ECHA
European Chemicals Agency

For final decision: TPE-D-0000000882-72-06/F Helsinki, 5 October 2010

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

For [redacted]
egistration Numbe[redacted]

Addressee: [redacted]

I. Procedure

Pursuant to Article 40(1) of Regulation (EC) No 1907/2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (the REACH Regulation), the European Chemicals Agency (ECHA) has examined testing proposals set out in the registration dossier for [redacted] by [redacted] (the "Registrant"), latest submission number [redacted] for the tonnage band [redacted]

In accordance with Article 12(1)(d) of the REACH Regulation, the Registrant submitted the following testing proposals as part of the registration dossier to fulfil information requirements:

- testing proposal for stability in organic solvents and identity of relevant degradation products to fulfil the information requirement of section 7.15 of Annex IX (stability in organic solvents and identity of relevant degradation products)
- testing proposal for screening for reproductive/developmental toxicity (OECD 421 guideline) in order to fulfil the information requirement of section 8.7.1 of Annex VIII (screening for reproductive/developmental toxicity)
- and the same testing proposal for screening for reproductive/developmental toxicity (the testing proposal refers to the OECD 421 guideline study proposed to fulfil the information requirement of section 8.7.1 of Annex VIII) in order to fulfil the information requirement of section 8.7.2 of Annex IX (pre-natal developmental toxicity study)

The examination of testing proposals was initiated on 13 August 2009.

On 4 December 2009 ECHA invited third parties to submit information and studies that address the relevant substance and the relevant hazard end-points by 18 January 2010.

After having examined the information received from third parties, ECHA drafted a decision in accordance with Article 40 of REACH. On 9 February 2010, ECHA notified the registrant of its draft decision and invited him to provide comments by 11 March 2010.

The registrant did not provide comments on ECHA's draft decision by the deadline set.

On 11 June 2010, ECHA notified the Member State Competent Authorities of its draft decision and invited them to provide proposals for amendment.

After receiving proposals for amendments from the Member State Competent Authorities, ECHA forwarded the proposals for amendment to the registrant on 13 July 2010 and did not amend the draft decision.

On 26 July 2010, the draft decision was referred to the Member State Committee.

The registrant did not provide comments on the proposals for amendment.

After discussion in the Member State Committee meeting on 14-16 September 2010, the draft decision was modified by the Member State Committee and a unanimous agreement of the Member State Committee on the modified draft decision was reached on 15 September 2010.

II. Testing required

ECHA has taken the following decision in accordance with the procedure set out in Articles 50 and 51 of the REACH Regulation.

Pursuant to Article 40(3)(a) and 40(3)(c) of the REACH Regulation, the Registrant must carry out the following tests:

- Stability in organic solvents and identity of relevant degradation products
- Pre-natal developmental toxicity study (method B.31 of Regulation (EC) No 440/2008; OECD test guideline 414)
- Sub-chronic toxicity study (90-day) in rats, oral route (method B.26 of Regulation (EC) No 440/2008; OECD test guideline 408)

Pursuant to Articles 40(4) and 22 of the REACH Regulation the Registrant must submit to ECHA by 2 years from the date of the decision an update of the registration containing the information required by this decision.

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.

III. Statement of reasons

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

a) Stability in organic solvents and identity of relevant degradation products

According to section 7.15 of Annex IX of the REACH Regulation stability in organic solvents and identity of relevant degradation products is required to fulfil the standard information requirements.

The test for stability in organic solvents, proposed by the Registrant, is thus necessary to fulfil the information requirement pursuant to section 7.15 of Annex IX to the REACH Regulation.

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Pursuant to Article 40(3)(a) of the REACH Regulation, the Registrant is thus requested to carry out this test.

b) Reproductive toxicity

i) Information requirement of section 8.7.1 of Annex VIII of the REACH Regulation

The Registrant has submitted a testing proposal for screening for reproductive/developmental toxicity (OECD 421 guideline) to meet the information requirement of section 8.7.1 of Annex VIII. Pursuant to Article 12(1)(d) of the REACH Regulation Registrants are required to provide the information specified in Annexes VII and VIII. The REACH Regulation therefore does not permit Registrants to submit testing proposals for the information requirements set out in these annexes. Accordingly the Registrant should not have submitted a testing proposal for the information requirement of section 8.7.1 of Annex VIII. Therefore, ECHA cannot evaluate this proposal under Article 40 of REACH.

ii) Information requirement of section 8.7.2 of Annex IX of the REACH Regulation

According to section 8.7.2 of Annex IX of the REACH Regulation a pre-natal developmental toxicity study is required to fulfil the standard information requirements.

The Registrant has, however, proposed a study according to OECD test guideline 421 to fulfil this information requirement (the Registrant refers in his testing proposal to the screening for reproductive/developmental toxicity study, proposed to fulfil the information requirement of section 8.7.1 of Annex VIII mentioned in III(b)(i) above). No reasoning has been provided by the Registrant why his testing proposal is deviating from the standard information required in section 8.7.2 of Annex IX of the REACH Regulation. The proposed study therefore does not meet the requirements of the REACH Regulation.

ECHA has further examined the scientific information submitted by third parties following the public consultation (4 December 2009 – 18 January 2010) in order to determine whether there is already scientifically valid information that addresses the relevant substance and hazard endpoint.

1. National Toxicology Programme (NTP), Study on Hexanamide: http://ntp.niehs.nih.gov/?objectid=BCE6B71F-123F-7908-7B786E83B6F2AC6D
   The substance covered in the report is hexanamide. [redacted]

2. Fleischman, R.W., Baker, J.R., Hagopian, M., Wade, G.G., Hayden, D.W., Smith, E.R., Weisburger, J.H., Weisburger, E.K., 1980. Carcinogenesis bioassay of acetamide, hexanamide, adipamide, urea and P-tolylurea in mice and rats. J. Environ. Pathol. Toxicol. 3 (5-6), 149-170.
   The substances covered in the report are acetamide, hexanamide, adipamide, urea and P-tolylurea [redacted]

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3. Huang, T.L., Dredar, S.A., Manneh, V.A., Blankenship, J.W., Fries, D.S., 1992. Inhibition of N8-acetylspermidine deacetylase by active-site-directed metal coordinating inhibitors. J. Med. Chem. 35 (13), 2414-2418.
The substance covered in the report is 6-((3-aminopropyl)amino)-N-hydroxyhexanamide. [redacted]

The information submitted by the third parties has been generated using substances that are different from the registered substance. Such information may be used if the physicochemical, toxicological and ecotoxicological properties are likely to be similar to the registered substance (read-across approach). However, on the basis of the information currently provided, ECHA concludes that there is insufficient evidence for read-across to permit the Registrant to adapt the standard testing requirement in section 8.7.2 of Annex IX.

Pursuant to Article 40(3)(c) of the REACH Regulation, the Registrant is thus requested to carry out the following test: Pre-natal developmental toxicity study in rats, oral route (method B.31 of Regulation (EC) No 440/2008; OECD test guideline 414).

Additional testing required

c) Sub-chronic toxicity study (90-day), oral route

According to section 8.6.2 of Annex IX of the REACH Regulation the sub-chronic toxicity study (90-day) is required to fulfil the standard information requirements.

The Registrant has proposed to adapt the required standard information for this information requirement by waiving the test for the 3 routes of exposure. The Registrant concludes for the waiving for the 90-day sub-chronic toxicity study: "*Taken together,* [redacted] *shows no substance related signs of toxicity in vertebrate animals. Based on these results, together with the chemical structure of the substance, no adverse effects in a sub-chronic repeated dose 90-day toxicity study are expected…*" However, this waiving justification does not meet any of the conditions for adaptation according to column 2 of section 8.6.2, Annex IX. Further, it does not meet the criteria for waiving according to Annex XI. More specifically, it does not constitute a valid weight of evidence or read-across approach according to sections 1.2 and 1.5 of Annex XI. The Registrant refers to absence of effects in acute and subacute tests, absence of irritating and sensitising properties and a negative mutagenicity test. However, the absence of effects in these tests, as described by the Registrant, does not provide enough evidence that no effects will occur in the 90-day sub-chronic toxicity study. Further, the Registrant did not provide a justification for the prediction of absence of effects based on the structure of the substance.

Therefore, the Registrant has failed to provide a compliant analysis why rules for adaptation according to Annex IX or Annex XI of the REACH Regulation are deemed to be applicable for the standard testing requirement for sub-chronic toxicity (90-day).

ECHA concludes that the information requirement for the sub-chronic toxicity study (90-day), pursuant to section 8.6.2 of Annex IX to the REACH Regulation, is not fulfilled.

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Pursuant to Article 40(3)(c) of the REACH Regulation, the Registrant is thus requested to carry out the following test: sub-chronic toxicity study (90-day), oral route (method B.26 of Regulation (EC) No 440/2008; OECD test guideline 408).

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 1907/2008 adapted to the technical progress by Commission Regulation (EC) No 761/2009 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. The procedure is described in the Board of Appeal's "Preliminary instructions to Appellants" that can be found at the ECHA website. The notice of appeal will be deemed to be filed only when the appeal fee has been paid.

Done at Helsinki,

[redacted]

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