ECHA
EUROPEAN CHEMICALS AGENCY

Decision number: CCH-D-2114300740-66-01/F Helsinki, 4 June 2015

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

For 2-methylpropane-2-thiol, CAS No 75-66-1 (EC No 200-890-2), 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 2-methylpropane-2-thiol, CAS No 75-66-1 (EC No 200-890-2), submitted by [redacted] (Registrant).

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 5 March 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. ECHA notes, in particular, that the information requirement of Annex IX/X, Section 8.7.3 has not been addressed in this decision.

The compliance check was initiated on 28 November 2013.

On 25 November 2014 ECHA sent the draft decision to the Registrant and invited him to provide comments within 45 days of the receipt of the draft decision.

On 16 January 2015 ECHA received comments from the Registrant agreeing to ECHA's draft decision.

The ECHA Secretariat considered the Registrant's comments.

On 5 March 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.

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

II. Information required

A. Information in the technical dossier derived from the application of Annexes VII to XI – request for robust study summaries

Pursuant to Articles 41(1)(a), 41(3), 12(1)(e), 3(28) and 10(a)(vii) as well as Annexes I, VII and IX of the REACH Regulation the Registrant shall submit for the registered substance a revised robust study summary for the following key study:

> Reproductive Toxicity (Annex IX, 8.7.2.), Pre-natal developmental toxicity study in mice (Endpoint study record: Developmental toxicity/teratogenicity. 2 methylpropane-2-thiol, [redacted], mouse key study, study title: Inhalation Teratology Study of n-Butyl Mercaptan and t-Butyl Mercaptan in Rats and Mice) as further specified in Section III.A.

B. 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 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, Section 8.4.1.; test method: Bacterial reverse mutation test, EU B.13/14. /OECD 471) using one of the following strains: E. coli WP2 uvrA, or E. coli WP2 uvrA (pKM101), or S. typhimurium TA102, as specified in section III.B below.

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.

C. Deadline for submitting the required information

Pursuant to Articles 41(4) and 22(2) of the REACH Regulation the Registrant shall submit to ECHA by **11 December 2015** 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.

Information related to robust study summaries

Pursuant to Articles 10(a)(vii) and 3(28) of the REACH Regulation, the technical dossier of a registration shall include robust study summaries if required under Annex I. With regard to the human health hazard assessment under Annex I, 1.1.4. of the REACH Regulation, robust study summaries are required for all key data used in the hazard assessment. Article 3(28) defines a robust study summary (RSS) as 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 minimising the need to consult the full study report. A practical guide to the preparation of robust study summaries is provided on the ECHA website[1].

The Registrant has not reported a complete robust study summary within the meaning of Article 3(28) of the REACH Regulation for the key studies of the following endpoints:

> Reproductive Toxicity (Annex IX, 8.7.2), Pre-natal developmental toxicity study in mice (Endpoint study record: Developmental toxicity/teratogenicity. 2 methylpropane-2-thiol, [redacted], mouse key study, study title: Inhalation Teratology Study of n-Butyl Mercaptan and t-Butyl Mercaptan in Rats and Mice)).

The ECHA practical guide on how to report robust study summaries indicates that for pre-natal developmental toxicity studies, the robust study summary should include (among other things), information on the following for the fetuses:

- external, soft tissue and skeletal malformations and other relevant alterations;
- number and percent of fetuses and litters with malformations (including runts) and/or variations as well as description and incidences of malformations and main variations (and/or retardations);
- criteria for categorisation of external, soft tissue, and skeletal malformations and other relevant alterations.

ECHA notes that the results of the pre-natal developmental toxicity study on mice reported in the technical dossier of the Registrant states the following:

Vertebral anomalies was present in 16.7% of the litters in both the control group and the 10 ppm group, in 43.5% of the litters in the group 100 ppm and in 23.8% of the litters in the 200 ppm. The only other malformation present in the 200 ppm group was a single instance of rib anomalies. In the 10 and 100 ppm groups, the remaining malformations did not occur in a dose-related pattern and/or were within the range of the historical control data. An increase in the total litters with malformations, due primarily to the increased incidence of the malformation vertebral anomaly, was noted in the tbutyl Mercaptan treated groups when compared to the control group. However, this incidence did not occur in a dose-related pattern (47.8% and 28.6% of the litters in the 100 and 200 ppm groups, respectively, had malformed fetuses) and was not statistically significant (p>0.05).

However, there is no further information in the dossier on the nature of the vertebral anomalies. It is unclear if these anomalies refer to variations or malformations, or a combination of both. Therefore, it is not possible to assess the severity and relevance of these reported anomalies, and the summary provided cannot be considered to meet the criteria of a robust study summary.

[1] How to report robust study summaries - Practical Guide 3. Version 2.0 – ECHA, November 2012. http://echa.europa.eu/documents/10162/13643/pg_report_robust_study_summaries_en.pdf

Therefore, pursuant to Article 41(1) and (3), 10(a)(vii) and Annex I, 1.1.4. of the REACH Regulation, the Registrant is requested to provide robust study summaries as defined by Article 3(28) and as further described in the ECHA Practical Guide 3.

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.

In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.)

An "*In vitro* gene mutation study in bacteria" is a standard information requirement as laid down in Annex VII, Section 8.4.1. 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.

According to Article 13(3) of the REACH Regulation, tests required to generate information on intrinsic properties of substances shall be conducted in accordance with the test methods recognised by the Commission or ECHA.

Other tests may be used if the conditions of Annex XI are met. More specifically, Section 1.1.2 of Annex XI provides that existing data on human health properties from experiments not carried out according to GLP or the test methods referred to in Article 13(3) may be used if the following conditions are met:

(1) Adequacy for the purpose of classification and labelling and/or risk assessment;
(2) Adequate and reliable coverage of the key parameters foreseen to be investigated in the corresponding test methods referred to in Article 13(3);
(3) Exposure duration comparable to or longer than the corresponding test methods referred to in Article 13(3) if exposure duration is a relevant parameter; and
(4) adequate and reliable documentation of the study is provided.

According to paragraph 13 of the current OECD 471 test guideline (updated 1997) at least five strains of bacteria should be used. These should include four strains of *S. typhimurium* (TA1535; TA1537 or TA97a or TA97; TA98; and TA100) that have been shown to be reliable and reproducibly responsive between laboratories. These four *S. typhimurium* strains have GC base pairs at the primary reversion site and it is known that they may not detect certain oxidising mutagens, cross-linking agents and hydrazines. Such substances may be detected by E.coli WP2 strains or *S. typhimurium* TA102 which have an AT base pair at the primary reversion site.

The Registrant has provided a test from the year 1982 according OECD 471 and GLP with an assigned reliability score of 2. The test used five different strains of *S. typhimurium* TA TA98, TA100, TA1535, TA1537, and TA1538. However, since the test was conducted, significant changes have been made to OECD guideline 471 and this means that the study does not meet the current guidelines, nor can it be considered as providing equivalent data according to the criteria in Annex XI, 1.1.2. of the REACH Regulation.

ECHA concludes that a test using *E. coli* WP2 uvrA, or *E. coli* WP2 uvrA (pKM101), or *S. typhimurium* TA102 has not been submitted by the Registrant and that the test using one of these is required to conclude on *in vitro* gene mutation in bacteria.

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.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, the Registrant is requested to complete the following information derived with the registered substance subject to the present decision: Bacterial reverse mutation test (test method: EU B.13/14. / OECD 471) using one of the following strains: E. coli WP2 uvrA, or E. coli WP2 uvrA (pKM101), or S. typhimurium TA102.

IV. Adequate identification of the composition of the tested material

In relation to the information required by the present decision, the sample of substance used for the new study 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 study 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 study 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 study 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.

[redacted]
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