~~Confidential~~

Helsinki, 22 February 2024

Addressee(s)
Registrant(s) of JS_C12C18unsatAKD as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
24 May 2022

Registered substance subject to this decision ("the Substance")
Substance name: (4E)-4-(C13-C17)alkylidene-3-(C12-C16)alkyloxetan-2-one
EC/List number: 939-401-9

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 ***31 May 2027***.

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.)
   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. *In vitro* gene mutation study in bacteria (Annex VII, Section 8.4.1.; test method: Bacterial reverse mutation test, OECD TG 471 (2020))

3. Long-term toxicity testing on aquatic invertebrates also requested below (triggered by Annex VII, Section 9.1.1., column 2)

4. Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.; test method: EU C.3./OECD TG 201)

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

5. *In vitro* micronucleus study (Annex VIII, Section 8.4.2., test method: OECD TG 487). The aneugenic potential of the Substance must be assessed with an additional control group for aneugenicity on top of the control group for clastogenicity, if the Substance induces an increase in the frequency of micronuclei

6. Only if a negative result in Annex VII, Section 8.4.1. and Annex VIII, Section 8.4.2. is obtained, *in vitro* gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.; test method: EU B.17./OECD TG 476 or EU B.67./OECD TG 490)

7. Justification for an adaptation of the short-term repeated dose toxicity study (28 days) (Annex VIII, Section 8.6.1., Column 2) based on the request 8. below.

   or in case the sub-chronic toxicity study (90 days) is not requested:

   Short-term repeated dose toxicity (28 days), oral route (Annex VIII, Section 8.6.1.; test method: OECD TG 407) in rats

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

8. Sub-chronic toxicity study (90 days), oral route (Annex IX, Section 8.6.2.; test method: OECD TG 408) in rats

9. 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)

10. Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.; test method: EU C.20./OECD TG 211)

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 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[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

Reasons common to several requests

0.1. Read-across adaptation rejected

1 You have adapted the following standard information requirements by using grouping and read-across approach under Annex XI, Section 1.5.:

- Skin sensitisation (Annex VII, Section 8.3.)
- *In vitro* gene mutation study in bacteria (Annex VII, Section 8.4.1.)
- *In vitro* micronucleus study (Annex VIII, Section 8.4.2.)
- *In vitro* gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.)
- Sub-chronic toxicity study (90-day), (Annex IX, Section 8.6.2.)
- Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)
- Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.)
- Long-term toxicity to aquatic invertebrates (Annex IX, Section 9.1.5.)

2 ECHA has considered the scientific and regulatory validity of your read-across approach(es) in general before assessing the specific standard information requirements in the following sections.

3 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. 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.

4 Additional information on what is necessary when justifying a read-across approach can be found in the Guidance on IRs and CSA, Chapter R.6. and related documents (RAAF, 2017; RAAF UVCB, 2017).

0.1.1. Predictions for (eco)toxicological properties

5 You provide a read-across justification document in IUCLID Section 13.

6 You predict the properties of the Substance from information obtained from the following source substance(s):

- Solid AKD, 2-Oxetanone, 3-C14-16-alkyl-4-C15-17-alkylidene derivs. (AKDs) EC 308-760-8, (source substance 1);
- Behenic AKD, PMC D-532, EC 401-210-9, (source substance 2);
- Surrogate for Solid AKD, Reaction product containing 2-Oxetanone, 3-(C14-16 and C16-unsatd. branched and linear alkyl) 4-(C15-17 and C17-unsatd. branched and linear alkylidene) derivs. CAS 849705-80-2 (source substance 3).

7 You provide the following reasoning for the prediction of toxicological properties: ”Based on their chemical structure and similar physico-chemical properties, as well as availability of data, the following substances are considered suitable to be used as source chemicals (analogues) for the REACH registration of liquid AKD ”.

8 ECHA understands that your read-across hypothesis assumes that different compounds have the same type of effects. You predict the properties of your Substance to be quantitatively equal to those of the source substance.

9 Annex XI, Section 1.5. requires that whenever read-across is used adequate and reliable documentation of the applied method must be provided. Such documentation must include an explanation why the properties of the Substance may be predicted from other substances in the group, i.e. a read-across hypothesis. This hypothesis should be based on recognition of the structural similarities and differences between the substances (Guidance on IRs and

CSA, Section R.6.).It should explain why the differences in the chemical structures should not influence the toxicological properties or should do so in a regular pattern, taking into account that variations in chemical structure can affect both toxicokinetics (uptake and bioavailability) and toxicodynamics (e.g. interactions with receptors and enzymes) of substances (Guidance on IRs and CSA, Section R.6.2.1.3.).

10 Your read-across hypothesis is only based on structural similarities and similarities in the physico-chemical properties of the source substance(s). You consider that these elements are a sufficient basis for predicting the toxicological properties of the Substance.

11 You have not substantiated how structural and physico-chemical similarity alone would explain similarity in the predicted endpoint(s) and thus be sufficient to justify the (eco)toxicological predictions.

12 In your read-across justification document you have stated: 'Structurally the source and target substances are unsaturated lactones with similar physico-chemical properties and differ only slightly in size of the alkyl chains and have no additional unsaturation (both sources) or one unsaturation in the alkyl chain (target)'. There is no assessment how these structural differences may impact the prediction.

13 Physico-chemical similarity alone does not necessarily lead to predictable or similar toxicological properties. You have not provided a well-founded hypothesis to establish a reliable prediction for an (eco)toxicological property, explaining why the structural differences do not influence toxicokinetics and toxicodynamics of the substances, and thus why the properties of the Substance may be predicted from information on the source substance(s). ECHA concludes that you have not addressed the structural differences between the source substances and the target substance and did not explain, why those differences would not lead to differences in the (eco)toxicity profile of target and source substances. These differences could lead to a different reactivity and potentially to a different (eco)toxicity profile.

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

14 Annex XI, Section 1.5. requires that whenever read-across is used adequate and reliable documentation of the applied method must be provided. Such documentation must provide supporting information to scientifically justify the read-across explanation for prediction of properties. The set of supporting information should strengthen the rationale for the read-across in allowing to verify the crucial aspects of the read-across hypothesis and establishing that the properties of the Substance can be predicted from the data on the source substance(s) (Guidance on IRs and CSA R.6., Section R.6.2.2.1.f.).

15 Supporting information must include supporting information (e.g. bridging studies) to compare properties of the substances.

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

17 For the source substances, you provide the study used in the prediction in the registration dossier. Apart from that study, your read-across justification or the registration dossier does not include any robust study summaries or descriptions of data for the Substance that would confirm that both substances cause the same type of effects. In particular, you provided no study on the target substance relevant to the adapted information requirements with e.g. lower shorter exposure duration (bridging study). Furthermore, the

relevant physico-chemical properties, that are not available as experimental studies but only modelled, did not take into account all relevant constituents (i.e. the lower end of the range of constituents for the target substance, the upper end for the sources).

18 In the absence of such information, 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 scientifically justify the read-across.

0.1.1.2. Read-across hypothesis/prediction contradicted by existing data

19 Annex XI, Section 1.5. requires that whenever read-across is used adequate and reliable documentation of the applied method must be provided. Such documentation must provide supporting information to scientifically justify the read-across explanation for prediction of properties. The set of supporting information must strengthen the rationale for the read-across in allowing to verify the crucial aspects of the read-across hypothesis and establishing that the properties of the Substance can be predicted from the data on the source substance(s) (Guidance on IRs and CSA R.6, Section R.6.2.2.1.f.).

20 The observation of differences in the toxicological properties between the source substance(s) and the Substance would contradict the hypothesis that the properties of the Substance can be predicted from the data on the source substance(s). An explanation why such differences do not affect the read-across hypothesis must to be provided and supported by scientific evidence.

21 As indicated above, your read-across hypothesis is based on the assumption that the structurally similar Substance and source substance(s) cause the same type of effect(s). On that basis, you predict that the Substance has no hazardous properties and should not be classified.

22 However, the results of the information on repeated dose toxicity obtained with the source substance(s) deviate from your prediction of properties of the Substance. Specifically, positive results are observed in the two repeated dose toxicity studies (OECD TG 408 and 422) conducted with the source substance 1. show adverse effects in blood system and liver, inflammatory changes in a variety of tissues in both sexes which may have an impact on classification as STOT RE. You have not addressed these results in your read-across justification.

23 The available set of data on the on the source substances indicates adverse effects in the (eco)toxicological properties of the substances. This contradicts your read-across prediction of no hazardous properties for the Substance and no classification.

0.1.2. Conclusion

24 Based on the above, you have not established that relevant properties of the Substance can be predicted from data on the source substance(s). Your read-across approach under Annex XI, Section 1.5. is rejected.

Reasons related to the information under Annex VII of REACH

1. Skin sensitisation

25 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

26 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:

(i) A guinea pig maximisation test (2002) with the source substance 2-Oxetanone, 3-C14-16-alkyl-4-C15-17-alkylidene derivs. (AKDs) EC 308-760-8, Solid AKD

1.2. Assessment of the information provided

1.2.1. Assessment whether the Substance causes skin sensitisation

1.2.1.1. Read-across adaptation rejected

27 As explained under Reasons common to several requests, your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5. is rejected.

28 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

29 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).

30 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.

31 Therefore, the information requirement is not fulfilled.

1.3. Specification of the study design

32 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.

33 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.

34 In your comments on the initial draft decision you agree with the request.

2. *In vitro* gene mutation study in bacteria

35 An in vitro gene mutation study in bacteria is an information requirement under Annex VII, Section 8.4.1.

2.1. Information provided

36 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:

(i) an *in vitro* gene mutation study in bacteria (2019) with the source substance 2-Oxetanone, 3-C14-16-alkyl-4-C15-17-alkylidene derivs. (AKDs) EC 308-760-8, Solid AKD,

(ii) an *in vitro* gene mutation study in bacteria (2004) with the source substance PMC D-53, EC 401-210-9, Behenic AKD.

(iii) an *in vitro* gene mutation study in bacteria (2004) with the source substance PMC D-532, EC 401-210-9, Behenic AKD.

2.2. Assessment of the information provided

2.2.1. Read-across adaptation rejected

37 As explained under Reasons common to several requests, your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5. is rejected.

38 Therefore, the information requirement is not fulfilled.

2.3. Specification of the study design

39 To fulfil the information requirement for the Substance, the in vitro gene mutation study in bacteria (OECD TG 471) is considered suitable.

40 In your comments on the initial draft decision you agree with the request.

3. Long-term toxicity testing on aquatic invertebrates

41 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.

3.1. Triggering of the information requirement

42 In the provided QSAR estimation (2022), the saturation concentration of the Substance in water was calculated to be 3.94e-10 mg/L (WSKOWwin v1.42- Estimation methodology).

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

3.2. Information requirement not fulfilled

44 The information provided, its assessment and the specifications of the study design are addressed under request 10.

4. Growth inhibition study aquatic plants

45 Growth inhibition study on aquatic plants is an information requirement under Annex VII to REACH (Section 9.1.2.).

4.1. Information provided

46 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:

(i) Growth inhibition study on aquatic plants/algae with the source substance Solid AKD, 2-Oxetanone, 3-C14-16-alkyl-4-C15-17-alkylidene derivs. (AKDs) EC 308-760-8, (source substance 1);

(ii) Growth inhibition study on aquatic plants/algae (2001) with the source substance Behenic AKD, PMC D-532, EC 401-210-9, (source substance 2).

4.2. Assessment of the information provided

4.2.1. Read-across adaptation rejected

47 As explained in Section 0.1., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5. is rejected.

48 Therefore, the information requirement is not fulfilled.

49 In your comments on the initial draft decision you agree with the request.

4.3. Study design

50 The Substance is difficult to test due to the low water solubility (3.94e-10 mg/L) and/or adsorptive properties (log K_{oc} 9.1). OECD TG 201 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 201. 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.

51 For multi-constituents/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).

52 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.

Reasons related to the information under Annex VIII of REACH

5. *In vitro* micronucleus study

53 An in vitro cytogenicity study in mammalian cells or an in vitro micronucleus study is an information requirement under Annex VIII, Section 8.4.2.

5.1. Information provided

54 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:

(i) an *in vitro* cytogenicity study in mammalian cells (2003) with the source substance 2-Oxetanone, 3-C14-16-alkyl-4-C15-17-alkylidene derivs. (AKDs) EC 308-760-8, Solid AKD,

(ii) an *in vitro* cytogenicity study in mammalian cells (2004) with the source substance PMC D-532, EC 401-210-9, Behenic AKD.

5.2. Assessment of the information provided

5.2.1. Read-across adaptation rejected

55 As explained under Reasons common to several requests, your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5. is rejected.

56 Therefore, the information requirement is not fulfilled.

5.3. Specification of the study design

57 According to the Guidance on IR & CSA, Section R.7.7.6.3., either the in vitro mammalian chromosomal aberration ("CA") test (test method OECD TG 473) or the in vitro mammalian cell micronucleus ("MN") test (test method OECD TG 487) can be used to investigate chromosomal aberrations in vitro. However, while the MN test detects both structural chromosomal aberrations (clastogenicity) and numerical chromosomal aberrations (aneuploidy), the CA test detects only clastogenicity, as OECD TG 473 is not designed to measure aneuploidy (see OECD TG 473, paragraph 2).Therefore, you must perform the MN test (test method OECD TG 487), as it enables a more comprehensive investigation of the chromosome damaging potential in vitro.Moreover, in order to demonstrate the ability of the study to identify clastogens and aneugens, you must include two concurrent positive controls, one known clastogen and one known aneugen [1] (OECD TG 487, paragraphs 33 to 35).

5.3.1. Assessment of aneugenicity potential

58 If the result of the MN test is positive, i.e. your Substance induces an increase in the frequency of micronuclei, you must assess the aneugenic potential of the Substance.

59 In line with the OECD TG 487 (paragraph 4), you should use one of the centromere labelling or hybridisation procedures to determine whether the increase in the number of micronuclei is the result of clastogenic events (i.e. micronuclei contain chromosome fragment(s)) and/or aneugenic events (i.e. micronuclei contain whole chromosome(s)).

[1] According to the TG 487 (2016) "At the present time, no aneugens are known that require metabolic activation for their genotoxic activity" (paragraph 34).

60 In your comments on the initial draft decision you agree with the request.

6. *In vitro* gene mutation study in mammalian cells

61 An in vitro gene mutation study in mammalian cells is an information requirement under Annex VIII, Section 8.4.3., in case of a negative result in the in vitro gene mutation test in bacteria and the in vitro cytogenicity test.

6.1. Triggering of the information requirement

62 Your dossier contains an adaptation for an in vitro gene mutation study in bacteria, and an adaptation for an in vitro cytogenicity study in mammalian cells or in vitro micronucleus study.

63 The information for the in vitro gene mutation study in bacteria and for the in vitro cytogenicity study in mammalian cells or in vitro micronucleus study provided in the dossier are rejected for the reasons provided in requests 2 and 5.

64 The result of the requests for an in vitro gene mutation study in bacteria and for an in vitro cytogenicity study in mammalian cells will determine whether the present requirement for an in vitro mammalian cell gene mutation study in accordance with Annex VIII, Section 8.4.3. is triggered.

65 Consequently, you are required to provide information for this information requirement, if the in vitro gene mutation study in bacteria and the in vitro micronucleus study provides a negative result.

6.2. Information provided

66 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:

(i) an *in vitro* gene mutation study in mammalian cells (2020) with the source substance 2-Oxetanone, 3-C14-16-alkyl-4-C15-17-alkylidene derivs. (AKDs) EC 308-760-8, Solid AKD,

(ii) an *in vitro* gene mutation study in mammalian cells (2004) with the source substance PMC D-532, EC 401-210-9, Behenic AKD.

6.3. Assessment of the information provided

6.3.1. Read-across adaptation rejected

67 As explained under Reasons common to several requests, your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5. is rejected.

68 In the comments to the draft decision you reiterate your intention to adapt the information requirement according to Annex XI, Section 1.5. You present a strategy relying on the generation of additional supporting information on the Substance and on the analogue substances without supporting information. You indicate your intention to provide this in a future update of your registration dossier.

69 ECHA acknowledges your intentions to improve the (eco)toxicological profile of the Substance and your plans to refine your read-across approach. As indicated in your comments, this strategy relies essentially on data which is yet to be generated, therefore no conclusion on the compliance can currently be made.

70 Therefore, the information requirement is not fulfilled.

6.4. Specification of the study design

71 To fulfil the information requirement for the Substance, either the in vitro mammalian cell gene mutation tests using the hprt and xprt genes (OECD TG 476) or the thymidine kinase gene (OECD TG 490) are considered suitable.

7. Short-term repeated dose toxicity (28 days)

72 A short-term repeated dose toxicity study (28 days) is an information requirement under Annex VIII, Section 8.6.1. This information may take the form of a study record or a valid adaptation in accordance with either a specific adaptation rule under Column 2 or a general adaptation rule under Annex XI.

7.1. Information provided

73 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:

(i) a sub-chronic toxicity study (2004) with the source substance 2-Oxetanone, 3-C14-16-alkyl-4-C15-17-alkylidene derivs. (AKDs) EC 308-760-8, Solid AKD,

(ii) a sub-acute toxicity study (2002) with the source substance 2-Oxetanone, 3-C14-16-alkyl-4-C15-17-alkylidene derivs. (AKDs) EC 308-760-8, Solid AKD.

7.2. Assessment of the information provided

7.2.1. Read-across adaptation rejected

74 As explained in Section 0.1., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5. is rejected.

75 Therefore, the information requirement is not fulfilled.

7.3. Study design

76 Following the criteria provided in Annex VIII, Section 8.6.1., Column 2, and considering the Guidance on IRs and CSA, Section R.7.5.6.3.1., the oral route is the most appropriate route of administration to investigate repeated dose toxicity of the Substance, because Substance is a liquid with very low vapour pressure (based on modelling).

77 According to the OECD TG 407, the rat is the preferred species.

78 Therefore, the study must be performed according to the OECD TG 407, in rats and with oral administration of the Substance.

7.4. Justification for an adaptation of the short-term repeated dose toxicity study (Annex VIII, Section 8.6.1., Column 2)

79 The present decision requests the registrants concerned to generate and submit a reliable sub-chronic toxicity study (90 days) (see request 8.).

80 According to Annex VIII, Section 8.6.1., Column 2 and to prevent unnecessary animal testing, a short-term toxicity study (28 days) does not need to be conducted. Therefore, to comply with the information requirement in Annex VIII, Section 8.6.1., you are requested to provide a justification for adaptation, as provided in Annex VIII, Section 8.6.1., Column 2.

81 In case the adopted decision no longer contains a request for a 90-day study, you are required to provide a 28-day study.

82 Therefore, you are requested to either submit:

- a justification for the adaptation according to Annex VIII, Section 8.6.1., Column 2, based on request 8.; or
- a 28-day study as per the study design described in 7.3. in case the 90-day study is not requested in the adopted decision.

83 In your comments on the initial draft decision you agree with the request.

Reasons related to the information under Annex IX of REACH

8. Sub-chronic toxicity study (90 days)

84 A sub-chronic toxicity study (90 days) is an information requirement under Annex IX, Section 8.6.2.

8.1. Information provided

85 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:

(i) a sub-chronic toxicity study (2004) with the source substance 2-Oxetanone, 3-C14-16-alkyl-4-C15-17-alkylidene derivs. (AKDs) EC 308-760-8, Solid AKD,

(ii) a sub-acute toxicity study (2002) with the source substance 2-Oxetanone, 3-C14-16-alkyl-4-C15-17-alkylidene derivs. (AKDs) EC 308-760-8, Solid AKD.

8.2. Assessment of the information provided

8.2.1. Read-across adaptation rejected

86 As explained under Reasons common to several requests, your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5. is rejected.

87 In the comments to the draft decision you reiterate your intention to adapt the information requirement according to Annex XI, Section 1.5. You present a strategy relying on the generation of additional supporting information on the Substance and on the analogue substances without supporting information. You indicate your intention to provide this in a future update of your registration dossier.

88 ECHA acknowledges your intentions to improve the (eco)toxicological profile of the Substance and your plans to refine your read-across approach. As indicated in your comments, this strategy relies essentially on data which is yet to be generated, therefore no conclusion on the compliance can currently be made.

89 Therefore, the information requirement is not fulfilled.

8.3. Specification of the study design

90 Following the criteria provided in Annex IX, Section 8.6.2., Column 2, and considering the Guidance on IRs and CSA, Section R.7.5.6.3.2., the oral route is the most appropriate route of administration to investigate repeated dose toxicity of the Substance, because the Substance is a liquid with very low vapour pressure (based on modelling).

91 According to the OECD TG 408, the rat is the preferred species.

92 Therefore, the study must be performed in rats according to the OECD TG 408 with oral administration of the Substance.

9. Pre-natal developmental toxicity study in one species

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

9.1. Information provided

94 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:

(i) a pre-natal developmental toxicity study in rabbit (2005). Performed with source substance Reaction product containing 2-Oxetanone, 3-(C14-16 and C16-unsatd. branched and linear alkyl) 4-(C15-17 and C17-unsatd. branched and linear alkylidene) derivs. CAS 849705-80-2. The source substance is presented as a surrogate substance for Solid AKD,

(ii) a pre-natal developmental toxicity study in rats (2020) with the source substance 2-Oxetanone, 3-C14-16-alkyl-4-C15-17-alkylidene derivs. (AKDs) EC 308-760-8, Solid AKD,

(iii) a pre-natal developmental toxicity study in rabbit (2020) with the source substance 2-Oxetanone, 3-C14-16-alkyl-4-C15-17-alkylidene derivs. (AKDs) EC 308-760-8, Solid AKD.

9.2. Assessment of the information provided

9.2.1. Read-across adaptation rejected

95 As explained under Reasons common to several requests, your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5. is rejected.

96 In the comments to the draft decision you reiterate your intention to adapt the information requirement according to Annex XI, Section 1.5. You present a strategy relying on the generation of additional supporting information on the Substance and on the analogue substances without supporting information. You indicate your intention to provide this in a future update of your registration dossier.

97 ECHA acknowledges your intentions to improve the (eco)toxicological profile of the Substance and your plans to refine your read-across approach. As indicated in your comments, this strategy relies essentially on data which is yet to be generated, therefore no conclusion on the compliance can currently be made.

98 Therefore, the information requirement is not fulfilled.

9.3. Specification of the study design

99 A PNDT study according to the test method OECD TG 414 should be performed in rats or rabbits as preferred species.

100 As the Substance is a liquid, the study must be conducted with oral administration of the Substance (Annex IX, Section 8.7.2., Column 1).

101 Therefore, the study must be conducted in rats or rabbits with oral administration of the Substance.

10. Long-term toxicity testing on aquatic invertebrates

102 Long-term toxicity testing on aquatic invertebrates is an information requirement under Annex IX to REACH (Section 9.1.5.).

10.1. Information provided

103 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:

(i) a long-term toxicity study on *Daphnia magna* (2001) with the source substance Solid AKD, 2-Oxetanone, 3-C14-16-alkyl-4-C15-17-alkylidene derivs. (AKDs) EC 308-760-8, (source substance 1);

(ii) a long-term toxicity study on *Daphnia magna* with the source substance Behenic AKD, PMC D-532, EC 401-210-9, (source substance 2).

10.2. Assessment of the information provided

10.2.1. Read-across adaptation rejected

104 As explained in Section 0.1., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5. is rejected.

105 In the comments to the draft decision you reiterate your intention to adapt the information requirement according to Annex XI, Section 1.5. You present a strategy relying on the generation of additional supporting information on the Substance and on the analogue substances without supporting information. You indicate your intention to provide this in a future update of your registration dossier.

106 ECHA acknowledges your intentions to improve the (eco)toxicological profile of the Substance and your plans to refine your read-across approach. As indicated in your comments, this strategy relies essentially on data which is yet to be generated, therefore no conclusion on the compliance can currently be made.

107 Therefore, the information requirement is not fulfilled.

10.3. Study design

108 OECD TG 211 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" under request 4.3.

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 22 November 2022.

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).

As a result of one or more changes of registration tonnage band or registration type, the request for a pre-natal developmental toxicity study in a second species was removed from the decision. The requests for a long term toxicity on fish study were removed as a final decision (dated 30/03/2023) has been published under testing proposal evaluation.

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 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 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[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

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

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

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,
- The reported composition must also include other parameters relevant for the property to be tested.

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 (https://echa.europa.eu/manuals).