~~Confidential~~

Helsinki, 04 September 2023

Addressee(s)
Registrant(s) of JS_713-95-1_[redacted] as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
17/01/2022

Registered substance subject to this decision ("the Substance")
Substance name: Dodecan-5-olide
EC/List number: 211-932-4

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

2. Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.; test method: EU C.2./OECD TG 202)

3. 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

4. *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

5. 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)

6. Short-term repeated dose toxicity (28 days) (Annex VIII, Section 8.6.1.) by oral route, in rats, to be combined with the screening for reproductive/developmental toxicity requested below

7. Screening study for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.; test method: EU B.64/OECD TG 422) by oral route, in rats

8. Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.; test method: EU C.1./OECD TG 203)

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.

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)

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Reasons common to several requests

0. Weight of evidence adaptation rejected

1 You have adapted the following standard information requirements by using Annex XI, Section 1.2. (weight of evidence) for the following standard information requirements:

- In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.)
- In vitro cytogenicity study in mammalian cells or in vitro micronucleus study (Annex VIII, Section 8.4.2.)
- In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.)
- Short-term repeated dose toxicity (28 day), (Annex VIII, Section 8.6.1.)
- Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)
- Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.)
- Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.)
- Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.)

2 You have provided experimental data on:

- Oxacycloheptadec-10-ene-2- one, EC 249-120-7;
- Docosanoic acid, EC 204-010-8;
- Decanal, EC 203-957-4;
- Decan-5-olide EC 211-889-1;
- Dodecan-1-ol, ethoxylated EC 500-002-6.
- Octan-1-ol EC 203-917-6
- Hexan-1-ol EC 203-852-3

3 The test material used is different than the Substance. Therefore, the studies conducted with this substance (hereafter referred to as the "source substance") will be evaluated as a read-across adaptation under Annex XI, Section 1.5 of REACH.

4 Annex XI, Section 1.2. states that there may be sufficient weight of evidence from several independent sources of information enabling, through a reasoned justification, a conclusion on the information requirement, while the information from each single source alone is insufficient to fulfil the information requirement.

5 The justification must have regard to the information that would otherwise be obtained from the study that must normally be performed for this information requirement.

6 According to ECHA Guidance R.4, a weight of evidence adaptation involves an assessment of the relative values/weights of the different sources of information submitted. The weight given is based on the reliability of the data, consistency of results/data, nature and severity of effects, and relevance and coverage of the information for the given regulatory information requirement. Subsequently, relevance, reliability, coverage, consistency and results of these sources of information must be balanced in order to decide whether they together provide sufficient weight to conclude on the corresponding information requirement.

0.1. Lack of documentation justifying the weight of evidence adaptation

7 Annex XI, Section 1.2. requires that adequate and reliable documentation is provided to describe a weight of evidence approach. This documentation must include robust study summaries of the studies used as sources of information and a justification explaining why the sources of information together provide a conclusion on the information requirement.

8 You have not included a justification for your weight of evidence adaptation for each of the relevant information requirement, which would include an adequate and reliable (concise) documentation as to why the sources of information provide sufficient weight to conclude on the information requirements under consideration.

9 In spite of this critical deficiency, ECHA has nevertheless assessed the validity of your adaptation.

10 Your weight of evidence approach has deficiencies that are common to all information requirements under consideration and also deficiencies that are specific for these information requirements individually.

11 The common deficiencies are set out here, while the specific ones are set out under the information requirement concerned in the requests below.

0.2. Read-across adaptation rejected

12 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.

13 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.

14 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).

0.2.1. Absence of read-across documentation

15 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 information on the source substance(s).

16 In your registration dossier, you have provided robust study summaries for studies conducted with other substances than the Substance in order to comply with the REACH information requirements. However, you have not provided documentation as to why this information is relevant for the Substance and thus why the properties of the Substance may be predicted from information on the source substance(s).

17 In your comments to the initial draft decision you provided a read-across justification document "[redacted]", which addresses the lack of justification for these information requirements.

18 In the absence of justification documents for all source substances and all information requirements (except 28-day study and screening study, on one of the source substances),

the properties of the Substance cannot be reliably predicted from the data on the source substance(s).

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

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 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.).

20 Supporting information must include, for example, toxicokinetic information on the formation of the common compound or supporting information/bridging studies to compare properties of the category members.

21 In this context, relevant, reliable and adequate information allowing to compare the properties of the 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).

22 For the source substances, you provide the study used in the prediction in the registration dossier. Apart from those studies, your registration dossier does not include any robust study summaries or descriptions of data for the Substance that would confirm that the source and target substances cause the same type of effects.

23 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.

0.2.3. Conclusion on the read-across approach

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 is not reliable.

Reasons related to the information under Annex VII of REACH

1. *In vitro* gene mutation study in bacteria

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

1.1. Information provided

26 You have adapted this information requirement by using Annex XI, Section 1.2. (weight of evidence) based on experimental data from the following substances:

(i) an *in vitro* gene mutation study in bacteria (2019) with the source substance Oxacycloheptadec-10-ene-2- one, EC 249-120-7;

(ii) an *in vitro* gene mutation study in bacteria (2018) with the source substance Docosanoic acid, EC / 204-010-8.

1.2. Assessment of the information provided

27 As explained under Reasons common to several requests the weight of evidence adaptation already has critical deficiencies.

28 In addition, as explained under Reasons common to several request, the adaptation must fulfil the information requirement based on relevant and reliable sources of information. These sources of information must provide sufficient weight to conclude that the Substance has or has not the dangerous property investigated by the required study.

29 Relevant information that can be used to support weight of evidence adaptation for information requirement of Section 8.4.1 at Annex VII include:

- Detection and quantification of gene mutations (base pairs, substitution or frame shift) in cultured bacteria including data on the number of revertant colonies; and
- Data provided on 5 bacterial strains: four strains of *S. typhimurium* (TA98; TA100; TA1535; TA1537 or TA97a or TA97) and one strain which is either *S. typhimurium* TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101).

30 Both sources of information (i) and (ii) provide such information.

1.2.1. Reliability of the provided information

31 The information from (i) and (ii) with read across source substances is already rejected under Reasons common to several requests. Therefore they cannot be used as part of the weight of evidence adaptation.

1.2.2. Conclusion

32 In summary, the sources of information (i) and (ii) provide relevant information on in vitro gene mutation study in bacteria. However, these sources of information have significant reliability issues as described above and cannot contribute to the conclusion on the information requirement for in vitro gene mutation study in bacteria.

33 It is not possible to conclude, based on any source of information alone or considered together, on the information requirement for *in vitro* gene mutation study in bacteria.

34 Based on the above, your adaptation is rejected.

35 Therefore, the information requirement is not fulfilled.

1.3. Comments on the draft decision

36 In your comments to the draft decision you agree to perform the requested study.

1.4. Specification of the study design

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

2. Short-term toxicity testing on aquatic invertebrates

38 Short-term toxicity testing on aquatic invertebrates is an information requirement under Annex VII to REACH (Section 9.1.1.).

2.1. Information provided

39 You have adapted this information requirement by using Annex XI, Section 1.2. (weight of evidence) based on experimental data from the following substances:

(i) a short-term toxicity study on aquatic invertebrates (*Gammarus italicus*) (2006) with the source substance dodecan-1-ol, ethoxylated EC 500-002-6.

(ii) a short-term toxicity study on *daphnia magna* (2013) with the source substance octan-1-ol EC 203-917-6 .

2.2. Assessment of the information provided

40 As explained under Reasons common to several requests the weight of evidence adaptation already has critical deficiencies.

41 In addition, as explained under Reasons common to several request, the adaptation must fulfil the information requirement based on relevant and reliable sources of information. These sources of information must provide sufficient weight to conclude that the Substance has or has not the dangerous property investigated by the required study.

42 Relevant information that can be used to support weight of evidence adaptation for information requirement of Section 9.1.1. at Annex VII include:

- the concentration of the test material leading to the immobilisation of 50% of the test organisms (aquatic invertebrates) at the end of the test

43 This information is covered by OECD TG 202.

44 Both sources of information provide such information.

2.2.1. Reliability of the provided information

45 The information from (i) and (ii) with read across source substances is already rejected under Reasons common to several requests. Therefore they cannot be used as part of the weight of evidence adaptation.

2.2.2. The provided studies do not meet the specifications of the test guideline(s)

46 OECD TG 202 provide the following specifications:

Validity criteria

a) the percentage of immobilised daphnids is ≤ 10% at the end of the test in the controls (including the solvent control, if applicable);

b) the dissolved oxygen concentration is ≥ 3 mg/L in all test vessels at the end of the test.

Technical specifications impacting the sensitivity/reliability of the test

c) the test duration is 48 hours or longer;

d) *Daphnia magna* (or other suitable Daphnia species) is used as test species;

e) at least five concentrations are tested. If less than five concentrations are included in the test design a justification must be provided.

Characterisation of exposure

f) analytical monitoring must be conducted. A reliable analytical method for the quantification of the test material in the test solutions with reported specificity, recovery efficiency, precision, limits of determination (i.e. detection and quantification) and working range must be available.

47 In study (i) and (ii):

Validity criteria

g) There is no information on the percentage of immobilised daphnids at the end of the test in the controls;

h) There is no information on the dissolved oxygen concentration at the end of the test.

Technical specifications impacting the sensitivity/reliability of the test

i) the test duration was 24 hours;

j) the test (only study i) was conducted on *Gammarus italicus*;

k) There is no information on the concentrations that were tested.

Characterisation of exposure

l) no analytical monitoring of exposure was conducted.

48 Based on the above,

- it is not possible to verify that the validity criteria of OECD TG 202 are met
- there are critical methodological deficiencies resulting in the rejection of the study results. More, specifically information on analytical monitoring and analytical method is missing. Without analytical monitoring, it is not possible to determine whether and to what extent the tested organisms were exposed to the test material and thus the study is not reliable. In study (i) there is no justification explaining why another species was used instead of a *Daphnia* species. Furthermore, both studies are not reliable as the test duration was only 24 hours.

49 On this basis, the specifications of OECD TG 202 are not met.

2.2.3. Conclusion

50 In summary, the sources of information (i) and (ii) provide relevant information on short-term toxicity testing on aquatic invertebrates. However, these sources of information have

significant reliability issues as described above and cannot contribute to the conclusion on the information requirement for short-term toxicity testing on aquatic invertebrates.

51 It is not possible to conclude, based on any source of information alone or considered together, on the information requirement for *s*hort-term toxicity testing on aquatic invertebrates.

52 Based on the above, your adaptation is rejected.

2.3. Comments on the draft decision

53 In your comments to the draft decision and in your updated dossier you provided new information, a short-term toxicity study (2022) on aquatic invertebrates on the Substance.

54 We have assessed this information and identified the following issue:

55 Toxicological and eco-toxicological tests and analyses on substances must be carried out in compliance with the principles of good laboratory practice (GLP) provided for in Directive 2004/10/EC or other international standards recognised as being equivalent by the Commission or ECHA and with the provisions of Directive 86/609/EEC, if applicable (Article 13(4) of REACH). According to Article 141(2), Article 13 applies from 1 June 2008.

56 Based on the information in your dossier, the study you provided is not performed in compliance with GLP.

57 Therefore, the information requirement is not fulfilled.

3. Growth inhibition study aquatic plants

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

3.1. Information provided

59 You have adapted this information requirement by using Annex XI, Section 1.2. (weight of evidence) based on experimental data from the following substances:

(i) Growth inhibition study on aquatic plants/algae (2006) with the source substance dodecan-1-ol, ethoxylated EC 500-002-6;

(ii) Growth inhibition study on aquatic plants/algae (2018) with the source substance hexan-1-ol EC 203-852-3.

3.2. Assessment of the information provided

60 As explained under Reasons common to several requests the weight of evidence adaptation already has critical deficiencies.

61 In addition, as explained under Reasons common to several request, the adaptation must fulfil the information requirement based on relevant and reliable sources of information. These sources of information must provide sufficient weight to conclude that the Substance has or has not the dangerous property investigated by the required study.

62 Relevant information that can be used to support weight of evidence adaptation for information requirement of Section 9.1.2. at Annex VII include:

- the concentration in the test substance leading to a 50 % inhibition of growth at the end of the test. Growth must be expressed as the logarithmic increase in biomass (average specific growth rate) during the exposure period;

63 This information is covered by OECD TG 201 or OECD TG 221.

64 Sources of information (i) and (ii) provide such information.

3.2.1. Reliability of the provided information

65 The information from (i) and (ii) with read across source substances is already rejected under Reasons common to several requests. Therefore they cannot be used as part of the weight of evidence adaptation.

3.2.2. The provided studies do not meet the specifications of the test guideline(s)

66 OECD TG 201 provides the following specifications:

Validity criteria

a) exponential growth in the control cultures is observed over the entire duration of the test;
b) at least 16-fold increase in biomass is observed in the control cultures by the end of the test;
c) the mean coefficient of variation for section-by-section specific growth rates (days 0-1, 1-2 and 2-3, for 72-hour tests) in the control cultures is ≤ 35%.

Technical specifications impacting the sensitivity/reliability of the test

d) the test duration is 72 hours.

Characterisation of exposure

e) analytical monitoring must be conducted. Alternatively, a justification why the analytical monitoring of exposure concentrations is not technically feasible must be provided.

67 In study (i) and (ii):

Validity criteria

a) to c) you claim that the validity criteria are fulfilled, however there are no raw data to verify the validity criteria.

Technical specifications impacting the sensitivity/reliability of the test

d) in study (ii) the test duration was 24 h.

Characterisation of exposure

b) no analytical monitoring of exposure was conducted.

68 Based on the above,

- there are critical methodological deficiencies resulting in the rejection of the study results. More specifically, information on analytical monitoring and analytical method is missing. Without analytical monitoring, it is not possible to determine whether and to what extent the tested organisms were exposed to the test material and thus the study is not reliable.
- the reporting of the studies is not sufficient to conduct an independent assessment of its reliability. More specifically, there are no raw data to check and confirm that the validity criteria are fulfilled.

69 On this basis, the specifications of OECD TG 201 are not met and there are significant reliability issues.

3.2.3. Conclusion

70 As a conclusion, the sources of information as indicated above, provide information on the growth rate of algal cultures but the information provided is not reliable.

71 Accordingly, it is not possible to conclude, based on any source of information alone or considered together, whether your Substance has or has not the particular dangerous property foreseen to be investigated in an OECD TG 201 study.

72 Based on the above, your adaptation is rejected.

73 Therefore, the information requirement is not fulfilled.

3.3. Comments on the draft decision

74 In your comments to the draft decision you agree to perform the requested study.

Reasons related to the information under Annex VIII of REACH

4. *In vitro* micronucleus study

75 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.

4.1. Information provided

76 You have adapted this information requirement by using Annex XI, Section 1.2. (weight of evidence) based on experimental data from the following substances:

(i) an *in vitro* cytogenicity/chromosome aberration study in mammalian cells (1984) with the source substance Decanal, EC 203-957-4;

(ii) an *in vitro* cytogenicity/chromosome aberration study in mammalian cells (2018) with the source substance docosanoic acid, EC 204-010-8.

4.2. Assessment of the information provided

77 As explained under Reasons common to several requests the weight of evidence adaptation already has critical deficiencies.

78 In addition, as explained under Reasons common to several request, the adaptation must fulfil the information requirement based on relevant and reliable sources of information. These sources of information must provide sufficient weight to conclude that the Substance has or has not the dangerous property investigated by the required study.

79 Relevant information that can be used to support weight of evidence adaptation for information requirement of Section 8.4.2. at Annex VIII includes:

- Detection and quantification of structural or numerical chromosomal aberrations in cultured mammalian cells or in mammals, including data on the cytotoxicity and the frequency of cells with chromosomal aberrations or micronuclei.

80 This information is covered by OECD TG 473 or OECD 487.

81 Both sources of information (i) and (ii) provide such information.

4.2.1. Reliability of the provided information

82 The information from (i) and (ii) with read across source substances is already rejected under Reasons common to several requests. Therefore they cannot be used as part of the weight of evidence adaptation.

4.2.2. Conclusion

83 In summary, the sources of information (i) and (ii) provide relevant information on cytogenicity. However, these sources of information have significant reliability issues as described above and cannot contribute to the conclusion on the information requirement for *in vitro* cytotoxicity study in mammalian cells or *in vitro* micronucleus study.

84 It is not possible to conclude, based on any source of information alone or considered together, on the information requirement for *in vitro* cytotoxicity study in mammalian cells or *in vitro* micronucleus study.

85 Based on the above, your adaptation is rejected.

86 Therefore, the information requirement is not fulfilled.

4.3. Comments on the draft decision

87 In your comments to the draft decision you agree to perform the requested study.

4.4. Specification of the study design

88 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).

4.4.1. Assessment of aneugenicity potential

89 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.

90 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).

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

91 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.

5.1. Triggering of the information requirement

92 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.

93 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 1 and 4.

94 The result of the requests for an *in vitro* gene mutation study in bacteria and for an *in vitro* micronucleus study 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.

95 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.

5.2. Information provided

96 You have adapted this information requirement by using Annex XI, Section 1.2. (weight of evidence) based on experimental data from the following substances:

(i) an *in vitro* gene mutation study in mammalian cells (2015) with the source substance Decan-5-olide EC 211-889-1;

(ii) an *in vitro* gene mutation study in mammalian cells (1991) with the source substance Dodecan-1-ol, ethoxylated EC 500-002-6.

5.3. Assessment of the information provided

97 As explained under Reasons common to several requests, the weight of evidence adaptation already has critical deficiencies.

98 In addition, as explained under Reasons common to several request, the adaptation must fulfil the information requirement based on relevant and reliable sources of information. These sources of information must provide sufficient weight to conclude that the Substance has or has not the dangerous property investigated by the required study.

99 Relevant information that can be used to support weight of evidence adaptation for information requirement of Section 8.4.3 at Annex VIII includes similar information that is produced by the OECD TG 476/490 and OECD TG 488. This includes:

- Detection and quantification of gene mutations (point mutations, frame-shift mutations, small deletions, etc.) including data on the frequency of mutant colonies in cultured mammalian cells (*in vitro*) or mutant frequency for each tissue in mammals (*in vivo*).

100 Both sources of information (i) and ii) provide such information.

5.3.1. Reliability of the provided information

101 OECD TG 476 or OECD TG 490 provides the following specification/condition:

a) One positive control must be included in the study. The positive control substance must produce a statistically significant increase in the response compared with the concurrent negative control.

102 The reported data for study (i) did not include:

a) A statistically significant increase in the response in the positive control for cultures with metabolic activation (7,12-dimethylbenz(a) anthracene) compared with the concurrent negative control.

103 Therefore, the information requirement is not fulfilled.

104 The information from (i) and (ii) with read across source substances is already rejected under Reasons common to several requests. Therefore they cannot be used as part of the weight of evidence adaptation.

5.3.2. Conclusion

105 In summary, the sources of information (i) and (ii) provide relevant information on in vitro gene mutation study in mammalian cells. However, these sources of information have significant reliability issues as described above and cannot contribute to the conclusion on the information requirement for *in vitro* gene mutation study in mammalian cells.

106 It is not possible to conclude, based on any source of information alone or considered together, on the information requirement for *in vitro* gene mutation study in mammalian cells.

107 Based on the above, your adaptation is rejected.

108 Therefore, the information requirement is not fulfilled.

5.4. Comments on the draft decision

109 In your comments to the draft decision you agree to perform the requested study.

5.5. Specification of the study design

110 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.

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

111 A short-term repeated dose toxicity study (28 days) is an information requirement under Annex VIII, Section 8.6.1.

6.1. Information provided

112 You have adapted this information requirement by using Annex XI, Section 1.2. (weight of evidence) based on experimental data from the following substances:

(i) short-term repeated dose toxicity: oral (2018) with the source substance decan-5-olide, EC 211-889-1;

(ii) short-term repeated dose toxicity: oral (2018) with the source substance Oxacycloheptadec-10-en-2-one, EC 249-120-7.

6.2. Assessment of the information provided

113 As explained under Reasons common to several requests, which also addresses your comments on the draft decision, the weight of evidence adaptation already has critical deficiencies.

114 In addition, as explained under Reasons common to several request, the adaptation must fulfil the information requirement based on relevant and reliable sources of information. These sources of information must provide sufficient weight to conclude that the Substance has or has not the dangerous property investigated by the required study.

115 Relevant information that can be used to support weight of evidence adaptation for information requirement of Section 8.6.1 at Annex VIII includes, at general level, information on systemic toxicity in intact, non-pregnant and young adult males and females from: 1) in-life observations, 2) blood chemistry, 3) organ and tissue toxicity. Information should address effects on the following physiological systems: circulatory system, digestive/excretory system, endocrine system, immune system, integumentary system,

musculoskeletal system, nervous system, renal/urinary system, reproductive system, and respiratory system.

116 Both sources of information (i) and ii) provide such information.

6.2.1. Reliability of the provided information

117 The information from (i) and (ii) with read across source substances is already rejected under Reasons common to several requests. Therefore they cannot be used as part of the weight of evidence adaptation.

6.2.2. Conclusion

118 In summary, the sources of information (i) and (ii) provide relevant information on short-term repeated dose toxicity study (28 days). However, these sources of information have significant reliability issues as described above and cannot contribute to the conclusion on the information requirement for short-term repeated dose toxicity study (28 days).

119 It is not possible to conclude, based on any source of information alone or considered together, on the information requirement for short-term repeated dose toxicity study (28 days).

120 Based on the above, your adaptation is rejected.

121 Therefore, the information requirement is not fulfilled.

6.3. Specification of the study design

122 ECHA considers that a sub-acute toxicity study should be performed in rats with oral administration because although the information indicate that human exposure to the Substance by the inhalation route is likely, there is no concern for severe local effects following inhalation exposure. Furthermore, no repeated dose toxicity study by the oral route is available.

123 When there is no information available neither for the 28-day repeated dose toxicity (EU B.7, OECD TG 407), nor for the screening study for reproductive/developmental toxicity (OECD TG 421 or TG 422), the conduct of a combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (OECD TG 422) is preferred to ensure that unnecessary animal testing is avoided (Guidance on IRs and CSA, Section R.7.6.2.3.2.).

124 The study design is addressed in request 7.

7. Screening study for reproductive/developmental toxicity

125 A screening study for reproductive/developmental toxicity study (OECD 421 or OECD 422) is an information requirement under Annex VIII, Section 8.7.1., if there is no evidence from analogue substances, QSAR or in vitro methods that the substance may be a developmental toxicant.

7.1. Information provided

126 You have adapted this information requirement by using Annex XI, Section 1.2. (weight of evidence) based on experimental data from the following substances:

(i) a screening study for reproductive/developmental toxicity (2018) with the source substance decan-5-olide , EC 211-889-1;

(ii) a screening study for reproductive/developmental toxicity (2018) with the source substance oxacycloheptadec-10-en-2-one, EC 249-120-7.

7.2. Assessment of the information provided

127 As explained in under Reasons common to several requests, which also addresses your comments on the draft decision, the weight of evidence adaptation already has critical deficiencies.

128 In addition, as explained under Reasons common to several request, the adaptation must fulfil the information requirement based on relevant and reliable sources of information. These sources of information must provide sufficient weight to conclude that the Substance has or has not the dangerous property investigated by the required study.

129 Relevant information that can be used to support weight of evidence adaptation for information requirement of Section 8.7.3 at Annex VIII includes similar information that is produced by the EU B.63/OECD TG 421 or EU B.64/OECD TG 422. At general level, it includes information on the following key elements: 1) sexual function and fertility, 2) toxicity to offspring, and 3) systemic toxicity.

130 Both sources of information (i) and ii) provide such information.

7.2.1. Reliability of the provided information

131 The information from (i) and (ii) with read across source substances is already rejected under Reasons common to several requests. Therefore they cannot be used as part of the weight of evidence adaptation.

7.2.2. Conclusion

132 In summary, the sources of information (i) and (ii) provide relevant information on screening study for reproductive/developmental toxicity study. However, these sources of information have significant reliability issues as described above and cannot contribute to the conclusion on the information requirement for screening study for reproductive/developmental toxicity study.

133 It is not possible to conclude, based on any source of information alone or considered together, on the information requirement for screening study for reproductive/developmental toxicity study.

134 Based on the above, your adaptation is rejected.

135 Therefore, the information requirement is not fulfilled.

7.3. Specification of the study design

136 A study according to the test method EU B.64/OECD TG 422 must be performed in rats.

137 As the Substance is a liquid, the study must be conducted with oral administration of the Substance (Annex VIII, Section 8.7.1, Column 1).

138 Therefore, the study must be conducted in rats with oral administration of the Substance.

8. Short-term toxicity testing on fish

139 Short-term toxicity testing on fish is an information requirement under Annex VIII to REACH (Section 9.1.3.).

8.1. Information provided

140 You have adapted this information requirement by using Annex XI, Section 1.2. (weight of evidence) based on experimental data from the following substances:

(i) a short-term toxicity study on fish (2013) with the source substance docosanoic acid, EC 204-010-8;

(ii) a short-term toxicity study on fish (1984) with the source substance dodecan-1-ol, ethoxylated, EC 500-002-6.

8.2. Assessment of the information provided

141 As explained under Reasons common to several requests the weight of evidence adaptation already has critical deficiencies.

142 In addition, as explained under Reasons common to several request, the adaptation must fulfil the information requirement based on relevant and reliable sources of information. These sources of information must provide sufficient weight to conclude that the Substance has or has not the dangerous property investigated by the required study.

143 Relevant information that can be used to support weight of evidence adaptation for information requirement of Section 9.1.3. at Annex VIII include

- the concentration in the test substance leading to the mortality of 50% of the test organisms (fish) at the end of the test

144 This information is covered by OECD TG 203.

145 Sources of information (i) and (ii) provide such information.

8.2.1. Reliability of the provided information

146 The information from (i) and (ii) with read across source substances is already rejected under Reasons common to several requests. Therefore they cannot be used as part of the weight of evidence adaptation.

8.2.2. The provided studies do not meet the specifications of the test guideline(s)

147 To fulfil the information requirement, a study must comply with OECD TG 203 (Article 13(3) of REACH). Therefore, the following specification(s) must be met:

Validity criteria

a) the analytical measurement of test concentrations is conducted.

Technical specifications impacting the sensitivity/reliability of the test

b) the test duration is 96 hours or longer.

Characterisation of exposure

c) analytical monitoring must be conducted. A reliable analytical method for the quantification of the test material in the test solutions with reported specificity, recovery efficiency, precision, limits of determination (i.e. detection and quantification) and working range must be available.

148 In studies (i) and (ii):

Validity criteria

a) no analytical measurement of test concentrations was conducted;

Technical specifications impacting the sensitivity/reliability of the test

b) the test duration was 24 hours.

Characterisation of exposure

c) no analytical monitoring of exposure was conducted.

149 Based on the above,

- the validity criteria of OECD TG 203 are not met
- there are critical methodological deficiencies resulting in the rejection of the study results. More, specifically information on analytical monitoring and analytical method is missing. Without analytical monitoring, it is not possible to determine whether and to what extent the tested organisms were exposed to the test material and thus the study is not reliable. Furthermore the study is not reliable ad it was stopped after only 24 hours.

150 On this basis, the specification(s) of OECD TG 203 are not met.

8.2.3. Conclusion

151 In summary, the sources of information (i) and (ii) provide relevant information on short-term toxicity testing on fish. However, these sources of information have significant reliability issues as described above and cannot contribute to the conclusion on the information requirement for short-term toxicity testing on fish.

152 It is not possible to conclude, based on any source of information alone or considered together, on the information requirement for short-term toxicity testing on fish.

153 Based on the above, your adaptation is rejected.

8.3. Comments on the draft decision

154 In your comments to the draft decision and in your updated dossier you provided new information, a short-term toxicity study (2022) on fish on the Substance.

155 We have assessed this information and identified the following issue:

156 Toxicological and eco-toxicological tests and analyses on substances must be carried out in compliance with the principles of good laboratory practice (GLP) provided for in Directive 2004/10/EC or other international standards recognised as being equivalent by the Commission or ECHA and with the provisions of Directive 86/609/EEC, if applicable (Article 13(4) of REACH). According to Article 141(2), Article 13 applies from 1 June 2008.

157 Based on the information in your dossier, the study you provided is not performed in compliance with GLP.

158 Therefore, the information requirement is not fulfilled.

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).

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]
[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.

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

- 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 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).