EUROPEAN CHEMICALS AGENCY

For final decision: TPE-D-0000002591-77-04/F Helsinki, 14 November 2012

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

For Amides C8-18 (even-numbered) and C18 (unsaturated), N-(2-hydroxypropyl), EC No. 931-596-9, 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 Amides C8-18 (even-numbered) and C18 (unsaturated), N-(2-hydroxypropyl), EC No 931-596-9, by [redacted] (Registrant), latest submission number [redacted] for the tonnage band of 1000 tonnes or more per year:

- Repeated dose 90-day oral toxicity in rodents (OECD 408) with the registered substance;
- Pre-natal developmental toxicity (OECD 414) with the registered substance

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.

This decision does not imply that the information provided by the Registrant in his registration dossier is in compliance with the REACH requirements. The decision does not prevent ECHA from initiating a compliance check on the present dossier at a later stage.

On 9 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 third party consultation for the testing proposals from 16 August 2011 until 30 September 2011. ECHA did receive information from a third party (see section III below).

On 8 March 2012 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 10 April 2012 the Registrant did not provide any comments on the draft decision to ECHA.

On 16 May 2012 the Registrant updated his registration dossier.

ECHA considered the Registrant's updated registration dossier. However, as the update did not concern testing proposals, there was no need to amend the draft decision.

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 not to amend the draft decision.

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

The Registrant did not provide any 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.

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 substance subject to the present decision:

1. Sub-chronic toxicity study (90-day) in rats, oral route (Annex IX, 8.6.2.; test method: EU B.26/OECD 408);
2. Pre-natal developmental toxicity study in rats, oral route (Annex IX, 8.7.2.; test method: EU B.31/OECD 414).

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.

Pursuant to Articles 40(4) and 22 of the REACH Regulation, the Registrant shall submit to ECHA by **14 November 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, subject to the Annex IX, 8.7.2. column 2 requirements. If the Registrant considers that testing is necessary to fulfil this information requirement taking into account the outcome of the pre-natal developmental toxicity study on a first species and all other relevant and available data, 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 proposals submitted by the Registrant for the registered substance and scientific information submitted by a third party.

1. Sub-chronic 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.

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 proposes to the test the registered substance by the oral 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 oral route is appropriate.

The Registrant did not specify the species to be used for testing. According to the test method EU B.26/OECD 408 the rat is the preferred rodent species. ECHA considers this species as being appropriate.

b) Consideration of the information received during third party consultation

ECHA received third party information concerning the testing proposal during the public consultation. For the reasons explained further below the information provided by third parties is not sufficient to fulfil this information requirement.

A third party has proposed a read-across approach to adapt the information requirements according to Annex XI for ECHA to take into account before further tests on vertebrate animals are required. As part of this approach the third party referred to results from an oral repeated dose toxicity study (28-day) using a first analogue substance amides, coco, N-(hydroxyethyl) (CAS No. 68140-00-1); and results from an oral repeated dose toxicity study (90-day) using a second analogue substance dodecanamide, N,N-bis (2-hydroxyethyl)- (CAS No. 120-40-1). The third party also provided results of a (Q)SAR profiling of the substance octadecanamide, n-(2-hydroxypropyl)- (CAS No. 35627-96-4) using the OECD Toolbox 2.0.

ECHA has taken the information provided into account and concludes that it is insufficient for demonstrating that the conditions of Annex XI, Section 1.3 and 1.5 of the REACH Regulation are met. More specifically, the results of the OECD Toolbox do not address the hazard endpoint for which testing was proposed. As a result, the proposed a read-across approach is not sufficient to assume that the substance has or has not the dangerous property at stake and that the standard information requirement for a sub-chronic toxicity

study (90-day) could be adapted. Furthermore; the documentation justifying the proposed read-across approach did not demonstrate that human health effects may be predicted from data on the reference substance.

Although ECHA recognises that the information as provided by the third party might be scientifically valid, it does not fulfil Annex XI requirements and is therefore not sufficient to allow ECHA to reject the testing proposal. Nevertheless, ECHA acknowledges that the Registrant may himself supplement under its own responsibility the argumentation and information provided by the third party in order to make use of adaptation possibilities. This would require that the Registrant documents, using several independent sources of information, that there is a sufficient weight of evidence leading to the assumption/conclusion that a substance has or has not particular dangerous properties, according to the criteria laid down in Annex XI of the REACH Regulation.

c) 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, oral route (test method: EU B.26/OECD 408) using the registered substance Amides C8-18 (even-numbered) and C18 (unsaturated), N-(2-hydroxypropyl).

2. Prenatal 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.

A pre-natal developmental toxicity study for a first species is a standard information requirement as laid down in Annex IX, section 8.7.2. of the REACH Regulation. According to section 8.7.2 of Annex X subject to the Annex IX, 8.7.2 column 2 requirements of the REACH Regulation, a further pre-natal developmental toxicity study performed in a second species is required to fulfil the standard information requirements. The information available on this endpoint for the registered substance in the technical dossier does not meet these information requirements. Consequently there is an information gap and it is necessary to generate the data for this endpoint.

The Registrant did not specify the species and route to be used for testing. According to the test method EU B.31/OECD 414, the rat is the preferred rodent species, the rabbit the preferred non-rodent species and the test substance is usually administered orally. ECHA considers these default parameters appropriate and testing should be performed by the oral route with the rat as a first species to be used.

b) Consideration of the information received during third party consultation

ECHA received third party information concerning the testing proposal during the public consultation. For the reasons explained further below the information provided by third parties is not sufficient to fulfil this information requirement.

A third party has proposed a read-across approach to adapt the information requirements according to Annex XI for ECHA to take into account before further tests on vertebrate animals are required. As part of this approach the third party referred to results from a pre-natal developmental toxicity study using an analogue substance dodecanamide, N,N-bis (2-hydroxyethyl)- (CAS No. 120-40-1). The third party also provided results of a (Q)SAR

profiling of the substance octadecanamide, n-(2-hydroxypropyl)- (CAS No. 35627-96-4) using the OECD Toolbox 2.0.

ECHA has taken the information provided into account and concludes that it is insufficient for demonstrating that the conditions of Annex XI, Section 1.3 and 1.5 of the REACH Regulation are met. More specifically, the results of the OECD Toolbox do not address the hazard endpoint for which testing was proposed. As a result, the proposed a read-across approach is not sufficient to assume that the substance has or has not the dangerous property at stake and that the standard information requirement for a pre-natal developmental toxicity study could be adapted. Furthermore; the documentation justifying the proposed read-across approach did not demonstrate that human health effects may be predicted from data on the reference substance.

Although ECHA recognises that the information as provided by the third party might be scientifically valid, it does not fulfil Annex XI requirements and is therefore not sufficient to allow ECHA to reject the testing proposal. Nevertheless, ECHA acknowledges that the Registrant may himself supplement under its own responsibility the argumentation and information provided by the third party in order to make use of adaptation possibilities. This would require that the Registrant documents, using several independent sources of information, that there is a sufficient weight of evidence leading to the assumption/conclusion that a substance has or has not particular dangerous properties, according to the criteria laid down in Annex XI of the REACH Regulation.

c) 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, oral route (test method: EU B.31/OECD 414) using the registered substance Amides C8-18 (even-numbered) and C18 (unsaturated), N-(2-hydroxypropyl).

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]
Geert Dancet
Executive Director