~~Confidential~~

Helsinki, 22 June 2023

Addressees
Registrants of JS_synthetic amorphous silica as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
18/10/2022

Registered substance subject to this decision ("the Substance")
Substance name: Silicon dioxide
EC/List number: 231-545-4

Registered form subject to this decision ("the Set of Nanoforms")
Name of Set of similar nanoforms: synthetic amorphous silica, nanostructured material_Set 1

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 OF A SET OF NANOFORMS

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 Set of Nanoforms "synthetic amorphous silica, nanostructured material_Set 1" (hereafter, "the Set of Nanoforms") into compliance with the information requirements listed below by the deadline of ***2 April 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 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 1. The procedural history is described in Appendix 2.

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

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.

2 In a generic comment to the draft decision, you explain that "*boundaries are determined as result of a complex iteration process that the lead registrant must perform in cooperation with other joint registrants. Following this collection exercise, the parameters, as defined in 2.4.2 - 2.4.5 of REACH Annex VI will be carefully reviewed*." ECHA takes note of your intention to address the incompliances identified in the decision on the characterisation of clearly defined boundaries of the set of nanoforms.

1.1.1. Information provided

3 The lead registrant of the joint submission has reported "*synthetic amorphous silica, nanostructured material*" as a Set of Nanoforms. The boundaries of the Set of Nanoforms are identified in Section 1.2 of the lead registrant's dossier and in a document entitled "[redacted]".

1.1.2. Assessment of the information provided

4 We have assessed the information you provided and we have identified the following issue 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 particle size distribution

5 Annex VI section 2.4.2. of the REACH Regulation requires reporting of "number-based particle size distribution with indication of the number fraction of constituent particles in the size range within 1 nm – 100 nm".

6 Further, the Section 4.1 of ECHA Guidance document 'Appendix for nanoforms applicable to the Guidance on Registration and Substance Identification' outlines the principles for reporting particle size distribution and number fraction of constituent particles for a set of nanoforms. It stipulates that for a set of nanoforms, you must report the particle size distribution and the number fraction of constituent particles of the nanoforms included in the set with the smallest and largest d10, d50, and d90 value.

7 You have reported the number fraction of constituent particles as 50-100 % and range for d10, d50 and d90 values as 1-100 nm. In the document "[redacted].pdf" you state that "[t]*ypical particle size distribution on commercial SAS grades is provided on mass based. For commercially relevant are the d10, d50 and d90 values. The mass based particle size distribution is measured through standard industrial particle size measurement either in suspension or in air*".

8 However, mass-based particle size distribution values are not relevant for the determination of "*number-based particle size distribution*".

9 Further, Annex VI, Section 2.4.2 requires "indication of the number fraction of constituent particles in the size range within 1 nm – 100 nm". Thus, the reported number fraction values imply that:

- **all the particles** of the nanoform with the **largest number fraction** (100 %) of the constituent particles in the set have at least one of the external dimensions in the size range 1-100 nm
- **50 % of the particles** of the nanoform with the **smallest number fraction** (50 %) of the constituent particles in the set have at least one of the external dimensions in the size range 1-100 nm

10 However, the reported maximum d90 value is not consistent with the minimum number fraction of constituent particles. The maximum d90 value of 100 nm implies that there can be only 10 % of particles of which smallest external dimension is larger than 100 nm and thus number fraction of constituent particles cannot be smaller than 90 %.

11 Therefore, you are requested to report d10, d50 and d90 values based on the number-based particle size distributions as well as the values of the number fraction of constituent particles, which are consistent with each other, and which are based on values of nanoforms setting the boundaries for the Set of Nanoforms. The information must be included in Section 1.2 of the IUCLID dossier reporting the Set of Nanoforms.

12 In your comments to the draft decision, you indicate that "*we will clarify the wording, adjust the numbers (d10-d50-d90) and provide a justification for the updated ranges in line with the current nanomaterial definition in REACH annex VI*." ECHA takes note of your intention to report the required information.

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)

13 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

14 The lead registrant of the joint submission has reported the Set of Nanoforms to which you refer in your own dossier. A justification of the Set of Nanoforms is provided in a document entitled "[redacted]" in section 1.2. of the lead registrant's registration dossier .

1.2.2. Assessment of the information provided

15 We have assessed the information you 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. Missing explanation addressing the physicochemical, environmental fate, ecotoxicity and toxicity properties of nanoforms in the Set

16 Section 4. of the 'Appendix for nanoforms applicable to the Guidance on Registration and Substance Identification' explains how to justify that the variation of a characterisation parameter of the nanoforms covered by the set does not change the hazard profile of those nanoforms[1]. More specifically, the justification must contain documented evidence that the registrant has investigated the threshold beyond which a variation of a characteriser will affect the property of the nanoforms included in the set. More specifically, the justification must investigate at minimum the following:

- Does the variation of the characterisation parameters of the different nanoforms within the set impact their dissolution rate and solubility?
- Does the variation of the characterisation parameters of the different nanoforms within the set impact their toxicokinetic behaviour, as well as their fate and (bio)availability set?
- Does the variation of the characterisation parameters of the different nanoforms within the set impact their (eco)toxicity? Is there a direct relationship between that variation and the (eco)toxicity?

17 The justification must address separately each characterisation parameter set out in Annex VI, Section, 2.4. for which there is a variation among the different nanoforms within the Set.

18 The boundaries of the Set of Nanoforms report a variation of particle size distribution with minimum and maximum d10, d50 and d90 values as 1 nm and 100 nm, respectively. This implies that the nanoform setting the lower boundary for the Set of Nanoforms has 80 % of particles with at least one external dimension exactly 1 nm (i.e., all d-values are 1 nm) and the nanoform setting the upper boundary has 80 % of particles with at least one external dimension exactly 100 nm (i.e., all d-values are 100 nm).

19 However, your justification does not investigate whether this variation impacts the dissolution rate, solubility, toxicokinetic behaviour, fate, (bio)availability or (eco)toxicity of the nanoforms in the Set of Nanoforms.

20 Similarly, while the boundaries of the Set of Nanoforms report a variation of specific surface area by mass and by volume as 4-1000 m^2/g and 8.8-2200 m^2/cm^3, respectively, your justification does not investigate whether this variation impacts the dissolution rate, solubility, toxicokinetic behaviour, fate, (bio)availability or (eco)toxicity of the nanoforms in the Set of Nanoforms.

21 Therefore, your justification does not demonstrate that the variation of particle size distribution and specific surface area of the nanoforms in the Set of Nanoforms do not affect the joint hazard assessment of these nanoforms. Consequently, you have not established that the hazard assessment of the nanoforms within the Set can be performed jointly.

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

22 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'.

23 In your justification to demonstrate that the variation of the particle size distribution and specific surface area of the nanoforms in the Set does not affect the hazard assessment, you refer to: *"same hazard (eco)toxicological profile because" [these characterisers] "do not have any impact on toxicokinetic, fate and (bio)availability as evidenced in "key*

[1] 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

[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

(eco)toxicological studies", "*reliable in vivo (eco)toxicological studies*", "*various in vitro experiments", "key in vivo studies"* and "*two recent 90-day toxicity studies in rats"*.

24 However, you have not provided any detailed information on these specific studies and you have not linked your statements to specific studies in order to substantiate your justification.

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

1.2.2.3. Missing (robust) study summaries

26 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.

27 You state that "*the nanoforms in this set are expected to have the same (eco)toxicological profile because particle size, although influencing dissolution rate and solubility under laboratory conditions, did not have an impact on in vivo toxicokinetic behaviour, fate, and (bio)availability as evidenced in key (eco)toxicological studies*". In this context you refer to several publications ([redacted], 2007, [redacted], 2019, [redacted], 2018, and [redacted], 2019).

28 You further explain that the silanol density is not a driver for toxicity and you refer to the publication [redacted], 2019. However, you have not provided any (robust) study summaries or study summaries for these studies.

29 In the absence of robust study summaries or study summaries, ECHA cannot assess the reliability of your justification.

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

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

31 Annex VI of the 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.

32 Section 4 of the 'Appendix for nanoforms applicable to the Guidance on Registration and Substance Identification' (Version 2.0 – January, 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 in the set 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

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

minimum by similar dispersion stability, dissolution behaviour and surface functionalisation of all nanoforms within the set.

33 You have not provided information on the potential release of the nanoforms. Therefore, you have not demonstrated that there is no variation of the potential release of the nanoforms and that the exposure assessment of all the nanoforms in the Set can be performed jointly.

34 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 similar Nanoforms cannot be performed jointly.

35 In your comments to the draft decision, you indicate that the "*Justification will be enhanced. For this purpose, in vitro and in vivo screening tests as well as PC data are appropriate indicators"*. ECHA takes note of your intention to address the incompliances addressed in this decision relating to the justification of the set of nanoforms.

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

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 05 July 2021.

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

ECHA took into account your comments and did not amend the requests.

In the comments on the draft decision, you requested an extension of the deadline to provide information, from 3 months initially indicated in the draft decision to 12 months from the date of adoption of the decision.

On the 5th of September 2022 ECHA requested clarifications to substantiate your request for an extension of the deadline, in order for ECHA to understand the need for an extension of the deadline and evaluate a proportionate time. More specifically, ECHA requested information on the detailed actions you intended to take; measurements and the precise nature of the tests you intend to perform; and information on the precise nature of the literature searches (scope, sources, search and quality criteria) you intend to perform.

In your reply, you do not specify any action, measurement or test you intend to perform to justify that the hazard assessment can be performed jointly within the set. You refer only generically to the "*re-evaluation of available studies*". You also explain that you "*focus on additional literature searches to elucidate possible influence of surface modification on human- or environmental toxicity of SAS*". You indicate that the "*selection of keywords, sources and quality criteria is currently being discussed*". Without more detailed information, ECHA has no ground to assess the time you would need to perform any specific action, measurement or study. In addition, ECHA cannot foresee the precise nature of the literature searches you intend to perform, and thereby, the time needed to perform them. Consequently, we are therefore unable to justify an extension of the deadline.

Nevertheless, in your reply you indicate generically that data must be collected from several hundreds of registrants, while you do not specify the data concerned. This data collection exercise is comparable to the efforts performed by registrants subject to previous compliance check decision who also requested a deadline extension. In these cases, ECHA considered that the 9 months deadline requested was a reasonable time given the number of registrants (ca. 350) and the actions these registrants undertook to perform. In order to provide a level playing field between registrants of nanoforms and to align the deadline between registrants subject to compliance check decision regarding nanoforms in similar circumstances, ECHA has extended the deadline indicated in the decision from 3 months to 9 months.

ECHA notes that in the absence of information relating to the performance of any test and on their anticipated duration, there is no legitimate reason to extend the indicated deadline beyond the 9 months already provided.

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

ECHA received proposals for amendment and modified the draft decision.

ECHA invited you to comment on the proposed amendments and referred the modified draft decision to the Member State Committee.

Three addressees of this decision provided comments agreeing on the proposed amendment. These comments were taken into account by the Member State Committee.

In addition, the same addressees have also provided comments on the draft decision. These comments do not address the proposed amendment(s). Therefore, these comments were not taken into account by the Member State Committee as they were considered to be outside of the scope of Article 51(5).

The Member State Committee unanimously agreed on the draft decision in its MSC-82 written procedure. 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]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
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[redacted]	[redacted]
[redacted]	[redacted]
[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.