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EUROPEAN CHEMICALS AGENCY

For final decision: TPE-D-0000001903-75-05/F Helsinki, 6 June 2012

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

For 2,2-bis(hydroxymethyl)propionic acid, CAS: 4767-03-7 (EC No: 225-306-3), 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 2,2-bis(hydroxymethyl)propionic acid, CAS No 4767-03-7 (EC No 225-306-3) submitted by [redacted] (Registrant), latest submission number: [redacted], for >1000 tonnes per year.

In accordance with Articles 10(a)(ix) and 12(1)(e) 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:

- Sub-chronic repeated-dose oral toxicity study (OECD 408);
- Pre-natal developmental toxicity study (OECD 414).

The examination of the testing proposals was initiated on 20 July 2010.

ECHA opened a third party consultation for the testing proposals including testing on vertebrate animals that was held from 5 April until 20 May 2011. ECHA received the following input from third parties:

(a) A proposal for evaluation based on existing data and alternative testing strategies in a weight-of-evidence approach.

(b) Results of a non-linear classification ANN QSAR model for sub-chronic repeated dose oral toxicity and of a non-linear classification ANN QSAR model for pre-natal developmental toxicity.

On 27 September 2011 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 27 October 2011 the Registrant did not provide any comments on the draft decision to ECHA.

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On 20 January 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 submitted proposals for amendment to the draft decision.

On 23 February 2012 ECHA notified the Registrant of proposals for amendment to the draft decision and invited him pursuant to Article 51(5) of the REACH Regulation to provide comments on those proposals within 30 days of the receipt of the notification.

On 26 March 2012 the Registrant provided comments on the proposals for amendment. The Member State Committee took the comments of the Registrant into account.

After discussion in the Member State Committee meeting on 24-27 April 2012, the Member State Committee reached unanimous agreement on the draft decision as amended during the meeting on 25 April 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

Pursuant to Article 40(3)(a) of the REACH Regulation, the registrant shall carry out the following tests using these indicated test method(s):

- Sub-chronic repeated-dose oral toxicity study (Annex IX, 8.6.2., EU Method B.26 of Regulation (EC) No. 440/2008; OECD 408) in the rat by the oral route; following administration with the registered substance.

- Pre-natal developmental toxicity study (Annex X, 8.7.2., EU Method B. 31 of Regulation (EC) No. 440/2008; OECD 414) in the rat by the oral route; following administration with the registered substance.

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.

Pursuant to Articles 40(4) and 22 of the REACH Regulation, the registrant shall submit to ECHA by **6 June 2014** an update of the registration dossier containing the information required by this decision.

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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

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

The sub-chronic repeated dose toxicity and pre-natal developmental toxicity study endpoints are standard information requirements under Annex IX, 8.6.2., and Annex X, 8.7.2., respectively. As the necessary information on these endpoints is not available for the registered substance but needs to be present in the technical dossier, it follows that there is an information gap and that it is necessary to generate the data for these endpoints.

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.

(a) Response to third party comment – sub-chronic repeated-dose oral toxicity and pre-natal developmental toxicity:

One third party has proposed a testing strategy for the Agency to take into consideration (see above 1(a)).

ECHA has invited the submission of 'scientifically valid information with studies which address the relevant substance and hazard end-point', as specified by Article 40(2). This proposed strategy cannot be considered as scientifically valid information, or an appropriate replacement for sub-chronic repeated-dose or pre-natal developmental toxicities.

ECHA therefore concludes that this is an insufficient basis for rejecting the testing proposals for the above mentioned endpoints.

(b) Response to third party comments – sub-chronic repeated-dose oral toxicity and pre-natal developmental toxicity:

A second third party has provided ECHA with predictions using a non-linear classification ANN QSAR model for sub-chronic repeated-dose oral toxicity and pre-natal developmental toxicity endpoints (see above 1(b)). The predictions provide results of dependent variables of the model which are in the form "toxic/non-toxic".

In accordance with Annex XI, section 1.3., results of QSAR may be used instead of testing when the following conditions are met:

- results are derived from a QSAR model whose scientific validity has been established;
- the substance falls within the applicability domain of the QSAR model;

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- results are adequate for the purpose of classification and labelling and/or risk assessment, and;
- adequate and reliable documentation of the applied method is provided.

As such, the results provided cannot be utilised or extrapolated directly to fulfil these information requirements.

ECHA therefore concludes that this is an insufficient basis for rejecting testing which has been proposed for these endpoints.

(c) Deadline for submitting the required information

In the draft decision, ECHA requested that the Registrant shall submit an update of the registration dossier containing the required information within 12 months from the date of the decision. During the commenting period on the proposals for amendment, the Registrant indicated that 18 months would be more appropriate to update the registration dossier when considering the estimated time to plan, conduct and analyse the studies. Taking this into account and considering ECHA's current practice of providing sufficient time for the Registrant to conduct the studies sequentially, ECHA is requesting the Registrant to provide the required information for the 90-day sub-chronic toxicity study and the pre-natal developmental toxicity study within 24 months of the date of the final decision.

IV. Adequate identification of the composition of the tested material

The process of evaluation of testing proposals set out in Article 40 of the REACH Regulation aims at ensuring that the generation of information is tailored to real information needs in order to prevent unnecessary testing. The information submitted in the dossier was sufficient to confirm the identity of the substance for the purpose of assessing the testing proposal. The registrant must note, however, that this information, or the information submitted by other registrants of the same 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 relation to the proposed tests, the sample of substance used for the new studies 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 the joint registrants of the same substance to agree with the tests proposed in the testing proposal (as applicable to their tonnage level) and to document the necessary information on its composition. The substance identity information of the registered substance and of the sample tested must enable ECHA to confirm the relevance of the testing for the substance actually registered by each joint registrant. Finally, the studies must be shared by the joint registrants concerned.

V. 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

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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 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.

[redacted]

Jukka MALM
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