

Helsinki, 17 January 2023

**Addressees**

Registrant(s) of JS\_700-897-5 as listed in Appendix 3 of this decision

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

05/10/2020

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

Substance name: bis[2-(4,4-dimethylpentan-2-yl)-5,7,7-trimethyloctyl] (2E)-but-2-enedioate

EC number: 700-897-5

**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 **23 July 2024**.

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

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

1. Long-term toxicity testing on aquatic invertebrates (triggered by Annex VII, Section 9.1.1., column 2; test method: EU C.20./OECD TG 211)

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.

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 related to the information under Annex VII of REACH****1. Long-term toxicity testing on aquatic invertebrates**

1 Short-term toxicity testing on aquatic invertebrates is an information requirement under Column 1 of Annex VII to REACH (Section 9.1.1.). However, long-term toxicity testing on aquatic invertebrates must be considered (Section 9.1.1., Column 2) if the substance is poorly water soluble.

*1.1. Trigger*

2 Poorly water soluble substances require longer time to reach steady-state conditions. As a result, the short-term tests does 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 In the provided OECD TG 105 (GLP compliant, 2013), the saturation concentration of the Substance in water was determined to be  $\leq 0.085$  mg/L.

4 Therefore, the Substance is poorly water soluble and information on long-term toxicity on aquatic invertebrates must be provided.

*1.2. Information provided*

5 In your dossier, you have provided an OECD TG 202 study with the Substance (GLP compliant) but no information on long-term toxicity on aquatic invertebrates for the Substance.

6 In your comments, ECHA understands that you raised an adaptation under the first indent of Section 9.1.1., Column 2 of Annex VII of REACH.

*1.3. Assessment of the adaptation provided*

7 Under Annex VII, Section 9.1.2., Column 2, first indent, the study may be omitted if aquatic toxicity is unlikely, for instance if the Substance is highly insoluble in water. Guidance on IRs and CSA, Section R.7.8.5 explains that there is no scientific basis to define a cut off limit for solubility below which toxicity is unlikely. Therefore, the justification must demonstrate very low water solubility and low likelihood to cross biological membranes. For the latter, the indicators used for low likelihood of a high bioaccumulation potential (Guidance on IRs and CSA, Figure R.11-4) must be considered, including:

- physico-chemical indicators of hindered uptake due to large molecular size (e.g.  $D_{\max} > 17.4 \text{ \AA}$  and  $MW > 1100$  or  $MML > 4.3 \text{ nm}$ ) or high octanol-water partition coefficient ( $\log K_{ow} > 10$ ) or low potential for mass storage (octanol solubility (mg/L)  $< 0.002 \times MW$ ), and
- supporting experimental evidence of hindered uptake (no chronic toxicity for mammals and birds, no chronic ecotoxicity, no uptake in mammalian toxicokinetic studies, very low uptake after chronic exposure).

8 Your registration dossier provides:

- Information on the solubility of the Substance in water ( $\leq 0.083$  mg/L at pH 5.3 at 20° C; GLP based on OECD TG 105);

9 In your comments:

- a. You provide a statement that you consider that your Log  $K_{ow}$  of the Substance is significantly greater than 9.4.
- b. You indicate that there are 2 components that have Molecular weights < 500 Daltons. These two substances are isopropyl alcohol (60 g/mol, present at [REDACTED] and 2-(4,4-dimethylpentan-2-yl)-5,7,7-trimethyloctan-1-ol (270 g/mol, present at [REDACTED]). Based on the available data for the two components having molecular weights below 500, these are not classified for long term chronic aquatic toxicity thereby leading to the conclusion that the probability of substance EC700-897-5 having long term effects or being bioavailable in the chronic Daphnia study is negligible.
- c. You argue that the OECD TG 202 study is valid and shows no effect at water saturation.

10 However:

- a. Even though the water solubility of the Substance is low, you did not provide any new information on the low likelihood to cross biological membranes and did not substantiate your claim of a Log  $K_{ow}$  significantly greater than 9.4.
- b. You do not mention your main constituent, Fumaric diester = (E)-But-2-enedioic acid, di- {1-octanol,5,7,7-trimethyl-2-(1,3,3-trimethylbutyl)-}-ester which has a molecular weight of 621 g/mol and represents [REDACTED] of the Substance.
- c. A valid OECD TG 202 study is not indicative of unlikely toxicity for the reasons developed above, even less in case of reliability issue such as, here, absence of an adequately sensitive analytical method. In this study, you state that the Total Organic Carbon (TOC) analysis of the 100 mg/L loading rate WAF at 0 and 48 hours showed measured concentrations below the limit of quantitation (assessed as 1.0 mg Carbon/L) (no specific raw analytical results provided). You did not demonstrate the attainment of equilibrium in WAF preparation, presence of the Substance in the test medium (i.e., initial concentration), compositional stability and maintenance of exposure concentrations. In addition, you have not demonstrated that the method used is the most sensitive method available for the determination of the Substance in the concentration range used in the test.
- d. Further, guidance on IRs and CSA, Section R.7.8.5 specifies that it is not reliable to correct the measured parameters by applying an acute to chronic ratio (ACR) for the toxicity on aquatic invertebrates: '*Especially the extrapolation from acute to chronic toxicity is hardly possible. Analysis of a large number of validated data on new and existing chemicals revealed that acute data have only limited predictive value for long-term effects in aquatic ecosystems.*'
- e. Absence of classification is very poorly indicative of unlikely toxicity.

11 Therefore, your adaptation is rejected and the information requirement is still not fulfilled.

#### 1.4. Study design and test specifications

12 The Substance is difficult to test due to the low water solubility ( $\leq 0.085$  mg/L), UVCB nature and adsorptive properties ( $\log K_{ow} > 9.4$ ) of the Substance. 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 solutions.

- 13 For UVCBs, the analytical method must be adequate to monitor qualitative and quantitative changes in exposure to the dissolved fraction of the test material during the test (e.g. by comparing mass spectral full-scan GC or HPLC chromatogram peak areas or by using targeted measures of key constituents or groups of constituents).
- 14 If you decide to use the Water Accommodated Fraction (WAF) approach, in addition to the above, you must:
- use loading rates that are sufficiently low to be in the solubility range of most constituents (or that are consistent with the PEC value). This condition is mandatory to provide relevant information for the hazard and risk assessment (Guidance on IRs and CSA, Appendix R.7.8.1-1, Table R.7.8-3);
  - provide a full description of the method used to prepare the WAF (including, among others, loading rates, details on the mixing procedure, method to separate any remaining non-dissolved test material including a justification for the separation technique);
  - prepare WAFs separately for each dose level (i.e. loading rate) and in a consistent manner.

## 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**

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 03 May 2021.

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

ECHA took into account your comments and amended the deadline.

In your comments on the draft decision, you requested an extension of the deadline to provide information from 9 months to 13 or 30 months from the date of adoption of the decision. You justified your request with letters from two testing laboratories, each indicating one of these two potential extensions. The deadline of the draft decision was set based on standard practice for carrying out OECD TG tests. It has been exceptionally extended by 6 months from the standard deadline granted by ECHA to take into account currently longer lead times in contract research organisations. On this basis, ECHA has extended the deadline to 15 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 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
[REDACTED]	[REDACTED]	[REDACTED]
[REDACTED]	[REDACTED]	[REDACTED]

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>.

#### 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 the careful identification and description of the characteristics of the Tests Materials in accordance with OECD GLP (ENV/MC/CHEM(98)16) and EU Test Methods Regulation (EU) 440/2008 (Note, Annex), namely all the constituents must be identified as far as possible as well as their concentration. Also any constituents that have harmonised classification and labelling according to the CLP Regulation must be identified and quantified using the appropriate analytical methods.

With that detailed information, ECHA can confirm 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>