Decision number: TPE-D-2114314147-58-01/F Helsinki, 08 January 2016

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

For tetrahydro-2-methylfuran, EC No 202-507-4 (CAS No 96-47-9), 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)(d) thereof for tetrahydro-2-methylfuran, EC No 202-507-4 (CAS No 96-47-9), submitted by [redacted] (Registrant).

- 90-day toxicity study (OECD 413) in rats, inhalation route using the registered substance;
- Developmental toxicity / teratogenicity study (OECD 414) in rats, inhalation route using the registered substance.

This decision is based on the registration as submitted with submission [redacted], for the tonnage band of 100 to 1000 tonnes per year.

This decision does not take into account any updates after 14 September 2015, i.e. 30 calendar days after the end of the commenting period.

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 proposals for further examination pursuant to Article 40(1) on 2 August 2013.

ECHA held a third party consultation for the testing proposals from 23 January 2015 until 9 March 2015. ECHA received information from third parties (see section III below).

On 7 July 2015 ECHA sent the draft decision to the Registrant and invited him to provide comments on the draft decision in accordance with Article 50(1).

By 13 August 2015 ECHA did not receive comments from the Registrant.

On 29 October 2015, ECHA notified the competent authorities of the Member States of its draft decision and invited them to propose amendments to the draft decision under Article 51 of the REACH Regulation.

As no amendments were proposed, 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. Sub-chronic toxicity study (90-day), inhalation route (Annex IX, Section 8.6.2.; test method: OECD 413) in rats;

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 method and the registered substance subject to the present decision:

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

while the originally proposed developmental toxicity / teratogenicity study (OECD 414) in rats, inhalation route, is rejected according to the Article 40(3)(d) of the REACH Regulation.

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 **15 January 2018** an update of the registration dossier containing the information required by this decision, including, where relevant, an update of the Chemical Safety Report. 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 and scientific information submitted by third parties.

A. Tests required pursuant to Article 40(3)

1. Sub-chronic toxicity study (90-day), inhalation route (Annex IX, Section 8.6.2.)

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 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 inhalation (OECD 413) without providing further justification. The registered substance is reported to be a liquid at ambient temperature of high vapour pressure (14 kPa at 20°C). Hence, inhalation exposure of humans to vapours is likely and in the CSR human exposure by inhalation is reported. Therefore, testing by the inhalation route is appropriate according to REACH Annex IX, Section 8.6.2., column 2. Furthermore, since the Registrant has classified the substance for skin and eye irritation, respiratory tract irritation might be expected following inhalation exposure. Hence, testing by the inhalation route could provide information on local and systemic effects following inhalation exposure. Therefore, ECHA agrees that the inhalation route is the most appropriate route of administration for testing.

The Registrant proposed testing in rats. According to the test method OECD 413 the rat is the preferred species. ECHA considers this species as being appropriate and testing should be performed with the rat.

ECHA notes that the study in the dossier reported to use oral repeat dosing in rats with an unknown test guideline, insufficient documentation to assess adequacy of the study and no effects reported at the top dose tested of 26 mg/kg bw/day is inadequate to provide information on the potential for local toxicity following repeated inhalation exposure nor is it adequate for the purposes of classification and labelling.

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: Sub-chronic toxicity study (90-day) in rats, inhalation route (test method: OECD 413).

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

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 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 in rats according to EU B.31/OECD 414 to be performed with the registered substance by the inhalation route.

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

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 notes that the Registrant has proposed the test to be performed by the inhalation route without providing further justification. Due to the high vapour pressure of the substance (14 kPa at 20°C) inhalation could be an appropriate route of administration as it is for testing for repeated dose toxicity. However, since the Registrant has classified the substance for skin and eye irritation, respiratory tract irritation might be expected following inhalation exposure. If respiratory tract irritation occurs in a pre-natal developmental toxicity study performed by the inhalation route at lower concentrations than systemic toxicity in the dams, it may hamper the interpretation of the results of this study. Hence, for irritating substances the oral route of administration seems to be more appropriate than the inhalation route. Furthermore, even if the substance is of high vapour pressure, it does not prevent testing by the oral route. Therefore, ECHA considers that the oral route is the most appropriate route of administration for a pre-natal developmental toxicity study performed with the registered substance subject to the present decision.

b) Consideration of the information received during third party consultation

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

The third party has referred to the corrosive property of the substance and therefore proposed that the test is conducted the test via oral route of administration. The third party supports this proposal with information from a related compound, tetrahydrofuran, for which he reports that it has potentially irritating properties whilst an approximate dose of 111 mg/kg bw/d in a sub-acute toxicity study did not induce gastric irritation/corrosion. In addition, the third party pointed out that the potential for local tracheobronchial effects will be addressed by the proposed sub-chronic toxicity via the inhalation route.

As already stated under section III.1 above, ECHA acknowledges that the possible local effects on respiratory tract may be further investigated in the sub-chronic study conducted by inhalation route, as the potential for such effects may not be obtained using oral route of administration.

ECHA also acknowledges that – as specified in the general part of Annexes VII-X – "*in vivo* testing with corrosive substances at concentration/dose levels causing corrosivity shall be avoided". The test methods for repeated dose toxicity and reproductive toxicity specify that the highest dose level should induce "toxicity but not death or severe suffering". Therefore, it is the Registrant's responsibility to ensure that appropriate dose/exposure levels are used in the requested studies.

c) Outcome

Therefore, pursuant to Article 40(3)(b) of the REACH Regulation, the Registrant is requested to carry out the modified 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).

IV. Adequate identification of the composition of the tested material

The process of examination of testing proposals set out in Article 40 of the REACH Regulation aims at ensuring that the new studies meet real information needs. Within this context, the Registrant's dossier was sufficient to confirm the identity of the substance to the extent necessary for examination of the testing proposal. The Registrant must note, however, that this information, or the information submitted by other registrants of the same substance, has not been checked for compliance with the substance identity requirements set out in Section 2 of Annex VI of the REACH Regulation.

In relation to the proposed tests, the sample of substance used for the new studies must be suitable for use by all the joint registrants. Hence, the sample should have a composition that is within the specifications of the substance composition that are given by the joint registrants. It is the responsibility of all joint registrants of the same substance to agree to the tests proposed (as applicable to their tonnage level) and to document the necessary information on their substance composition.

In addition, 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 by each registrant. If the registration of the substance by any registrant covers different grades, the sample used for the new studies must be suitable to assess these grades.

Finally 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.

Authorised[1] by Leena Ylä-Mononen, Director of Evaluation

[1] As this is an electronic document, it is not physically signed. This communication has been approved according to ECHA's internal decision-approval process.