ECHA
EUROPEAN CHEMICALS AGENCY

Decision number: TPE-D-2114306098-53-01/F Helsinki, 22 July 2015

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

For 2-Butyne-1,4-diol, polymer with 2-(chloromethyl)oxirane, brominated, dehydrochlorinated, methoxylated, CAS No 68441-62-3 (EC No 614-503-3), 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 2-Butyne-1,4-diol, polymer with 2-(chloromethyl)oxirane, brominated, dehydrochlorinated, methoxylated, CAS No 68441-62-3 (EC No 614-503-3), submitted by [redacted] (Registrant).

- OECD Guideline 414 (Prenatal Developmental Toxicity Study) in rabbits, oral route

This decision is based on the registration dossier as submitted with submission number [redacted], for the tonnage band 1000 tonnes or more per year. This decision does not take into account any updates after 8 April 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 updated registration dossier containing the above-mentioned testing proposal for further examination pursuant to Article 40(1) on 19 June 2014.

ECHA held a third party consultation for the testing proposal from 17 September 2014 until 31 October 2014. ECHA did not receive information from third parties.

On 30 January 2015 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 5 March 2015 ECHA received comments from the Registrant on the draft decision indicating consent to perform a pre-natal developmental toxicity study in rabbits for which however more time would be required (18 months).

The ECHA Secretariat considered the Registrant's comments. On basis of this information, only the deadline in Section II was amended from 12 to 18 months.

On 11 June 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:

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

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.

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 **30 January 2017** 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

A. Tests required pursuant to Article 40(3)

Pre-natal developmental toxicity study (Annex X, 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.

Pre-natal developmental toxicity studies on two species are part of the standard information requirements for substance registered for 1000 tonnes or more per year (Annex IX, Section 8.7.2., column 1, Annex X, Section 8.7.2., column 1, and sentence 2 of introductory paragraph 2 of Annex X of the REACH Regulation).

The dossier contains a pre-natal developmental toxicity study in rats as first species. However, there is no information available for a pre-natal developmental toxicity study in a second species. Consequently there is an information gap for Annex X, Section 8.7.2. 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 a second species rabbits according to EU B.31/OECD 414 with the following justification: "The outcome of the first developmental toxicity study with Polyol IXOL B350 in rat is negative. Therefore a pre-natal developmental toxicity study in a second species (rabbit) is proposed via the oral route. Based on the low toxicity observed in the repeated dose studies and the absence of developmental toxicity in the rat, it is proposed to conduct the developmental study in rabbit as a limit test preceded by a Dose Range Finder".

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

The Registrant proposed testing in rabbits. He proposed testing by the oral route. The test in the first species was carried out by testing a rodent species and ECHA therefore considers that the test in a second species should be carried out in a non-rodent species. According to the test method EU B.31/OECD 414, the rabbit is 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 rabbit.

However, ECHA notes that the Registrant mentioned the intention to perform the developmental study in rabbit as a limit test. The OECD Guideline 414 (Prenatal Developmental Toxicity Study) includes the possibility of performing that deviation to the standard protocol of three dose levels (paragraph 16):
"If a test at one dose level of at least 1000 mg/kg body weight/day by oral administration, using the procedures described for this study, produces no observable toxicity and if an effect would not be expected based upon existing data (e.g., from structurally and/or metabolically related compounds), then a full study using three dose levels may not be considered necessary." The responsibility of selecting the appropriate study design is at the Registrant's discretion. The Registrant should justify why he deems it not necessary to perform the full study using three dose levels.

Nevertheless, ECHA notes that, even if low, some toxicity was observed in the repeated dose and pre-natal developmental toxicity studies in rat present in the dossier. Furthermore, all those studies were performed in rats, while the proposed study is to be conducted in rabbits, which has a different sensibility. There are no rabbit studies to base the "no effect" prediction for the proposed species. Therefore, the second criterion set in the OECD test guideline 414, paragraph 16, i.e. an "effect would not be expected based upon existing data", does not appear to be met.

On this basis, ECHA considers that effects may be expected based on the existing data. If the Registrant ultimately considers it adequate to perform the study by means of a limit test, a dose level of at least 1000 mg/kg body weight/day must be used. In case effects are observed in a limit test, then the study needs to be repeated using the full protocol, in order to comply with the requirements for pre-natal developmental toxicity study in a second species with a guideline conform and acceptable study that allows to derive a no observed adverse effect level (NOAEL).

b) Outcome

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation, the Registrant is thus requested to carry out the proposed study with the registered substance subject to the present decision: Pre-natal developmental toxicity study in 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 study 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 has not been checked for compliance with the substance identity requirements set out in Section 2 of Annex VI of the REACH Regulation.

In addition, 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.

Finally, 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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