of the substance with similar characterisation parameters in a set of similar nanoforms. Consequently, the incompliance(s) described above can be resolved by implementing one of the following actions:

1) by reporting and assessing each single nanoform covered by the currently reported set. This implies:

   a. the characterisation of each nanoform in accordance with section 2.4.2 to 2.4.5 of Annex VI; and

   b. the submission of information on hazards, exposure and risk specific to each nanoform; and

   c. the reporting of the above information in such a manner that it is clear which hazards, exposure and risk information pertains to each nanoform.

2) by correcting the incompliances of the currently reported set.

3) by grouping the nanoforms covered by the currently reported set in different sets of similar nanoforms. This implies that:

    a. the boundaries of each set are clearly defined in the parameters in the points 2.4.2 to 2.4.5;

    b. justification is provided for each set of nanoforms demonstrating that the hazard, exposure and risk assessment of the nanoforms in the set can be performed jointly.

    c. the reporting of the above information in such a manner that it is clear which hazards, exposure and risk information pertains to each set of nanoforms.

4) by reporting some of the nanoforms covered by the current set as single nanoforms and grouping the other nanoforms covered by that set in one or different sets of nanoforms. Each reporting approach would have to fulfil the conditions set out respectively in option 1) and option 3).

Under Annex VI, a set of similar nanoforms is a group of nanoforms defined by clear boundaries. Based on the information currently in the dossier (Section 2.4.2 to 2.4.5), ECHA cannot determine the actual nanoforms that the Registrants agreed to cover within the set. Only the Registrant of each nanoform in the set knows the characterisation of that nanoform. Therefore, it is each Registrant's exclusive responsibility 1) to ensure that the boundaries of the set of similar nanoforms are clearly defined in accordance with the points 2.4.2 to 2.4.5 of Annex VI and 2) to justify and demonstrate that a variation within the boundaries of the set of nanoforms does not affect the hazard assessment, exposure assessment and risk assessment of the similar nanoforms in the set.

Consequently, if the information eventually submitted by a Registrant does not enable ECHA to verify that the information in the dossier complies with the requirements set out in this decision, the set of nanoforms will not be considered valid. As a result, all the nanoforms that the set was supposed to cover will be considered as not registered. This could result in national enforcement authorities deciding on possible enforcement actions. The reasons of this decision are set out in Appendix A. The procedural history is described in Appendix B.

The scope of this compliance check decision is limited to the standard information requirements of Annex VI applicable to the set of similar nanoforms.

How to comply with your information requirements

To comply with your information requirements, you must submit the information requested by this decision in an updated registration dossier by the deadline indicated above. You must also update the chemical safety report, where relevant, including any changes to classification and labelling, based on the newly generated information.

Appeal

This decision, when adopted under Article 51 of REACH, may be appealed to the Board of Appeal of ECHA within three months of its notification to you. Please refer to

http://echa.europa.eu/regulations/appeals for further information.

Failure to comply

If you do not comply with the information required by this decision by the deadline indicated above, ECHA will notify the enforcement authorities of your Member State.

Authorised[1] under the authority of Mike Rasenberg, Director of Hazard Assessment

Appendix 1: Reasons to request information on the submitted set of similar nanoforms under Annex VI of the REACH Regulation
Appendix 2: Procedure
Appendix 3: Addressees of this decision and their corresponding information requirements

[1] As this is an electronic document, it is not physically signed. This communication has been approved according to ECHA's internal decision-approval process.

Appendix 1: Reasons for the decision

1. Reasons to request information on the submitted set of similar nanoforms under Annex VI of the REACH Regulation

1.1. Characterisation of the clearly defined boundaries of a set of similar nanoforms in accordance with the parameters set out in the points 2.4.2 to 2.4.5 of Annex VI (introduction to Annex VI)

1 Annex VI of REACH requires that each set of similar nanoforms is identified by clearly defined boundaries in the parameters in the points 2.4.2 to 2.4.5 of the individual nanoforms within the set.

1.1.1. Information provided

2 The lead registrant of the joint submission has reported the Set of Nanoforms in the form of a boundary composition and identified the boundaries of the Set of Nanoforms in Section 1.2 of their registration dossier and in a document entitled "[redacted]".

1.1.2. Assessment of the information provided

3 We have assessed the information provided and we have identified the following issues on the basis of which we consider that the Set of Nanoforms does not fulfil the requirement for clearly defined boundaries in the parameters in section 2.4.2 of Annex VI:

1.1.2.1. Unclear boundaries of the shape and morphology – Crystallinity

4 The REACH Annex VI section 2.4.4. requires reporting of "shape, aspect ratio and other morphological characterisation: crystallinity, information on assembly structure including e.g., shell like structures or hollow structures, if appropriate".

5 Further, Section 4.2 of 'Appendix for nanoforms applicable to the Guidance on Registration and Substance Identification' outlines the principles for reporting of shape, aspect ratio and other morphological characterisation for a set of similar nanoforms. It stipulates that when reporting the information on the crystallinity of a set of nanoforms, you must specifically provide:

6 For a set including only crystalline nanoforms with one specific crystal structure:

- The name of the specific crystal structure covered;
- A clear indication that the set includes nanoforms consisting of particles with only specific crystal structure.

7 For a set including crystalline nanoforms where the individual nanoforms consist of particles with more than one crystal structure:

- The names and the ranges (as w/w percentage) of different crystal structures covered by the set (e.g., 20-40%(w/w) of crystal structure 1, 80-60%(w/w) of crystal structure 2).

8 For a set including partially crystalline nanoforms:

- The range(s) (as w/w percentage) and the name of different crystal structure(s) and the range of amorphous fraction covered by the set.

9 You have reported that the crystal structure of the nanoforms in the Set [redacted]. You report that nanoforms consists of [redacted]. However, you have also specified in your dossier that the [redacted]. This information indicates that [redacted].

10 Therefore, the information you have reported describing the crystal structure(s) of the nanoforms in the Set of Nanoforms is inconsistent.

11 You must report consistent information describing crystal structure of the nanoforms so that the boundaries of the Set of Nanoforms are clear. If the nanoforms covered by the set consist of [redacted]. If the nanoforms covered by the set consist of [redacted]. The information must be included in Section 1.2 of the IUCLID dossier reporting the Set of Nanoforms.

1.2. Justification demonstrating that a variation within the boundaries of the set of similar nanoforms does not affect the hazard assessment, exposure assessment and the risk assessment of the similar nanoforms in the set (introduction to Annex VI)

12 Annex VI of the REACH regulation requires that a "justification shall be provided to demonstrate that a variation within these boundaries does not affect the hazard assessment, exposure assessment and risk assessment of the similar nanoforms in the set".

1.2.1. Information provided

13 The lead registrant's dossier includes a justification document for the Set of Nanoforms entitled "[redacted]" under IUCLID section 1.2.

1.2.2. Assessment of the information provided

14 We have assessed the information provided and we have identified the following issues on the basis of which we consider that the Set of Nanoforms does not fulfil the requirement for a justification demonstrating that a variation within these boundaries does not affect the hazard assessment, exposure assessment and risk assessment of the similar nanoforms in the set:

1.2.2.1. Lack of scientific evidence on which this justification is based

15 Section 4 of Appendix for nanoforms applicable to the Guidance on Registration and Substance Identification (Version 2.0 – January, pages 22-30)[2] states that the 'registrant must also submit the adequate and reliable scientific evidence on which this justification is based'.

16 In your justification to demonstrate that the hazard assessment of the nanoforms covered by the Set can be performed jointly, you state that, regarding environmental fate and ecotoxicity, "*mobility, bioavailability and toxicity can be expected to be low for all TiO2 nanoforms*" and conclude lack of environmental hazard.

[2] Section 4.1 (Page 22) and 4.2.2.1 (page 23) of the Appendix for Nanoforms applicable to the Guidance on Registration and the Guidance on Substance Identification, ECHA (2022)

17 In relation to human health, to support the lack of repeated dose toxicity, you state that "*There is currently no animal data available on the repeated dose toxicity via oral route for nano forms of titanium dioxide. However, based on the fact that (a)* [redacted] *did not show any adverse effects in two chronic oral feeding studies and several other repeated dose toxicity studies via gavage (b)* [redacted] *and therefore need to be considered as* [redacted]" and "*it appears unlikely that nano forms of titanium dioxide show a significantly different toxicological profile to* [redacted]".

18 You have neither provided detailed information on bioaccumulation, adsorption and (eco)toxicology on nanoforms relevant to the Set in your justification nor have you linked your statements to specific studies in order to substantiate your justification.

19 Similarly, you claim that the "*studies in the REACH dossier have been thoroughly reviewed and there is no evidence in any of the studies for any endpoints for any differences in hazard due to crystal phase*". However, you do not specifiy to which studies, in (or outside) the dossier, you are referring to.

20 Finally, you refer to "[redacted]", with regards to the impact of aspect ratio variation on hazards, where you mention "*no differences in hazard between any of the materials* [redacted]*".* The reported aspect ration of the Set of Nanoforms is [redacted]. Hence, the referred study is considered not to provide relevant information for the Set of Nanoforms.

21 Therefore, in the absence of scientific evidence substantiating the justification, you have not demonstrated that the hazard assessment of the nanoforms can be performed jointly.

1.2.2.2. Missing (robust) study summaries

22 The ECHA manual "How to prepare registration dossiers covering nanoforms"[3] clarifies in section 2.2.6. that "each scientific evidence summarised in the justification must refer to a study summary or robust study summary." Whether based on unpublished data or on publicly available literature, each scientific evidence, and the characterisers of the nanoforms it refers to must be provided in the justification in the form of a (robust) study summary. Article 3(28) and (29) of REACH regulation, states that a (robust) study summary must comprise a (detailed) summary of the objectives, methods, results and conclusions of a full study report providing sufficient information to make an (independent) assessment of the study or of the relevance of the study.

23 In the justification document, you refer to several studies, namely:

- You also refer to several publications in support of your arguments (e.g. [redacted] 2005 and references therein; [redacted] 2018a-c, 2019a-c; [redacted] 2014 a,b and [redacted] 1998 and references therein), with regards to stability and mobility of TiO2 nanoforms. Specifically, in support of nanoforms stability, you provide tabulated data on "[redacted]", referring to [redacted] 2018a-c, 2019a-c. However, limited details on test conditions (e.g. pH and separation method) and no comprehensive information of the test materials is reported.
- [redacted] 2014, in support of the dustiness data provided.

[3] Section 2 How to prepare registration dossiers covering nanoforms, ECHA (2021)

24 However, you have not provided a robust study summary or study summaries for any of these studies.

25 In the absence of robust study summaries or study summaries, ECHA cannot assess the reliability of your justification. Furthermore, in the absence of comprehensive information on the test materials, ECHA cannot assess the relevance of the provided data to the Set of Nanoforms.

26 Therefore, you have not demonstrated that the hazard assessment of the nanoforms can be performed jointly.

1.2.2.3. Hazard/fate data provided on nanoforms outside the Set of Nanoforms

27 In accordance with Annex VI of REACH, the parameters in the points 2.4.2 to 2.4.5 of the individual nanoforms are used to define the boundaries of a 'set of similar nanoforms' which "allow to conclude that the hazard assessment, exposure assessment and risk assessment of these nanoforms can be performed jointly." This implies that the justification can be based only on hazard information resulting from nanoforms with characterisation parameter values within the boundaries of this set.

28 You have defined the boundaries of the Set of Nanoforms as follows:

29 [redacted] You have provided data on solubility and dustiness in the justification document.

30 The provided dustiness tests ([redacted] 2014) were performed on [redacted] nanoforms: [redacted]. None of the nanoforms tested for dustiness can pertain to this Set of Nanoforms due to [redacted]. That is, only the tested nanomaterial [redacted] listed above could be relevant for this Set based on the reported crystal phase (i.e. [redacted]). However, as [redacted] tested nanomaterials [redacted] are claimed to [redacted] (i.e. [redacted]) and to [redacted] they fall outside this ([redacted]) Set of Nanoforms. As a result, they are necessarily outside the boundary of the Set of Nanoforms.

31 The solubility tests ([redacted] 2018a-c, 2019a-c) were performed on [redacted] nanoforms [redacted] at pH 6 and 8. However, [redacted] nanoforms tested for dissolution cannot pertain to this Set of Nanoforms due to [redacted]. Therefore, only one potentially relevant data point is available on dissolution for the Set of Nanoforms. However, ECHA notes the following:

- Firstly the test material is not appropriately characterised as described in section 1.2.1.4, and
- Secondly, according to Annex VI of REACH regulation, a "*justification shall be provided to demonstrate that a variation within these boundaries does not affect the hazard assessment, exposure assessment and risk assessment of the similar nanoforms in the Set.*". Thus, in relation to variation of each characterisation

parameter, the registrant must provide hazard information demonstrating that there is a common pattern in the potency of the (eco)toxicological properties despite the variation of the characterisers of the nanoforms in the Set. Only one data point for the Set of Nanoforms cannot demonstrate that there is a common pattern.

32 Therefore, in the absence of hazard information relating to the nanoforms covered by the Set, you have not justified that the hazard assessment of the nanoforms in this Set can be performed jointly.

1.2.2.4. Hazard/fate data provided only on an unknown nanoform

33 Recital 12 of the COMMISSION REGULATION (EU) 2018/1881, stipulates that "to allow for adequate assessment of the relevance of any physicochemical, toxicological and ecotoxicological information for the different nanoforms, the test material should be appropriately characterised. For the same reasons, test conditions documented and a scientific justification for the relevance and adequacy of the utilised test material as well as documentation for the relevance and adequacy of the information obtained from means other than testing for the different nanoforms should be provided."

34 As explained in section 1.2.1.3, you have provided information on dissolution ([redacted] 2018a-c, 2019a-c) on only one nanoform potentially relevant to the Set of Nanoforms. You have reported only few characterisation parameters of the test material. Specifically, you have reported [redacted]. However, you have not provided all required characterisation parameters of the particles of the test material, as listed under Section 2.4.2.to 2.4.5 of REACH Annex VI. Namely, you have not specified the particle size distribution, the aspect ratio, the purity of the crystal phase and the shape of the particles of the test material.

35 In the absence of appropriate characterisation of the test material used in the generation of the data, it is not possible to conclude whether the tested nanoform is representative for the nanoforms included in the Set. Hence, cannot be concluded that the data provided in the justification is relevant for a nanoform in a specific set. Therefore, it cannot be concluded that the hazard assessment of the nanoforms in this Set can be performed jointly.

1.2.2.5. Missing justification for joint exposure assessment of the Set of Nanoforms

36 Annex VI of REACH regulation requires a justification to demonstrate that a variation within the boundaries of the Set of Nanoforms does not affect joint performance of the hazard assessment, exposure assessment and risk assessment of the nanoforms.

37 Section 4 of the 'Appendix for nanoforms applicable to the Guidance on Registration and Substance Identification' (Version 2.0 – January 2022, page 22-23) states that a justification must be provided as to "why the exposure (…) can also be performed jointly for the set of nanoforms". It specifically requires that "a common conclusion on exposure assessment can be reached for the set". This is demonstrated when the potential release is similar for all the nanoforms with regards to all their respective exposure routes. For example, for airborne exposure, this is demonstrated by similar value of dustiness (or by using a dustiness value that is conservative); for aquatic exposure, it is demonstrated as a minimum by similar dispersion stability, dissolution behaviour and surface functionalisation of all nanoforms within the set.

38 While you provide information on dissolution ([redacted] 2018a-c, 2019a-c) and dustiness ([redacted] 2014) which are relevant properties for the assessment of the exposure, this information is not relevant to the Set of Nanoforms as explained in sections 1.2.1.3

and 1.2.1.4 above. As a consequence, you have not demonstrated that the potential release of the nanoforms is similar and that the exposure assessment of all the nanoform in the Set can be performed jointly.

39 Therefore, it is not demonstrated that a common conclusion on exposure assessment can be reached for the Set. Hence, the risk assessment of the Set of Nanoforms cannot be performed jointly.

References

The following documents may have been cited in the decision.

Guidance on registration of nanoforms
Appendix for nanoforms applicable to the Guidance on Registration and Substance Identification' (version 2.0, January 2022)
How to prepare registration dossiers covering nanoforms (version 1.2, October 2021)

All Guidance on REACH is available online: https://echa.europa.eu/guidance-documents/guidance-on-reach

Appendix 2: Procedure

The Substance is listed in the Community rolling action plan (CoRAP) for the start of substance evaluation in 2018.

This decision does not prevent ECHA from initiating further compliance checks at a later stage on the registrations present.

ECHA followed the procedure detailed in Articles 50 and 51 of REACH.

The compliance check was initiated on 07 July 2021.

ECHA notified you of the draft decision and invited you to provide comments.

In the comments on the draft decision, the Lead Registrant of the Joint Submission, on behalf of all co-registrants, requested an extension of the deadline to provide information, from 3 months initially indicated in the draft decision to 10 months from the date of adoption of the decision. Following ECHA's request for clarifications substantiating this extension on 05 September 2022, the Lead Registrant provided a detailed work plan to address the incompliances set out in the draft decision. Based on these clarifications, ECHA consider that actions described to address the incompliances identified in the decision justify reasonnably the request for deadline extension. Therefore, ECHA has extended the deadline to 10 months.

ECHA notified the draft decision to the competent authorities of the Member States for proposals for amendment.

ECHA received proposal(s) for amendment and modified the draft decision.

ECHA invited you to comment on the proposed amendment(s) and referred the modified draft decision to the Member State Committee.

You did not provide any comments on the proposed amendment(s).

The Member State Committee unanimously agreed on the draft decision during its MSC-81 meeting. ECHA adopted the decision under Article 51(6) of REACH.

Appendix 3: Addressees of this decision and their corresponding information requirements

In accordance with Articles 10(a) and 12(1) of REACH, the information requirements for individual registrations are defined as follows:

Registrant Name	Registration number
[redacted]	[redacted]

Where applicable, the name of a third party representative (TPR) may be displayed in the list of recipients whereas ECHA will send the decision to the actual registrant.