EUROPEAN CHEMICALS AGENCY

Decision number: TPE-D-0000002000-98-05/F Helsinki, 21 June 2012

DECISION ON A TESTING PROPOSAL SET OUT IN A REGISTRATION PURSUANT TO ARTICLE 40(3) OF REGULATION (EC) NO 1907/2006

For Silicon, CAS No 7440-21-3 (EC No 231-130-8), registration number: [redacted]

Addressee: [redacted]

The European Chemicals Agency (ECHA) has taken the following decision in accordance with the procedure set out in Articles 50 and 51 of Regulation (EC) No 1907/2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH Regulation).

I. Procedure

Pursuant to Article 40(1) of the REACH Regulation, ECHA has examined a testing proposal set out in the registration dossier for Silicon, CAS No 7440-21-3 (EC No 231-130-8), submitted by [redacted] (Registrant), latest submission number [redacted], for > 1000 tonnes per year.

In accordance with Articles 10(a)(ix) and 12(1)(e) of the REACH Regulation, the Registrant submitted the following testing proposal as part of the registration dossier to fulfil the information requirements set out in Annex IX:

Annex IX, 8.6.2: Sub-chronic toxicity study (90-day), inhalation route

The examination of the testing proposal was initiated on 20 September 2010.

ECHA opened a third party consultation for the testing proposals including testing on vertebrate animals that was held from 14 February until 31 March 2011. ECHA received comments on the testing proposal, which are described and analysed in Section III (statement of reasons).

On 3 November 2011 ECHA sent a draft decision to the Registrant for comments. The Registrant did not provide any comments on the draft decision.

On 20 January 2012 ECHA notified the Competent Authorities of the Member States of its draft decision and invited them pursuant to Article 51(1) of the REACH Regulation to submit proposals to amend the draft decision within 30 days of the receipt of the notification.

Subsequently, Competent Authorities of the Member States submitted one proposal for amendment to the draft decision.

On 23 February 2012 ECHA notified the Registrant of proposals for amendment to the draft decision and invited him pursuant to Article 51(5) of the REACH Regulation to provide comments on those proposals for amendment within 30 days of the receipt of the notification.

ECHA has reviewed the proposal for amendment received and decided not to amend the draft decision.

On 5 March 2012, the draft decision was referred to the Member State Committee.

On 20 March 2012 the Registrant provided comments on the proposed amendment. The Member State Committee took the comments of the Registrant into account.

After discussion in the Member State Committee meeting on 24-27 April 2012, a unanimous agreement of the Member State Committee on the draft decision as modified at the meeting was reached on 26 April 2012 and ECHA took the decision pursuant to Article 51(6) of the REACH Regulation.

This decision does not imply that the information provided by the Registrant in his registration dossier is in compliance with the requirements of the REACH Regulation. The decision does not prevent ECHA to initiate a compliance check on the present dossier at a later stage.

II. Testing required

Pursuant to Article 40(3)(a) of the REACH Regulation, the Registrant shall carry out the following test using the indicated test method:

- Sub-chronic toxicity study (90-day) toxicity study (Annex IX, 8.6.2, EU Method B.29, OECD Guideline 413) in rat by the inhalation route

Pursuant to Articles 40(4) and 22 of the REACH Regulation, the Registrant shall submit to ECHA by **23 June 2014** an update of the registration dossier containing the information required by this decision.

At any time, the Registrant shall take into account that there may be an obligation to make every effort to agree on sharing of information and costs with other registrants.

III. Statement of reasons

Pursuant to Article 40(3)(a) of the REACH Regulation, ECHA may take a decision requiring the Registrant to carry out the proposed test.

The decision of ECHA is based on the examination of the testing proposal of the Registrant for the registered substance, scientific information submitted by third parties, comments from the Registrant on the draft decision, and proposals for amendment submitted by Member States.

For the reasons set out below ECHA has decided to accept the Registrant's testing proposal.

1. Examination of the Registrant's testing proposal

The technical dossier does not contain the results of any sub-chronic toxicity study (90-day) on the registered substance silicon via the inhalation route. Instead, the dossier contains the following information:

- Statements for the use of a read-across approach from a supporting substance for the registered substance. The dossier contains the results of an OECD Guideline 452 study on the substance synthetic amorphous silica by the inhalation route. In addition, the dossier contains the results of the OECD assessment of the available test data on synthetic amorphous silica for the endpoint on repeated dose toxicity. However, the Registrant concludes that *although the surface of silicon is covered*

with amorphous silicon dioxide and the dissolution of silicon from silicon particles in vitro is not very different from that of synthetic amorphous silica, no read-across from synthetic silicon dioxide is performed for this end-point due to different particle characteristics.

- The results of epidemiological studies on workers in the silicon and ferrosilicon industries, showing some effects on the workers in these industries. However, the Registrant concludes that *since silicon particles are only a minor component of these dusts present in silicon/ferrosilicon factories, no conclusions on the inhalation toxicity of silicon can be made based on these studies. Repeated dose inhalation toxicity testing of silicon is proposed.*

- The section on toxicokinetics contains several studies performed on synthetic amorphous silica, including studies on the lung kinetics of this substance. However, the Registrant concludes that *because of the different particle characteristics between synthetic amorphous silica and silicon, the usability of these studies in the assessment of the toxicokinetics of silicon after inhalation is limited.* Furthermore, the dossier contains the results of a study on the *in vitro* dissolution kinetics of silicon. For these studies, the Registrant concludes that *studies on in vitro dissolution kinetics of silicon suggest that silicon may have slightly lower lung clearance compared to the lung clearance of synthetic amorphous silica.*

ECHA agrees that the read-across from synthetic amorphous silica to silicon is not justified according to Annex XI, 1.5. A read-across from synthetic amorphous silica to silicon for the endpoint on repeated dose toxicity via inhalation depends on the premise that silicon is covered by a layer of amorphous silicon dioxide, and that silicon and silicon dioxide have similar dissolution behaviour. Although the surface of silicon is covered with amorphous silicon dioxide, the *in vitro* dissolution data does not provide sufficient information on the behaviour of silicon particles in the lung. Furthermore, even if silicon and silicon dioxide exhibit similar dissolution behaviour, this would only account for the toxicity of the resulting silicon ion, but does not provide any information about the toxicity of silicon, including local effects, prior to its clearance from the lungs.

In addition, while the surface of silicon may be covered by silicon dioxide, the read-across from synthetic amorphous silica does not address the potential hazard from another structurally similar compound. Silicon dioxide can exist in different forms, which are chemically identical (SiO2), but structurally different: amorhpous silicon dioxide and crystalline silicon dioxide (quartz). This is significant because quartz is known to cause silicosis after repeated inhalation exposure, which is not seen in amorphous silicon dioxide. No justification is provided for the use of only the less hazardous synthetic amorphous silica instead of the more hazardous crystalline silicon in the read-across.

Therefore, as the information on this endpoint is not sufficient for the registered substance but needs to be present in the technical dossier to meet the information requirements it is necessary to generate the data and to perform the test. Regarding the additional parameters suggested by the Registrant, The EU Method B.29/OECD 413 guideline states that "animals in a satellite group scheduled for follow up observations should be kept for at least a further 28 days without treatment to detect recovery from, or persistence of toxic effects", but does not set an upper limit on the length of the observation period. The guidelines allow for control and vehicle control groups, but do not provide guidance on positive controls.

The inclusion of an additional positive control during the sub-chronic toxicity test may be helpful for the Registrant to conclude on the outcome of this study but the performance of

such a control treatment is by itself not necessary to fulfil the REACH information requirement. Therefore the inclusion of this positive control group during a sub-chronic repeated dose toxicity study is at the Registrant's discretion. However, the Registrant should ensure that the performance of any such additional investigations does not interfere with the performance of the sub-chronic toxicity study according to OECD Guideline 413.

2. Examination of the comments submitted by third parties

As a result of the public consultation, ECHA received comments from two parties. These are described and analysed below

I. Before a sub-chronic toxicity (Subchronic Inhalation Toxicity Study, OECD Guideline 413) is conducted, consideration should be given to the following:

1. Results from sub-chronic and chronic inhalation studies with amorphous silica (IUCLID dossier, OECD SIDS from 2004)

The third party points out that the Registrant has already applied read across from silica to silicon for the endpoints on oral repeated-dose toxicity and toxicokinetics, and that one of the read-across studies suggested by the Registrant under the section on toxicokinetics is an inhalation toxicity study, where rats were exposed to amorphous silica for 3-12 months, and points out additional inhalation studies on silica in an attached OECD SIDS report on silicates.

According to section 1.5 of Annex XI of the REACH Regulation, grouping of substances and read-across approach can be applied for substances whose physicochemical, toxicological and ecotoxicological properties are likely to be similar or follow a regular pattern as a result of structural similarity, and when the conditions in section 1.5 of Annex XI are met.

ECHA has evaluated this comment and has identified several deficiencies in the information provided by the third party with regard to the fulfilment of the conditions laid down in section 1.5 of Annex XI of the REACH Regulation and in particular that:

- One of the conditions laid down in section 1.5 of Annex XI of the REACH Regulation is that adequate and reliable information of the applied method is provided. The justification provided by the third party for read-across is limited to a statement that the Registrant has applied a similar read-across for information on toxicokinetics and oral repeated dose toxicity, but provides no justification for why read-across is applicable for inhalation repeated dose toxicity. The documentation of the applied method provided is not considered adequate to justify the read-across.

- The absence of information on toxicological properties of silicon in the dossier or the third party comment prevents an assessment of whether the inhalation toxicity, or toxicity in general, of silicon and silicon dioxide are likely to be similar or follow a regular pattern as a result of structural similarity.

Therefore, ECHA concludes that on this occasion, the information submitted does not meet the conditions for the grouping of substances and read-across set out in Annex XI, Section 1.5. Therefore, it cannot constitute an acceptable adaptation to the test in question.

2. Human data on repeated inhalation exposure to amorphous silica

The third party suggests using data obtained from a monitoring programme and morbidity study on workers in synthetic amorphous silica-production plants in a weight of evidence

assessment, and attached the OECD SIDS report for amorphous silica and silicates.

ECHA has evaluated this comment and notes the third party mentions that silicon is used in industry, with particles <10 microns, and that the measured particle size of amorphous silica is between 1-350 microns. However, there is no justification for why this information from synthetic amorphous silica would be applicable to silicon. In addition, due to insufficient information, no judgement can be made if the criteria specified in Annex XI, 1.1.3 of the REACH Regulation are met for this study.

Therefore, ECHA concludes that on this occasion, the information submitted does not meet the conditions for the use of historical human data set out in Annex XI, Section 1.1.3. Therefore, it cannot constitute an acceptable adaptation to the standard test in question.

3. Exposure considerations: use the TTC for repeated dose end point.

The third party states that since testing can be exempted based on negligible exposure, exposure should be thoroughly analysed before conducting the test. In addition, they suggest that the Threshold of Toxicological Concern (TTC) concept should be adopted and cut-off values (human exposure threshold values below which there is no significant risk to human health) for oral (90/540/1800 mg/kg bw/day) exposure should be used. No cut-off values are provided for inhalation exposure.

According to Annex XI, Section 3 of the REACH Regulation, the testing can be omitted if it can be demonstrated that there is no or no significant exposure. The Registrant did not use substance-tailored exposure-driven testing according to Annex XI, Section 3 for this endpoint, but indicated that for several uses, the opportunity for exposure arises.

Therefore, ECHA concludes that on this occasion, the information submitted does not meet the conditions for the use of substance tailored exposure driven testing in Annex XI, Section 3..Therefore, ECHA concludes that testing cannot be omitted based on negligible exposure.

II. A suggestion to use read-across from existing inhalation toxicity studies on Synthetic Amorphous Silica (SAS), EINECS 231-545-4

The third party comment suggests performing read-across from synthetic amorphous silica to silicon, with the justification that silicon will be covered with a layer of amorphous silicon dioxide. This is a justification based on structural similarity, as exposure to silicon particles will result in exposure to silicon dioxide. However, the read-across from synthetic amorphous silica does not address the potential hazard from another structurally similar compound. Silicon dioxide can exist in different forms, which are chemically identical (SiO2), but structurally different: amorphous silicon dioxide and crystalline silicon dioxide (quartz). This is significant because quartz is known to cause silicosis after repeated inhalation exposure, which is not seen in amorphous silicon dioxide. The third party provides no rationale for choosing the less hazardous form of silicon dioxide to perform the read-across from. They only state that *the difference between crystalline and amorphous silica can be at least partly explained by the better transformation/dissolution properties of amorphous silica in lung tissue as compared to crystalline silica like quartz and cristoballite.*

However, the limited toxicokinetic data on dissolution of silicon shows it has slightly slower dissolution compared to silicon dioxide, and therefore may have slightly lower lung clearance. There is no *in vivo* toxicokinetic data on the dissolution or clearance of silicon particles from lungs.

Therefore, ECHA concludes that on this occasion, the information submitted does not meet

the conditions for the grouping of substances and read-across set out in Annex XI, Section 1.5. Therefore, it cannot constitute an acceptable adaptation to the test in question.

In addition to the above, the third party comment suggests there may be technical difficulties in producing silicon particles <5 micron for the inhalation toxicity tests, and that the resulting particles may be contaminated by the milling process. However, the granulometry data in the technical dossier submitted by the Registrant shows that silicon is produced in different forms, and one of these forms includes jetmilled powders <10 micron in size. The data presented on the particle size distribution of these powders shows that for at least one of the tested samples, the particle size falls under the required 5 microns. This shows that silicon can and indeed is produced by industry with sufficiently small particle sizes.

IV. Adequate identification of the composition of the tested material

The process of evaluation of testing proposals set out in Article 40 of the REACH Regulation aims at ensuring that the generation of information is tailored to real information needs in order to prevent unnecessary testing. The information submitted in the dossier was sufficient to confirm the identity of the substance for the purpose of assessing the testing proposal. The Registrant must note, however, that this information, or the information submitted by other registrants of the same substance, has not been checked for compliance with the substance identity requirements set out in Section 2 of Annex VI of the REACH Regulation.

In relation to the proposed tests, the sample of substance used for the new studies must be suitable for use by all the joint registrants. Hence, the sample should have a composition that is within the specifications of the substance composition that are given by the joint registrants. It is the responsibility of all the joint registrants of the same substance to agree with the tests proposed in the testing proposal (as applicable to their tonnage level) and to document the necessary information on its composition. The substance identity information of the registered substance and of the sample tested must enable ECHA to confirm the relevance of the testing for the substance actually registered by each joint registrant. Finally, the studies must be shared by the joint registrants concerned.

V. General requirements for the generation of information and Good Laboratory Practice

ECHA always reminds registrants of the requirements of Article 13(4) of the REACH Regulation that ecotoxicological and toxicological tests and analyses shall be carried out in compliance with the principles of good laboratory practice (GLP). National authorities monitoring GLP maintain lists of test facilities indicating the relevant areas of expertise of each facility.

According to Article 13(3) of the REACH Regulation, tests that are required to generate information on intrinsic properties of substances shall be conducted in accordance with the test methods laid down in a Commission Regulation or in accordance with other international test methods recognised by the Commission or the European Chemicals Agency as being appropriate. Thus, the Registrant shall refer to Commission Regulation (EC) No 440/2008 laying down test methods pursuant to Regulation (EC) No 1907/2006 as adapted to technical progress or to other international test methods recognised as being appropriate and use the applicable test methods to generate the information on the endpoints indicated above.

VI. Information on right to appeal

An appeal may be brought against this decision to the Board of Appeal of ECHA under Article 51(8) of the REACH Regulation. Such appeal shall be lodged within three months of receiving notification of this decision. Further information on the appeal procedure can be found on the ECHA's internet page at http://echa.europa.eu/appeals/app_procedure_en.asp. The notice of appeal will be deemed to be filed only when the appeal fee has been paid.

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