ECHA
EUROPEAN CHEMICALS AGENCY

Decision number: CCH-D-2114311254-64-01/F Helsinki, 9 December 2015

DECISION ON A COMPLIANCE CHECK OF A REGISTRATION PURSUANT TO ARTICLE 41(3) OF REGULATION (EC) NO 1907/2006

For Antimony, CAS No 7440-36-0 (EC No 231-146-5), 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 41(1) of the REACH Regulation ECHA has performed a compliance check of the registration for Antimony, CAS No 7440-36-0 (EC No 231-146-5), submitted by [redacted] (Registrant).

This decision is based on the registration as submitted with submission [redacted], for the tonnage band 1000 tonnes or more per year. This decision does not take into account any updates submitted after 23 July 2015, the date upon which ECHA notified its draft decision to the Competent Authorities of the Member States pursuant to Article 51(1) of the REACH Regulation.

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

The compliance check was initiated on 7 November 2013.

On 13 December 2013 ECHA sent the draft decision to the Registrant and invited him to provide comments within 30 days of the receipt of the draft decision. That draft decision was based on submission number [redacted].

On 27 January 2014 ECHA received comments from the Registrant on the draft decision, concerning the information requirements of Annex I, Sections 1.4.1., 5. and 6., Annex VI, Sections 2.3. and 2.3.7. and Annex IX, Section 8.7.2. and Annex X, Sections 8.7.2. and 8.7.3. On 25 February 2014 the Registrant updated his registration with the submission number [redacted]

The compliance check requirement to submit information of a two-generation reproductive toxicity study (EU B.35, OECD TG 416) or an extended one-generation reproductive toxicity study (EU B.56, OECD TG 443) has been removed from this draft decision due to the legislative amendments to the REACH Regulation regarding Annex X, Section 8.7.3. In light of this, ECHA Secretariat did not consider further the Registrant's comments and update(s) concerning the information requirement of Annex X, Section 8.7.3. However, ECHA Secretariat did consider further the Registrant's comments and update(s) concerning the information requirements of Annex I, Sections 1.4.1, 5 and 6, Annex VI, Sections 2.3 and

2.3.7. and Annex X, Section 8.7.2. On the basis of all this information and change of scope, Section II was amended. The Statement of Reasons (Section III) was changed accordingly.

On 23 July 2015 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 for amendment of the draft decision within 30 days of the receipt of the notification. Subsequently, a proposal for amendment was submitted.

On 28 August 2015 ECHA notified the Registrant of the proposal for amendment to the draft decision and invited him pursuant to Article 51(5) of the REACH Regulation to provide comments on the proposal for amendment within 30 days of the receipt of the notification.

The ECHA Secretariat reviewed the proposal for amendment received and amended Section I (Procedural Section) of the draft decision.

On 7 September 2015 ECHA referred the draft decision to the Member State Committee.

By 28 September 2015, in accordance to Article 51(5), the Registrant provided comments on the proposal for amendment. In addition, the Registrant provided comments on the draft decision. The Member State Committee took the comments on the proposal for amendment of the Registrant into account. The Member State Committee did not take into account the Registrant's comments on the draft decision as they were not related to the proposal(s) for amendment made and are therefore considered outside the scope of Article 51(5).

A unanimous agreement of the Member State Committee on the draft decision was reached on 13 October 2015 in a written procedure launched on 1 October 2015.

ECHA took the decision pursuant to Article 51(6) of the REACH Regulation.

II. Information required

A. Information in the technical dossier derived from the application of Annexes VII to XI

Pursuant to Articles 41(1), 41(3), 10(a)(vi) and/or (vii), 12(1)(e), 13 and Annex X of the REACH Regulation the Registrant shall submit the following information using the indicated test method and the registered substance subject to the present decision:

Pre-natal developmental toxicity study, second species (Annex X, Section 8.7.2.; test method: EU B.31./OECD 414) in rabbits, oral route.

Note for consideration by the Registrant:

The Registrant may adapt the testing requested above according to the specific rules outlined in Annexes VI to X and/or according to the general rules contained in Annex XI of the REACH Regulation. In order to ensure compliance with the respective information requirement, any such adaptation will need to have a scientific justification, referring to and conforming with the appropriate rules in the respective Annex, and an adequate and reliable documentation.

Failure to comply with the request(s) in this decision, or to fulfil otherwise the information requirement(s) with a valid and documented adaptation, will result in a notification to the Enforcement Authorities of the Member States.

B. Deadline for submitting the required information

Pursuant to Article 41(4) and 22(2) of the REACH Regulation the Registrant shall submit the information in the form of an updated registration to ECHA by **16 June 2017** an update of the registration dossier containing the information required by this decision[, including, where relevant, an update of the Chemical Safety Report].

III. Statement of reasons

Pursuant to Article 41(3) of the REACH Regulation, ECHA may require the Registrant to submit any information needed to bring the registration into compliance with the relevant information requirements.

A. Information in the technical dossier derived from the application of Annexes VII to XI

Pursuant to Articles 10(a)(vi) and/or (vii), 12(1)(e) of the REACH Regulation, a technical dossier for a substance manufactured or imported by the Registrant in quantities of 1000 tonnes or more per year shall contain as a minimum the information specified in Annexes VII to X of the REACH Regulation.

Pre-natal developmental toxicity study, second species (Annex X, Section 8.7.2.)

Pre-natal developmental toxicity studies on two species are part of the standard information requirements for a substance registered for 1000 tonnes or more per year (Annex IX, Section 8.7.2., column 1, Annex X, Section 8.7.2., column 1, and sentence 2 of introductory paragraph 2 of Annex X of the REACH Regulation).

ECHA notes that the Registrant has adapted the information requirement for a pre-natal developmental toxicity study, first species (Annex IX, 8.7.2.) for the registered substance by using read-across from data generated with diantimony trioxide. The Registrant has included information to support this read-across approach. ECHA has assessed this adaptation of the standard information requirement and considers that the Registrant has provided an adequate and reliable documentation of the read-across applied in line with the requirements established in Annex XI, 1.5. of the REACH Regulation. Therefore, ECHA has accepted the read-across approach as used by the Registrant.

As for the second species, the Registrant has sought to adapt the information requirement by referring to the provisions of Annex X, section 8.7., column 2 and also submitted a weight of evidence approach according to Annex XI, Section 1.2.

Firstly, ECHA assessed the adaptation submitted by the Registrant based on Annex X, section 8.7., column 2 and concludes that the conditions for adaptation of the standard testing regime are not all met for the following reasons:

According to Annex X, Section 8.7., column 2, "*the studies do not need to be conducted if the substance is of low toxicological activity (no evidence of toxicity seen in any of the tests available), it can be proven from toxicokinetic data that no systemic absorption occurs via relevant routes of exposure (e.g. plasma/blood concentration below detection limit using a sensitive method and absence of the substance and of metabolites of the substance in urine, bile or exhaled air) and there is no or no significant human exposure*".

a) Based on the available information, the Registrant considers that the registered substance is of low toxicity. The Registrant claims in their adaptation of the information requirement and comments to the draft decision an absence of systemic adverse toxicological effects in studies with single or repeated dosing and indicates that "*local effects are the sole effect of toxicological concern*" in chronic inhalation studies of diantimony trioxide. ECHA notes that the diantimony trioxide has been assessed in an EU Risk Assessment Report (RAR) (available at the following link: https://echa.europa.eu/.../trd_rar_sweden_diantimony_trioxide_en.rtf) which concludes that diantimony trioxide causes lung tumours in rats following inhalation exposure. The EU RAR considered that this is a threshold effect and that the relevance for humans could be discussed but concluded that in the absence of mechanistic data to the contrary, it must be assumed that the rat model of tumourigenicity can identify potential carcinogenic hazards to humans. Consequently, ECHA considers that, on the basis of the above considerations, the registered substance cannot be regarded as of "low toxicological activity", i.e. there is evidence of toxicity seen in the chronic inhalation toxicity studies. Therefore, ECHA concludes that the specific criteria for adaptation of the information requirement specified in Annex X, Section 8.7 column 2 referring to the low toxicological activity of the substance is not met.

b) In addition, the Registrant refers in his justification of the adaptation of the standard testing regime to the "*poor bioavailability of diantimony trioxide via oral (0.05-0.3%), dermal (0.01-0.1%) and inhalation (<<1%) routes at doses expected to be used for any reproductive toxicity study (i.e. 100-1000mg/kg/d)*" and to tissue distribution data to support their adaptation of the standard information requirement. As indicated above, according to the provisions of Annex X, section 8.7 column 2, absence of systemic absorption via relevant route of exposure is one of the conditions to be met to waive further testing with regard to the information requirement of Annex X, section 8.7. ECHA points out that the information provided by the Registrant in their adaptation and in section 5.1.3 of the Chemical Safety Report (CSR), as outlined in the initial draft decision, suggest that limited systemic exposure occurs after administration of diantimony trioxide. Section 5.1.3 of the CSR also reports on tissue distribution of antimony measured after a single oral administration of diantimony trioxide. Although the study is regarded as having a Klimisch score of 4, the consistent tissue distribution pattern reported in a 24-week oral repeated dose toxicity study in male rats ([redacted]) with antimony detected in spleen, lung liver, kidney, testes and brain is compatible with the Registrant's claim that diantimony trioxide is bioavailable, even if only to a limited degree. On the basis of this information, ECHA considers that the condition for adaptation of the information requirement specified in Annex X, Section 8.7 column 2 referring to the absence of systemic absorption is not met.

c) The Registrant elaborates on the limited worker and consumer exposure and refers to risk characterisation ratios (RCRs) of "≤ 0.75" and to risk management measures controlling the risks for local effects via inhalation to demonstrate safe use of the substance subject to this decision. ECHA outlines that RCRs of 0.75 derived based on inhalation exposure suggest that significant worker exposure occurs. Based on this information, ECHA considers that the condition laid down in Annex X, Section 8.7. column 2 of no or no significant exposure is not fulfilled.

Based on the above, ECHA concludes that the conditions for adaptation of the standard testing regime according to Annex X, Section 8.7. column 2 are not all met. Consequently the adaptation according to the provisions of Annex X, section 8.7., column 2 submitted by the Registrant cannot be accepted.

Secondly, ECHA has assessed the weight of evidence provided by the Registrant and concludes that no adequate and reliable documentation as required by Annex XI, 1.2 of the REACH Regulation was provided for the information requirement of Annex X, Section 8.7.2. ECHA points out that no information on the pre-natal developmental toxicity of the substance subject to this decision or the substance used as source substance in the read-across approach in a species other than the rat has been provided.

The technical dossier contains a pre-natal developmental toxicity study performed in rats via the inhalation route using the analogue substance diantimony trioxide that ECHA considers adequate to fulfil the information requirement of Annex IX, Section 8.7.2. i.e. for a first species. The information obtained from the dose-range finding study and included in the technical dossier provides little new information for the endpoint under consideration. The scope of the investigations performed in this study is limited compared to the definitive study performed in the same species with the same test material administered via the same route. The Registrant also reported data from a "Study of the embryotoxic effects of antimony oxide under experimental conditions" in the registration dossier. The Registrant considered this study performed in rats as not reliable and "not useful for risk assessment" due to limitations in the reporting of the test conditions. Based on the information provided in the study summary, ECHA concludes that this study provides supporting information of limited relevance on the pre-natal developmental toxicity of diantimony trioxide in rats and does not provide insights on the toxicity of this substance in a second species.

The Registrant further refers to the weight of evidence from the short- and long-term toxicity/fertility studies in rodents and the relevant information on the toxicokinetic behaviour in rats to conclude that diantimony trioxide does not present a reproductive toxicity hazard. ECHA observes that the lines of evidence mentioned by the Registrant address endpoints other than pre-natal developmental toxicity and do not provide information on the developmental toxicity of antimony in a non-rodent species.

Consequently ECHA considers that the weight of the evidence provided by the Registrant does not meet the requirements of Annex XI, Section 1.2. and is not sufficient to assess whether the substance subject to this decision has or has not the potential to cause developmental toxicity in a second species.

Accordingly, ECHA concludes that the waiving argument based on the conditions for adaptation of the information requirements laid down in Annex X, Section 8.7.2, column 2 proposed by the Registrant cannot be accepted. ECHA also considers that the proposed weight of evidence does not meet the requirements of Annex XI, Section 1.2. and is not sufficient to assess whether antimony has or has not the potential to cause developmental

toxicity in a second species. Consequently there is an information gap for Annex X, Section 8.7.2. and it is necessary to provide information for this endpoint.

The test in the first species was carried out by testing a rodent species and ECHA therefore considers that the test in a second species should be carried out in a non-rodent species. According to the test method EU B.31/OECD 414, the rabbit is the preferred non-rodent species and the test substance is usually administered orally. ECHA considers these default parameters appropriate and testing should be performed by the oral route with the rabbit as a second species to be used.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, the Registrant is requested to submit the following information derived with the registered substance subject to the present decision: Pre-natal developmental toxicity study (test method: EU B.31./OECD 414) in rabbits by the oral route.

B. Deadline for submitting the required information

In the draft decision communicated to the Registrant the time indicated to provide the requested information was 30 months from the date of adoption of the decision. This period of time took into account the fact that the draft decision also contained a two-generation reproductive toxicity study (EU B.35, OECD TG 416) (Annex X, Section 8.7.3.) and information requests based on Annex I, Sections 1.4.1, 1.5 and 1.6 and Annex VI, Sections 2.3 and 2.3.7. As these requests are not addressed in the present decision, ECHA Secretariat considers that a reasonable time period for providing the required information in the form of an updated IUCLID5 dossier is 18 months from the date of the adoption of the decision.

The Registrant submitted comments to the draft decision in which an extension to the deadline for submitting the information was requested. The Registrant's justification for this request was that the time required to organise and complete the entire test programme would exceed the 30-month period indicated in the draft decision and requested an extension to the deadline to 36 months. ECHA evaluated the justification provided and, taking into account the change in scope of this decision, decided to add six months to the standard deadline for the only remaining information requirement changing the deadline from 12 months to 18 months.

IV. Adequate identification of the composition of the tested material

ECHA stresses that the information submitted by other joint registrants for identifying the 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 information required by the present decision, 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 joint registrants who manufacture or import the same substance to agree on the appropriate composition of the test material and to document the necessary information on their substance composition.

In addition, it is important to ensure that the particular sample of substance tested in the new studies is appropriate to assess the properties of the registered substance, taking into account any variation in the composition of the technical grade of the substance as actually manufactured by each registrant. If the registration of the substance by any registrant covers different grades, the sample used for the new studies must be suitable to assess these grades.

Finally there must be adequate information on substance identity for the sample tested and the grade(s) registered to enable the relevance of the studies to be assessed.

V. 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 an appeal shall be lodged within three months of receiving notification of this decision. Further information on the appeal procedure can be found on ECHA's internet page at http://www.echa.europa.eu/regulations/appeals. The notice of appeal will be deemed to be filed only when the appeal fee has been paid.

Authorised[1] by Guilhem de Seze, Head of Unit, Evaluation E1

[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.