~~Confidential~~

Helsinki, 04 September 2023

Addressee
Registrant of Oxacycloheptadecan-2-one as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
20/04/2018

Registered substance subject to this decision ("the Substance")
Substance name: Oxacycloheptadecan-2-one
EC number/List number: 203-662-0

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 ***11 September 2025***.

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

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

1. Skin sensitisation (Annex VII, Section 8.3.; test method:)

   a) in vitro/in chemico skin sensitisation information on molecular interactions with skin proteins (OECD TG 442C), inflammatory response in keratinocytes (OECD TG 442D) and activation of dendritic cells (OECD TG 442E) (Annex VII, Section 8.3.1.); and

   b) only if the in vitro/in chemico test methods specified under point a) above are not applicable for the Substance or the results obtained are not adequate for classification and risk assessment, in vivo skin sensitisation (Annex VII, Section 8.3.2.; test method: EU B.42./OECD TG 429);

2. 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)

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

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

The reasons for the request(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 addressee of the decision and its corresponding information requirements based on registered tonnage band are listed in Appendix 3.

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[1] under the authority of Mike Rasenberg, Director of Hazard Assessment

Appendix 1: Reasons for the request(s)
Appendix 2: Procedure
Appendix 3: Addressees of the decision and their individual information requirements
Appendix 4: Conducting and reporting new tests under REACH

[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 1: Reasons for the request(s)

Contents

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Reasons related to the information under Annex VII of REACH

1. Skin sensitisation

1 Skin sensitisation is an information requirement under Annex VII, Section 8.3. Under Section 8.3., Column 1, the registrants must submit information allowing (1) a conclusion whether the substance is a skin sensitiser and (2) whether it can be presumed to have the potential to produce significant sensitisation in humans (Cat. 1A).

1.1. Information provided

2 You have provided:

i. a Human Patch Test (1972) with the Substance.

3 In addition, you have adapted this information requirement by using Annex XI, Section 1.5. (grouping of substances and read-across approach) based on experimental data from the following substances:

ii. a Local Lymph Node Assay (2009) with the source substance oxacyclohexadecan-2-one, EC 203-354-6.

4 You also provide a read-across justification document in the CSR.

5 You provide the following reasoning for the prediction of this information requirement: "The read-across source chemical oxacyclohexadecan-2-one and the target chemical oxacycloheptadecan-2-one are structural homologues of each other, with the only difference between the two being one additional carbon atom in the cyclic aliphatic chain (C15 and C16, respectively). Considering a very long aliphatic chain in both substances, the presence of additional carbon atom (CH2 moiety) in oxacycloheptadecan-2-one is not expected to influence its toxicological properties in comparison to oxacyclohexadecan-2-one. Therefore read-across from oxacyclohexadecan-2-one to oxacycloheptadecan-2-one is considered to be justified."

6 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.

1.2. Assessment of the information provided

1.2.1. Assessment whether the Substance causes skin sensitisation

1.2.1.1. Adequacy of the provided study for hazard identification

7 A study must be adequate for the corresponding information requirement. According to the Guidance on IRs and CSA, Section R.4. (page 1), "The evaluation of data quality includes assessment of adequacy of the information for hazard/risk assessment and C&L purposes". The Guidance on IRs and CSA, Section R.4. (page 1) defines adequacy as "the usefulness of data for hazard/risk assessment purposes". As a consequence, a study must be relevant for hazard assessment and for classification and labelling purposes.

8 You have provided a study according to the Human Patch Test (study i.) where 54 volunteers were exposed to 2% of the Substance. The study resulted in no indication of

skin sensitisation. You consider that due to lack of proof of proper induction, the absence of sensitisation is not sufficient to conclude that the test substance does not have skin sensitising properties. You have assigned the study as reliability 4 (non assignable).

9 The study (i.) appears to have been designed to establish safe levels for specific intended uses due to low concentration used in the study, rather than to investigate the intrinsic properties of the Substance as required for the purpose of hazard identification. ECHA agrees that the study outcome cannot be used to establish whether the Substance has the properties to induce skin sensitisation in humans.

10 Therefore, the study is rejected and does not allow to make a conclusion whether the Substance causes skin sensitisation.

1.2.1.2. Read-across adaptation rejected

11 We have identified the following issue(s) with the prediction of toxicological properties:

1.2.1.2.1. Bias from selection of the source study

12 When a grouping and read-across approach is used, the results must be adequate for the purpose of classification and labelling and risk assessment.

13 In this respect, where more than one study addressing the same effect are available on the source substance, the one giving rise to the highest concern must be used as a key study to identify the properties of the substance and to be considered for establishing DNELs and PNECs, unless justified (Sections 1.1.4. and 3.1.5., Annex I).

14 You predict the properties of the Substance from the following study: Local Lymph Node Assay (2009) with the source substance oxacyclohexadecan-2-one, EC 203-354-6 and consider the outcome negative.

15 There are available studies that gives rise to a higher concern than the study that you use to predict the properties of the Substance for the endpoint. Based on the studies available for the source substance (ECHAs dissemination site: https://echa.europa.eu/registration-dossier/-/registered-dossier/5937/7/5/1), it has been considered that the source substance is a skin sensitiser and a self-classification of skin sensitiser cat 1B has been selected. You have not provided any justification why you have selected this particular study and why other studies for the source substance has been disregarded.

16 In the absence of any justification on the selection of the study used in the prediction, your predictions may underestimate the hazards of the Substance and the results are not adequate for the purpose of classification and labelling and risk assessment.

17 As explained above, you have not established that relevant properties of the Substance can be predicted from data on the source substance. On this basis, your read-across approach under Annex XI, Section 1.5. is rejected.

18 On this basis, the information provided does not contribute to the assessment whether the Substance causes skin sensitisation.

1.2.2. No assessment of potency

19 To be considered compliant and enable a conclusion in cases where the substance is considered to cause skin sensitisation, the information provided must also allow a conclusion whether it can be presumed to have the potential to produce significant sensitisation in humans (Cat. 1A).

20 As the currently available data does not allow to conclude whether the Substance causes skin sensitisation (see section 1.2.1. above), this condition cannot be assessed.

21 Therefore, the information requirement is not fulfilled.

1.3. Specification of the study design

22 To fulfil the information requirement for the Substance, information on molecular interaction with skin proteins and inflammatory response in keratinocytes and activation of dendritic cells (OECD TG 442C and OECD TG 442D and OECD TG 442E) must be provided. Furthermore an appropriate risk assessment is required if a classification of the Substance as a skin sensitiser (Cat 1A or 1B) is warranted.

23 In case no conclusion on the skin sensitisation potency can be made for the Substance based on the existing data or newly generated *in vitro/in chemico* data, *in vivo* skin sensitisation study must be performed and the murine local lymph node assay (EU Method B.42/OECD TG 429) is considered as the appropriate study for the potency estimation.

2. Long-term toxicity testing on aquatic invertebrates

24 Short-term toxicity testing on aquatic invertebrates is an information requirement under Annex VII, Column 1, Section 9.1.1. However, under Column 2, long-term toxicity testing on aquatic invertebrates may be required by the Agency if the substance is poorly water soluble, i.e. solubility below 1 mg/L.

2.1. Triggering of the information requirement

25 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.

26 In the provided OECD TG 105 study (2016), the saturation concentration of the Substance in water was determined to be 0.103 mg/L.

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

28 In your registration dossier, you have provided a short-term toxicity study on aquatic invertebrates but no information on long-term toxicity on aquatic invertebrates for the Substance.

29 In the absence of information on long-term toxicity on aquatic invertebrates, this information requirement is not fulfilled.

30 In the comments to the draft decision ECHA understands that you claim an adaptation under Section 9.1.1, Column 2, first hyphen. You provided the following information in support:

"The substance is poorly soluble in water and biodegradable. For those reason the possibility that a long term exposure of an aquatic organism to the substance is zero in reality."

31 ECHA understands that you intend to provide a data waiver under Column 2 of Annex VII, Section 9.1.1.

32 By its term, the data waiver you provide in your comments applies to short-term toxicity testing on aquatic invertebrates. However, it is not applicable to long-term toxicity testing on aquatic invertebrates, requested on the basis of the poor water solubility of the Substance, under Column 2 of Annex VII.

33 Therefore, the information requirement is not fulfilled.

2.2. Study design and test specifications

34 The Substance is difficult to test due to the low water solubility (0.13 mg/L) and adsorptive properties (log K_{OC}: 5.58). 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.

Reasons related to the information under Annex VIII of REACH

3. Long-term toxicity testing on fish

35 Short-term toxicity testing on fish is an information requirement under Annex VIII, Column 1, Section 9.1.3. However, long-term toxicity testing on fish may be required by the Agency (Section 9.1.3., Column 2) if the substance is poorly water soluble, i.e. solubility below 1 mg/L.

3.1. Triggering of the information requirement

36 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.

37 As already explained in Request 2, the Substance is poorly water soluble and information on long-term toxicity on fish must be provided.

3.2. Information provided and its assessment

38 In your registration dossier, you have provided a short-term toxicity study on fish but no information on long-term toxicity on fish for the Substance.

39 In the absence of information on long-term toxicity on fish, this information requirement is not fulfilled.

40 In the comments to the draft decision ECHA understands that you claim an adaptation under Section 9.1.3, Column 2, first hyphen. You provided the following information in support:

"The substance is poorly soluble in water and biodegradable. For those reason the possibility that a long term exposure of an aquatic organism to the substance is zero."

41 By its term, the data waiver you provide in your comments applies to short-term toxicity testing on fish. However, it is not applicable to long-term toxicity testing on fish, requested on the basis of the poor water solubility of the Substance, under Column 2 of Annex VIII.

42 Therefore, the information requirement is not fulfilled.

3.3. Study design and test specifications

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

44 OECD TG 210 specifies that, for difficult to test substances, OECD GD 23 must be followed. As already explained above, the Substance is difficult to test. Therefore, you must fulfil the requirements described in "Study design and test specifications" under Request 2.

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).
Guidance for monomers and polymers; ECHA (2012).
Guidance on intermediates; ECHA (2010).
All guidance documents are 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 17 November 2021.

The deadline of the decision is set based on standard practice for carrying out OECD TG tests. It has been exceptionally extended by 12 months from the standard deadline granted by ECHA to take into account currently longer lead times in contract research organisations.

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

ECHA took into account your comments and did not amend the request(s) or the deadline. In the comments related to the deadline stated in this draft decision, you provided socio-economic information about the company addressed in the draft decision (i.e., the registrant of the Substance).

The REACH Regulation establishes the information requirements specified in the relevant Annexes (in the present case, Annexes VII and VIII) and grounds for adaptation (Column 2 of Annexes VII-X and Annex XI), which do not include socio-economic information.

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: Addressee(s) 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;

Registrant Name	Registration number	Highest REACH Annex applicable to you
[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[2].

(4) Under the introductory part of Annexes VII/VIII/IX/X to REACH, 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 must ensure that the data generated are adequate for hazard identification and risk assessment.

1.2. Test material

(5) 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.

(6) 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.

With that detailed information, ECHA can confirm 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 (https://echa.europa.eu/manuals).

[2] https://echa.europa.eu/practical-guides