EUROPEAN CHEMICALS AGENCY

For final decision: TPE-D-0000002018-81-05/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 [redacted] 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 [redacted] submitted by [redacted] (Registrant), latest submission number [redacted].

The Registrant notified the substance pursuant to the national legislation implementing Directive 67/548/EEC relating to the classification, packaging and labelling of dangerous substances (as amended) by submitting a notification to the [redacted] in accordance with Article 7 of Directive 67/548/EEC. The notification number allocated was [redacted]

Article 24(1) of the REACH Regulation provides that the notification is regarded as a registration and ECHA has assigned a registration number. Article 24(2) of the REACH Regulation specifies that "*If the quantity of a notified substance manufactured or imported per manufacturer or importer reaches the next tonnage threshold under Article 12, the additional required information corresponding to that tonnage threshold, as well as to all the lower tonnage thresholds, shall be submitted in accordance with Articles 10 and 12, unless it has already been submitted in accordance with those Articles.*" This is the case for the current dossier, when the Registrant submitted to ECHA an updated dossier [redacted]

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 Annexes IX and X:

a) Pre-natal developmental toxicity study according to OECD Guideline 415 (one-generation reproduction toxicity study), Annex IX, 8.7.2.

b) Two-generation reproductive toxicity study according to OECD Guideline 415 (one-generation reproduction toxicity study), Annex X, 8.7.3.

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

The examination of the testing proposals was initiated [redacted]

ECHA opened a third party consultation for the testing proposals including testing on vertebrate animals that was held from 23 June until 8 August 2011. ECHA did not receive comments from a third party for the pre-natal developmental toxicity endpoint.

[redacted] 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.

[redacted] the Registrant provided to ECHA comments on the draft decision. ECHA took into account the information received and amended the draft decision accordingly.

[redacted] 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.

[redacted] 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.

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

[redacted] ECHA referred the draft decision to the Member State Committee.

[redacted] 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 [redacted], 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 proposal for a pre-natal developmental toxicity study (present decision).

The Member State Committee reached unanimous agreement on the draft decision relating to the testing proposal for a pre-natal developmental toxicity study at the meeting [redacted] 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)(c) of the REACH Regulation, the Registrant shall carry out the following tests using the indicated test method:

> Annex IX, 8.7.2.; Pre-natal developmental toxicity study, in the rat via the oral route (test method: EU B. 31/ OECD 414);

while the originally proposed one-generation reproduction toxicity study, test method: OECD 415 for provision of Annex IX 8.7.2. is rejected in accordance with Article 40(3)(d) of the REACH Regulation.

Pursuant to Articles 40(4) and 22 of the REACH Regulation, the Registrant shall submit to ECHA by **6 June 2013** 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.

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.

1) Examination of testing proposals

Pre-natal developmental toxicity study is part of the standard information requirements as laid down in Annex IX, section 8.7.2. of the REACH Regulation. The information on this endpoint is not available for the substance subject to the present decision, 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 has submitted a testing proposal for a one-generation reproduction toxicity study according to test method OECD 415 to fulfil the information of Annex IX 8.7.2.: pre-natal developmental toxicity. The test was proposed to be modified to include an additional group for developmental examination and prolonged exposure (parental animals).

Pursuant to Article 40(3)(c) of the REACH Regulation, ECHA may reject a testing proposal and require the Registrant to carry out one or more additional tests in case of non-compliance of the testing proposal with Annexes IX and X of the REACH Regulation.

The proposed one-generation test, with the inclusion of an additional group is not suitable

to generate data that would be equivalent to a pre-natal developmental toxicity study. A modified one-generation reproductive toxicity study as proposed does not test for potential effects on post weaning development and maturation, and pre-natal effects such as malformations can also not be detected. Thus, the one-generation study cannot be accepted as a valid replacement for a pre-natal developmental toxicity endpoint (Annex IX, 8.7.2.) and is therefore rejected in accordance with Article 40(3)(d) of the REACH Regulation.

ECHA notes that in the comments, submitted during the 30-days commenting period, the Registrant has accepted conducting a pre-natal developmental toxicity study according to EU Test Method B.31 (OECD 414).

Therefore, pursuant to Article 40(3)(c) of the REACH Regulation, the Registrant is requested to carry out the following test: Pre-natal developmental toxicity study in rats, oral route (test method: EU B.31/OECD Guideline 414) using the registered substance.

When considering the need for a testing proposal for a pre-natal 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.

2) Deadline for submitting the required information

In the draft decision 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 decision included also a request for a reproductive toxicity study (Annex X, 8.7.3.). 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 12 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 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.

[redacted]

Jukka Malm
Director of Regulatory Affairs