

Helsinki, 20 September 2023

Addressee(s)

Registrant(s) of C4-C6_diisobutylester as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision

27/09/2021

Registered substance subject to this decision ("the Substance")

Substance name: Reaction mass of bis(2-methylpropyl) pentanedioate and bis(2-methylpropyl) butanedioate and bis(2-methylpropyl) hexanedioate

EC/List number: 907-870-9

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

Under Article 40 of Regulation (EC) No 1907/2006 (REACH), you must submit the information listed below by **4 January 2027**.

Requested information must be generated using the Substance unless otherwise specified.

Information required from all the Registrants subject to Annex X of REACH

1. Pre-natal developmental toxicity study (Annex X, Section 8.7.2.; test method: OECD TG 414) by oral route, in a second species (rat/rabbit)

The reasons for the decision(s) are explained in Appendix 1.

Information required depends on your tonnage band

You must provide the information listed above for all REACH Annexes applicable to you in accordance with Articles 10(a) and 12(1) of REACH. The addressee(s) of the decision and their corresponding information requirements based on registered tonnage band are listed in Appendix 3.

You are only required to share the costs of information that you must submit to fulfil your information requirements.

How to comply with your information requirements

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

You must follow the general requirements for testing and reporting new tests under REACH, see Appendix 4.

Appeal

This decision, when adopted under Article 51 of REACH, may be appealed to the Board of

Appeal of ECHA within three months of its notification to you. Please refer to <http://echa.europa.eu/regulations/appeals> for further information.

Failure to comply

If you do not comply with the information required by this decision by the deadline indicated above, ECHA will notify the enforcement authorities of your Member State.

Authorised¹ under the authority of Mike Rasenberg, Director of Hazard Assessment

Appendix 1: Reasons for the decision

Appendix 2: Procedure

Appendix 3: Addressees of the decision and their individual information requirements

Appendix 4: Conducting and reporting new tests under REACH

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 for the decision

Contents

Reasons for the decision(s) related to the information under Annex X of REACH	4
1. Pre-natal developmental toxicity study.....	4
References	7

Reasons for the decision(s) related to the information under Annex X of REACH**1. Pre-natal developmental toxicity study**

1 A pre-natal developmental toxicity (PNDT) study (OECD TG 414) in two species is a standard information requirement under Annex X, Section 8.7.2.

1.1. Information provided to fulfil the information requirement

2 You have submitted a testing proposal for a PNDT study according to the OECD TG 414 by the oral route with the analogue substance Reaction mass of Dimethyl adipate, Dimethyl glutarate and Dimethyl succinate (EC No. 906-170-0).

3 ECHA requested your considerations for alternative methods to fulfil the information requirement for Developmental toxicity. 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.

4 ECHA agrees that a PNDT study in a second species is necessary.

1.2. Grouping of substances and read-across approach

5 Annex XI, Section 1.5. specifies two conditions which must be fulfilled whenever a read-across approach is used. Firstly, there needs to be structural similarity between substances which results in a likelihood that the substances have similar physicochemical, toxicological and ecotoxicological properties so that the substances may be considered as a group or category. Secondly, it is required that the relevant properties of a substance within the group may be predicted from data for reference substance(s) within the group.

6 Additional information on what is necessary when justifying a read-across approach can be found in the Guidance on IRs and CSA, Chapter R.6. and related documents (RAAF, 2017; RAAF UVCB, 2017).

1.2.1. Predictions for toxicological properties

7 You provide a read-across justification document in IUCLID Section 7.8.

8 You justify the grouping of the substances as: "There are no data available on the developmental toxicity of the diisobutyl esters of adipic, succinic and glutaric acid (DBE-IB). However developmental toxicity data (in rats) exist for the methyl esters of these acids (DBE), and for isobutanol in rats and rabbits".

9 You intend to predict the properties of the Substance from information obtained from the following source substance(s) via testing in rats:

- Reaction mass of dimethyl adipate, dimethyl glutarate and dimethyl succinate (Dibasicesters, DBE), EC 906-170-0;
- 2-methylpropan-1-ol, EC 201-148-0.

10 You provide the following reasoning for the prediction of toxicological properties: "Dosing of the diisobutyl esters will result in the release of the acids and isobutanol, therefore read across to the requested study in rabbits with dimethyl esters is considered appropriate since the major hydrolysis products of the dimethyl esters are the acids. In support of this, data on isobutanol are also provided to address the isobutanol that would be released from the diisobutyl esters once entering the body".

11 ECHA understands that your read-across hypothesis assumes that different compounds have the same type of effect and includes information on a common (bio)trans-formation product. You predict the properties of your Substance to be quantitatively equal to those of the source substance based on an identified trend within the group.

12 We have identified the following issue(s) with the prediction(s) of toxicological properties:

1.2.1.1. Missing supporting information to compare properties of the substances(s)

13 Annex XI, Section 1.5. requires that whenever read-across is used adequate and reliable documentation of the applied method must be provided. Such documentation must provide supporting information to scientifically justify the read-across explanation for prediction of properties. The set of supporting information should strengthen the rationale for the read-across in allowing to verify the crucial aspects of the read-across hypothesis and establishing that the properties of the Substance can be predicted from the data on the source substance(s) (Guidance on IRs and CSA R.6., Section R.6.2.2.1.f.).

14 Supporting information must include bridging studies to compare properties of the category members.

15 As indicated above, your read-across hypothesis is based on the assumption that the structurally similar substance(s) cause the same type of effect(s). In this context, relevant, reliable and adequate information allowing to compare the properties of the substance(s) is necessary to confirm that the substances cause the same type of effects. Such information can be obtained, for example, from bridging studies of comparable design and duration for the Substance and of the source substance(s).

16 You provided several studies on source substances.

17 You provided no study on the target substance relevant to the adapted information requirement.

18 In the absence of such information, you have not established that the Substance and the source substance(s) are likely to have similar properties. Therefore, you have not provided sufficient supporting information to scientifically justify the read-across.

1.2.2. Conclusion on the read-across approach

19 Based on the above, you have not established that relevant properties of the Substance can be predicted from data on the source substance(s). Your read-across approach under Annex XI, Section 1.5. is rejected.

20 Therefore, the information requirement is not fulfilled.

21 In your comments, you submitted a new read across justification document. In that document you present a strategy relying on the generation of additional supporting information on the Substance and on the analogue substances ECs 906-170-0, 211-020-6, 936-196-8, 214-277-2 and 203-419-9. ECHA acknowledges your intention. As indicated in your comments, this strategy relies essentially on data, which is yet to be generated, therefore no conclusion on the compliance can currently be made. You remain responsible for complying with this decision by the set deadline.

1.3. Specification of the study design

22 Under the OECD TG 414, the rat or the rabbit are the preferred species (Guidance on IRs & CSA, Section R.7.6.2.3.2.). Therefore, a PNDT study according to the OECD TG 414 must be performed in rabbit or rat as the second species, depending on choice of species for the first PNDT study.

- 23 As the Substance is a liquid, the study must be conducted with oral administration of the Substance (Annex X, Section 8.7.2, Column 1).

1.4. Outcome

- 24 Your testing proposal is rejected under Article 40(3) (d) of REACH. Under Article 40(3)(c) you are requested to carry out the additional test with the Substance, as specified above.

References

The following documents may have been cited in the decision.

Guidance on information requirements and chemical safety assessment (Guidance on IRs & CSA)

- Chapter R.4 Evaluation of available information; ECHA (2011).
- Chapter R.6 QSARs, read-across and grouping; ECHA (2008).
Appendix to Chapter R.6 for nanoforms; ECHA (2019).
- Chapter R.7a Endpoint specific guidance, Sections R.7.1 – R.7.7; ECHA (2017).
Appendix to Chapter R.7a for nanomaterials; ECHA (2017).
- Chapter R.7b Endpoint specific guidance, Sections R.7.8 – R.7.9; ECHA (2017).
Appendix to Chapter R.7b for nanomaterials; ECHA (2017).
- Chapter R.7c Endpoint specific guidance, Sections R.7.10 – R.7.13; ECHA (2017).
Appendix to Chapter R.7a for nanomaterials; ECHA (2017).
Appendix R.7.13-2 Environmental risk assessment for metals and metal compounds; ECHA (2008).
- Chapter R.11 PBT/vPvB assessment; ECHA (2017).
- Chapter R.16 Environmental exposure assessment; ECHA (2016).

Guidance on data-sharing; ECHA (2017).

Guidance for monomers and polymers; ECHA (2012).

Guidance on intermediates; ECHA (2010).

All guidance documents are available online: <https://echa.europa.eu/guidance-documents/guidance-on-reach>

Read-across assessment framework (RAAF)

- RAAF, 2017 Read-across assessment framework (RAAF); ECHA (2017)
- RAAF UVCB, 2017 Read-across assessment framework (RAAF) – considerations on multi- constituent substances and UVCBs); ECHA (2017).

The RAAF and related documents are available online:

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

OECD Guidance documents (OECD GDs)

- OECD GD 23 Guidance document on aquatic toxicity testing of difficult substances and mixtures; No. 23 in the OECD series on testing and assessment, OECD (2019).
- OECD GD 29 Guidance document on transformation/dissolution of metals and metal compounds in aqueous media; No. 29 in the OECD series on testing and assessment, OECD (2002).
- OECD GD 150 Revised guidance document 150 on standardised test guidelines for evaluating chemicals for endocrine disruption; No. 150 in the OECD series on testing and assessment, OECD (2018).
- OECD GD 151 Guidance document supporting OECD test guideline 443 on the extended one-generation reproductive toxicity test; No. 151 in the OECD series on testing and assessment, OECD (2013).

Appendix 2: Procedure

The information requirement for an Extended One-Generation Reproductive Toxicity Study (EOGRTS; Annexes IX or X, Section 8.7.3.) is not addressed in this decision. This may be addressed in a separate decision once the information from the sub-chronic toxicity study (90-day) requested in a compliance check decision is provided; due to the fact that the results from the 90-day study requested in the parallel CCH decision are needed for the design of the EOGRTS.

ECHA started the testing proposal evaluation in accordance with Article 40(1) on 28 September 2021.

ECHA held a third-party consultation for the testing proposal(s) from 22 September 2022 until 7 November 2022. ECHA did not receive information from third parties.

ECHA followed the procedure detailed in Articles 50 and 51 of REACH.

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

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

The deadline of the decision is set based on standard practice for carrying out OECD TG tests. It has been exceptionally extended by 12 months from the standard deadline granted by ECHA to take into account currently longer lead times in contract research organisations.

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 3: Addressee(s) of this decision and their corresponding information requirements

In accordance with Articles 10(a) and 12(1) of REACH, the information requirements for individual registrations are defined as follows:

- the information specified in Annex VII to REACH, for registration at 1-10 tonnes per year (tpa), or as a transported isolated intermediate in quantity above 1000 tpa;
- the information specified in Annexes VII and VIII to REACH, for registration at 10-100 tpa;
- the information specified in Annexes VII, VIII and IX to REACH, for registration at 100-1000 tpa;
- the information specified in Annexes VII to X to REACH, for registration at more than 1000 tpa.

Registrant Name	Registration number	Highest REACH Annex applicable to you
██████████	████████████████████	██████
██████████	████████████████████	██████

Where applicable, the name of a third-party representative (TPR) may be displayed in the list of recipients whereas ECHA will send the decision to the actual registrant.

Appendix 4: Conducting and reporting new tests for REACH purposes

1. Requirements when conducting and reporting new tests for REACH purposes

1.1. Test methods, GLP requirements and reporting

- (1) Under Article 13(3) of REACH, all new data generated as a result of this decision must be conducted according to the test methods laid down in a European Commission Regulation or to international test methods recognised by the Commission or ECHA as being appropriate.
- (2) 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.
- (3) 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 on How to report robust study summaries².
- (4) Under the introductory part of Annexes VII/VIII/IX/X to REACH, where a test method offers flexibility in the study design, for example in relation to the choice of dose levels or concentrations, the chosen study design must ensure that the data generated are adequate for hazard identification and risk assessment.

1.2. Test material

Before generating new data, you must agree within the joint submission on the chemical composition of the material to be tested (Test Material) which must be relevant for all the registrants of the Substance.

- (1) Selection of the Test material(s)
The Test Material used to generate the new data must be selected taking into account the following:
 - the variation in compositions reported by all members of the joint submission,
 - the boundary composition(s) of the Substance,
 - the impact of each constituent/ impurity 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.
- (2) Information on the Test Material needed in the updated dossier
 - You must report the composition of the Test Material selected for each study, under the "Test material information" section, for each respective endpoint study record in IUCLID.
 - The reported composition must include all constituents of each Test Material and their concentration values and other parameters relevant for the property to be tested.

² <https://echa.europa.eu/practical-guides>

This information is needed to assess whether the Test Material is relevant for the Substance and whether it is suitable for use by all members of the joint submission.

Technical instructions on how to report the above is available in the manual on How to prepare registration and PPORD dossiers³.

³ <https://echa.europa.eu/manuals>