

For final decision: TPE-D-0000002565-72-05/F

Helsinki, 5 April 2013

DECISION ON A TESTING PROPOSAL SET OUT IN A REGISTRATION PURSUANT TO ARTICLE 40(3) OF REGULATION (EC) NO 1907/2006**For 1,3-dioxepane, CAS NO 505-65-7 (EC No 208-015-6) 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 the following testing proposals submitted as part of the registration dossier in accordance with Articles 10(a)(ix) and 12 (1)(e) thereof for 1,3-dioxepane, CAS No. 505-65-7 (EC No. 208-015-6), submitted by [REDACTED] (Registrant), latest submission number [REDACTED], for 1000 tonnes or more per year:

- 90-Day inhalation toxicity study (OECD 413) in rats with an extended assessment of the male/female reproductive system.
- Prenatal developmental toxicity study (OECD 414) in rats, inhalation route.

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 14 June 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.

On 23 November 2010, pursuant to Article 40(1) of the REACH Regulation, ECHA initiated the examination of the testing proposals set out by the Registrant in the registration dossier for the substance mentioned above.

ECHA held a consultation of third parties for the testing proposals including testing on vertebrate animals from 15 July 2011 until 29 August 2011. ECHA did not receive information from third parties for the tests subject to the current decision.

On 27 February ECHA received comments and new update for the dossier from the Registrant. In the update the Registrant has removed one of previously three testing proposals.

ECHA considered the Registrant's comments received and the dossier update and did amend the draft decision accordingly.

On 14 June 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, one Competent Authority of a Member State submitted a proposal for amendment to the draft decision.

On 18 July 2012 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.

ECHA reviewed the proposal for amendment received and decided to amend the draft decision.

On 30 July 2012 ECHA referred the draft decision to the Member State Committee.

On 30 July 2012, the Registrant actively provided no comments on the proposed amendment.

A unanimous agreement of the Member State Committee on the draft decision was reached on 3 September 2012 in a written procedure launched on 22 August 2012 and ECHA took the decision pursuant to Article 51(6) 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 requirements of the REACH Regulation. The decision does not prevent ECHA to initiate a compliance check on the present dossier at a later stage.

II. Testing required

The Registrant shall carry out the following proposed tests pursuant to Article 40(3)(a) of the REACH Regulation using the indicated test methods and the registered substance subject to the present decision:

1. Sub-chronic toxicity study (90-day) in rats, inhalation route (Annex IX, 8.6.2., test method: EU B.29/OECD 413).
2. Pre-natal developmental toxicity study in rats, inhalation route (Annex IX, 8.7.2., test method: EU B.31/OECD 414).

It is at the Registrant's discretion to perform the intended additional examinations during the Sub-chronic toxicity study (90-day).

The Registrant shall determine the appropriate order of the studies taking into account the possible outcomes and considering the possibilities for adaptations of the standard information requirements according to column 1 or 2 provisions of the relevant Annexes of the REACH Regulation.

Pursuant to Articles 40(4) and 22 of the REACH Regulation, the Registrant shall submit to ECHA by **5 April 2015** an update of the registration dossier containing the information required by this decision.

Data from a second pre-natal developmental toxicity study on another species is a standard information requirement according to Annex X, 8.7.2. of the REACH Regulation. 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, 8.7. column 2, or according to Annex XI. If the Registrant considers that testing is necessary to fulfil 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.

III. Statement of reasons

The decision of ECHA is based on the examination of the testing proposal submitted by the Registrant for the registered substance..

1. Sub-chronic toxicity (90 day)

a) Examination of the testing proposal

Pursuant to Article 40(3)(a) of the REACH Regulation, ECHA may require the Registrant to carry out the proposed test.

A sub-chronic toxicity study (90 day) is a standard information requirement as laid down in Annex IX, section 8.6.2. of the REACH Regulation. The information on this endpoint is not available for the registered substance but needs to be present in the technical dossier to meet the information requirements. Consequently there is an information gap and it is necessary to generate the data for this endpoint.

The Registrant proposed to perform a sub-chronic inhalation toxicity study in rats according to OECD guideline 413. Besides the standard assay parameters of the guideline, the Registrant proposed to perform an extended assessment of the male/female reproductive system (e.g. spermatogenesis). Additionally, in his testing strategy, the Registrant intends to perform this study after a 14-day day range finding study in time-mated female rats and the pre-natal developmental toxicity study.

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

ECHA also acknowledges the tiered testing strategy proposed by the Registrant. The outcomes from the 14-day day range finding study in time-mated female rats and the pre-natal developmental toxicity study could be used to ensure a better design of the inhalation sub-chronic toxicity study (90 day). However, the Registrant is reminded that the 14-day day range finding study in time-mated female rats and the pre-natal developmental toxicity study are not enough to fulfil the standard information requirements in the registration dossier for repeated dose toxicity set out in Annex IX, 8.6.2.

The Registrant proposed testing by the inhalation route. In the light of the physico-chemical properties of the substance and the information provided on the uses and human exposure, ECHA considers that testing by the inhalation route is appropriate.

b) Outcome

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation, the Registrant is required to carry out the proposed study: Sub-chronic toxicity study (90-day) in rats, inhalation route (test method: EU B.29/OECD 413) using the registered substance subject to the present decision.

2. Pre-natal developmental toxicity

a) Examination of the testing proposal

Pursuant to Article 40(3)(a) of the REACH Regulation, ECHA may require the Registrant to carry out the proposed test.

Pre-natal developmental toxicity studies are part of the standard information requirements as laid down in Annexes IX and X, section 8.7.2. of the REACH Regulation. The information on this endpoint is not available for the registered substance but needs to be present in the technical dossier to meet the information requirements. Consequently there is an information gap and it is necessary to generate the data for this endpoint.

The Registrant proposed testing by the inhalation route. In the light of the physico-chemical properties of the substance and the information provided on the uses and human exposure, ECHA considers that testing by the inhalation route is appropriate.

b) Outcome

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation, the Registrant is required to carry out the proposed study: Pre-natal developmental toxicity study in rats, inhalation route (test method: EU B.31/OECD 414) using the registered substance subject to the present decision.

When considering the need for a testing proposal for a prenatal developmental toxicity study in a second species, the Registrant should take into account the outcome of the pre-natal developmental toxicity study on the first species and all available data to determine if the conditions are met for adaptations according to Annex X, 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.

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.

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 ecotoxicological and toxicological tests and analyses shall be carried out in compliance with the principles of good laboratory practice (GLP). National authorities monitoring GLP maintain lists of test facilities indicating the relevant areas of expertise of each facility.

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.

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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