~~CONFIDENTIAL~~

European Chemicals Agency

Decision number: TPE-D-0000001673-74-05/F Helsinki, 01/12/2011

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

For 126-30-7 master 2,2-dimethylpropane-1,3-diol (IUC4 DSN 517), CAS 126-30-7 (EC No 204-781-0), 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 40(1) of the REACH Regulation, ECHA has examined testing proposals set out in the registration dossier for **126-30-7 master 2,2-dimethylpropane-1,3-diol (IUC4 DSN 517)**, CAS 126-30-7 (EC NO 204-781-0) submitted by [redacted] (the 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 and X:

- Sub-chronic toxicity study (90-day study and additional examinations concerning reproductive toxicity)

- Pre-natal developmental toxicity study

The examination of the testing proposals was initiated upon the date when receipt of the complete registration dossier was confirmed on 20 September 2010.

ECHA opened a third party consultation for the testing proposals including testing on vertebrate animals that was held from 26 January 2011 until 14 March 2011. ECHA received the following information from third parties (TPI):

TPI 1. Before a 90-day sub-chronic toxicity study and a developmental toxicity study is conducted, consideration should be given to the following alternative testing strategies:

a. *Evaluate the need to conduct a sub-chronic toxicity study based on results of existing data.*
b. *Evaluate the need to conduct a Prenatal Developmental Toxicity Study in light of the results of the existing 28-day or 90-day study and other toxicological data.*
c. *Perform in vitro (pre-) validated tests for the evaluation of the embryotoxic and endocrine disruption potential and apply QSAR classification models for developmental toxicity. Use results to waive developmental toxicity study.*
d. *Exposure considerations: use the TTC for repeated dose and reproduction toxicity end points*

TPI 2. Result of a nonlinear classification ANN QSAR Model for prenatal developmental toxicity study: toxic

ECHA examined the testing proposals and the information received from third parties and drafted a decision in accordance with Article 40 of REACH.

On 10 June 2011 ECHA notified the Registrant of its draft decision and invited him pursuant to Article 50(1) of the REACH Regulation to provide comments on the draft decision.

On 11 July 2011 the Registrant provided to ECHA comments on the draft decision. ECHA considered the information received and did not amend the draft decision.

On 29 July 2011 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. Subsequently, Competent Authorities of the Member States submitted proposals for amendments to the draft decision.

On 31 August 2011 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 for amendment within 30 days of the receipt of the notification. Based on the proposed amendments ECHA decided not to modify its draft decision.

On 12 September 2011, the draft decision was referred to the Member State Committee.

On 30 September 2011, the Registrant provided comments on the proposed amendments. The Member State Committee took the comments of the Registrant into account.

After discussion in the Member State Committee meeting on 2-4 November 2011, the Member State Committee amended the draft decision and a unanimous agreement of the Member State Committee on the amended draft decision was reached on 3 November 2011.

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 the indicated test method:

a. Sub-chronic toxicity study (90-day) (Annex IX, 8.6.2, EU Method B.26) in rat by the oral route.

   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 to include additional examinations concerning reproductive toxicity may not fulfil the standard information requirements in the registration dossier for reproductive toxicity set out in Annex X, 8.7.3..

b. Pre-natal developmental toxicity study (Annex IX and X, 8.7.2, EU Method B 31) in rat by the oral route. The Registrant shall consider the need for testing the substance in a second species (preferably rabbit) depending on the outcome of the test in rats and include a testing proposal or a justification, why testing is not needed in the updated dossier; and

Pursuant to Articles 40(4) and 22 of the REACH Regulation, the Registrant shall submit to ECHA by **03/06/2013** an update of the registration dossier containing the information required by this decision.

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 the examination of the testing proposal of the Registrant for the registered substance and scientific valid information submitted by third parties.

a) Sub-chronic toxicity

A sub-chronic toxicity study (90-day) is a standard information requirement of Annex IX, 8.6.2 at the present tonnage level. ECHA notes that this standard information is not available in the present registration dossier, but a testing proposal concerning a sub-chronic toxicity study (90-day) has been made.

ECHA has examined the information submitted by third parties, as follows:

TPI 1. The third party has proposed four testing strategies (a, b, c, and d, as referred to under section I above) for ECHA to consider. However, ECHA invited submission of "scientifically valid information and studies that address the relevant substance and hazard end-point, addressed by the testing proposal", as specified by Article 40(2), and the proposal for a strategy cannot be considered as such information. Consequently, ECHA concludes that this is not a sufficient basis for rejecting the testing proposed.

Accordingly, the Registrant is requested to provide information on the Annex IX, 8.6.2 endpoint by carrying out a sub-chronic toxicity study (90-day) in rat by the oral route by using EU Method B.26. It should be noted that the Registrant's proposed extension of this study to additional examinations concerning reproductive toxicity may not fulfil the standard information requirement in the registration dossier for reproductive toxicity set out in Annex X, 8.7.3. ECHA may therefore verify the compliance of this end-point in a compliance check at a later stage. It is however 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.

b) Prenatal developmental toxicity

A pre-natal developmental toxicity study on a first species is required under Annex IX, 8.7.2 to the REACH Regulation, and a pre-natal developmental toxicity study on a second species is required according to Annex X, 8.7.2, subject to all appropriate column 2 or Annex XI data adaptations.

The Registrant has suggested meeting this standard information requirement by proposing a pre-natal developmental toxicity study in one species.

ECHA has examined the information submitted by third parties, as follows:

TPI 1. The third party has proposed four strategies for ECHA to consider. However, ECHA invited submission of "scientifically valid information and studies that address the relevant substance and hazard end-point, addressed by the testing proposal", as specified by Article 40(2), and the proposal for a strategy cannot be regarded as such information. Consequently, ECHA concludes that this is not a sufficient basis for rejecting the testing proposed.

TPI 2. A prediction using the nonlinear classification ANN QSAR Model for prenatal developmental toxicity study giving the result toxic was provided. The dependent variable of the model is in the form "toxic/non-toxic". Annex XI, 1.3 governing QSAR models requires that information concerning the validity, applicability domain, adequacy for classification & labelling, and documentation of the method be provided. As this information was not provided, ECHA considers that the model fails to meet the requirements of Annex XI, 1.3. The predicted result can therefore not be directly used or extrapolated to fill the information requirements in question.

ECHA agrees with the Registrant that a pre-natal developmental toxicity test is needed to address the information requirements of Annexes IX and X, 8.7.2 of the REACH Regulation. Since the information for developmental toxicity in one species is required by both Annexes IX and X and the requirements are additive, the information requirements from these two Annexes comprise pre-natal developmental toxicity tests in two species. However, according to column 2 of Annex IX, 8.7.2, the decision on the need for performing the test in a second species should be based on the outcome of the study in the first species and all other relevant data.

Once the information from the first study is available, and taking into account all relevant information, the Registrant is requested to consider whether the information requirements for pre-natal developmental toxicity studies in two species are met and update his dossier accordingly. The updated dossier shall either include an explanation, why the Registrant considers the information requirements as being met, or a testing proposal for a pre-natal developmental toxicity study in a second species, preferably in rabbit.

c) Deadline for submitting the required information

In the draft decisions communicated to the Registrant the time indicated to provide the requested information was 24 months from the date of adoption of the decision. This period of time took into account the fact that the draft decisions also requested a 2-generation reproductive toxicity study. As the request for a 2-generation reproductive toxicity study was removed from the draft decision ECHA considers that a reasonable time period for providing the remaining required information in the form of an updated IUCLID5 dossier is 18 months from the date of the adoption of the decision. The decision was therefore modified accordingly.

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.*"

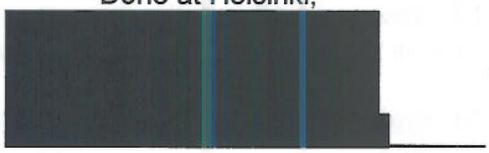
According to Article 13(3) of the REACH Regulation, tests that are required to generate information on intrinsic properties of substances shall be conducted in accordance with the test methods laid down in a Commission Regulation or in accordance with other international test methods recognised by the 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 the technical progress 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.

Done at Helsinki,



Jukka Malm
Director of Regulatory Affairs