

Helsinki, 20 June 2022

**Addressees**

Registrant(s) of JS-Tetrakis14 as listed in Appendix 3 of this decision

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

21 June 2021

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

Substance name: Tetrakis(phenylmethyl)thioperoxydi(carbothioamide)

EC number: 404-310-0

**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 **25 September 2024**.

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

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

1. Long-term toxicity testing on fish (triggered by Annex VIII, Section 9.1.3., column 2; test method: EU C.47./OECD TG 210).

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

2. Sub-chronic toxicity study (90-day) (Annex IX, Section 8.6.2.; test method: OECD TG 408) by oral route, in rats;
3. 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);
4. Long-term toxicity testing on fish (Annex IX, Section 9.1.6.; test method: EU C.47./OECD TG 210).

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 addressees of the decision and their corresponding information requirements based on registered tonnage band are listed in Appendix 3.

In the requests above, the same study has been requested under different Annexes. This is because some information requirements may be triggered at lower tonnage band(s). In

such cases, only the reasons why the information requirement is triggered are provided for the lower tonnage band(s). For the highest tonnage band, the reasons why the standard information requirement is not met, and the specification of the study design are provided. Only one study is to be conducted; all registrants concerned must make every effort to reach an agreement as to who is to carry out the study on behalf of the others under Article 53 of REACH.

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.

Authorised<sup>1</sup> 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

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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 1: Reasons for the decision**

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**Reasons for the decision(s) related to the information under Annex VIII of REACH****1. Long-term toxicity testing on fish**

- 1 Short-term toxicity testing on fish is an information requirement under Column 1 of Annex VIII to REACH (Section 9.1.3.). However, long-term toxicity testing on fish must be considered (Section 9.1.3., Column 2) if the substance is poorly water soluble.
- 2 Poorly water soluble substances require longer time to reach steady-state conditions. As a result, the short-term tests do not give a true measure of toxicity for this type of substances and the long-term test is required. A substance is regarded as poorly water soluble if, for instance, it has a water solubility below 1 mg/L or below the detection limit of the analytical method of the test material (Guidance on IRs and CSA, Section R.7.8.5).
- 3 Under Section 4.8 of your technical dossier, you have provided two OECD 105 studies both of which indicate low water solubility (<10 µg/l).
- 4 Therefore, the Substance is poorly water soluble and information on long-term toxicity on fish must be provided.
- 5 The examination of the information provided, your considerations of alternative methods, of third party comments (if applicable), as well as the selection of the requested test and the test design are addressed under the reasons for Request 4.

**Reasons for the decision(s) related to the information under Annex IX of REACH****2. Sub-chronic toxicity study (90-days)**

6 A sub-chronic toxicity study (90 day) is an information requirement under Annex IX to REACH (Section 8.6.2.).

2.1. *Information provided to fulfil the information requirement*

7 You have submitted a testing proposal for a Sub-chronic toxicity study (90 day) according to OECD TG 408 with the Substance.

8 ECHA requested your considerations for alternative methods to fulfil the information requirement for Repeated dose 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.

9 ECHA received third party information concerning the testing proposal during the third-party consultation. A third party has indicated that the existing OECD TG 407 study with the Substance reports a NOAEL of 1000 mg/kg bw/day and appears to meet the definition of a "low toxicity substance". Also, published analysis of toxicological data in REACH registration dossiers demonstrate no added value from a 90-day study for the human risk assessment in case of a "low toxicity substance".

10 ECHA understands that the third-party comments refer to the adaptation possibility under Annex IX, Section 8.6.2., column 2, fourth indent. This adaptation specifies that a sub-chronic toxicity study (90-day) does not need to be conducted if "*the substance is unreactive, insoluble and not inhalable and there is no evidence of absorption and no evidence of toxicity in a 28-day study, particularly if such a pattern is coupled with limited human exposure*". ECHA notes that all criteria need to be met.

11 ECHA observes that the third-party comments addressed only the criterion concerning "no evidence of toxicity". The third party did not submit information regarding the other cumulative criteria (the substance is unreactive, insoluble and not inhalable and there is no evidence of absorption) under Annex IX, Section 8.6.2., column 2, fourth indent. Therefore, based on the information submitted by the third party alone, the cumulative criteria listed in Annex IX, section 8.6.2., column 2, fourth indent are not met.

12 ECHA notes that it is your responsibility to consider and justify in the registration dossier any adaptation of the information requirements in accordance with Annex IX, Section 8.6.2., column 2, fourth indent.

13 Considering the data gap in the dossier, ECHA agrees that a 90-day study is necessary.

2.2. *Specification of the study design*

14 You proposed testing in the rat. ECHA agrees with your proposal because the rat is the preferred species according to the OECD TG 408. Therefore, the study must be conducted in the rat.

15 You proposed testing by the oral route. ECHA agrees with your proposal because this route of administration is appropriate to investigate systemic toxicity; Guidance on IRs and CSA, Section R.7.5.4.3.2.

### 2.3. Outcome

- 16 Your testing proposal is accepted under Article 40(3)(a) and you are requested to conduct the test with the Substance, as specified above.

## 3. Pre-natal developmental toxicity study

- 17 A pre-natal developmental toxicity (PNDT) study (OECD TG 414) in one species is an information requirement under Annex IX to REACH (Section 8.7.2.).

### 3.1. Information provided to fulfil the information requirement

- 18 You have submitted a testing proposal for a PNDT study according to OECD TG 414 by the oral route with the Substance.
- 19 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.
- 20 ECHA agrees that a PNDT study in a first species is necessary.

### 3.2. Specification of the study design

- 21 You proposed testing in the rat as a first species. You may select between the rat or the rabbit because both are preferred species under the OECD TG 414 (ECHA Guidance R.7a, Section R.7.6.2.3.2.).
- 22 You proposed testing by the oral route. ECHA agrees with your proposal because this route of administration is the most appropriate to investigate reproductive toxicity (ECHA Guidance R.7a, Section R.7.6.2.3.2.).

### 3.3. Outcome

- 23 Your testing proposal is accepted under Article 40(3)(a) and you are requested to conduct the test with the Substance, as specified above.

## 4. Long-term toxicity testing on fish

- 24 Long-term toxicity testing on fish is an information requirement under Annex IX to REACH (Section 9.1.6.).

### 4.1. Information provided to fulfil the information requirement

- 25 You have submitted a testing proposal for a Fish, Early-Life Stage Toxicity Test (test method: OECD TG 210).
- 26 Your registration dossier does not include any information on long-term toxicity on fish.
- 27 ECHA requested your considerations for alternative methods to fulfil the information requirement for long-term toxicity on fish. 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.

28 ECHA did not receive third party information concerning the testing proposal during the third-party consultation.

29 ECHA agrees that an appropriate study on long-term toxicity on fish is needed.

#### *4.2. Test selection and study specifications*

30 The proposed Fish, Early-Life Stage Toxicity Test (test method: OECD TG 210) is appropriate to cover the information requirement for long-term toxicity on fish (Guidance on IRs and CSA, Section R.7.8.4.1.).

31 The Substance is difficult to test due to the low water solubility (10 µg/L). OECD TG 210 specifies that, for difficult to test substances, you must consider the approach described in OECD GD 23 or other approaches, if more appropriate for your substance. In all cases, the approach selected must be justified and documented. Due to the properties of Substance, it may be difficult to achieve and maintain the desired exposure concentrations. Therefore, you must monitor the test concentration(s) of the Substance throughout the exposure duration and report the results. If it is not possible to demonstrate the stability of exposure concentrations (i.e. measured concentration(s) not within 80-120% of the nominal concentration(s)), you must express the effect concentration based on measured values as described in OECD TG 210. In case a dose-response relationship cannot be established (no observed effects), you must demonstrate that the approach used to prepare test solutions was adequate to maximise the concentration of the Substance in the test solutions.

#### *4.3. Outcome*

32 Your testing proposal is accepted under Article 40(3)(a) and you are requested to conduct the 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).

All Guidance on REACH is 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**

ECHA received your testing proposal(s) on 21 June 2021 and started the testing proposal evaluation in accordance with Article 40(1).

ECHA held a third party consultation for the testing proposal(s) from 30 September 2021 until 15 November 2021. ECHA received information from third parties (see Appendix 1, Section 2).

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 amended the deadline.

The timeline indicated in the draft decision to provide the information requested was 18 months from the date of adoption of the decision. In your comments on the draft decision, you requested an extension of the timeline to 24 months. You justified your request by referring to documentation from your selected test laboratory.

Based on the information provided, ECHA has extended the deadline to 24 months.

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: Addressees 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 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;

<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.

## 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 summaries<sup>2</sup>.
- (4) 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 shall 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.

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>3</sup>.

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

<sup>3</sup> <https://echa.europa.eu/manuals>