EUROPEAN CHEMICALS AGENCY

Decision number: TPE-D-2114296627-33-01/F Helsinki, 18 March 2015

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

For nitromethane, CAS No 75-52-5 (EC No 200-876-6), 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)(e) thereof for nitromethane, CAS No 75-52-5 (EC No 200-876-6), submitted by [redacted] (Registrant).

- Developmental toxicity / teratogenicity study (OECD 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 15 January 2015, 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.

On 18 January 2014, pursuant to Article 40(1) of the REACH Regulation, ECHA initiated the examination of the testing proposal set out by the Registrant in the registration dossier for the substance mentioned above.

ECHA held a third party consultation for the testing proposal from 4 April 2014 until 18 May 2014. ECHA received information from third parties (see section III below).

On 30 July 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 2 September 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 15 January 2015 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 method and the registered substance subject to the present decision:

1. 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 **27 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.

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

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 and scientific information submitted by third parties.

A. Tests required pursuant to Article 40(3)

1. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)

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 proposed testing in rats. 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.

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

In his comments the Registrant did not agree with the route of administration and requested that the route for testing is changed to the inhalation route. The Registrant provided the following justification: "*(a) REACH Annex IX, Column I 8.7.2 defines that the study should be performed '[...] by the most appropriate route of exposure, having regard to the likely route of human exposure'. Considering the [...] vapour pressure (37.1 hPa @ 20 °C) and boiling point (101.2 oC @1013 hPa) and that the uses of nitromethane mainly involve industrial intermediate uses and a minor use as gasoline additive, inhalation exposure is the most likely route of human exposure. (b) Technical feasibility:There is sufficient experience with rat prenatal studies conducted with whole body chamber exposures, so that it can be expected to obtain relevant and reliable results out of whole body inhalation exposure of rats, comparable to the oral route of administration. Prior inhalation studies with nitromethane and similar nitroparaffins indicate that the substance only has a slight respiratory tract irritation potential at concentrations relevant for systemic effects. Hence, neither oral nor inhalation exposure are expected to cause inacceptable local effects. Expected systemic dose via different exposure routes: As reported in the registration dossier, systemic availability of nitromethane via the oral and inhalation route of exposure are expected to be equally high, while dermal availability is lower.*"

ECHA has considered the Registrant's comment as follows:

The Registrant argues that the physicochemical properties and uses indicate that testing by inhalation exposure should be conducted. Furthermore, he states that inhalation studies are technically feasible, result in systemic availability of the registered substance whereas the substance has only a slight potential for respiratory tract irritation.

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 subchronic and chronic repeated dose toxicity studies by the inhalation route ([redacted]) the highest dose tested was ~3.8 g/m³ (1500 ppm) and this demonstrates 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 (NOAEC = 94 ppm; hematologic parameters). ECHA also notes that exposure by inhalation is a likely route of exposure when considering that the substance has a vapour pressure of 4.75 kPa at 25 °C and is used as an additive in gasoline.

Therefore, based on the considerations above, ECHA has changed the route of administration to inhalation.

b) Consideration of the information received during third party consultation

ECHA has received third party information concerning the testing proposal during the third party consultation.

A third party has provided information on an OECD 422 screening study performed with the analogue substance 1-nitropropane.

However, ECHA notes that an OECD 422 screening study is not a test method that corresponds to the standard information requirement of Annex IX, Section 8.7.2 for a pre-natal developmental toxicity study because it does not provide equivalent information. The screening study does not cover adequate and reliable the key parameters of a pre-natal developmental toxicity study which are, for example, examinations of the foetuses for skeletal and visceral malformations.

Therefore, as the OECD 422 screening study would not even cover the standard information requirement of Annex IX, Section 8.7.2 for a pre-natal developmental toxicity study for the analogue substance (Annex XI, Section 1.1.2.) a read-across on the basis of this information can already for that reason not be justified. Consequently, the information provided by third parties is not sufficient to adapt this information requirement.

ECHA notes that the substance is registered for the tonnage band 100 to 1000 tonnes per year (Annex IX dossier). For that tonnage band a pre-natal developmental toxicity study is a standard information requirement as laid down in Annex IX, Section 8.7.2. of the REACH Regulation. Therefore, the test proposed by the Registrant is adequate to fulfil the information requirements.

Furthermore, the third party has stated that "*the substance has been self-classified as Category 2 carcinogen which implies the implementation of risk management measures.*" However, this self-classification is not sufficient to meet the adaptation criteria according to column 2 of Section 8.7.2., Annex IX as the provision explicitly states that the substance must be classified as genotoxic carcinogen. This condition is not met.

c) 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).

B. Deadline for submitting the required information

In the draft decision communicated to the Registrant the time indicated to provide the requested information was 12 months from the date of adoption of the decision. In his comments on the draft decision of 2 September 2014, the Registrant requested an extension of the timeline to 15 months. He sought to justify this request by outlining issues in relation to the capacity of the internal [redacted] to which he refers for higher tier testing. The Registrant supported his justification by submitting documentary evidence from the laboratory regarding available slots and timelines. ECHA has found the justification and the evidence provided appropriate. Therefore, ECHA has granted the request and set the deadline to 15 months.

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.

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