EUROPEAN CHEMICALS AGENCY

Decision number: CCH-D-0000004928-60-04/F Helsinki, 25 August 2014

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

For tin, CAS No 7440-31-5 (EC No 231-141-8), 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 41(1) of the REACH Regulation ECHA has performed a compliance check of the registration for tin, CAS No 7440-31-5 (EC No 231-141-8), submitted by [redacted] (Registrant). The scope of this compliance check is limited to the standard information requirements of Annex IX, Section 8.7.2., and Annex X, Section 8.7.2. of the REACH Regulation.

This decision is based on the registration as submitted with submission number [redacted], for the tonnage band of 1000 tonnes or more per year. This decision does not take into account any updates submitted after 6 March 2014, 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 5 March 2013.

On 22 August 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 19 September 2013 the Registrant updated his registration dossier with the submission number [redacted]

On 23 September 2013 ECHA received comments from the Registrant on the draft decision. The ECHA Secretariat considered the Registrant's comments and update. On basis of this information, Section II was amended. The Statement of Reasons (Section III) was changed accordingly.

On 6 March 2014 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 to the draft decision was submitted.

On 10 April 2014 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 modified Section III of the draft decision.

On 22 April 2014 ECHA referred the draft decision to the Member State Committee.

By 12 May 2014 in accordance to Article 51(5), the Registrant provided comments on the proposal for amendment. The Member State Committee took the comments of the Registrant on the proposal for amendment into account.

A unanimous agreement of the Member State Committee on the draft decision was reached on 26 May 2014 in a written procedure launched on 15 May 2014. ECHA took the decision pursuant to Article 51(6) of the REACH Regulation.

II. Information required

Pursuant to Articles 41(1)(a) 41(3), 10(a)(vii), 12(1)(e), 13 and Annex IX, 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 in rats or rabbits, oral route (Annex IX, 8.7.2.; test method: EU B.31/OECD 414).

Pursuant to Article 41(4) of the REACH Regulation the Registrant shall submit the information in the form of an updated registration to ECHA by **3 March 2016.**

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 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 pre-natal developmental toxicity study is a standard information requirement as laid down in Annex IX, section 8.7.2. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

In the technical dossier the Registrant provided information with which he sought to fulfil this standard information requirement of Annex IX, Section 8.7.2. The provided information stems from a Reproduction/Developmental Toxicity Screening Test (OECD 421). However, this study does not provide the information required by Annex IX, Section 8.7.2., because it lacks, amongst others, sound data on pre- and post-implantation losses, external, soft tissue and skeletal malformations, types and incidences of individual anomalies. Therefore, ECHA concludes that this study does not fulfil the standard information requirement of Annex IX, 8.7.2.

The draft decision sent to the Registrant on 22 August 2013 referred to submission number [redacted] Under this submission number the Registrant had submitted some information related to Annex IX, Section 8.7.2. under an inappropriate heading of the registration dossier (i.e. in the endpoint summary of chapter 7.8 of the IUCLID dossier ("Toxicity to reproduction")), but did not provide the respective robust study summaries. Thus, ECHA could not assess whether the information given by the Registrant was sufficient to meet the information requirements of Annex IX, Section 8.7.2. and Annex X, Section 8.7.2. and the Registrant was requested to submit robust study summaries with a view to fulfilling the information requirements on Pre-natal developmental toxicity in one species (Annex IX, 8.7.2.) and on Pre-natal developmental toxicity in another species (Annex X, 8.7.2.).

In the dossier update from 19 September 2013 (submission number [redacted] the Registrant has removed these references and now refers to Annex XI, Section 1, which is interpreted by ECHA as a weight of evidence approach.

The Registrant claims that the pre-natal developmental toxicity study has been omitted since it is considered to be not scientifically necessary to conduct. According to the Registrant, "the available data show that the substance is insoluble and unavailable to the body, at a significant level, to cause an adverse effect. Furthermore, results of a reproductive/developmental toxicity screening study, performed in accordance with OECD 421, showed that the substance, tin metal, demonstrated no developmental toxicity at the highest dosage group of 1000 mg/kg bw/day in rats. The lack of toxicity observed at such a high dose level indicates that performing a longer term study is scientifically unnecessary and inappropriate on animal welfare grounds."

ECHA notes that according to the data on toxicokinetics studies submitted in the dossier there were still some 10 % of the administered dose recovered in the faeces 48 hours after a single oral administration to rats. The absorption through the gastrointestinal tract may be regarded as low due to the results of the excretion study, but is still considerable in absolute terms. In humans with no occupational exposure to tin compounds blood tin concentrations of 2-9 ng/mL are reported in a WHO publication (Tin and Inorganic Tin Compounds, Cicad 65, 2005; http://www.inchem.org/documents/cicads/cicads.cicad65.htm). The submitted biodistribution study shows tin concentrations in blood of rats up to 44 ng/mL after a single administration of a high dose of 2000 mg tin/kg body weight, indicating that tin is systemically availably after oral administration.

Although ECHA agrees that the test substance, tin metal, did not show toxicity in the test provided by the Registrant, it also notes that none of the studies submitted, in particular the reproductive/developmental screening study according to OECD 421, provides the information required by Annex IX, Section 8.7.2.

Whereas ECHA acknowledges the efforts undertaken by the Registrant and the information supplied, ECHA considers that an adaptation based on low toxicity, low absorption and low water solubility (0.004 mg/L) is neither covered by Annex XI, 1.2, nor by Annexes IX and X, 8.7., column 2 adaptation possibilities. A weight of evidence approach requires input from several independent sources of information leading to the assumption/conclusion that a substance has or has not a particular dangerous property, while the information from each single source alone is regarded insufficient to support this notion. The Registrant has not shown that the substance has not a particular dangerous property (in this case: pre-natal developmental toxicity), as required in a weight of evidence approach. The OECD 421 screening study provided by the Registrant does not cover key parameters of a pre-natal developmental toxicity study, like e.g. skeletal and soft tissue malformations or types and incidences of individual anomalies. There is systemic absorption (although low), and there is significant human exposure.

As explained above, the information available on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.

In ECHA's draft decision from 22 August 2013 it was clearly indicated that the request for information is driven by the necessity to achieve compliance for the endpoint Annex IX, section 8.7.2, which can only be achieved by the use of robust study summaries of existing data, valid adaptation or generation of a study. The Registrant was therefore informed that the consequence of not providing robust study summaries of existing data or valid adaptation would be the necessity to generate new data. The Registrant, by removing the relevant references to pre-natal developmental toxicity studies, confirms that there are no available pre-natal developmental toxicity studies for this substance which could be used to achieve compliance with the dossier. The updated adaptation argument is considered not valid, as outlined before, and ECHA deems generation of a pre-natal developmental toxicity study on the first species necessary to achieve compliance.

A Member State Competent Authority submitted a proposal for amendment suggesting that the Registrant could make a more robust weight of evidence adaptation argument to meet the information requirement. ECHA notes that it is in the Registrant's responsibility to justify an adaptation of standard information requirements and that ECHA shall not take over that responsibility in compliance checks. As the Registrant has not included a justified and documented adaptation argument in the registration dossier the non compliance has to be addressed by a request to provide information for the respective endpoint in form of an experimental study.

Moreover, ECHA notes that the suggestion that the weight of evidence approach could be rendered more robust was based on the comparison of internal doses (systemic levels of tin) with external doses (NOAELs and LOAELs of tin compounds). The internal doses of tin (estimated to be 12-20 µg per kg body weight) after a single oral administration of 2000 mg tin per kg body weight are lower than the equivalent tin NOAELs of the tin compounds *Dioctyltin dichloride* and *Dibutyltin dichloride* (119-140 or 390 µg per kg body weight, resp.). Therefore the Member State Competent Authority concluded that it would not be possible to achieve a systemic dose of tin that is associated with developmental toxicity from known hazardous tin compounds by oral administration of tin.

ECHA does not agree with that approach for two main reasons:

- Effects after administration of tin at one single high dose are compared with effects after several consecutive administrations of tin compounds at low doses. There may be different mechanisms of absorption of tin and tin compounds for single and repeated dosing and for high and low doses.

- Whereas the absorption and internal dose of tin after single oral administration were investigated in an experiment using tin, no data are given for the internal dose of tin after consecutive administration of tin compounds. ECHA is of the opinion that it is therefore not possible to conclude from the NOAEL of tin compounds, i.e. from an external dose, on the internal doses of tin. Consequently, it is not possible to compare the data for tin with those of the abovementioned tin compounds.

The Registrant, in their comments to the above proposal for amendment of a Member State Competent Authority, did not agree with the proposal for different reasons, in particular because they considered the organotin compounds referred to in the proposal for amendments not to be representative of tin metal. The Registrant however agreed to perform a pre-natal developmental toxicity study in rats.

According to the test method EU B.31/OECD 414, the rat is the preferred rodent species, the rabbit 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 rat or the rabbit as a first 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 rats or rabbits by the oral route.

Deadline for submitting the required information:

As the request in Section II was substantially amended from a request to provide robust study summaries to a request for an experimenatl study, the timeline given to the Registrant to submit the information was prolonged first from 3 months to 12 months.

In response to the proposal for amendment submitted by a Competent Authority of a Member State the Registrant submitted comments in which an extension to the deadline for submitting the information was requested. Due to the change of the request from robust study summaries to an experimental study this was the first occasion at which the Registrant could react on the request for an pre-natal developmental toxicity study and the time that ECHA considered sufficient to perform the assay. For this reason ECHA assessed the comments made and notes that the Registrant's justification for this request to extend the deadline concerning possible diffculties in obtaining an appropriate test sample appears to be valid. Therefore ECHA decided to extend the deadline to provide the requested information by 6 months so that a total of 18 months is available to generate the required study.

Notes for consideration by the Registrant:

In addition, a pre-natal developmental toxicity study on a second species is part of the standard information requirements as laid down in Annex X, Section 8.7.2. for substances registered for 1000 tonnes or more per year (see sentence 2 of introductory paragraph 2 of Annex X).

The Registrant should firstly take into account the outcome of the pre-natal developmental toxicity on a first species and all other relevant available data to determine if the conditions are met for adaptations according to Annex X, Section 8.7. column 2, or according to Annex XI; for example if the substance meets the criteria for classification as toxic for reproduction Category 1B: May damage the unborn child (H360D), and the available data are adequate to support a robust risk assessment, or alternatively, if weight of evidence assessment of all relevant available data provides scientific justification that the study in a second species is not needed. If the Registrant considers that testing is necessary to fulfill this information requirement, he should include in the update of his dossier a testing proposal for a pre-natal developmental toxicity study on a second species. If the Registrant comes to the conclusion that no study on a second species is required, he should update his technical dossier by clearly stating the reasons for adapting the standard information requirement of Annex X, Section 8.7.2.

IV. 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://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.

[redacted]

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