

Helsinki, 11 March 2022

**Addressees**

Registrant(s) of JS\_Di-tert-amyl peroxide as listed in the last Appendix of this decision

**Date of submission of the dossier subject to this decision**

18/11/2020

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

Substance name: Di-tert-pentyl peroxide

EC number: 234-042-8

**Decision number:** Please refer to the REACH-IT message which delivered this communication (in format CCH-D-XXXXXXXXXX-XX-XX/F)**DECISION ON A COMPLIANCE CHECK**

Under Article 41 of Regulation (EC) No 1907/2006 (REACH), you must submit the information listed below, by the deadline of **18 December 2023**.

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

**A. Information required from all the Registrants subject to Annex VIII of REACH**

1. Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.; test method: EU B.63/OECD TG 421 or EU B.64/OECD TG 422) by oral route, in rats

**B. Information required from all the Registrants subject to Annex IX of REACH**

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

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

- Appendix entitled "Reasons common to several requests";
- Appendix/Appendices entitled "Reasons to request information" required under Annexes VII to IX of REACH respectively.

**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 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.

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 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, 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.

Authorised<sup>1</sup> under the authority of Mike Rasenberg, 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 on Reasons common to several requests

### 1. Assessment of your read-across approach under Annex XI, Section 1.5.

You seek to adapt the information requirements for the following standard information requirements by grouping substances in the category and applying a read-across approach in accordance with Annex XI, Section 1.5:

- Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)
- Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)

### Grouping of substances and read-across approach

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 (addressed under 'Scope of the grouping'). 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 (addressed under 'Prediction for toxicological properties').

Additional information on what is necessary when justifying a read-across approach can be found in the ECHA Guidance R.6 and related documents.

#### A. Predictions for toxicological properties

You predict the properties of the Substance from the structurally similar substance di-tert-butyl peroxide (DTB, EC 203-733-6), referred hereafter as "source substance".

You have provided a document "[REDACTED]", in IUCLID, section 13, referred hereafter as "justification document". In this document you have addressed chemical and structural considerations, toxicokinetics and (eco)toxicological properties of the substances.

You have provided the following reasoning for the prediction of toxicological properties: you state that the Substance and the source substance are structurally "very close and differ only by a methyl group from each side of the organic peroxide function". Further, you indicate that they have similar reactivity, defined by the formation of free alkyloxy radicals – CH<sub>3</sub><sup>o</sup> for the source and CH<sub>3</sub>-CH<sub>2</sub><sup>o</sup> for the Substance, as well as similar physical-chemical and toxicological properties.

ECHA understands that you predict the properties of the Substance using a read-across hypothesis which assumes that different compounds have the same type of effects. The properties of your Substance are predicted to be quantitatively equal to those of the source substance.

ECHA notes the following deficiencies with regards to prediction of toxicological properties.

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

Annex XI, Section 1.5 of the REACH Regulation states that "physicochemical properties, human health effects and environmental effects or environmental fate may be predicted from data for reference substance(s)". For this purpose "it is important to provide supporting information to strengthen the rationale for the read-across" (Guidance on IRs and CSA R.6, Section R.6.2.2.1.f.). The set of supporting information should allow to verify the crucial

aspects of the read-across hypothesis and establish that the properties of the Substance can be predicted from the data on the source substance(s).

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

In order to support your hypothesis you refer to the acute toxicity, eye irritation and genotoxicity properties of the Substance and of the source substance. In addition you have compared the toxicological properties using QSAR Toolbox (v.4.2.) profilers and concluded that the substances have a similar toxicological profile, including among others for *“reproductive toxicity based on endocrine effects”*.

The acute toxicity, eye irritation and genotoxicity studies do not inform on the reproductive and developmental toxicity properties of the Substance and of the source substance. Accordingly, this information is not considered as relevant to support your hypothesis. Further, ECHA notes that the data set reported in the technical dossier does not include any experimental data of comparable design and duration for the Substance to compare the reproductive toxicity properties between the Substance and the source substance. In the absence of such information it is not possible to compare the reproductive and developmental toxicity properties of the Substance and the source substance.

Also, as you have not provided any experimental data to compare the relevant properties of the Substance and source substance, information from QSAR Toolbox profilers do not constitute, on their own, a reliable basis for establishing similarities in reproductive toxicological properties. In fact, the complexity of the systemic interactions and the reproductive process and the large number of targets/mechanisms associated with those broad areas of toxicity cannot currently be covered only by computational tools.

Based on the above 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 strengthen the rationale for the read-across.

## **B. Conclusions on the read-across approach**

As explained above, you have not established that relevant properties of the Substance can be predicted from data on the analogue substance. Therefore, your adaptation does not comply with the general rules of adaptation as set out in Annex XI, Section 1.5. and your grouping and read-across approach is rejected.

**Appendix A: Reasons to request information required under Annex VIII of REACH****1. Screening for reproductive/developmental toxicity**

A Screening for reproductive/developmental toxicity study (test method: EU B.63/OECD TG 421 or EU B.64/OECD TG 422) is a standard information requirement under Annex VIII to REACH, if there is no evidence from analogue substances, QSAR or *in vitro* methods that the Substance may be a developmental toxicant. There is no information available in your dossier indicating that your Substance may be a developmental toxicant.

You have adapted this information requirement by using a Grouping of substances and read-across approach under Annex XI, Section 1.5. You have provided the following information:

- (i) Screening for reproductive/developmental toxicity study (key study; according to OECD TG 422, GLP) performed with the source substance di-tert-butyl peroxide (DTB, EC 203-733-6).

As explained in the Appendix of Reasons common to several requests, your adaptation in accordance with Annex XI, Section 1.5. is rejected. Therefore, the information requirement is not fulfilled.

In your comments to the draft decision you agreed to perform the requested study.

*Study design*

A study according to the test method EU B.63/OECD TG 421 or EU B.64/OECD TG 422 must be performed in rats with oral<sup>2</sup> administration of the Substance.

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<sup>2</sup> ECHA Guidance R.7a, Section R.7.6.2.3.2.

## Appendix B: Reasons to request information required under Annex IX of REACH

### 1. Pre-natal developmental toxicity study in one species

A Pre-natal developmental toxicity (PNDT) study (OECD TG 414) in one species is a standard information requirement under Annex IX to REACH.

You have adapted this information requirement by using a Grouping of substances and read-across approach under Annex XI, Section 1.5. You have provided the following information:

- i. Prenatal developmental toxicity study in rats (according to OECD TG 414, GLP), performed with the source substance di-tert-butyl peroxide (DTB, EC 203-733-6).

As explained in the Appendix of Reasons common to several requests, your adaptation in accordance with Annex XI, Section 1.5. is rejected.

In your comments to the draft decision you propose first to perform the Screening for reproductive/developmental toxicity study (OECD TG 421/422) with the Substance and to use it as bridging information to strengthen the read-across approach and to assess the need to perform the prenatal developmental toxicity study (OECD TG 414). Based on this, you request ECHA "to re-evaluate the validity of the read-across proposed in the reach registration dossier for the OECD TG 414 rat study when the results of the OECD TG 421/422 study will be available".

ECHA acknowledges your intentions to improve the toxicological profile of the Substance and your plans to refine your read-across approach. As indicated in your comments, this refined adaptation relies essentially on data which is yet to be generated, therefore no conclusion on the compliance can currently be made. Please note that this decision does not consider updates of the registration dossiers after the date on which you were notified of the draft decision according to Article 50(1) of REACH (see section 5.4. of ECHA's Practical Guide "How to act in Dossier Evaluation"). You remain responsible for complying with this decision by the set deadline

Therefore, the information requirement is not fulfilled.

#### *Study design*

A PNDT study according to the test method OECD TG 414 must be performed in rat or rabbit as preferred species with oral<sup>3</sup> administration of the Substance.

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<sup>3</sup> ECHA Guidance R.7a, Section R.7.6.2.3.2.

## **Appendix C: 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 summaries<sup>4</sup>.

### **B. 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.

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 dossiers<sup>5</sup>.

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<sup>4</sup> <https://echa.europa.eu/practical-guides>

<sup>5</sup> <https://echa.europa.eu/manuals>

**Appendix D: Procedure**

This decision does not prevent ECHA from initiating further compliance checks at a later stage on the registrations present.

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

The compliance check was initiated on 01 February 2021.

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

ECHA took into account your comments and did not amend the request(s).

**Deadline to submit the requested information in this decision**

In your comments on the draft decision, you requested an extension of the deadline from 18 to 30 months from the date of adoption of the decision to provide the requested information. In support of your request you state that the given deadline "*will not allow proceeding in two steps and deciding of the need for the pre-natal developmental toxicity study*".

ECHA considers that 18 months is the default timeline that allows for the conduct of the two requested studies (OECD TG 422/421 and OECD TG 414) to fulfil the standard information requirements addressed in the decision. As indicated in Appendix B, section 1 above, you stated your intention to fulfil the information requirement under consideration by other means than by generating the requested information.

The timeline set in this decision allows for generating the required data on the Substance as a result of incompliances identified in the dossier submission identified in the header of the document. The objective of this compliance check decision is for you to fulfil the standard information requirements by the set deadline. Therefore, a further extension of the deadline set in the decision to accommodate your statement of intention to provide an adaptation is considered unjustified.

In conclusion, ECHA did not amend the deadline of the draft decision.

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 E: List of references - ECHA Guidance<sup>6</sup> and other supporting documents**Evaluation 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)<sup>7</sup>

RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017)<sup>8</sup>

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 documents<sup>9</sup>

<sup>6</sup> <https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment>

<sup>7</sup> <https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across>

<sup>8</sup> [https://echa.europa.eu/documents/10162/13630/raaf\\_uvcb\\_report\\_en.pdf/3f79684d-07a5-e439-16c3-d2c8da96a316](https://echa.europa.eu/documents/10162/13630/raaf_uvcb_report_en.pdf/3f79684d-07a5-e439-16c3-d2c8da96a316)

<sup>9</sup> <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 F: Addressees of this decision and their corresponding information requirements**

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

<b>Registrant Name</b>	<b>Registration number</b>	<b>Highest REACH Annex applicable to you</b>
██████████	██████████████████	██████
██████████	██████████████████	██████████

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.