ECHA
EUROPEAN CHEMICALS AGENCY

Decision number: TPE-D-0000002016-85-03/F Helsinki, 12 November 2012

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

**For Pentaerythritol tetrakis (3-mercaptopropionate), CAS No 7575-23-7 (EC No 231-472-8), 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 testing proposals set out in the registration dossier for Pentaerythritol tetrakis (3-mercaptopropionate), CAS No 7575-23-7 (EC No 231-472-8), submitted by [redacted] (Registrant).

This decision is based on the registration dossier as submitted with submission number [redacted], for 100-1000 tonnes per year. This decision does not take into account any updates after 19 July 2012, 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 decision does not imply that the information provided by the Registrant in his registration dossier is in compliance with the REACH requirements. The decision does not prevent ECHA from initiating a compliance check on the present dossier at a later stage.

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

- Annex IX, 8.6.2. OECD Guideline 408 (Repeated Dose 90-Day Oral Toxicity, in Rodents), including determination of sperm parameters and oestrus cycle length in order to cover reproductive endpoints;
- Annex IX, 8.7.2. Pre-natal developmental toxicity study according to OECD Guideline 414; and
- Annex IX, 8.7.3. Extended OECD 408 in rats, oral route. Reproductive toxicity would be assessed by conducting a 90-day oral study in the rat. This study would be extended to include an assessment of reproductive organs, including determination of sperm parameters and oestrus cycle length in order to cover reproductive endpoints.

ECHA opened a third party consultation for testing proposals including testing on vertebrate animals that was held from 1 July to 15 August 2011 and received comments (see Section III below).

The examination of the testing proposal was initiated on 4 October 2010.

On 3 January 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.

By 2 February 2012 the Registrant did not provide any comments on the draft decision to ECHA.

On 19 July 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 did not propose amendments to the draft decision and ECHA took the decision pursuant to Article 51(3) of the REACH Regulation.

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.

II. Testing required

Pursuant to Article 40(3)(a) of the REACH Regulation, the Registrant shall carry out the following tests using the indicated test method and the registered substance subject to the present decision:

a) Sub-chronic toxicity study (90-day) in rats: oral route, according to EU Method B.26 (OECD Guideline 408), Annex IX, 8.6.2.;
b) Pre-natal developmental toxicity study in rats: oral route, according to EU Method B.31 (OECD Guideline 414), Annex IX, 8.7.2.;

While pursuant to Article 40(3)(d) of the REACH Regulation

c) The extended OECD 408 study for provision of information to fulfil Annex IX, 8.7.3. is rejected.

If the results of the sub-chronic toxicity study (90-day) required by this decision indicate adverse effects on reproductive organs or tissues then the Registrant shall submit a testing proposal to cover the endpoint of Annex IX, 8.7.3. for reproductive toxicity unless the Registrant considers that the specific rules for adaptation from this information requirement mentioned in Column 2, Annex IX, 8.7. apply.

The Registrant may also consider submitting a testing proposal for this end-point at an earlier time on the basis of other considerations and justify the need to perform the study.

Pursuant to Articles 40(4) and 22(2) of the REACH Regulation, the Registrant shall submit to ECHA an update of the dossier by **12 November 2014**.

III. Statement of reasons

The decision of ECHA is based on the examination of the testing proposals of the Registrant for the registered substance and scientific information submitted by third parties.

a) Sub-chronic toxicity study (90-day)

According to Section 8.6.2. of Annex IX of the REACH Regulation the sub-chronic toxicity study (90 day) is a standard information requirement that is currently not available in the technical dossier.

The Registrant has proposed testing according to the OECD 408, extended to some reproductive endpoints. According to the Registrant this study shall be extended to include an assessment of reproductive organs: "Sperm parameters and oestrus cycle length shall be determined in order to cover reproductive endpoints."

ECHA notes that it is at the Registrant's discretion to perform the intended additional examinations during the testing proposal and use the results to ensure the safe use of the substance. However the Registrant is reminded that the proposed extension of this study will not fulfil the standard information requirement for reproductive toxicity set out in Annex IX, 8.7.3., unless Annex IX 8.7. column 2 adaptation is applied.

The Registrant also suggests Read-across from methyl 3-mercaptopropionate (MMP; CAS 2935-90-2). The duration in the study with MMP is shorter, i.e. 28 days versus 90 days which is the duration of the study that is required at this tonnage according to REACH Regulation. Furthermore, the arguments concerning the metabolism of the registered substance are not supported by any of the studies provided by the Registrant. Therefore, the read-across proposed by the Registrant does not fulfil the requirements set in Annex XI, 1.5., of the REACH Regulation for grouping and read-across.

The Registrant did not specify the species to be tested. According to the test method EU B.26/OECD 408 the rat is the preferred rodent species. ECHA considers this species as being appropriate.

During the third party consultation, ECHA received no relevant comments/information on the testing proposal for the endpoint on repeated dose toxicity.

Therefore, according to the testing proposal submitted, the Registrant is requested to carry out Sub-chronic toxicity study (90-day) in rats: oral route, according to EU Method B.26 (OECD Guideline 408).

b) Pre-natal developmental toxicity study

According to Section 8.7.2. of Annex IX of the REACH Regulation the pre-natal developmental toxicity study is a standard information requirement that is currently not available in the technical dossier.

The Registrant did not specify the species to be tested or the route of administration. According to the test method B.31/OECD 414 the rat is the preferred species and oral route is the preferred route of administration. ECHA considers this species and route of administration as being appropriate.

During the third party consultation, ECHA received no comments concerning the testing proposal for the pre-natal developmental toxicity study:

The Registrant is requested to carry out pre-natal developmental toxicity study, oral route, according to EU Method B.31 (OECD Guideline 414), Annex IX, 8.7.2.

c) Rejection of the proposed OECD 408 study for provision of information to fulfil Annex IX, 8.7.3.

The Registrant has proposed: "Reproductive toxicity will be assessed by conducting a 90-day oral study in the rat. This study shall be extended to include an assessment of reproductive organs. Sperm parameters and oestrus cycle length shall be determined in order to cover reproductive endpoints." ECHA assumes that this statement is referring to the same study described under a) i.e. Sub-chronic toxicity study (90-day) in rats: oral route, according to EU Method B.26 (OECD Guideline 408), including determination of sperm parameters and oestrus cycle length.

As stated above under point a), the extension of the 90-day study will not fulfil the information requirement for reproductive toxicity set out in Annex IX, 8.7.3., unless Annex IX 8.7. column 2 adaptation is applied.
According to Section 8.7.3., of Annex IX of the REACH regulation a two-generation reproductive toxicity study is required if the 28-day or 90-day study indicates adverse effects on reproductive organs or tissues. The conditions for requiring a two-generation reproductive toxicity study are not currently fulfilled. ECHA concludes that at this moment in time the legal requirements of Annex IX for the mandatory performance of the two-generation study are not met. If the 90-day study shows adverse effects on reproductive organs or tissues, the Registrant shall submit a testing proposal to cover the endpoint of Annex IX, 8.7.3. as this would then constitute a standard information requirement for substances registered at 100 to 1000 tonnes per year.

In any event, based on the information generated from the other studies or on the basis of any other considerations the Registrant may also consider submitting a testing proposal for this end-point at an earlier stage. However, in such situation justification for the need to perform the study should be provided.

During the third party consultation, ECHA received the following comment/information on the testing proposal for the two-generation reproductive study:

- Third party asks ECHA to consider requesting the Extended One-Generation Reproductive Toxicity Study (EOGRTS).

ECHA examined this proposal and concluded that, as explained above, there is no respective information requirement at the moment. ECHA concludes that therefore the third party proposal does not affect the decision on this testing proposal.

In conclusion, ECHA rejects the testing proposal made for Annex IX, 8.7.3. This rejection does not affect the decision made on testing proposal for the endpoint Annex IX, 8.6.2. Repeated dose toxicity, sub-chronic toxicity study in rats: oral route.

IV. 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 reads:

> *"Ecotoxicological and toxicological tests and analyses shall be carried out in compliance with the principles of good laboratory practice provided for in Directive 2004/10/EC or other international standards recognised as being equivalent by the Commission or the Agency and with the provisions of Directive 86/609/EEC, if applicable."*

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.

National authorities monitoring good laboratory practice (GLP) maintain lists of test facilities indicating the relevant areas of expertise of each facility.

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 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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