~~Confidential~~

Helsinki, 17 October 2022

Addressees
Registrant(s) of JS_rm of geraniol and nerol as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
08 November 2018

Registered substance subject to this decision ("the Substance")
Substance name: Reaction mass of geraniol and nerol
EC/list number: 906-125-5

Decision number: Please refer to the REACH-IT message which delivered this communication (in format CCH-D-XXXXXXXXXX-XX-XX/F)

DECISION ON A COMPLIANCE CHECK

Under Article 41 of Regulation (EC) No 1907/2006 (REACH), you must submit the information listed below, by the deadline of ***24 April 2026***.

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: OECD TG 471, 2020);

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

2. Justification for an adaptation of a Short-term repeated dose toxicity (28 days) based on the results of the Sub-chronic toxicity study (90 days) requested below (Annex VIII, Section 8.6.1.);

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

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

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

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

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

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

7. Pre-natal developmental toxicity study (Annex X, Section 8.7.2.; test method: OECD TG 414) by oral route, in a second species (rabbit).

The reasons for the decision(s) are explained in Appendix 1.

Information required depends on your tonnage band

You must provide the information listed above for all REACH Annexes applicable to you in accordance with Articles 10(a) and 12(1) of REACH. The addressees of the decision and their corresponding information requirements based on registered tonnage band are listed in Appendix 3.

You are only required to share the costs of information that you must submit to fulfil your information requirements.

How to comply with your information requirements

To comply with your information requirements, you must submit the information requested by this decision in an updated registration dossier by the deadline indicated above. You must also **update the chemical safety report, where** relevant, including any changes to classification and labelling, based on the newly generated information.

You must follow the general requirements for testing and reporting new tests under REACH, see Appendix 4.

Appeal

This decision, when adopted under Article 51 of REACH, may be appealed to the Board of Appeal of ECHA within three months of its notification to you. Please refer to http://echa.europa.eu/regulations/appeals for further information.

Failure to comply

If you do not comply with the information required by this decision by the deadline indicated above, ECHA will notify the enforcement authorities of your Member State.

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

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

[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 decision

Contents

Reasons related to the information under Annex VII of REACH

1. In vitro gene mutation study in bacteria

1 An *in vitro* gene mutation study in bacteria is an information requirement under Annex VII to REACH (Section 8.4.1.).

1.1. Information provided

2 You have adapted this information requirement by using a Grouping of substances and read-across approach and provided the following information:

i. *in vitro* gene mutation study in bacteria (1984) with the source substance geraniol, EC number 203-377-1.

ii. *in vitro* gene mutation study in bacteria (2000) with the source substance nerol, EC number 203-378-7.

3 You have provided studies with test materials, indicated to be the source substances, identified as main constituents of the Substance.

4 On the basis of this information ECHA understands that you have applied a constituent-based approach whereby you conclude on the properties of the Substance using the results obtained from independent studies conducted with the constituents of the Substance as source substances.

5 ECHA understands that you predict the properties of the Substance using a read-across hypothesis which assumes that different compounds have the same type of effects. Thus, the toxicological properties of the Substance are predicted to be quantitatively equal to those of the source substances.

1.2. Assessment of the information provided

6 We have assessed this information and identified the following issue(s):

1.2.1. Read-across adaptation rejected

7 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.

8 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).

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

Adequacy and reliability of study on the source substance

10 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 the OECD TG 471. Therefore, the following specifications must be met:

a) The test must be performed with 5 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)
b) The maximum dose tested must induce a reduction in the number of revertant colonies per plate compared to the negative control, or the precipitation of the tested substance. If no precipitate or limiting cytotoxicity is observed, the highest test dose must correspond to 5 mg/plate or 5 µl/plate.
c) At least 5 doses must be evaluated, in each test condition.
d) Triplicate plating must be used at each dose level.
e) One positive control must be included in the study. The positive control substance must produce a statistically significant increase in the number of revertant colonies per plate compared with the concurrent negative control.
f) The mean number of revertant colonies per plate must be reported for the treated doses and the controls.

11 Your registration dossier provides a study (i) similar to an OECD TG 471 showing the following:

a) the required fifth strain, *S. typhimurium* TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101) is missing.
b) a maximum dose of 5 mg/plate or 5 ml/plate was not tested nor a dose that induced a reduction in the number of revertant colonies per plate compared to the negative control, nor the precipitation of the tested substance was used. The highest concentration tested was 0.5 mg/plate and no information was provided whether it induced a reduction in the number of revertant colonies per plate compared to the negative control.
c) the evaluation of at least 5 doses in each test condition did not occur. The dossier contains information that doses "up to 0.5 mg/ plate" were tested, however the number of dose levels evaluated is not given.
d) triplicate plating at each dose level was not used, instead only duplicates were tested.
e) information on a positive control was not provided.
f) data on the number of revertant colonies per plate for the treated doses and the controls was not provided.

12 Therefore, the study submitted in your adaptation, as currently reported in your dossier, does not provide an adequate and reliable coverage of the key parameter(s) of the corresponding OECD TG.

1.2.2. Conclusion on the read-across approach

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

14 Therefore, the information requirement is not fulfilled.

1.3. Specification of the study design

15 To fulfil the information requirement for the Substance, the *in vitro* gene mutation study in bacteria (OECD TG 471, 2020) is considered suitable.

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

Reasons related to the information under Annex VIII of REACH

2. Justification for an adaptation of a Short-term repeated dose toxicity (28 days) based on the results of the Sub-chronic toxicity study (90 days)

17 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 of Annex VIII or a general adaptation rule under Annex XI.

2.1. Information provided

18 While you have not indicated a specific legal reference for your adaptation, ECHA understands that you have adapted this information requirement according to Annex VIII, Section 8.6.1, Column 2, paragraph 1, first indent. According to that legal provision, 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 an appropriate species, dosage, solvent and route of administration are used.

19 You have provided a sub-chronic toxicity study in rats (1967) with the source substance explained as a mixture of 3,7-dimethyl-2,6-octadienol and 3,7-dimethyl-1,6-octadienol (named "[redacted]) (study i).

2.2. Assessment of the information provided

20 We have assessed this information and identified the following issue(s):

2.2.1. Adaptation under Annex VIII, Section 8.6.1, Column 2 is rejected

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

22 You have provided a sub-chronic toxicity study (i) conducted with the source substance geraniol.

23 As explained in Section 6, your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5 for the information requirement sub-chronic toxicity study (90-day) is rejected. Therefore, you have not provided a reliable sub-chronic toxicity study as required under Annex VIII, Section 8.6.1, Column 2 and as a result your adaptation is rejected.

24 On this basis, the information requirement is not fulfilled.

2.3. Specification of the study design

25 Annex VIII, Section 8.6.1., Column 2 provides that an experimental study for this information requirement is not needed if a reliable sub-chronic (90 days) or chronic toxicity study is available.

26 The present decision requests the registrants concerned to generate and submit a reliable sub-chronic toxicity study (90 days) (see request 6). 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 therefore need to be conducted.

27 Because you still must comply with the information requirement in Annex VIII, Section 8.6.1., you are requested to submit a justification for the adaptation provided in Column 2 of that provision.

28 In the comments to the draft decision, you agree with the request.

3. Short-term toxicity testing on fish

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

3.1. Information provided

30 You have adapted this information requirement by using a Grouping of substances and read-across approach based on the following experimental data:

i. Short-term toxicity to fish study (1996) with the source substance geraniol, EC number 203-377-1.

31 You provide the following reasoning for the prediction of this information requirement: "*The studies on daphnia and algae toxicities have been performed with the substance reaction mass of geraniol and nerol (consisting of the stereoisomers geraniol and nerol (E- and Z-isomer), the fish [..] tests have been performed with the main component geraniol. Relevant differences in toxicity are not expected for geraniol and nerol and thus the read-across is considered as justified*."

32 On the basis of this information ECHA understands that you have applied a constituent-based approach whereby you conclude on the properties of the Substance using the results obtained from an independent study conducted with the source substance, identified as one of the main constituent of your multi-constituent Substance.

33 ECHA understands that you predict the properties of the Substance using a read-across hypothesis which assumes that different compounds have the same type of effects. The properties of your Substance are predicted to be quantitatively equal to those of the source substance.

3.2. Assessment of the information provided

34 We have assessed this information and identified the following issue(s):

3.2.1. Read-across adaptation rejected

35 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.

36 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).

37 We have identified the following issue(s) with the prediction of this information requirement:

Missing supporting information

38 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.).

39 Supporting information must include bridging studies to compare properties of the Substance and source substance.

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

41 As indicated above, in order to support your hypothesis you provide the following statement: "*the fish [..] tests have been performed with the main component geraniol. Relevant differences in toxicity are not expected for geraniol and nerol and thus the read-across is considered as justified*."

42 You have provided a short-term toxicity to fish study with the source substance Geraniol, and no information on short-term toxicity to fish for the whole Substance or for the other constituent nerol.

43 You refer to an assumbed absence of differences in toxicity to justify the prediction for short-term toxicity to fish. However, in the absence of adequate information allowing to compare the short-term toxicity to fish properties of the Substance and of the source substance, it cannot be confirmed that both substances cause the same type of effects for the information requirement.

44 Therefore you have not provided sufficient supporting information to scientifically justify the read-across.

Adequacy and reliability of study on the source substance(s)

45 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 203. Therefore, the following specifications must be met:

46 Technical specifications impacting the sensitivity/reliability of the test

a. the test is conducted on juveniles of similar age (or size);

47 Reporting of the methodology and results

b. adequate information on the analytical method (including information on the sampling intervals) and on the results of the analytical determination of exposure concentrations are provided;

48 The study (i) is described as an OECD 203 study. However, the following specifications are not according to the requirements of the OECD TG 203:

49 Technical specifications impacting the sensitivity/reliability of the test

a. the mean size of fish at study initiation was 3.9 cm, which does not correspond to juveniles for *Danio rerio* (1-2 cm, Annex 2 of OECD TG 203);

50 Reporting of the methodology and results

b. you report measured concentrations without specifying when they were measured and on the analytical method, adequate information, i.e. information on the sampling intervals, is not reported.;

51 Based on the above, the study does not provide an adequate and reliable coverage of the key parameter(s) addressed by the OECD TG 203 and thist study is not an adequate basis for your read-across predictions.

52 As explained above, you have not established that relevant properties of the Substance can be predicted from data on the source substance(s). Therefore, your read-across approach under Annex XI, Section 1.5. is rejected and the information requirement is not fulfilled.

53 On this basis, the information requirement is not fulfilled.In the comments to the draft decision, you agree that the study provided does not meet the current standards of an OECD TG 203 study. Instead of performing a new OECD TG 203 study as requested, you propose to perform the long-term toxicity to fish study (OECD TG 210) requested in Appendix 1, Section 6.

54 REACH Annex VIII section 9.1.3. column 2 specifies that the short-term toxicity study does not need to be conducted if a long-term aquatic toxicity study on fish is available. At present no long-term toxicity study on fish is provided in the IUCLID dossier, therefore no conclusion on the compliance can currently be made. You remain responsible for complying with this decision by the set deadline.

Reasons related to the information under Annex IX of REACH

4. Sub-chronic toxicity study (90-day)

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

4.1. Information provided

56 You have adapted this information requirement by using a Grouping of substances and read-across approach based on the following experimental data:

i. sub-chronic toxicity study in rats (1967) with the source substance explained as a mixture of 3,7-dimethyl-2,6-octadienol and 3,7-dimethyl-1,6-octadienol ("[redacted]").

57 You provide the following reasoning for the prediction of this information requirement: "*No data concerning the repeated dose toxicity of the reaction mass of geraniol and nerol is available. However, the oral repeated dose toxicity was evaluated in a study (Hagan, 1967) with a mixture of 3,7-dimethyl-2,6-octadienol and 3,7-dimethyl-1,6-octadienol (named "[redacted]" by the authors). Due to the structural analogy, this study is used for read across, expecting the reaction mass of geraniol and nerol to have similar effects*."

58 ECHA understands that you predict the properties of the Substance using a read-across hypothesis which assumes that different compounds have the same type of effects. The properties of your Substance are predicted to be quantitatively equal to those of the source substance.

4.2. Assessment of the information provided

59 We have assessed this information and identified the following issue(s):

4.2.1. Read-across adaptation rejected

60 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.

61 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).

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

Missing supporting information

63 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.).

64 Supporting information must include supporting information/bridging studies to compare properties of the Substance and source substance(s) as well as information on the impact of exposure to non-common compounds on the prediction.

65 As indicated above, your read-across hypothesis is based on the assumption that the structurally similar substances cause the same type of effect(s). In this context, where the Substance and the source substance(s) are composed of more than one constituent, exposure to the Substance and of the source substance(s) may also lead to exposure to other compounds than the common compound of interest. The impact of exposure to these non-common compounds on the prediction of properties of the target needs to be assessed to ensure that a reliable prediction can be made.

66 The Substance is a multi-constituent substance comprised of the following two main constituents:

67 ([redacted]You have provided information on the source substance which is a mixture of 3,7-dimethyl-2,6-octadienol and 3,7-dimethyl-1,6-octadienol.

68 ECHA understands that the source substance contains [redacted] as the common compound with the Substance. However, you have not explained and established that the properties of the Substance, i.e. [redacted], can be predicted using the information from the source substance. In particular, you have not explained whether and how the other constituent in the Substance, [redacted] contributes to the properties of the Substance and how this is accounted for the prediction made from the source substance.

69 In addition, the source substance contains a non-common compound [redacted]. You have not provided experimental data or other adequate and reliable information addressing the impact of exposure to this non-common compound in the documentation of your read-across approach.

70 In the absence of such information, you have not established that a reliable prediction of the property under consideration of the Substance can be derived on the basis of your read-across hypothesis. Therefore, you have not provided sufficient supporting information to scientifically justify the read-across.

Adequacy and reliability of study on the source substance(s)

71 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. testing of at least three dose levels (unless conducted at the limit dose) with concurrent controls;

b. highest dose level should aim to induce toxicity or reach the limit dose;

c. at least 10 male and 10 female animals for each test and control group;

d. clinical signs observed daily and functional observations week 11 or after, i.e. sensory activity, grip strength and motor activity assessments;

e. haematological and clinical biochemistry tests as specified in paragraphs 30-38 of

the test guideline;

f. the oestrus cycle in females at necropsy;
g. terminal organ and body weights;
h. gross pathology as specified in paragraphs 43-46 of the test guideline;
i. full histopathology as specified in paragraphs 47-49 of the test guideline.

72 Your registration dossier provides a study similar to an OECD TG 408 showing the following:

a. only one dose level at the time used and this dose was changed during the experiment;
b. no justification for the dose setting while the highest dose levels tested was 550/55 mg/kg/bw/day which is below the limit dose of the test guideline, and no adverse effect were observed;
c. 5 males/ 5 females in each test and control group were used, which is an inadequate number of animals;
d. data on clinical signs and functional observations are missing: nature, severity and duration;
e. data on haematology and clinical biochemistry findings are missing: incidence and severity with relevant base-line values as specified in paragraphs 30-38 of the test guideline;
f. data on oestrus cycle are missing;
g. data on terminal organ weights and organ/body weight ratios are missing, in the methods section you claim that these were measured but no information on results is provided;
h. data on gross pathology findings are missing: incidence and severity;
i. data on histopathology findings are missing: incidence and severity.

73 Therefore, the study submitted in your adaptation, as currently reported in your dossier, does not provide an adequate and reliable coverage of the key parameter(s) of the corresponding OECD TG.

4.2.2. Conclusion on the read-across approach

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

75 Therefore, the information requirement is not fulfilled.

Specification of the study design

76 Following the criteria provided in Annex IX, Section 8.6.2, Column 2, the oral route is the most appropriate route of administration to investigate repeated dose toxicity of the Substance; Guidance on IRs and CSA, Section R.7.5.6.3.2.

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

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

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

5. Long-term toxicity testing on aquatic invertebrates

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

5.1. Information provided

81 You have adapted this information requirement by using Column 2 of Annex IX, Section 9.1. To support the adaptation, you have provided the following justification:

(i) *"In Annex IX of Regulation (EC) No 1907/2006, it is laid down that chronic toxicity tests shall be proposed by the registrant if the chemical safety assessment indicates the need to investigate further the effects on aquatic invertebrates. According to Annex I of this regulation, the chemical safety assessment triggers further action when the substance or the preparation meets the criteria for classification as dangerous according to Directive 67/548/EEC or Directive 1999/45/EC or is assessed to be a PBT or vPvB. The hazard assessment of geraniol reveals neither a need to classify the substance as dangerous to the environment, nor is it a PBT or vPvB substance, nor are there any further indications that the substance may be hazardous to the environment. Therefore a chronic toxicity test in Daphnia magna is not provided."*

5.2. Assessment of the information provided

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

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

83 Annex IX, Section 9.1., Column 2 does not allow omitting the need to submit information on long-term toxicity to aquatic invertebrates under Column 1. It must be understood as a trigger for providing further information on aquatic invertebrates if the chemical safety assessment according to Annex I indicates the need (Decision of the Board of Appeal in case A-011-2018).

84 Your adaptation is therefore rejected.

85 On this basis, the information requirement is not fulfilled.

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

6. Long-term toxicity testing on fish

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

6.1. Information provided

88 You have adapted this information requirement by using Column 2 of Annex IX, Section 9.1. To support the adaptation, you have provided following justification:

(i) *"In Annex IX of Regulation (EC) No 1907/2006, it is laid down that chronic toxicity tests shall be proposed by the registrant if the chemical safety assessment indicates the need to investigate further the effects on fish. According to Annex I of this regulation, the chemical safety assessment triggers further action when the substance or the preparation meets the criteria for classification as dangerous according to Directive 67/548/EEC or Directive 1999/45/EC or is assessed to be a PBT or vPvB. The hazard assessment of geraniol reveals neither a need to classify the substance as dangerous to the environment, nor is it a PBT or vPvB substance, nor are there any further indications that the substance may be hazardous to the environment. Therefore, and for reasons of animal welfare a chronic toxicity test in fish is not provided."*

6.2. Assessment of the information provided

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

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

90 Annex IX, Section 9.1., Column 2 does not allow omitting the need to submit information on long-term toxicity to fish under Column 1. It must be understood as a trigger for providing further information on long-term toxicity to fish if the chemical safety assessment according to Annex I indicates the need (Decision of the Board of Appeal in case A-011-2018).

91 In addition, minimisation of vertebrate animal testing is not on its own a legal ground for adaptation under the general rules of Annex XI.

92 Your adaptation is therefore rejected.

93 On this basis, the information requirement is not fulfilled.

6.3. Study design and test specifications

94 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.).In the comments to the draft decision, you agree to perform the requested study.

Reasons related to the information under Annex X of REACH

7. Pre-natal developmental toxicity study in a second species

95 Pre-natal developmental toxicity (PNDT) studies (OECD TG 414) in two species is an information requirement under Annex X, Section 8.7.2.

7.1. Information provided

96 While you have not provided a specific legal reference for your adaptation of this information requirement, ECHA understands that you have adapted this information requirement in accordance with Column 2 of Annex X, Section 8.7.

97 To support your adaptation you have referred to the results from the available pre-natal developmental toxicity study and the screening test for reproduction/development toxicity conducted with the Substance. You report that in the OECD TG 421 study "*None of the developmental parameters evaluated […] gave any evidence of a treatment-related or dose-related effect*." You also point out that in the OECD TG 414 study the Substance elicited maternal toxicity but did not affect gestational parameters and did not reveal effects on morphological structures of the fetus up to the highest dose tested. You also refer to the absence of teratogenic effects in the pre-natal developmental toxicity study conducted in rats with the Substance and included in the dossier (study ii below).

98 You consider that the rat is the most sensitive species for reproductive and general systemic toxicity when compared to other rodent and non-rodent species including rabbits. On that basis you conclude that "*Since rats are most susceptible for systemic toxicity and developmental effects were not observed or found to be a secondary non-specific consequence of general systemic toxicity in the dams, no additional information related to classification and risk characterization is expected to be gained by performing a developmental toxicity test with the reaction mass of geraniol and nerol in a second non-rodent species*". You support this statement by referring to a reproductive/developmental screening test and a pre-natal development study in rats conducted with the Substance:

i. reproduction / developmental toxicity screening test (2010), OECD TG 421, with the Substance;

ii. prenatal developmental toxicity study (2015) in rats, OECD TG 414, with the Substance.

7.2. Assessment of the information provided

99 We have assessed this information and identified the following issue(s):

7.2.1. Column 2 adaptation rejected

Under Annex IX, Section 8.7., Column 2, the study does not need to be conducted if the substance is of low toxicological activity. This needs to be demonstrated with a set of concomitant criteria, *inter alia*:

- that there is a comprehensive and informative dataset showing no toxicity in any of the tests available;
- that it can be proven from toxicokinetic data that no systemic absorption occurs via relevant routes of exposure;

100 You have not demonstrated:

- that there is no evidence of toxicity seen in any of the tests available. Toxicity was seen in the reproduction / developmental toxicity screening test and prenatal developmental toxicity study with the Substance, e.g. number of liveborn pups was statistically significantly decreased in high-dose females, viability index during early lactation (PND 0 - 4) was distinctly reduced, and there was reduction in body weights both for parental animals and progeny.
- that it can be proven from toxicokinetic data that no systemic absorption occurs via relevant routes of exposure. You have provided toxicokinetic data in the IUCLID dossier Section 7.1 'Toxicokinetics, metabolism and distribution' on the constituents of the reaction mass that clearly show systemic exposure. Therefore, you have not demonstrated that there is no systemic absorption of the Substance via relevant routes of exposure.

101 Furthermore, while you claim that the rat is the most sensitive species, you do not provide any information in support of this claim.

102 ECHA concludes that the above mentioned criteria for demonstrating low toxicological activity are not met.

103 Therefore, your adaptation is rejected.

7.3. Specification of the study design

104 A PNDT study according to the test method OECD TG 414 should be performed in rat or rabbit as preferred species. The study in the first species was carried out by using a rodent species (rat).

105 Therefore, a PNDT study in a second species must be performed in the rabbit as preferred non-rodent species.

106 The study must be performed with oral administration of the Substance (Guidance on IRs and CSA, Section R.7.6.2.3.2.).

107 Based on the above, the study must be conducted in rabbits with oral administration of the Substance.

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

References

The following documents may have been cited in the decision.

Guidance on information requirements and chemical safety assessment (Guidance on IRs & CSA)

Chapter R.4 Evaluation of available information; ECHA (2011).
Chapter R.6 QSARs, read-across and grouping; ECHA (2008).
Appendix to Chapter R.6 for nanoforms; ECHA (2019).
Chapter R.7a Endpoint specific guidance, Sections R.7.1 – R.7.7; ECHA (2017).
Appendix to Chapter R.7a for nanomaterials; ECHA (2017).
Chapter R.7b Endpoint specific guidance, Sections R.7.8 – R.7.9; ECHA (2017).
Appendix to Chapter R.7b for nanomaterials; ECHA (2017).
Chapter R.7c Endpoint specific guidance, Sections R.7.10 – R.7.13; (ECHA 2017).
Appendix to Chapter R.7a for nanomaterials; ECHA (2017).
Appendix R.7.13-2 Environmental risk assessment for metals and metal compounds; ECHA (2008).
Chapter R.11 PBT/vPvB assessment; ECHA (2017).
Chapter R.16 Environmental exposure assessment; ECHA (2016).

Guidance on data-sharing; ECHA (2017).

All Guidance on REACH is available online: https://echa.europa.eu/guidance-documents/guidance-on-reach

Read-across assessment framework (RAAF)

RAAF, 2017 Read-across assessment framework (RAAF), ECHA (2017)
RAAF UVCB, 2017 Read-across assessment framework (RAAF) – considerations on multi- constituent substances and UVCBs), ECHA (2017).

The RAAF and related documents are available online:
https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across

***OECD Guidance documents* (OECD GDs)**

OECD GD 23 Guidance document on aquatic toxicity testing of difficult substances and mixtures; No. 23 in the OECD series on testing and assessment, OECD (2019).
OECD GD 29 Guidance document on transformation/dissolution of metals and metal compounds in aqueous media; No. 29 in the OECD series on testing and assessment, OECD (2002).
OECD GD 150 Revised guidance document 150 on standardised test guidelines for evaluating chemicals for endocrine disruption; No. 150 in the OECD series on testing and assessment, OECD (2018).
OECD GD 151 Guidance document supporting OECD test guideline 443 on the extended one-generation reproductive toxicity test; No. 151 in the OECD series on testing and assessment, OECD (2013).

Appendix 2: Procedure

The information requirement for an Extended one-generation reproductive toxicity study (EOGRTS; Annexes IX or X, Section 8.7.3.) is not addressed in this decision. This may be addressed in a separate decision once the information from the Sub-chronic toxicity study (90-day) requested in the present decision is provided; due to the fact that the results from the 90-day study is needed for the design of the EOGRTS.

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 04 June 2021.

You have provided comments during the decision-making phase which were found to be compliant with the information required in the draft decision. Therefore the original requests ("In vitro gene mutation study in mammalian cells" and "Growth inhibition study aquatic plants") were removed.

In the comments to the draft decision, you requested an extension of the deadline from 18 to 39 months from the date of adoption of the decision. You justified the request by additional time required to complete the testing due to anticipated delays in finding an appropriate laboratory to conduct the studies. Based on the documentary evidence provided, ECHA has agreed with your request for a deadline extension and has extended the deadline to 39 months.

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

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

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

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

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

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

Where applicable, the name of a third party representative (TPR) may be displayed in the list of recipients whereas ECHA will send the decision to the actual registrant.

Appendix 4: Conducting and reporting new tests for REACH purposes

1. Requirements when conducting and reporting new tests for REACH purposes

1.1. Test methods, GLP requirements and reporting

(1) Under Article 13(3) of REACH, all new data generated as a result of this decision must be conducted according to the test methods laid down in a European Commission Regulation or to international test methods recognised by the Commission or ECHA as being appropriate.

(2) Under Article 13(4) of REACH, ecotoxicological and toxicological tests and analyses must be carried out according to the GLP principles (Directive 2004/10/EC) or other international standards recognised by the Commission or ECHA.

(3) Under Article 10(a)(vi) and (vii) of REACH, all new data generated as a result of this decision must be reported as study summaries, or as robust study summaries, if required under Annex I of REACH. See ECHA Practical Guide on How to report robust study summaries[2].

(4) Under the introductory part of Annexes VII/VIII/IX/X to REACH, where a test method offers flexibility in the study design, for example in relation to the choice of dose levels or concentrations, the chosen study design must ensure that the data generated are adequate for hazard identification and risk assessment.

1.2. Test material

Before generating new data, you must agree within the joint submission on the chemical composition of the material to be tested (Test Material) which must be relevant for all the registrants of the Substance.

(1) Selection of the Test material(s)
The Test Material used to generate the new data must be selected taking into account the following:
- the variation in compositions reported by all members of the joint submission,
- the boundary composition(s) of the Substance,
- the impact of each constituent/ impurity on the test results for the endpoint to be assessed. For example, if a constituent/ impurity of the Substance is known to have an impact on (eco)toxicity, the selected Test Material must contain that constituent/ impurity.

(2) Information on the Test Material needed in the updated dossier
- You must report the composition of the Test Material selected for each study, under the "Test material information" section, for each respective endpoint study record in IUCLID.
- The reported composition must include all constituents of each Test Material and their concentration values and other parameters relevant for the property to be tested.

This information is needed to assess 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[3].

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