EUROPEAN CHEMICALS AGENCY

Decision number: TPE-D-2114292026-51-01/F Helsinki, 5 February 2015

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

For Reaction Mass of Cis-4-(isopropyl) cyclohexanemethanol and Trans-4-(isopropyl) cyclohexanemethanol, EC No 939-719-8, 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)(d) thereof for Reaction Mass of Cis-4-(isopropyl) cyclohexanemethanol and Trans-4-(isopropyl) cyclohexanemethanol, EC No 939-719-8, submitted by [redacted] (Registrant).

- Developmental toxicity / teratogenicity study (OECD 414)
- 90-day oral toxicity study (OECD 408) in rats, oral route

This decision is based on the registration dossier as submitted with submission number [redacted] for the tonnage band of 100 to 1000 tonnes per year. This decision does not take into account any updates after 30 October 2014, 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 registration at a later stage.

ECHA received the registration dossier containing the above-mentioned testing proposal for further examination pursuant to Article 40(1) on 30 May 2013.

ECHA held a third party consultation for the testing proposals from 2 June 2014 until 17 July 2014. ECHA did not receive information from third parties.

On 19 August 2014 ECHA sent the draft decision to the Registrant and invited him to provide comments within 30 days of the receipt of the draft decision.

On 24 September 2014 ECHA received comments from the Registrant on the draft decision.

The ECHA Secretariat considered the Registrant's comments. The information is reflected in the Statement of Reasons (Section III) whereas no amendments to the Testing Required (Section II) were made.

On 30 October 2014 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 for amendment of the draft decision within 30 days of the receipt of the notification.

As no proposal for amendment was submitted, ECHA took the decision pursuant to Article 51(3) of the REACH Regulation.

II. Testing required

A. Tests required pursuant to Article 40(3)

The Registrant shall carry out the following proposed test pursuant to Article 40(3)(a) and 13(4) of the REACH Regulation using the indicated test methods and the registered substance subject to the present decision:

1. Pre-natal developmental toxicity study in rats or rabbits, oral route (Annex IX, Section 8.7.2.; test method: EU B.31/OECD 414).

The Registrant shall carry out the following modified test pursuant to Article 40(3)(b) and 13(4) of the REACH Regulation using the indicated test methods and the registered substance subject to the present decision:

2. Sub-chronic toxicity study (90-day) in rats, oral route (Annex IX, Section 8.6.2.; test method: EU B.26/OECD 408). The study protocol shall be modified to include additional clinical pathology and histopathological evaluations (sperm parameters) as described in Section III.2, to evaluate effects on male reproductive organs.

Note for consideration by the Registrant:

The Registrant may adapt the testing requested above according to the specific rules outlined in Annexes VI to X and/or according to the general rules contained in Annex XI of the REACH Regulation. In order to ensure compliance with the respective information requirement, any such adaptation will need to have a scientific justification, referring to and conforming with the appropriate rules in the respective Annex, and an adequate and reliable documentation.

Failure to comply with the requests in this decision, or to fulfil otherwise the information requirements with a valid and documented adaptation, will result in a notification to the Enforcement Authorities of the Member States.

B. Deadline for submitting the required information

Pursuant to Articles 40(4) and 22(2) of the REACH Regulation, the Registrant shall submit to ECHA by **13 February 2017** an update of the registration dossier containing the information required by this decision. The timeline has been set to allow for sequential testing as appropriate.

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.

A. Tests required pursuant to Article 40(3)

1. Pre-natal developmental toxicity study

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. 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 provide information for this endpoint.

The Registrant has submitted a testing proposal for a pre-natal developmental toxicity study according to EU B.31/OECD 414 with the justifications explained in a 23 pages document "[redacted]" included under IUCLID section 7.8.2.

The Registrant proposed testing in rats. He did not specify the route 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 or the rabbit as a first species to be used.

In his comments according to Article 50(1) of the REACH Regulation the Registrant agreed with the request of a pre-natal developmental toxicity study.

b) Outcome

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation, the Registrant is requested to carry out the proposed study with the registered substance subject to the present decision: Pre-natal developmental toxicity study in rats or rabbits, oral route (test method: EU B.31/OECD 414).

2. Sub-chronic toxicity study (90-day)

a) Examination of the testing proposal

Pursuant to Article 40(3)(b) of the REACH Regulation, ECHA may require the Registrant to carry out the proposed test under modified conditions.

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 provide information for this endpoint.

The Registrant has submitted a testing proposal for a sub-chronic toxicity study (90 day) in rats via the oral route (EU B.26/OECD 408) with the justifications explained in a 21 pages document "[redacted]" included under IUCLID section 7.5.1.

The Registrant proposed testing via the oral route. ECHA notes that the substance is a liquid with low vapour pressure (0.022 hPA) and it is not classified as irritating or corrosive to the skin or eye. ECHA notes further that although there is spray and roller application, it is with a mixture containing less than [redacted] of the registered substance. In light of the physic-chemical properties of the substance and the information provided on the uses and human exposure, ECHA considers that testing by the oral route is most appropriate.

The short-term repeated dose toxicity studies (14-day and 28-day) as well as the screening study for reproductive/developmental toxicity carried out with the registered substance revealed multiple, statistically significant effects on sperm parameters. While the Registrant concluded that these effects are not chemically-related, ECHA considers that sperm and the male reproductive tract, as the site of production of sperm, are likely to be target organs and that these parameters shall be investigated further in the proposed 90-day study. A chemically-related effect could thereby be clarified and either excluded or confirmed. The measurement of sperm parameters is not a default requirement of the B.26 (sub-chronic toxicity study, 90-day) test method. However, according to paragraph 1.5.2.3 of test method B.26 "Also any organs considered likely to be target organs based on the known properties of the test substance should be preserved". In the present case, ECHA considers that the male reproductive tract and sperm are likely to be target organs, and that these shall be preserved, and subject to histopathological examination, in accordance with this provision of test method B.26. Suitable methods of how to investigate the effects on male reproductive tract and sperm can be found in OECD test guideline 416 paragraphs 29-32, 39, 41-44.

In his comments according to Article 50(1) of the REACH Regulation the Registrant agreed with the request of a sub-chronic toxicity study. He, however pointed out that new in vitro data had become available indicating that the registered substance is a skin irritant category 2, but that the Registrant still considers the oral route of administration the most appropriate. He further specified that a new 14 days study in rats indicated that a trend in recovery was observed in the affected sperm parameters without any treatment-related degenerative changes in the testes. The Registrant nevertheless agreed with the request of the additional clinical pathology and histopathological evaluations (sperm parameters). ECHA considers that even if the new in vitro data cited by the Registrant indicate that the registered substance is a skin irritant category 2, the information on the physic-chemical properties and uses (as explained above) supports the conclusion that the requested oral route is indeed the most appropriate route of administration. ECHA further notes, that even with the new 14 days study in rats, there is (as explained above) a concern on the sperm findings based on existing repeated dose toxicity studies.

b) Outcome

Therefore, pursuant to Article 40(3)(b) of the REACH Regulation, the Registrant is requested to carry out the following study with the registered substance subject to the present decision: Sub-chronic toxicity study (90-day) in rats, oral route (test method: EU B.26/OECD 408). The study protocol shall be modified with additional clinical pathology and histopathological evaluations to evaluate effects on male reproductive organs as described in OECD 416, paragraphs 29-32, 39, 41-44.

IV. Adequate identification of the composition of the tested material

It is important to ensure that the particular sample of substance tested in the new studies is appropriate to assess the properties of the registered substance, taking into account any variation in the composition of the technical grade of the substance as actually manufactured. If the registration of the substance covers different grades, the sample used for the new studies must be suitable to assess these.

Furthermore, there must be adequate information on substance identity for the sample tested and the grade(s) registered to enable the relevance of the studies to be assessed.

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://www.echa.europa.eu/regulations/appeals. The notice of appeal will be deemed to be filed only when the appeal fee has been paid.

[redacted]

Leena Ylä-Mononen
Director of Evaluation