~~Confidential~~

Helsinki, 12 October 2023

Addressees
Registrants of JS_279_815_0 as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
08 February 2022

Registered substance subject to this decision ("the Substance")
Substance name: 4-methyl-3-decen-5-ol
EC/List number: 701-429-2

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 ***18 January 2027***.

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

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

1. *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.

2. 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).

3. 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 5 below.
   If the sub-chronic toxicity study (90 days) is not requested:
   Short-term repeated dose toxicity study (28 days) (Annex VIII, Section 8.6.1.; test method: EU B.7/OECD TG 407) by oral route, in rats.

4. Screening study for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.; test method: EU B.63/OECD TG 421 or EU B.64/OECD TG 422) by oral route, in rats.

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

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

6. 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).

7. Long-term toxicity testing on fish (Annex IX, Section 9.1.6.; test method: EU C.47./OECD TG 210)

The reasons for the requests 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)

Contents

Reasons common to several requests

0.1. Read-across adaptation (category approach) rejected

1 You have provided information derived from experimental data from source substances using the OECD QSAR Toolbox and flagged the information as (Q)SAR, for the following information requirements:

- *In vitro* micronucleus study (Annex VIII, Section 8.4.2.)
- *In vitro* gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.)
- *In vivo* micronucleus study (Annex IX, Section 8.4.2.)

2 The OECD QSAR Toolbox was not used to indicate the presence or absence of a certain dangerous property of the Substance as required in Annex XI, Section 1.3.

3 Instead, the OECD QSAR Toolbox was used to identify other substances that were themselves used as source substances to predict the property of the Substance using a read-across approach. Therefore, we understand that you have adapted the information requirements identified above not under Annex XI, Section 1.3., but under Annex XI, Section 1.5. (grouping of substances and read-across approach).

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

5 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.

6 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. Scope of the grouping of substances (category)

7 The documents attached under each study record for the information requirements identified above include some elements on the scope of the grouping.

8 In this decision, the following abbreviations are used for the category members:

9 For in vitro micronucleus study, in absence of S9:

- Cat. member No. 1, CAS 51-03-6
- Cat. member No. 2, CAS 106-32-1
- Cat. member No. 3, CAS 105-99-7
- Cat. member No. 4, CAS 112-31-2
- Cat. member No. 5, CAS 19700-21-1
- Cat. member No. 6, CAS 84-74-2
- Cat. member No. 7, CAS 110-54-3
- Cat. member No. 8, CAS 106-27-4
- Cat. member No. 9, CAS 110-82-7

- Cat. member No. 10, CAS 123-68-2

10 For in vitro micronucleus study, in presence of S9:

- Cat. member No. 1, CAS 57-83-0
- Cat. member No. 2, CAS 19700-21-1
- Cat. member No. 3, CAS 84-74-2
- Cat. member No. 4, CAS 2216-51-5
- Cat. member No. 5, CAS 110-82-7
- Cat. member No. 6, CAS [redacted]
- Cat. member No. 7, CAS 100-41-4
- Cat. member No. 8, CAS 1843-05-6
- Cat. member No. 9, CAS 3648-21-3
- Cat. member No. 10, CAS 67-64-1

11 For in vivo micronucleus study:

- Cat. member No. 1, CAS 68457-13-6
- Cat. member No. 2, CAS 105-99-7
- Cat. member No. 3, CAS 106-22-9
- Cat. member No. 4, CAS 150-84-5
- Cat. member No. 5, CAS 1724-39-6
- Cat. member No. 6, no CAS number
- Cat. member No. 7, CAS 112-53-8
- Cat. member No. 8, CAS 123-68-2
- Cat. member No. 9, CAS 95962-14-4
- Cat. member No. 10, CAS 24851-98-7

12 For in vitro gene mutation study in mammalian cells, in absence of S9:

- Cat. member No. 1, CAS 64741-54-4
- Cat. member No. 2, CAS 64741-55-5
- Cat. member No. 3, CAS 115-11-7
- Cat. member No. 4, CAS 68477-42-9
- Cat. member No. 5, CAS 68513-02-0
- Cat. member No. 6, CAS 68783-66-4
- Cat. member No. 7, CAS 64-17-5

13 For in vitro gene mutation study in mammalian cells, in presence of S9:

- Cat. member No. 1, CAS 64741-54-4
- Cat. member No. 2, CAS 64741-55-5
- Cat. member No. 3, CAS 68513-02-0
- Cat. member No. 4, CAS 115-07-1

- Cat. member No. 5, CAS 68783-66-4
- Cat. member No. 6, CAS 64-17-5

14 You justify the grouping of the substances as: "[the selected substances are the] nearest neighbours compared by prediction descriptors".

15 You have not provided a definition of the structural basis for the grouping.

16 We have identified the following issue with the proposed scope of the grouping:

0.1.1.1. Incomplete description of the applicability domain of the category

17 A category (grouping) hypothesis should address "the set of inclusion and/or exclusion rules that identify the ranges of values within which reliable estimations can be made for category members for the given endpoint" (Guidance on IRs and CSA, Section R.6.2.4.1.). Particularly, "the applicability domain of a (sub)category would identify the structural requirements and ranges of physico-chemical, environmental fate, toxicological or ecotoxicological properties within which reliable estimations can be made for the (sub)category members" (Guidance on IRs and CSA, Section R.6.2.1.2.). Therefore, to reliably predict properties within a category the applicability domain should be described including the borders of the category, for which chemicals the category does not hold and a justification for the inclusion and/or exclusion rules.

18 You describe the applicability domain of the substances covered by the grouping as: "Category members are single chemicals or mixtures and are selected based on the profile of the target chemical. Only chemicals having experimental data are listed in the category." You have not provided a description of the structural requirements and ranges of physico-chemical, environmental fate, toxicological or ecotoxicological properties for the category.

19 This applicability domain does not introduce unambiguous inclusion/exclusion criteria which would identify the structural requirements and ranges of physico-chemical, environmental fate, toxicological or ecotoxicological properties within which reliable estimations can be made for the (sub)category members.

0.1.2. Predictions for toxicological properties

20 The documents attached under each study record for the information requirements identified above include some elements of justification for the use of a read-across approach.

21 You predict the properties of the Substance from information obtained from several source substances relied upon under each specific information requirement (list of substances provided under 0.1.1.).

22 You provide the following reasoning for the prediction of toxicological properties: The substances have a similar profile based on Genotoxicity OASIS and/or ECHA CHEM.

23 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.

0.1.2.1. Missing supporting information to compare properties of the substances

24 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.).

25 Supporting information must include (bridging) studies to compare the properties of the category members.

26 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).

27 For the source substances, you provide the results ("negative", "positive", "equivocal") obtained from a database for each endpoint predicted and you include the profiling results from several prediction models. Apart from these records that are specific to the endpoint predicted, your justification or the registration dossier do not include any robust study summaries or descriptions of data for the Substance that would confirm that both the Substance as well as the source substances cause the same type of effects.

28 In the absence of such information, you have not established that the Substance and the source substances are likely to have similar properties. Therefore, you have not provided sufficient supporting information to scientifically justify the read-across.

0.1.2.2. Missing robust study summaries

29 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 robust study summary for each source study used in the adaptation.

30 Robust study summaries must provide a detailed summary of the objectives, methods, results, and conclusions of a full study report providing sufficient information to make an independent assessment of the study (Article 3(28)).

31 ECHA understands that your read-across adaptation relies on experimental data. You have not provided robust study summaries of the tests with the source substances, whose results are the basis for your prediction.

32 You have not provided detailed information on the methods, results, and conclusions, allowing for an independent assessment of the source studies. Therefore, you have failed to provide a robust study summary for each source study used in the adaptation as required by Annex XI, Section 1.5.

0.1.3. Conclusion

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

0.2. Read-across adaptation (analogue approach) rejected

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

- Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)
- Sub-chronic toxicity study (90 days) (Annex IX, Section 8.6.2.)
- Pre-natal developmental toxicity study, one species (Annex IX, Section 8.7.2.)

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

36 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.

37 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. Predictions for toxicological properties

38 You provide the same read-across justification document under each information requirement cited above.

39 You predict the properties of the Substance from information obtained from the following source substance:

- Source substance 1, geraniol, EC 203-377-1.

40 You provide the following reasoning for the prediction of toxicological properties: "the target substance and 1 source substances have the same expected mode of action and similar physicochemical properties relevant for the read-across endpoints".

41 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.

0.2.1.1. Missing supporting information to compare properties of the substances

42 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.).

43 Supporting information must include information to compare the properties of the substances, including the impurity profile, bridging studies to assess the impact of differences in chemical structure and metabolism on the predictions.

44 As indicated above, your read-across hypothesis is based on the assumption that the structurally similar source substance causes the same type of effect(s). In this context, relevant, reliable, and adequate information allowing to compare the properties of the source substance 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.

45 For the source substance and the Substance, you compare the results of an in vitro gene mutation study in bacteria, and acute oral toxicity studies. Apart from these limited study results, your read-across justification or the registration dossier does not include any robust study summaries or descriptions of data that would confirm that both substances cause the

same type of effects. Specifically, it does not include (short-term) studies on both the source substance and the Substance relevant to the adapted information requirements, which would allow a comparison of properties as a basis for the prediction.

46 Furthermore, you state in your justification document that the source substance contains terpene functional groups, which are not present in the Substance. However, you do not discuss the impact of this on the predicted properties of the Substance.

47 You provide a list of potential metabolites formed using the TIMES software. However, the output is not readable and ECHA is unable to assess the provided information.

48 In the absence of comparable information that is relevant to the adapted endpoints, 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.

0.2.1.2. Inadequate or unreliable studies on the source substance

49 According to Annex XI, Section 1.5., if the grouping concept is applied then in all cases the results to be read across must:

(1) have adequate and reliable coverage of the key parameters addressed in the corresponding study that shall normally be performed for a particular information requirement;

(2) cover an exposure duration comparable to or longer than the corresponding study that shall normally be performed for a particular information requirement if exposure duration is a relevant parameter.

50 Specific reasons why the studies on the source substance do not meet these criteria are explained further below under the applicable information requirement sections 4, 5 and 6. Therefore, no reliable predictions can be made for these information requirements.

0.2.2. Conclusion

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

Reasons related to the information under Annex VIII of REACH

1. *In vitro* micronucleus study

52 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.

1.1. Information provided

53 You have provided information derived from experimental data from a group of substances using the OECD QSAR Toolbox and flagged the information as QSAR.

54 As the group of substances is used as source substances to predict the property of the Substance, ECHA understands that you have adapted the standard information requirement under Annex XI, Section 1.5. (grouping of substances and read-across approach) based on experimental data from source substances (as described in section 0.1.).

55 In addition to the information on in vitro cytogenicity in mammalian cells, you also provide information on in vivo cytogenicity. While you did not claim an adaptation, for the sake of completeness, ECHA considers that you may have provided that information as an attempt to adapt this information requirement by using Annex VIII, Section 8.4.2., Column 2. Therefore, ECHA assesses the information provided against this legal basis.

1.2. Assessment of the information provided

1.2.1. Read-across adaptation (category approach) rejected

56 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.

1.2.2. The provided adaptation does not meet the criteria of Annex VIII, Section 8.4.2., Column 2

57 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.

58 On this basis, your adaptation under Annex VIII, Section 8.4.2., Column 2 is rejected.

59 Therefore, the information requirement is not fulfilled.

60 In your comments to the draft decision, you state that information on an in vitro micronucleus study is available and that you will provide this information in an updated registration dossier. However, ECHA notes that the information in your comments is not sufficient to make an assessment and therefore no conclusion on the compliance can currently be made.

61 Based on the above, you remain responsible for complying with this decision by the set deadline.

1.3. Study design

62 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).

1.3.1. Assessment of aneugenicity potential

63 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.

64 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).

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

65 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.

2.1. Triggering of the information requirement

66 Your dossier contains (I) a negative result for in vitro gene mutation study in bacteria, and (II) inadequate data for the other study (in vitro cytogenicity study in mammalian cells).

67 The in vitro cytogenicity study in mammalian cells provided in the dossier is rejected for the reasons provided in request 1.

68 The result of the request 1 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.

69 Consequently, you are required to provide information for this information requirement, if the in vitro micronucleus study provides a negative result.

2.2. Information provided

70 You have provided information derived from experimental data from a group of substances using the OECD QSAR Toolbox and flagged the information as QSAR.

71 As the group of substances is used as source substances to predict the property of the Substance, ECHA understands that you have adapted the standard information requirement under Annex XI, Section 1.5. (grouping of substances and read-across approach) based on experimental data from source substances (as described in section 0.1.).

2.3. Assessment of the information provided

2.3.1. Read-across adaptation (category approach) rejected

72 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. In addition, ECHA identified endpoint specific issue addressed below.

2.3.1.1. Read-across hypothesis contradicted by existing data

73 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.).

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

75 As indicated above, your read-across hypothesis is based on the assumption that the structurally similar Substance and source substances cause the same type of effect(s).

76 However, the results of the information on mutagenicity obtained with the source substances vary. Specifically, you indicate that in absence of S9, 1 value out of 7 values used for the prediction is positive. Similarly, you indicate that in presence of S9, 4 values out of 11 values indicate positive results, and 4 other values indicated equivocal results.

77 The available set of data on the Substance and on the source substances indicates differences in the toxicological properties of the substances. This contradicts your read-across hypothesis whereby the Substance and source substances cause the same type of effect(s). However, you have not supported and scientifically justified why such differences in the toxicological properties do not affect your read-across hypothesis.

78 Therefore, the information requirement is not fulfilled.

2.4. Study design

79 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.

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

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

81 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.

3.1. Information provided

82 You have adapted this information requirement by using Annex VIII, Section 8.6.1., Column 2. To support the adaptation, you have provided the following information:

(i) a 16-week oral study (1966) with the source substance 1, EC 203-377-1;

(ii) a 27-28 week oral study (1996) with the source substance 1, EC 203-377-1.

83 You provided two identical study records for study (i) ("Oral 16 weeks. [redacted]. (1966)_Geraniol_Target" and "Oral 16 weeks. [redacted] (1966)_Geraniol/_Source") and two identical study records for study (ii) ("Oral 27-28 weeks. [redacted]

(1966)_Geraniol/_Source" and "Oral 27-28 weeks. [redacted] (1966)_Geraniol_Target"). Therefore, only the sources of information (i) and (ii) were assessed.

3.2. Assessment of the information provided

3.2.1. Information requirement on Sub-chronic toxicity study (90 days) not met

84 Under Annex VIII, Section 8.6.1., Column 2, Paragraph 1, Indent 1, the study may be omitted if a reliable sub-chronic (90 days) or chronic toxicity study is available or proposed by the registrant, provided that appropriate species, dosage, solvent and route of administration are used.

85 The studies (i and ii) are described as sub-chronic (90 days) studies.

86 However, for the reasons explained in request 5, the information requirement on Sub-chronic toxicity study (90 days) is not met.

87 Based on the above, your adaptation is rejected.

88 Therefore, the information requirement is not fulfilled.

3.3. Study design

89 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.

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

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

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

92 The present decision requests the registrants concerned to generate and submit a reliable sub-chronic toxicity study (90 days) (see request 5).

93 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.

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

95 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 5; or
- a 28-day study as per the study design described in 3.3. in case the 90-day study is not requested in the adopted decision.

96 In your comments to the draft decision, you agree to provide a justification for the adaptation according to Annex VIII, Section 8.6.1., Column 2.

97 ECHA emphasizes that, to support the adaptation, an adequate 90-day study needs to be available. As explained under request 5, your dossier currently does not include adequate information on Sub-chronic toxicity study (90 days). Therefore, as the information in your

comments is not sufficient to make an assessment, no conclusion on the compliance can currently be made.

98 Based on the above, you remain responsible for complying with this decision by the set deadline.

4. Screening study for reproductive/developmental toxicity

99 A screening study for reproductive/developmental toxicity study (OECD 421 or OECD 422) is an information requirement under Annex VIII, Section 8.7.1.

4.1. Information provided

100 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 screening study for reproductive/developmental toxicity with dermal exposure (2010) with the source substance geraniol, EC 203-377-1.

4.2. Assessment of the information provided

4.2.1. Read-across adaptation (analogue approach) rejected

101 As explained in Section 0.2., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5. is rejected. In addition, ECHA identified endpoint-specific issue addressed below.

4.2.1.1. Inadequate study on the source substance

102 Under Annex XI, Section 1.5., the results to be read across must have an adequate and reliable coverage of the key parameters addressed in the test guideline for the corresponding study that shall normally be performed for a particular information requirement, in this case EU B.63/OECD TG 421 or EU B.64/OECD TG 422 and Annex VIII, Section 8.7.1. Therefore, the following specifications must be met:

a) the route of administration is oral (i) unless other routes of administration are considered more appropriate (OECD TG 421) and (ii) if the substance is a liquid (Annex VIII, Section 8.7.1.);

b) a justification is provided in case the route of administration is not oral (OECD TG 421 and Annex VIII, Section 8.7.1.).

103 In study (i):

a) the test material was administered via the dermal route;

b) no justification was provided to justify the route of administration.

104 The substance is a liquid and you do not provide any justification for the selected route. Therefore, it cannot be concluded that the dermal route is appropriate and the default route (oral) for liquid substances apply.

105 Based on the above, the study submitted in your adaptation, as currently reported in your dossier, does not provide an adequate and reliable coverage of the key parameters of the corresponding OECD TG.

106 Therefore, the information requirement is not fulfilled.

107 In your comments to the draft decision, you indicate that you understand "*there is essentially no possibility to resort to a read-across to fulfil this requirement*" as "*the*

Screening study for reproductive/developmental toxicity is the first study required for this type of endpoint" and therefore "*there will never be a possibility to address ECHA's rejection argument"* (see Section 0.2.1.1. 'Missing supporting information to compare properties of the substances').

108 ECHA disagrees with your statement. 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). ECHA emphasizes that the information necessary to support a read-across adaptation may differ depending on the type of read-across hypothesis. Bridging studies of comparable design and duration for the Substance and of the source substance may not be needed if the read-across adaptation relies on, for e.g.:

- the identification of a consistent trend within a category of structurally related substances;
- rapid (bio)transformation of the Substance and of the source substance(s) to common compound(s) where reliable and relevant information on the common and non-common compound(s) is available as well as experimental evidence supporting rapid (bio)transformation.

109 Therefore, your comments on the draft decision does not change the assessment outcome.

4.3. Study design

110 A study according to the test method EU B.63/OECD TG 421 or EU B.64/OECD TG 422 must be performed in rats.

111 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).

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

113 In case the adopted decision no longer contains a request for a sub-chronic (90 days) study (e.g., as a result of an overall tonnage band change of the joint submission), a screening study for reproductive/developmental toxicity performed according to the OECD TG 422 is preferred.

114 In your comments to the draft decision, you indicate that, if this information requirement remains in the final decision, you may consider combining the screening study for reproductive/developmental toxicity with the sub-chronic toxicity requested under section 5.

115 You do not provide arguments in your comments to indicate how a combined study would meet the specifications of OECD TG 421/422. You are reminded that under Annex VIII, Section 8.7.1., Column 1, a screening study according to the test method EU B.63/OECD TG 421 or EU B.64/OECD TG 422 must be performed. The information provided in your updated dossier will be assessed against these test guidelines.

116 In your comments to the draft decision, you also indicate your intention to conduct the study via dermal route. According to Annex VIII, Section 8.7.1., Column 1, "*the route of administration shall be oral if the substance is a solid or a liquid.* […]; *deviations may be made if scientifically justified, for example through evidence of equivalent or higher systemic exposure via another relevant route of human exposure or route-specific toxicity*".

117 The Substance is a liquid and you do not provide evidence of equivalent or higher systemic exposure via the dermal route, and you do not demonstrate dermal-specific toxicity (see Section 5.5). Therefore, the deviation from oral route to dermal route is not scientifically justified.

Reasons related to the information under Annex IX of REACH

5. Sub-chronic toxicity study (90 days)

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

5.1. Information provided in the registration dossier

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

(i) a 16-week oral study (1966) with the source substance 1, EC 203-377-1;

(ii) a 27-28 week oral study (1996) with the source substance 1, EC 203-377-1.

120 You provided two identical study records for study (i) ("Oral 16 weeks. [redacted] (1966)_Geraniol_Target" and "Oral 16 weeks. [redacted] (1966)_Geraniol/_Source") and two identical study records for study (ii) ("Oral 27-28 weeks. [redacted] (1966)_Geraniol/_Source" and "Oral 27-28 weeks. [redacted] (1966)_Geraniol_Target"). Therefore, only the sources of information (i) and (ii) were assessed.

5.2. Information provided in your comments to the draft decision

121 In your comments to the draft decision, you present arguments related to the risk assessment performed on the Substance. You indicate that "*the risk assessment demonstrates that during its entire life cycle, the handling and use of the registered substance is done in a safe manner*". You also indicate that "*Human exposure, whether workers or consumers, is always below appropriate safety levels. The appropriate safety levels, or DNEL (Derived No Effect Level) were calculated using appropriate Assessment Factors, among others to account for the uncertainties related to the read-across approach*". You conclude that "*there is no added value generating the requested OECD 408 study (REACH Annex IX, Section 8.6.2.), as the risk assessment is already ensuring the full protection and safety of both workers and consumers in the EU*".

122 A registrant may only adapt this information requirement based on the general rules set out in Annex XI or Annex IX, Section 8.6.2., Column 2. ECHA understands that you intend to adapt this information requirement based on exposure considerations, according to Annex XI, Section 3(2)(a).

5.3. Assessment of the information provided in the registration dossier

5.3.1. Weight of evidence adaptation rejected

123 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.

124 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.

125 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.

126 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.

127 You have not included a justification for your weight of evidence adaptation, 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.

128 Beside this critical deficiency, ECHA has also assessed the other aspects of your adaptation.

129 Information that can be used to support weight of evidence adaptation for the information requirement of Annex IX, Section 8.6.2. includes similar information that is produced by the OECD TG 408 with a design as specified in this decision. OECD TG 408 requires the study to investigate the following key elements:

(2) in-life observations;

(3) blood chemistry;

(4) organ and tissue toxicity.

130 The sources of information (i) and (ii) provide relevant information on in-life observations.

131 The sources of information (i) and (ii) provide limited information on blood chemistry. In particular, the following investigations on haematology and clinical biochemistry are missing: a measure of clotting potential, electrolyte balance (calcium, phosphorus, chloride, sodium, potassium), carbohydrate metabolism (fasting glucose), liver and kidney function (serum glutamic-pyruvic transaminase, serum glutamic oxaloacetic transaminase, ornithine decarboxylase, gamma glutamyl transpeptidase, urea nitrogen, albumen, blood creatinine, total bilirubin, total serum protein measurements).

132 The sources of information (i) and (ii) provide limited information on organ and tissue toxicity. In particular, the following organs were not included in the gross pathology or histopathology examinations: brain, pituitary gland, thyroid/parathyroid, thymus, trachea, lungs, aorta, adrenals, pancreas, gonads, uterus, oesophagus, stomach, duodenum, jejunum, ileum, caecum, colon, rectum, urinary bladder, representative lymph node, peripheral nerve.

133 Therefore, there is no information provided on some elements of blood chemistry and some elements of organ and tissue toxicity.

134 Furthermore, the reliability of the sources of information that provide relevant information is significantly affected by the following deficiencies:

5.3.1.1. Read-across adaptation (analogue approach) rejected

135 As explained in Section 0.2., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5. is rejected. In addition, ECHA identified issues specific information requirements, which are addressed below.

5.3.1.1.1. Inadequate or unreliable studies on the source substance

136 Under Annex XI, Section 1.5., the results to be read across must have an adequate and reliable coverage of the key parameters addressed in the test guideline for the corresponding study that shall normally be performed for a particular information

requirement, in this case OECD TG 408. Therefore, the following specifications must be met:

a) at least 10 male and 10 female animals are used for each concentration and control group;

b) clinical signs are observed daily and functional observations are reported.

137 In studies (i) and (ii):

a) only 5 males and 5 females were included in each test and control group;

This deficiency significantly affects the statistical power of the study.

b) signs of toxicity observations, cage-side observations, and ophthalmological examinations are missing.

Without information on these parameters, it is not possible to draw a conclusion in the overall absence of toxicity of the substance in rats following oral exposure.

138 Therefore, the provided studies cannot be considered a reliable source of information that could contribute to the conclusion on in-life observations investigated by the required study.

139 In summary:

- while you have provided information on in-life observations, blood chemistry, organ and tissue toxicity, the corresponding sources of information have deficiencies affecting their reliability. As in this case these deficiencies significantly affect the statistical power of these sources of information, it prevents drawing the conclusion on in-life observations;
- there is no information provided on some elements of blood chemistry and organ and tissue toxicity. Therefore, the sources of information you provided do not provide an adequate coverage of the key elements that should normally be investigated to meet this information requirement.

140 Therefore, it is not possible to conclude, based on any source of information alone or considered together, on the information requirement for sub-chronic toxicity study.

141 Based on the above, your weight of evidence adaptation under Annex XI, Section 1.2. is rejected.

5.4. Assessment of the information provided in the comments to the draft decision

5.4.1. Substance-tailored exposure-driven testing adaptation rejected

142 A substance-tailored exposure-driven testing adaptation must fulfil the cumulative conditions set out under Annex XI, Sections 3(1) as well as 3(2)(a) or (b) or (c).

5.4.1.1. Lack of appropriate DNEL

143 Under Annex XI, Section 3(2)(a)(ii), a relevant and appropriate derived no effect level (DNEL) must be derived. That DNEL must be "*relevant and appropriate both to the information requirement to be omitted and for risk assessment purposes*". In the present case, for a relevant and appropriate DNEL, the tested parameters in the study on which basis the DNEL was derived should cover the parameters of a sub-chronic study (90 days).

144 Specifically, a sub-chronic study (90 days) has the following parameters:

- dosing of the Substance is performed daily for a minimum of 90 days;

- 10 non-pregnant female animals are used for each concentration and control group;
- gross pathological examinations are performed as specified in paragraphs 43-46 of OECD TG 408;
- full histopathology is performed as specified in paragraphs 47-49 of OECD TG 408.

145 You have derived the worker long-term systemic DNEL from a screening study for reproductive and developmental toxicity on an analogue substance.

146 You state that "*The reproductive and developmental toxicity of the test material was investigated in a study performed in accordance with standardised guidelines OECD 421 and EPA OPPTS 870.3550 using an appropriate test material suitable for read-across to support 4-methyl-3-decen-5-ol. The study was performed in line with good scientific principles and reported to a high standard. In accordance with Klimisch (1997), the study was assigned a reliability score of 2, as the study was performed on a read-across substance. Under the conditions of the 08/02/2022 Generated by Chesar 3.7 Chemical Safety Report 75 (3E)-4-methyldec-3-en-5-ol study, the NOAEL for reproductive performance and fertility was determined to be 300 mg/kg bw/day and this value was used as the starting point for the calculation of systemic DNELs*."

147 In the screening study which you use to derive the DNEL:

- the exposure duration is limited to 28 days for males and 63 days for females;
- no non-pregnant females are included in each test and control group;
- gross pathology of non-reproductive organs is not performed;
- histopathology of non-reproductive organs is not performed.

148 In summary, the screening study does not cover the parameters of a sub-chronic study (90 days) complying with the OECD TG 408.

149 Moreover, the read-across for the screening study which you use to derive the DNEL is rejected, and that study does not cover the specifications of the OECD TG 421 (see reasons explained in request 4).Therefore, you have not demonstrated that the DNEL derived from the screening study is relevant and appropriate to both to the information requirement to be omitted (sub-chronic study) and for risk assessment purposes.

150 Based on the above, your adaptation under Annex XI, Section 3(2)(a) is rejected.

151 Therefore, the information requirement is not fulfilled.

5.5. Study design

152 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.

153 In your comments to the draft decision, you disagree with the request of oral exposure. You consider that the "*most likely and predominant route of human exposure of such substances during their life cycle is the dermal route, based on the likelihood of exposure of the skin compared to the digestive or respiratory tracts*". You refer to Annex IX, Section 8.6.2., and the Guidance on IRs and CSA, Section R.7.5.6.3.2.

154 According to Annex IX, Section 8.6.2., Column 2, Paragraph 2, testing by the dermal route is appropriate if:

(1) skin contact in production and/or use is likely; and

(2) the physicochemical properties suggest a significant rate of absorption through the skin; and

(3) one of the following conditions is met:

- toxicity is observed in the acute dermal toxicity test at lower doses than in the oral toxicity test, or
- systemic effects or other evidence of absorption is observed in skin and/or eye irritation studies, or
- in vitro tests indicate significant dermal absorption, or
- significant dermal toxicity or dermal penetration is recognised for structurally-related substances.

155 However, with regards to criteria (3) of Annex IX, Section 8.6.2., Column 2, Paragraph 2:

- In your dossier, you report the following acute effect values: LD_{50} > 5000 mg/kg/day following dermal exposure and LC_{50} > 8000 mg/kg/day following oral exposure. No toxicity was observed in these studies. Therefore, you do not provide evidence that the toxicity observed in the acute dermal toxicity test(s) is at lower doses than in the oral toxicity test(s).
- You do not provide evidence of systemic effects or other evidence of absorption in the provided skin irritation study (2000) nor in the eye irritation study (1980).
- There are no *in vitro* tests in your dossier that indicate significant dermal absorption.
- You do not demonstrate that significant dermal toxicity or dermal penetration is recognised for structurally-related substances.

156 Based on the above, you did not demonstrate that at least one of the conditions listed under criteria (3) are met and therefore that testing by the dermal route is appropriate. Therefore, the deviation from oral route to dermal route is not scientifically justified.

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

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

6. Pre-natal developmental toxicity study in one species

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

6.1. Information provided

160 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 screening study for reproductive and developmental toxicity (2010) with the source substance 1, EC 203-377-1.

6.2. Assessment of the information provided

6.2.1. Read-across adaptation (analogue approach) rejected

161 As explained in Section 0.2., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5. is rejected. In addition, ECHA identified endpoint-specific issue addressed below.

6.2.1.1. Inadequate or unreliable study on the source substance

162 Under Annex XI, Section 1.5., the results to be read across must have an adequate and reliable coverage of the key parameters addressed and cover an exposure duration comparable to or longer than the one specified in the test guideline for the corresponding study that shall be normally performed for a particular information requirement, in this case OECD TG 414.

163 Study (i) is a screening study for reproductive and developmental toxicity performed according to OECD TG 421.

164 Study (i) is not a pre-natal developmental toxicity study.

165 Therefore, the study submitted in your adaptation, as currently reported in your dossier, does not provide an adequate and reliable coverage of the key parameters of the corresponding OECD TG and does not cover an exposure duration comparable to or longer than the one specified in the corresponding OECD TG.

166 Based on the above, the adaptation is rejected.

167 Therefore, the information requirement is not fulfilled.

6.3. Study design

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

169 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).

170 In your comments to the draft decision, you disagree with the request of oral exposure. You explain that "*considering that the substance is a fragrance substance and based on the intended use and handling of the substance and the evidence of its past years on the fragrance market, all available information indicate that workers and consumers are majorly exposed to the registered fragrance substance via dermal contact and not at all orally*".

171 According to Annex IX, Section 8.7.2., Column 1, "*the route of administration shall be oral if the substance is a solid or a liquid.* […]; *deviations may be made if scientifically justified, for example through evidence of equivalent or higher systemic exposure via another relevant route of human exposure or route-specific toxicity*".

172 The Substance is a liquid and you do not provide evidence of equivalent or higher systemic exposure via the dermal route, and you do not demonstrate dermal-specific toxicity (see Section 5.5). Therefore, the deviation from oral route to dermal route is not scientifically justified.

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

7. Long-term toxicity testing on fish

174 Long-term toxicity testing on fish is an information requirement under Annex IX to REACH (Section 9.1.6.).

7.1. Information provided

175 You have adapted this information requirement by using Annex IX, Section 9.1., Column 2. To support the adaptation, you have provided following justification: "The Chemical Safety Assessment does not indicate the need for further investigation and so testing is therefore not required."

7.2. Assessment of the information provided

7.2.1. Annex IX, Section 9.1., Column 2 is not a valid basis to omit the study

176 Under Annex IX, Section 9.1., Column 2 is not a basis for omitting information on long-term toxicity to fish referred to under Column 1, Section 9.1.6.

177 Your adaptation is therefore rejected, and the information requirement is not fulfilled.

178 In your comments to the draft decision, you agree with ECHA's assessment. You intend to first assess whether non-animal testing methods could be used to meet the information requirement and you refer to the use of acute to chronic ratios (ACRs), QSAR and the fact that RCRs are below 1 for all life-cycle stage.

179 ECHA emphasizes that if you decide to submit an adaptation instead of conducting the requested study, you will need to specify an unambiguous legal basis for your adaptation (i.e., referring to the general rules set out in Annex XI). As indicated in your comments, your strategy relies on an approach that has not yet been fully described and justified. Therefore, no conclusion on the compliance of a potential adaptation can be made. You remain responsible for complying with this decision by the set deadline.

7.3. Study design and test specifications

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

181 The Substance is difficult to test due to the low surface tension (44.7 mN/m at 20 °C). OECD TG 210 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 210. 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.

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 (2023).
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 24 August 2022.

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).

However, ECHA agrees with your comment referring to the incorrect EC number for the Substance in the draft decision ('279-815-0'). Therefore, ECHA updated the EC number in this decision ('701-429-2') as also indicated by you in your comments.

ECHA notified the draft decision to the competent authorities of the Member States for proposals for amendment.

As no amendments were proposed, ECHA adopted the decision under Article 51(3) of REACH.

Appendix 3: Addressees of this decision and their corresponding information requirements

In accordance with Articles 10(a) and 12(1) of REACH, the information requirements for individual registrations are defined as follows:

- the information specified in Annex VII to REACH, for registration at 1-10 tonnes per year (tpa), or as a transported isolated intermediate in quantity above 1000 tpa;
- the information specified in Annexes VII and VIII to REACH, for registration at 10-100 tpa;
- the information specified in Annexes VII, VIII and IX to REACH, for registration at 100-1000 tpa;
- the information specified in Annexes VII to X to REACH, for registration at more than 1000 tpa.

Registrant Name	Registration number	Highest REACH Annex applicable to you
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[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 (https://echa.europa.eu/practical-guides).

(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 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).