ECHA
EUROPEAN CHEMICALS AGENCY

Decision number: TPE-D-2114294900-45-01/F Helsinki, 27 May 2015

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

For heptan-2-one, CAS No 110-43-0 (EC No 203-767-1), 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 proposal submitted as part of the registration dossier in accordance with Articles 10(a)(ix) and 12(1)(d) thereof for heptan-2-one, CAS No 110-43-0 (EC No 203-767-1, submitted by [redacted] (Registrant).

Pre-natal Developmental Toxicity (OECD Guideline 414).

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 2 January 2012.

ECHA held a third party consultation for the testing proposal from 3 March 2014 until 17 April 2014. ECHA did not receive information from third parties.

On 18 June 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 26 June 2014 ECHA received comments from the Registrant on the draft decision.

The ECHA Secretariat considered the Registrant's comments. On basis of this information, Section II was amended. The Statement of Reasons (Section III) was changed accordingly.

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.

Subsequently, a proposal for amendment to the draft decision was submitted.

On 5 December 2014 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.

The ECHA Secretariat reviewed the proposal for amendment received and modified Section III of the draft decision whereas no amendments to the Information Required (Section II) were made.

On 15 December 2014 ECHA referred the draft decision to the Member State Committee.

By 5 January 2015, in accordance to Article 51(5), the Registrant provided comments on the proposal for amendment. The Member State Committee took the comments of the Registrant on the proposal for amendment into account.

Unanimous agreement of the Member State Committee on the draft decision was reached on 19 January 2015 in the written procedure launched on 9 January 2015.

ECHA took the decision pursuant to Article 51(6) 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) of the REACH Regulation using the indicated test method and the registered substance subject to the present decision:

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

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 **3 June 2016** an update of the registration dossier containing the information required by this decision, including, where relevant, an update of the Chemical Safety Report.

III. Statement of reasons

The decision of ECHA is based on the examination of the testing proposal submitted by the Registrant for the registered substance.

Tests required pursuant to Article 40(3)

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.

ECHA considers that the proposed study is appropriate to fulfil the information requirement of Annex IX, Section 8.7.2. of the REACH Regulation.

The Registrant did not specify the species 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 that testing should be performed with the rat or the rabbit as a first species to be used.

The Registrant did not specify the route for testing. Originally ECHA considered that the test should be conducted by the oral route.

In his comments the Registrant agreed that "*the rat is the appropriate species for the study*". However, the Registrant did not agree with the route of administration and requested that the route of administration is changed to the inhalation route. The Registrant stated that inhalation would be the most relevant route of exposure as the substance is a volatile solvent. Moreover, the Registrant holds registrations for several other substances with similar structures, physical properties and uses, and for all of these inhalation studies have been conducted or proposed. Thus, an inhalation study would allow for a more relevant analysis of the data in light of the chemical class.

ECHA agrees with the Registrant that inhalation is an appropriate route of exposure and that it is relevant in terms of human exposure (i.e. reducing uncertainty in route-to-route extrapolation). Furthermore, ECHA notes that in the available repeated dose toxicity studies in rats and monkeys by the inhalation route ([redacted]) the highest dose tested was ~5.0 g/m³ (1025 ppm). According to ECHA Guidance R.8, route-to-route extrapolation of a limit concentration of 20 mg/L for vapours would yield an equivalent oral dose of 5.8-7.6 g/kg bw/day, and a concentration of 5 mg/L (approximately the concentration to be used in the rat study) would result in an equivalent oral dose of approximately 1.45-1.9 g/kg bw/day. ECHA therefore considers that sufficiently high concentrations can be achieved by the inhalation route for adequate evaluation of systemic toxicity. Furthermore, the provided studies show that the substance is systemically available after inhalation exposure (testing with ^{14}C-labelled substance). ECHA also notes that exposure by inhalation is a likely route of exposure when considering that the substance is used as a solvent in spraying applications (PROC 7).

Therefore, based on the considerations above, ECHA considers that inhalation is the most appropriate route of administration and has changed the route of administration to inhalation.

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, inhalation route (test method: EU B.31/OECD 414).

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 study 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 study 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 study 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]
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