

Helsinki, 14 April 2021

Addressees

Registrants of JS_2212-81-9 listed in the last Appendix of this decision

Date of submission of the dossier subject of a decision

29/10/2019

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

Substance name: [1,3-phenylenebis(1-methylethylidene)]bis[tert-butyl] peroxide

EC number: 218-664-7

CAS number: 2212-81-9

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)**

Based on Article 40 of Regulation (EC) No 1907/2006 (REACH), you must submit the information listed below by **21 April 2023**.

The requested information must be generated using the Substance unless otherwise specified.

A. Information required from the Registrants subject to Annex X of REACH

1. Extended one-generation reproductive toxicity study (Annex X, Section 8.7.3.; test method: EU B.56./OECD TG 443) by oral route, in rats, with the analogue substance [1,3(or 1,4)-phenylenebis(1-methylethylidene)]bis[tert-butyl] peroxide (EC no 246-678-3) 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; and
 - Cohorts 2A and 2B (Developmental neurotoxicity).

You must report the study performed according to the above specifications. Any expansion of the study must be scientifically justified.

Reasons for the request(s) are explained in the following appendix:

- Appendix entitled "Reasons to request information required under Annex X of REACH".

Information required depends on your tonnage band

You must provide the information listed above for all REACH Annexes applicable to you, and in accordance with Articles 10(a) and 12(1) of REACH:

- the information specified in Annexes VII to X to REACH, for registration at more than 1000 tpa.

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 testing and reporting requirements provided under the Appendix entitled "Requirements to fulfil when conducting and reporting new tests for REACH purposes". For references used in this decision, please consult the Appendix entitled "List of references".

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>.

Approved¹ under the authority of Christel Schilliger-Musset, Director of Hazard Assessment

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 A: Reasons to request information required under Annex X of REACH

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

1. Extended one-generation reproductive toxicity study

The basic test design of an extended one-generation reproductive toxicity study (EOGRTS) is a standard information requirement under Annex X to REACH.

You have submitted a testing proposal for an EOGRTS according to OECD TG 443 in rats with basic test design (Cohorts 1A and 1B without extension) with the analogue substance [1,3(or 1,4)-phenylenebis(1-methylethylidene)]bis[tert-butyl] peroxide (EC no 246-678-3).

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.

Evaluation of read-across

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.

You provide the following justification for your read-across approach:

- The mono-constituent Substance constitutes [REDACTED] of the multi-constituent source substance.
- The results from an OECD 422 study with the Substance demonstrate that the toxicological properties of the Substance and the source substance are similar.

ECHA agrees that the submitted information supports your hypothesis.

Therefore, you have established that relevant properties of the Substance can be predicted from data on the analogue substance.

ECHA emphasises that any final determination on the validity of your read-across adaptation will only be possible when the information on requested studies will be available in the dossier.

Details on the study

The proposed study design requires modification to fulfil the information requirement.

The following refers to the specifications of this required study.

Premating exposure duration and dose-level setting

You did not provide a proposal for premating exposure duration or dose-level setting.

Ten weeks premating exposure duration is required because there is no substance specific information in the dossier supporting shorter premating exposure duration as advised in the ECHA Guidance R.7a Ten weeks exposure duration is also supported by the lipophilicity of the analogue substance [1,3(or 1,4)-phenylenebis(1-methylethylidene)]bis[tert-butyl] peroxide

that you will use for testing to ensure that the steady state in parental animals has been reached before mating (Log Pow 7.3).

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 to induce systemic toxicity, but not death or severe suffering of the animals, to allow 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 shall be included.

Cohorts 2A and 2B

The developmental neurotoxicity Cohorts 2A and 2B need to be conducted in case of a particular concern on (developmental) neurotoxicity.

You proposed not to include Cohorts 2A and 2B.

ECHA notes that existing information on the analogue substance [1,3(or 1,4)-phenylenebis(1-methylethylidene)]bis[tert-butyl] peroxide derived from the available OECD TG 408 and 422 studies shows evidence of thyroid toxicity. Specifically, histopathological changes, i.e. hypertrophy of the follicular cells, were observed in both sexes. Signs of thyroid toxicity rise a particular concern on developmental neurotoxicity (ECHA Guidance R.7a).

The developmental neurotoxicity cohorts 2A and 2B must be conducted because there is a particular concern on (developmental) neurotoxicity.

Species and route selection

You proposed testing in rats. ECHA agrees with your proposal.

You did not specify the route for testing. ECHA considers that the oral route is the most appropriate route of administration, since the Substance to be tested is a solid.

Outcome

Under Article 40(3)(b) of REACH, you are to provide the data generated on the analogue substance [1,3(or 1,4)-phenylenebis(1-methylethylidene)]bis[tert-butyl] peroxide (EC no 246-678-3).

There is an adopted decision request for the same endpoint with the analogue substance, [1,3(or 1,4)-phenylenebis(1-methylethylidene)]bis[tert-butyl] peroxide (EC no 246-678-3), with a deadline of 16 May 2022 to submit the information, where you are listed as a registrant. No additional animal testing should be required. The sharing of the information and related costs is required.

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 Cohort 3 (developmental immunotoxicity) were identified. However, you may expand the study by including the extension of Cohort 1B 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 Guidance².

² ECHA Guidance R.7a, Section R.7.6.

Appendix B: Requirements to fulfil when conducting and reporting new tests for REACH purposes

A. 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 summaries³.

B. Test material

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 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.

Technical instructions on how to report the above is available in the manual on How to prepare registration and PPORD dossiers⁴.

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

⁴ <https://echa.europa.eu/manuals>

Appendix C: Procedure

ECHA started the testing proposal evaluation in accordance with Article 40(1) on 30 October 2019.

ECHA held a third party consultation for the testing proposal(s) from 25 May 2020 until 9 July 2020. 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 did not receive any comments within the notification period.

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 D: List of references - ECHA Guidance⁵ and other supporting documentsEvaluation of available information

Guidance on information requirements and chemical safety assessment, Chapter R.4 (version 1.1., December 2011), referred to as ECHA Guidance R.4 where relevant.

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 where relevant.

Read-across assessment framework (RAAF, March 2017)⁶

RAAF - considerations on multi-constituent substances and UVCBs (RAAF UVCB, March 2017)⁶

Physical-chemical properties

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.

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.

Data sharing

Guidance on data-sharing (version 3.1, January 2017), referred to as ECHA Guidance on data sharing in this decision.

OECD Guidance documents⁷

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

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

⁷ <http://www.oecd.org/chemicalsafety/testing/series-testing-assessment-publications-number.htm>

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

Guidance document on transformation/dissolution of metals and metal compounds in aqueous media – No 29, referred to as OECD GD 29.

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

Guidance Document supporting OECD test guideline 443 on the extended one-generation reproductive toxicity test – No 151, referred to as OECD GD 151.

Appendix E: Addressees of this decision and the corresponding information requirements applicable to them

You must provide the information requested in this decision for all REACH Annexes applicable to you.

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.