ECHA
EUROPEAN CHEMICALS AGENCY

Decision number: TPE-D-0000002028-80-04/F Helsinki, 25 June 2012

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

For Tris [2-[2-(2-methoxyethoxy)ethoxy]ethyl] orthoborate, CAS 30989-05-0 (EC No 250-418-4), 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 **Tris [2-[2-(2-methoxyethoxy) ethoxy]ethyl] orthoborate, CAS 30989-05-0 (EC No 250-418-4),** 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 and X:

- Viscosity (OECD guideline 114)
- Sub-chronic toxicity study (90-day), oral (EU test method B.26)
- Pre-natal developmental toxicity study (EU test method B.31)
- Two-generation reproductive toxicity study (EU test method B.35)

The present decision relates solely to the examination of the testing proposals for viscosity, sub-chronic toxicity study, and pre-natal developmental toxicity study. The testing proposal for the two-generation reproductive toxicity study is addressed in a separate decision although all testing proposals were initially addressed together in the same draft decision.

The examination of the testing proposals was initiated on 19 August 2010.

ECHA opened a third party consultation for the testing proposals including testing on vertebrate animals that was held from 28 February 2011 until 14 April 2011. ECHA received comments from third parties concerning the use of (i) human data, (ii) existing repeated dose toxicity data, (iii) Threshold of Toxicological Concern (TTC) concept, and (iv) *in vitro* testing and QSAR modelling, and conducting an extended one-generation reproductive toxicity studies instead of pre-natal developmental toxicity study.

ECHA
EUROPEAN CHEMICALS AGENCY

On 5 September 2011 ECHA notified the Registrant of its draft decision and invited him pursuant to Article 50(1) of the REACH Regulation to provide comments within 30 days of the receipt of the draft decision.

On 3 October 2011 the Registrant provided to ECHA comments on the draft decision.
ECHA has taken into account the information received and decided to amend the draft decision.

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. Subsequently, Competent Authorities of the Member States submitted proposals for amendment to the draft decision. ECHA has reviewed the proposals for amendment received and decided to modify 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 5 March 2012, the draft decision was referred to the Member State Committee.

On 22 March 2012 the Registrant provided comments on the proposals for amendment. The Member State Committee took the comments of the Registrant into account.

The draft decision was split into two draft decision documents: one relating to the testing proposal for a two-generation reproductive toxicity study and one relating to the testing proposals for viscosity, a sub-chronic toxicity study and a pre-natal developmental toxicity study.

A unanimous agreement of the Member State Committee on the draft decision relating to the testing proposals for viscosity, a sub-chronic toxicity study and a pre-natal developmental toxicity study was reached on 11 April 2012 in a written procedure launched on 28 March 2012.

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:

- Viscosity (Annex IX, 7.17, OECD test guideline 114)
- Sub-chronic toxicity study (90-day), (Annex IX, 8.6.2, method B.26 of Regulation (EC) No 440/2008, OECD test guideline 408) in rat by the oral route
- Pre-natal developmental toxicity study (Annex IX, 8.7.2, method B.31 of Regulation (EC) No 440/2008, OECD test guideline 414) in rat by the oral route

ECHA
EUROPEAN CHEMICALS AGENCY

Pursuant to Articles 40(4) and 22(2) of the REACH Regulation, the Registrant shall submit to ECHA **by 2 January 2014** 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.

The Registrant shall determine the appropriate order of the studies taking into account the possible outcome 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.

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 information submitted by third parties. A viscosity study is required under Annex IX, 7.17, a sub-chronic toxicity study (90-day) under Annex IX, 8.6.2, a pre-natal developmental toxicity study in one species under Annex IX, 8.7.2 and on a second species under Annexes IX and X, 8.7.2 of the REACH Regulation. The studies are subject to all appropriate column 2 or Annex XI data adaptations. Since information on these endpoints is missing in the registration dossier, and since no acceptable adaptations to omit these information requirements have been received, ECHA accepts the proposed tests. The tests shall be carried out using the EU test methods or in the case of viscosity, the OECD Test Guideline indicated in section II above.

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.

The third party information following the public consultation was evaluated in order to determine whether there is already scientifically valid information that addresses the relevant substance and hazard endpoint. This additional information does not, however, change the conclusion that a sub-chronic toxicity and a pre-natal developmental toxicity studies need to be requested, as explained below.

ECHA
EUROPEAN CHEMICALS AGENCY

The third party has proposed the following information for ECHA to consider, i.e. the use of human data, Threshold of Toxicological Concern (TTC) concept, and *in vitro* testing and QSAR modelling (OECD Toolbox) before further tests on animals are requested.

Considering that 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) of the REACH Regulation, ECHA has concluded that the proposed information does not sufficiently address the relevant end-point. Consequently, ECHA concludes that the information provided is not a basis for rejecting the testing proposed.

In addition, the third party has proposed to evaluate and consider using the existing 28-day and 90-day studies and other toxicological data before conducting the pre-natal developmental toxicity study.

ECHA notes that the pre-natal developmental toxicity study is a standard information requirement according to Annexes IX and X, 8.7.2. of the REACH Regulation. The information provided by the third party does not meet the specific rules for adaptation of the information requirement for reproductive toxicity studies under column 2 of Annexes IX and X, 8.7. Specifically, it was not shown from toxicokinetic data that no systemic absorption occurs via relevant routes of exposure. Therefore, the third party proposal does not provide a sufficient basis on which to reject the proposed tests.

In response to ECHA's draft decision, the Registrant submitted comments regarding tiered testing. ECHA agrees with the Registrant's comment on sequential testing, i.e. that the sub-chronic toxicity test should be performed prior to performing the prenatal developmental toxicity study, and that the Registrant should determine if the results of those tests provide basis for not conducting the two-generation reproductive toxicity test according to Column 2 provisions of Annex X, 8.7. of the REACH Regulation.

In the draft decision communicated to the Registrant the time indicated to provide the requested information was 36 months from the date of adoption of the decision. This period of time took into account the fact that the draft decision also requested a 2-generation reproductive toxicity study. As the testing proposal for this study is not addressed in the present draft decision, ECHA considers that a reasonable time period for providing the 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.*"

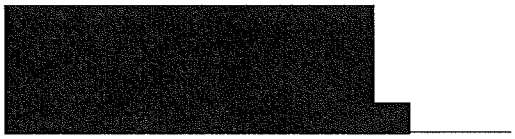
ECHA
EUROPEAN CHEMICALS AGENCY

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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