Decision number: CCH-D-0000004858-59-03/F Helsinki, 11 November 2014

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

For Sodium hexahydroxoantimonate, CAS No 33908-66-6 (EC No 251-735-0), 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 dossier for Sodium hexahydroxoantimonate, CAS No 33908-66-6 (EC No 251-735-0), submitted by [redacted] (Registrant). The scope of this compliance check is limited to the standard information requirements of Annex VII, Section 8.4. and Annex VIII, Section 8.4. of the REACH Regulation.

This decision is based on the registration dossier 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 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 dossier at a later stage.

The compliance check was initiated on 28 September 2012.

On 17 December 2012 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 11 January 2013 ECHA received comments from the Registrant. On 9 December 2013 the Registrant updated his registration dossier (submission number [redacted]).

The ECHA Secretariat considered the Registrant's comments and update. The information is reflected in the Statement of Reasons (Section III) whereas no amendments to the Information Required (Section II) were made.

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.

As no proposal for amendment was submitted, ECHA took the decision pursuant to Article 51(3) of the REACH Regulation.

II. Information required

Pursuant to Articles 41(1), 41(3), 10(a)(vi), 12(1)(e), 13 and Annex VII 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:

In vitro gene mutation study in bacteria (Annex VII, 8.4.1.; test method: EU B.13/14/OECD 471);

Pursuant to Article 41(4) of the REACH Regulation the Registrant shall submit the information in the form of an updated IUCLID dossier to ECHA by **18 May 2015**

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 requirement. The scope of the present decision is the *in vitro* gene mutation study in bacteria (Annex VII, 8.4.1. of the REACH Regulation). In accordance with Articles 10(a)(vi) and 12(1) of the REACH Regulation, any registration for a substance shall contain this information.

The technical dossier did not contain an *in vitro* gene mutation study in bacteria nor an adaptation argument to the standard information requirement that forms the scope of the present decision.

Following the draft decision the Registrant commented on the limitations of Ames regarding the testing of the metal compounds. In the updated dossier the following statement was included to waive the Ames testing:

"Tests on the mutagenic potential of antimony compounds in bacteria are considered dispensable for principal considerations, since inorganic metal compounds are frequently negative in this assay due to limited capacity for uptake of metal ions (Guidance on information requirements and chemical safety assessment, Chapter R.7a, p. 387; HERAG fact sheet mutagenicity, Chapter 2.1).
Supporting evidence: Kuroda et al (1991) conclude a negative testing outcome in bacterial reverse mutation assays using pentvalent SbCl5 (which because of comparative water solubility are considered suitable for read-aross to sodium hexahydroxoantimonate). This study can not be considered fully compliant with current testing requirements due to a limited number of tester strains used, among other minor shortcomings, and therefore does not qualify as a key study."

The Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 2.3. December 2013)(p.347-348) mentions this limitation in the context of ITS for mutagencity. Performing first a gene toxicity test with mammalian cells might increase the chance to identify in only one step a genotoxic inorganic compound and "would be a prefered **starting point** for this class of **Annex VII** substances". Nevertheless, in the event of a negative outcome it is still necessary to have the Ames test as there are some metal compounds which are positive in this test (e.g.chromium). Also it must be noted that the toxicity can vary not only between compounds of diverse metals but also between the different species of one metal.

The Registrant submitted also a suporting study with an Ames test performed in only two *Salmonella* strains with another antimony compound. However, if the Registrant intended to build a weight of evidence case showing that other antimony compounds are negative for Ames, the study reported by Kuroda K., et al. (1991) is not sufficient. REACH Annex XI 1.2. requests that " *There may be sufficient weight of evidence from several independent sources of information leading to the asssumtion/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.*" As the Registrant mentioned, the only study provided cannot be considered compliant with the current guideline (only two *Salmonella* strains TA 98 and T 100 were used) and no other data were provided for gene mutation in bacteria endpoint. Annex XI 1.1. regarding existing data also states the necessity for "adequate and reliable coverage of the key parameters foreseen to be investigated in the corresponding test method reffered to in Article 13 (3)." This is not the case with the study using only 2 *Salmonella* strains supplied by the Registrant.

The Registrant also brings up as evidence negative results in mammalian gene mutation and in vitro micronucleus test:

"It is concluded that Sodium hexahydroxoantimonate did not induce micronuclei in cultured human peripheral blood lymphocytes following treatments in the absence and presence of an Aroclor induced rat liver metabolic activation system (S-9). Concentrations were tested and analysed up to and in excess of the solubility limit in culture medium.
It is concluded that Sodium hexahydroxoantimonate did not induce mutation at the tk locus of L5178Y mouse lymphoma cells when tested under the conditions employed in this study. These conditions included treatments up to precipitating concentrations in two independent experiments, in the absence and presence of a rat liver metabolic activation system (S-9). Further testing of in vivo genetic toxicity tests is not considered necessary.
The following information is taken into account for any hazard / risk assessment: Sodium hexahydroxoantimonate did not induce micronuclei in cultured human lymphocytes and gene mutation in the tk locus of the L5178Y mouse lymphoma cell line. Therefore sodium hexahydroxoantimonate is considered as non-clastogenic and non-mutagenic."

While the negative result in a in vitro gene mutation in mammalian cells is indeed supportive for a non toxic potential for gene mutation in general it does not grant a negative result also for gene mutation in bacteria. As specified in Annex VIII, Column 2, 8.4. "*Appropriate in vivo mutagenicity studies shall be considered in case of a positive result **in any** of the genotoxicity studies in Annex VII or VIII.*". Thus, the Ames test is an important regulatory trigger for further *in vivo* genotoxicity studies that cannot be waived on the basis of another available *in vitro* study in mammalian cells.

Consequently there is an information gap and it is necessary to generate the data for this endpoint. Therefore, the Registrant is requested to submit the information for this endpoint using the abovementioned test method on the registered substance.

IV. Adequate identification of the composition of the tested material

ECHA stresses that the information submitted by the Registrant and 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 carrying out the studies required by the present decision it is important to ensure that the particular sample of substance tested 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. If the registration of the substance covers different grades, the sample used for the new studies must be suitable to assess these.

Furthermore, there must be adequate information on substance identity for the sample tested and the grade registered to enable the relevance of the studies to be assessed.

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

ECHA 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).

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 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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