

Helsinki, 19 May 2020

**Addressees**

Registrant of JS\_15834-04-5\_FEUC listed in the last Appendix of this decision

**Date of submission for the dossier subject of a decision**

8 November 2019

**Registered substance subject to this decision, hereafter 'the Substance'**

Substance name: 2,2-bis[[[(1-oxopentyl)oxy]methyl]propane-1,3-diyl divalerate

EC number: 239-937-7

CAS number: 15834-04-5

**Decision number:** [Please refer to the REACH-IT message which delivered this communication (in format TPE-D-XXXXXXXXXX-XX-XX/F)]**DECISION ON A TESTING PROPOSAL**

Based on Article 40 of Regulation (EC) No 1907/2006 (REACH), ECHA requests that you submit the information listed below by the deadline of **26 May 2022**.

**A. Requirements applicable to all the Registrants subject to Annex X of REACH**

1. Extended one-generation reproductive toxicity study (Annex X, Section 8.7.3.; test method: OECD TG 443) in rats, oral route (gavage), with the Substance, specified as follows:
  - Ten weeks pre-mating exposure duration for the parental (P0) generation;
  - Dose level setting shall aim to induce systemic toxicity at the highest dose level;
  - Cohort 1A (Reproductive toxicity);
  - Cohort 1B (Reproductive toxicity) without extension to mate the Cohort 1B animals to produce the F2 generation.

**Conditions to comply with the requests**

You are bound by the requests for information corresponding to the REACH Annexes applicable to your own registered tonnage of the Substance at the time of evaluation. Therefore, you have to comply with the requirements of Annexes VII to X of REACH, if you have registered a substance at above 1000 tonnes per year.

The Appendix entitled Observations and technical guidance addresses the generic approach for the selection and reporting of the test material used to perform the required studies and provides generic recommendations and references to ECHA guidance and other reference documents.

You must submit the information requested in this decision by the deadline indicated above in an updated registration dossier and also update the chemical safety report, where relevant, including any changes to classification and labelling, based on the newly generated information.

## **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<sup>1</sup> under the authority of Christel Schilliger-Musset, Director of Hazard Assessment

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<sup>1</sup> 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 A: Reasons for the requirement applicable to all the Registrants subject to Annex X of REACH**

This decision is based on the examination of the testing proposal you submitted.

**1. Extended one-generation reproductive toxicity study (Annex X, Section 8.7.3.)**

The basic test design of an extended one-generation reproductive toxicity study (EOGRTS) is a standard information requirement under Annex X to REACH. Furthermore, column 2 of Section 8.7.3. defines when the study design needs to be expanded.

You have submitted a testing proposal for an EOGRTS according to OECD TG 443 by the oral route. You have provided the following specification of the study design: *"An extended one generation reproductive toxicity study according to OECD 443 guideline, basic test design (cohorts 1A and 1B without extension to include a F2 generation) is proposed at the present time. The detailed study design of EOGRTS will be further assessed to ensure its adequate assessment of possible effects and avoid unnecessary vertebrate animal use. Gavage is suitable to be used in the study since the test substance likely will add a taste."*

You provided your considerations concluding that there were no alternative methods which could be used to adapt the information requirement(s) for which testing is proposed. ECHA has taken these considerations into account.

The proposed study design needs further specification to fulfil the information requirement.

The following refers to the specifications of this required study.

*Premating exposure duration and dose-level setting*

Ten weeks pre-mating exposure duration is required because there is no substance specific information in the dossier supporting shorter pre-mating exposure duration as advised in the ECHA Guidance R.7a. In this specific case ten weeks exposure duration is supported by the lipophilicity of the Substance (predicted logKow = 6.74) to ensure that the steady state in parental animals has been reached before mating.

In order to be compliant and not to be rejected due to too low dose levels, the study must include a highest dose level which must aim at inducing systemic toxicity, but not death or severe suffering of the animals, at allowing comparison of reproductive toxicity and systemic toxicity. The dose level selection should be based upon the fertility effects with the other cohorts being tested at the same dose levels. A descending sequence of dose levels should be selected in order to demonstrate any dose-related effect and to establish NOAELs.

If there is no existing relevant data to be used for dose level setting, it is recommended that results from a range-finding study (or range-finding studies) are reported with the main study.

You must provide a justification with your study report that demonstrate that the dose level selection meets the conditions described above.

*Cohorts 1A and 1B*

Cohorts 1A and 1B belong to the basic study design and must be included.

### *Species and route selection*

You proposed testing by oral route (gavage) in rats. ECHA agrees with your proposal.

You did not specify the species for testing. According to the test method OECD TG 443, the rat is the preferred species.

In your comments on the draft decision, you agree to conduct the requested test as specified in the decision.

Under Article 40(3)(a) of REACH, you are requested to carry out the proposed test with the Substance.

### *Further expansion of the study design*

The conditions to include the extension of Cohort 1B are currently not met. Furthermore, no triggers for the inclusion of Cohorts 2A and 2B (developmental neurotoxicity) and Cohort 3 (developmental immunotoxicity) were identified. However, you may expand the study by including the extension of Cohort 1B, Cohorts 2A and 2B and/or Cohort 3 if relevant information becomes available from other studies or during conduct of this study. Inclusion is justified if the available information meets the criteria and conditions which are described in Column 2, Section 8.7.3., Annex X. You may also expand the study due to other scientific reasons in order to avoid a conduct of a new study. The study design, including any added expansions, must be fully justified and documented. Further detailed guidance on study design and triggers is provided in ECHA Guidance<sup>2</sup>.

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<sup>2</sup> ECHA Guidance R.7a, Section R.7.6.

## **Appendix B: Procedural history**

ECHA started the testing proposal evaluation in accordance with Article 40(1) on 8 July 2019.

ECHA held a third party consultation for the testing proposals from 21 October 2019 until 5 December 2019. ECHA did not receive information from third parties.

For the purpose of the decision-making, this decision does not take into account any updates of registration dossiers after the date on which you were notified the draft decision according to Article 50(1) of REACH.

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

ECHA notified you of the draft decision and invited you to provide comments within 30 days of the notification.

ECHA took into account your comments and did not amend the requests.

ECHA notified the draft decision to the competent authorities of the Member States for proposals for amendment.

As no amendments were proposed, ECHA adopted the decision under Article 51(3) of REACH.

## Appendix C: Observations and technical guidance

1. This testing proposal examination decision does not prevent ECHA from initiating compliance checks at a later stage on the registrations present.
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 your Member State(s).

3. Test guidelines, GLP requirements and reporting

Under Article 13(3) of REACH, all new data generated as a result of this decision needs to be conducted according to the test methods laid down in a European Commission Regulation or according to international test methods recognised by the Commission or ECHA as being appropriate.

Under Article 13(4) of REACH, ecotoxicological and toxicological tests and analyses must be carried out according to the GLP principles (Directive 2004/10/EC) or other international standards recognised by the Commission or ECHA.

Under Article 10 (a) (vi) and (vii) of REACH, all new data generated as a result of this decision must be reported as study summaries, or as robust study summaries, if required under Annex I of REACH. See ECHA Practical Guide: 'How to report robust study summaries'<sup>3</sup>.

4. Test material

### *Selection of the test material(s)*

The composition of the test material(s) must fall within the boundary composition(s) of the Substance.

While selecting the test material you must take into account the impact of each constituent/impurity is known to have or could have on the test results for the endpoint to be assessed. For example, if a constituent/impurity of the Substance is known to have an impact on (eco)toxicity, the selected test material must contain that constituent/impurity.

### *Technical reporting of the test material*

The composition of the selected test material must be reported in the respective endpoint study record, under the Test material section. The composition must include all constituents of the test material and their concentration values. Without such detailed reporting, ECHA may not be able to confirm that the test material is relevant for the Substance and to all the registrants of the Substance.

Technical instructions are available in the manual "How to prepare registration and PPORD dossiers"<sup>4</sup>.

5. List of references of the ECHA Guidance and other guidance/ reference documents<sup>5</sup>

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<sup>3</sup> <https://echa.europa.eu/practical-guides>

<sup>4</sup> <https://echa.europa.eu/manuals>

<sup>5</sup> <https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment>

QSARs, read-across and grouping

Guidance on information requirements and chemical safety assessment, Chapter R.6 (version 1.0, May 2008), referred to as ECHA Guidance R.6 in this decision.

ECHA Read-across assessment framework (RAAF, March 2017)<sup>6</sup>

Toxicology

Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7c (version 3.0, June 2017), referred to as ECHA Guidance R.7c in this decision.

Environmental toxicology and fate

Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7b (version 4.0, June 2017), referred to as ECHA Guidance R.7b in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7c (version 3.0, June 2017), referred to as ECHA Guidance R.7c in this decision.

PBT assessment

Guidance on information requirements and chemical safety assessment, Chapter R.11 (version 3.0, June 2017), referred to as ECHA Guidance R.11 in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.16 (version 3.0, February 2016), referred to as ECHA Guidance R.16 in this decision.

OECD Guidance documents

Guidance Document on aqueous-phase aquatic toxicity testing of difficult test chemicals – No 23, referred to as OECD GD 23.

Guidance Document on Standardised Test Guidelines for Evaluating Chemicals for Endocrine Disruption – No 150, referred to as OECD GD 150.

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<sup>6</sup> <https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across>

**Appendix D: List of the registrants to which the decision is addressed and the corresponding information requirements applicable to them**

<b>Registrant Name</b>	<b>Registration number</b>	<b>(Highest) Data requirements to be fulfilled</b>
[REDACTED]	[REDACTED]	[REDACTED]

Note: where applicable, the name of a third party representative (TPR) may be displayed in the list of recipients whereas the decision is sent to the actual registrant.