EUROPEAN CHEMICALS AGENCY

Helsinki, 22 August 2018

Addressee: [redacted]

Decision number: TPE-D-2114440219-52-01/F
Substance name: a,a-dimethylphenethyl butyrate
EC number: 233-221-8
CAS number: 10094-34-5
Registration number: [redacted]
Submission number: [redacted]
Submission date: 10/10/2017
Registered tonnage band: 100-1000

DECISION ON A TESTING PROPOSAL

Based on Article 40 of Regulation ((EC) No 1907/2006) (the REACH Regulation), ECHA examined your testing proposal(s) and decided as follows.

While your originally proposed tests for Sub-chronic toxicity study (90-day), oral route (EU B.26./OECD TG 408) and Pre-natal developmental toxicity study (EU B.31./OECD TG 414) using the analogue substance 1,1-dimethyl-2-phenylethyl acetate (EC No 205-781-3) are rejected, you are requested to perform:

1. **Sub-chronic toxicity study (90-day), inhalation route (Annex IX, Section 8.6.2.; test method: OECD TG 413) in rats using the registered substance.**
2. **Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method: EU B.31./OECD TG 414) in a first species (rat or 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 to the REACH Regulation. 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 have to submit the requested information in an updated registration dossier by ***31 August 2020***. You also have to update the chemical safety report, where relevant. The timeline has been set to allow for sequential testing.

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

Appeal

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, has to 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 Kevin Pollard, Head of Unit, Evaluation E1

[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

0. Grouping of substances and read-across

The decision of ECHA is based on the examination of the testing proposals submitted by you for the registered substance 1,1-dimethyl-2-phenylethyl butyrate, CAS No 10094-34-5 (EC No 233-221-8), (hereafter referred to as "target substance"), proposed to be performed with a source substance 1,1-dimethyl-2-phenylethyl acetate, CAS No 151-05-3 (EC No 205-781-3). ECHA has considered first the scientific validity of the read-across hypothesis (preliminary considerations below), before assessing the testing proposed (sections 1 and 2 below).

Article 13(1) of the REACH Regulation requires information on intrinsic properties of substances on human toxicity to be generated whenever possible by means other than vertebrate animal tests, including from information from structurally related substances (grouping or read-across), "*provided that the conditions set out in Annex XI are met*".

According to Annex XI, Section 1.5. there needs to be structural similarity among the substances within a group or a category and furthermore, it is required that the relevant properties of a substance within the group can be predicted from the data for reference substance(s) by interpolation, and the data should be adequate for the purpose of classification and labelling and/or risk assessment. Furthermore, Annex XI, Section 1.5. lists several additional requirements, including that adequate and reliable documentation of the applied method is to be provided.

You have proposed to cover the standard information requirements for a sub-chronic toxicity study (90-days; Annex IX, Section 8.6.2.) and a pre-natal developmental toxicity study (Annex IX, Section 8.7.2.) by performing the test with a source substance 1,1-dimethyl-2-phenylethyl acetate, CAS No 151-05-3 (EC No 205-781-3).

ECHA observes that there is no documentation in the registration dossier establishing a basis whereby relevant human health properties of the registered substance may be predicted from data for the analogue substance 1,1-dimethyl-2-phenylethyl acetate, CAS No 151-05-3 (EC No 205-781-3). In the absence of any documentation supporting the proposed read-across approach, ECHA considers that you have failed to provide an adequate and reliable documentation of the applied method as required by Annex XI, Section 1.5 of the REACH Regulation. Therefore, ECHA is not in a position to evaluate the proposed read-across approach which could allow establishing that relevant properties of the registered substance can be predicted from those of the analogue substance. The proposed read-across has therefore to be rejected as not acceptable. Accordingly, it is necessary to perform testing on the registered substance.

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

Pursuant to Article 40(3)(d) and (c) of the REACH Regulation, ECHA may reject a proposed test and require the Registrant to carry out other tests in cases of non-compliance of the testing proposal with Annexes IX, X or XI.

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.

You have submitted a testing proposal for a sub-chronic toxicity study (90 day) in rats via the oral route according to EU B.26./OECD TG 408) to be performed with the analogue substance 1,1-dimethyl-2-phenylethyl acetate, CAS No 151-05-3 (EC No 205-781-3), with no further justification. In the absence of information, as explained above in section 0, Grouping of substances and read-across, ECHA is not in a position to conclude on the proposed read-across approach which could allow establishing that sub-chronic toxicity of the registered substance can be predicted from that of the analogue substance and therefore rejects the read-across adaptation.

ECHA requested your considerations for alternative methods to fulfil the information requirement for Sub-chronic toxicity (90-day): oral. ECHA notes that you provided your considerations and you applied read-across to fulfil the respective information requirement, and no other alternative methods were available. ECHA has taken these considerations into account.

You proposed testing by the oral route. It is noted that testing by the oral route of administration could be considered. The registered substance is reported to be a liquid at ambient temperature. However, judging from the information you provided, the inhalation route is considered the more appropriate route of administration. ECHA considers that, due to the reported vapour pressure of 8.5 kPa at ambient temperature, formation of vapours might be assumed during the described consumer and professional uses (e.g. use of cleaning & air care products and polishes & wax). The registered substance is classified for skin irritation and ECHA therefore notes a potential concern for local respiratory tract effects following inhalation exposure. Furthermore, uses with spray application indicate that the human exposure to the registered substance by inhalation route is likely. No exposure assessment or risk management measures were described or introduced in the chemical safety report.

Therefore, ECHA considers that a study performed by the inhalation route with the registered substance is appropriate to fulfil the information requirement of Annex IX, Section 8.6.2. of the REACH Regulation.

You did not specify the species to be used for testing. According to the test method EU B.26./OECD TG 413 the rat is the preferred species. ECHA considers this species as being appropriate and testing should be performed with the rat.

Therefore, pursuant to Article 40(3)(c) of the REACH Regulation, you are requested to carry out thestudy with the registered substance subject to the present decision: Sub-chronic toxicity study (90-day) in rats, inhalation route (test method: OECD TG 413). Your originally proposed test for a sub-chronic toxicity study (90 day) oral route (EU B.26./OECD TG 408) with the analogue substance 1,1-dimethyl-2-phenylethyl acetate, CAS No 151-05-3 (EC No 205-781-3), is rejected according to Article 40(3)(d) of the REACH Regulation.

2. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.) in a first species

Pursuant to Article 40(3)(d) and (c) of the REACH Regulation, ECHA may reject a proposed test and require the Registrant to carry out other tests in cases of non-compliance of the testing proposal with Annexes IX, X or XI.

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.

You have submitted a testing proposal for a pre-natal developmental toxicity study study according to EU B.31./OECD TG 414 to be performed with the analogue substance 1,1-dimethyl-2-phenylethyl acetate, CAS No 151-05-3 (EC No 205-781-3), with no further justification. In the absence of information, as explained above in section 0, Grouping of substances and read-across, ECHA is not in a position to conclude on the proposed read-across approach which could allow establishing that the developmental toxicity of the registered substance can be predicted from that of the analogue substance and therefore rejects the read-across adaptation.

ECHA requested your considerations for alternative methods to fulfil the information requirement for Reproductive toxicity (pre-natal developmental toxicity). ECHA notes that you provided your considerations and you applied read-across to fulfil the respective information requirement, and no other alternative methods were available. ECHA has taken these considerations into account.

ECHA considers that a study performed with the registered substance 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 TG 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 rat or rabbit as a first 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 6.0, July 2017) Chapter R.7a, Section 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)(c) of the REACH Regulation, you are requested to carry out the study with the registered substance subject to the present decision: Pre-natal developmental toxicity study in a first species (rats or rabbits), oral route (test method: EU B.31./OECD TG 414 while your originally proposed test for a pre-natal developmental toxicity study (EU B.31./OECD TG 414) with the analogue substance 1,1-dimethyl-2-phenylethyl acetate, CAS No 151-05-3 (EC No 205-781-3), is rejected according to Article 40(3)(d) of the REACH Regulation.
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 6.0, July 2017), Chapter R.7a, Section R.7.6.2.3.2.

ECHA notes that a revised version of OECD TG 414 was adopted this year by the OECD. This revised version contains enhancements of certain endocrine disrupting relevant parameters. You should test in accordance with the revised version of the guideline as published on the OECD website for adopted test guidelines (https://www.oecd-ilibrary.org/environment/oecd-guidelines-for-the-testing-of-chemicals-section-4-health-effects_20745788).

Appendix 2: Procedural history

ECHA received your registration containing the testing proposals for examination in accordance with Article 40(1) on 10 October 2017.

ECHA held a third party consultation for the testing proposals from 22 November 2017 until 8 January 2018. ECHA did not receive information from third parties.

This decision does not take into account any updates after **21 May 2018**, 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 did not receive any comments by the end of the commenting period.

ECHA notified the draft decision to the competent authorities of the Member States for proposals 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 requests in this decision, or to otherwise fulfil the information requirements with a valid and documented adaptation, will result in a notification to the enforcement authorities of the Member States.

3. In carrying out the tests required by the present decision, it is important to ensure that the particular sample of substance tested 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. If the registration of the substance covers different grades, the sample used for the new tests must be suitable to assess these.

   Furthermore, there must be adequate information on substance identity for the sample tested and the grades registered to enable the relevance of the tests to be assessed.