

Helsinki, 11 March 2021

**Addressees**

Registrants of CAS1283129-18-9 -- JS listed in the last Appendix of this decision

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

21/11/2019

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

Substance name: (1S)-1,5-anhydro-2,3,4,6-tetrakis-O-(2,2-dimethylpropanoyl)-1-(3-{{[5-(4-fluorophenyl)-2-thienyl]methyl}}-4-methylphenyl)-D-glucitol

EC number: 695-878-0

CAS number: 1283129-18-9

**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), you must submit the information listed below by **19 September 2022**.

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

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

1. Sub-chronic toxicity study (90-day), oral route (Annex IX, Section 8.6.2.; test method OECD TG 408) in rats;
2. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method OECD TG 414) in a first species (rat or rabbit), oral route
3. Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.; test method EU C.20./OECD TG 211);
4. Long-term toxicity testing on fish (Annex IX, Section 9.1.6.1.; test method OECD TG 210);

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

- Appendix entitled "Reasons to request information required under Annex IX 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, VIII and IX to REACH, for registration at 100-1000 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>.

Approved<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 to request information required under Annex IX of REACH**

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

**1. Sub-chronic toxicity study (90-day), oral route (Annex IX, Section 8.6.2.)**

A sub-chronic toxicity study (90 day) is a standard information requirement in Annex IX, Section 8.6.2. to REACH.

You have submitted a testing proposal for a sub-chronic toxicity study (90 day) in rats by the oral route according to OECD TG 408 with the Substance.

ECHA notes that 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.

You proposed testing by the oral route, in rats. ECHA agrees with your proposal. According to OECD TG 408, the rat is the preferred species and the most appropriate route of administration is the oral route<sup>2</sup> since the Substance is a solid of very low vapour pressure and no uses with spray application that could potentially lead to aerosols of inhalable size, are reported.

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

**2. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.) in one species**

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

You have submitted a testing proposal for a PNDT study according to OECD TG 414 with the Substance, in the rat by the oral route.

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.

*Species*

You proposed testing with 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<sup>3</sup>.

*Route*

You proposed testing by the oral route. ECHA agrees with your proposal.

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

**3. Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.)**

<sup>2</sup> ECHA Guidance R.7a, Section R.7.5.4.3

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

Long-term toxicity testing on aquatic invertebrates is a standard information requirement in Annex IX to the REACH Regulation.

You have submitted a testing proposal (OECD TG 211) for a *Daphnia magna* Reproduction Test.

ECHA agrees that OECD TG 211 is an appropriate method to study long-term toxicity to aquatic invertebrates.

To support the testing proposal, you indicate the following justification in your technical dossier:

“To cover relevant Annex IX endpoints a testing proposal should be submitted. No acute effects were seen (see 6.1.1.,6.1.3.,6.1.5), however the substance is insoluble and no effects were seen up to water solubility. Therefore the substance is classified as chronic 4. According to the CLP guidance, the acute ecotoxicity tests do not provide a true measure of the intrinsic toxicity and therefore a long-term study with invertebrates is needed.”

ECHA agrees that OECD TG 211 is an appropriate method to study long-term toxicity to aquatic invertebrates. Please also note that Annex IX, Section 9.1., Column 2 does not allow omitting the need to submit information on long-term toxicity to aquatic invertebrates under Column 1. It must be understood as a trigger for providing further information on aquatic invertebrates if the chemical safety assessment according to Annex I indicates the need (Decision of the Board of Appeal in case A-011-2018).

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

The Substance is difficult to test due to the low water solubility (<0.01 g/L). OECD TG 211 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 211. 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 solution.

#### **4. Long-term toxicity testing on fish (Annex IX, Section 9.1.6.1.)**

“Long-term toxicity testing on fish” is an information requirement under Annex IX (Section 9.1.6.).

Under Article 40(3)(c) of REACH, ECHA may require a registrant to carry out one or more additional tests in case of non-compliance of the testing proposal with Annexes IX, X or XI of the REACH Regulation. The endpoint for aquatic toxicity at Annex IX covers long-term toxicity testing for both aquatic toxicity and fish but you have submitted a testing proposal for aquatic invertebrates only, as explained in Appendix B.3. In case of data gap for fish, it is necessary to request a long-term toxicity testing on fish as an additional test to ensure compliance with the aquatic toxicity endpoint.

You have provided the following information:

In support of your adaptation, you provided the following justification: "No acute effects were seen (see 6.1.1, 6.1.3, 6.1.5). The substance is insoluble and has a classification chronic 4. Therefore a long-term daphnia experiment will be planned (see 6.1.4) to see if there are chronic effects and vertebrate testing can thus be avoided".

We have assessed this information and identified the following issue:

A registrant may adapt the standard testing regime in accordance with the specific rules set out in column 2 of Annexes VII to X or the general rules set out in Annex XI.

Your adaptation does not refer to any of the general adaptation possibilities under Annex XI. It is therefore unclear what adaptation possibility you refer to under Annex XI. In addition, column 2 of Annex IX, Section 9.1, does not allow omitting the need to submit information on long-term toxicity to fish under Column 1 (Decision of the Board of Appeal in case A-011-2018).

Your adaptation is therefore rejected.

Consequently, under Article 40(3)(c) of the REACH Regulation, you are requested to carry out the additional test with the Substance.

#### *Study design*

To fulfil the information requirement for the Substance, the Fish, Early-life Stage Toxicity Test (test method OECD TG 210) is the most appropriate (ECHA Guidance R.7.8.2.).

For further information on difficult to test substances, see Appendix A.3.

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

### **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.

This information is needed to assess whether the Test material is relevant for the Substance.

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 C: Procedure**

ECHA started the testing proposal evaluation in accordance with Article 40(1) on 11 December 2019.

ECHA held a third party consultation for the testing proposals from 24 February 2020 until 9 April 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 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 multi-constituent 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> <http://www.oecd.org/chemicalsafety/testing/series-testing-assessment-publications-number.htm>

<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 E: 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) Data requirements to be fulfilled</b>
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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.