EUROPEAN CHEMICALS AGENCY

Helsinki, 27 October 2016

Addressee: [redacted]

Decision number: TPE-D-2114346946-36-01/F
Substance name: 1-isopropyl-2,2-dimethyltrimethylene diisobutyrate
EC number: 229-934-9
CAS number: 6846-50-0
Registration number: [redacted]
Submission number: [redacted]
Submission date: 14.01.2015
Registered tonnage band: 1000+T

DECISION ON A TESTING PROPOSAL

Based on Article 40 of Regulation (EC) No 1907/2006 (the 'REACH Regulation'), ECHA has taken the following decision.

Your testing proposal is accepted and you are requested to carry out:

1. **Pre-natal developmental toxicity study (Annex X, Section 8.7.2.; test method: EU B.31./OECD TG 414) in a second species (rabbit), oral route using the registered substance.**

You 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 and conforming to the appropriate rules in the respective Annex, and an adequate and reliable documentation.

You are required to submit the requested information in an updated registration dossier by **4 May 2018**. You shall also update the chemical safety report, where relevant.

The reasons of this decision are set out in Appendix 1. The procedural history is described in Appendix 2. Advice and further observations are provided in Appendix 3.

Appeal

Applicable only for the final decision: This decision can be appealed to the Board of Appeal of ECHA within three months of its notification. An appeal, together with the grounds thereof, shall be submitted to ECHA in writing. An appeal has suspensive effect and is subject to a fee. Further details are described under http://echa.europa.eu/regulations/appeals.

Authorised[1] by Claudio Carlon, Head of Unit, Evaluation E2

[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.

Appendix 1: Reasons

The decision of ECHA is based on the examination of the testing proposal submitted by you.

1. Pre-natal developmental toxicity study (Annex X, Section 8.7.2.) in a second species

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.

You have submitted a testing proposal for a pre-natal developmental toxicity study in a second species (rabbits) according to EU B.31/OECD TG 414.

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

You proposed testing with the rabbit as a second species. The test in the first species was carried out with rats. According to the test method EU B.31/OECD 414, the rat is the preferred rodent species and the rabbit the preferred non-rodent species. On the basis of this default consideration, ECHA considers testing should be performed with the rabbit as a second species.

You did not specify the route for testing. ECHA considers that the oral route is the most appropriate route of administration for substances except gases to focus on the detection of hazardous properties on reproduction as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 4.1, October 2015) R.7a, chapter R.7.6.2.3.2. Since the substance to be tested is a liquid, ECHA concludes that testing should be performed by the oral route.

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation, you are thus requested to carry out the proposed study with the registered substance subject to the present decision: Pre-natal developmental toxicity study in a second species (rabbit), oral route (test method: EU B.31/OECD TG 414).

Notes for your consideration

For the selection of the appropriate species you are advised to consult ECHA *Guidance on information requirements and chemical safety assessment* (version 4.1, October 2015), Chapter R.7a, section R.7.6.2.3.2.

Deadline to submit the requested Information

In the draft decision communicated to you the time indicated to provide the requested information was 12 months from the date of adoption of the decision. In your comment(s) on the draft decision according to Article 50(1) of the REACH Regulation you requested an extension of the timeline by an additional 9 months to 21 months.

You sought to justify this request based on expected difficulties in administering the test substance orally via gavage due to inappetance. Furthermore, you argue that the stability of the substance could be affected by the vehicle which would require additional analytical studies. For administration of the substance in the diet you claim that the dietary formulation needs to be pelleted, and additional analytical work will be required to a) assess the stability of the test article to the pelleting process, and b) develop and validate a new analytical method to extract and analyze the test material that had been pelleted. Further, a palatability study needs to be performed in case the substance will be administered in the diet. You additionally noted in your comments that the availability of rabbits is low.
You provided documentary evidence supporting your case for extension of the deadline. This documentation strengthens your argumentation that administration via gavage may not be possible in this case. However, you do not base your request for an extended deadline upon a timetable provided by a CRO. Hence, it is not obvious from the provided documentation why preparation of the dietary formulation (including pelleting), additional analytical work for assessing the stability of the test article to the pelleting process, development and validation of a new analytical method to extract and analyse the pelleted test material, and performing a palatability study, would require an extension of the deadline by 9 months (i.e. a total of 21 months for performing the study). ECHA also notes that some of the preparatory work for the required test could start already before receiving the final decision.

The argument regarding shortage of rabbits was not further substantiated in your provided documentation.

ECHA is of the opinion that 18 months is sufficient time to conduct and report a dietary pre-natal developmental study in rabbits, including associated dose-range finding and palatability studies and other necessary preparations. The deadline was therefore extended to 18 months.

In conclusion, ECHA has evaluated your request and rejected an extension to 21 months. The deadline was instead extended to 18 months.

Appendix 2: Procedural history

ECHA received your registration containing the testing proposal(s) for examination pursuant to Article 40(1) on 14 January 2015.

ECHA held a third party consultation for the testing proposal(s) from 14 March 2016 until 28 April 2016. ECHA did not receive information from third parties.

This decision does not take into account any updates after **20 July 2016**, 30 calendar days after the end of the commenting period.

The decision making followed the procedure of Articles 50 and 51 of the REACH Regulation, as described below:

ECHA notified you of the draft decision and invited you to provide comments.

ECHA took your comments into account and amended the deadline.

ECHA notified the draft decision to the competent authorities of the Member States for proposal(s) for amendment.

As no amendments were proposed, ECHA took the decision according to Article 51(3) of the REACH Regulation.

Appendix 3: Further information, observations and technical guidance

1. This decision does not imply that the information provided in your 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.

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

3. In relation to the information required by the present decision, the sample of the substance used for the new test(s) must be suitable for use by all the joint registrants. Hence, the sample should have a composition that is suitable to fulfil the information requirement for the range of substance compositions manufactured or imported by the joint registrants. It is the responsibility of all joint registrants who manufacture or import the same substance to agree on the appropriate composition of the test material and to document the necessary information on their substance composition. In addition, it is important to ensure that the particular sample of the substance tested in the new test(s) 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 or imported by each registrant. If the registration of the substance by any registrant covers different grades, the sample used for the new test(s) 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 test(s) to be assessed.