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Helsinki, 13 April 2022

Addressees
Registrant(s) of JS_Octane-1,2-diol as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
07/05/2018

Registered substance subject to this decision ("the Substance")
Substance name: Octane-1,2-diol
EC number: 214-254-7

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 ***19 July 2024***.

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

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

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

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

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

3. In vitro cytogenicity study in mammalian cells (Annex VIII, Section 8.4.2.; test method: OECD TG 473) or In vitro micronucleus study (Annex VIII, Section 8.4.2.; test method: OECD TG 487);

4. If negative results are obtained in test performed for the information requirement of Annex VIII, Section 8.4.2. then: In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.; test method: OECD TG 476 or TG 490);

5. 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

6. Extended one-generation reproductive toxicity study (triggered by Annex IX, Section 8.7.3., column 1; test method: OECD TG 443) by oral route, in rats, specified as follows:
    - Ten weeks premating exposure duration for the parental (P0) generation;
    - The highest dose level in P0 animals must be determined based on clear evidence of an adverse effect on sexual function and fertility without severe

suffering or deaths in P0 animals as specified further in Appendix 1, or follow the limit dose concept. The reporting of the study must provide the justification for the setting of the dose levels;
- Cohort 1A (Reproductive toxicity); and
- Cohort 1B (Reproductive toxicity) without extension to mate the Cohort 1B animals to produce the F2 generation.

You must report the study performed according to the above specifications. Any expansion of the study must be scientifically justified.

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

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

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

[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.

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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

Appendix 1: Reasons for the decision

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Reasons related to the information under Annex VII of REACH

1. Short-term toxicity testing on aquatic invertebrates

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

1.1. Information provided

2 You have provided a study according to the OECD TG 202 on the Substance

1.2. Assessment of the information provided

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

1.2.1. The provided study does not meet the information requirement

4 To fulfil the information requirement, a study must comply with the OECD TG 202 and the requirements of the OECD GD 23 if the substance is difficult to test (Article 13(3) of REACH). Therefore, the following specifications must be met:

5 Characterisation of exposure:

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

6 Additional requirements applicable to difficult to test substances regarding:

7 Preliminary solubility study:

(b) if the test material is forming dispersion or emulsions (*e.g.* certain surfactants, aliphatic amines), the dispersibility limit or the critical micelle concentration of the test material in the specific test solution under the test conditions is determined.

8 Test solutions preparation methods:

(c) surface-active test chemicals are tested at concentrations below their critical micelle concentration (CMC) in the test medium.

9 Your registration dossier provides an OECD TG 202 study showing the following:

10 Characterisation of exposure:

(a) no analytical monitoring of exposure was conducted.

11 Additional requirements applicable to difficult to test substances regarding:

12 Preliminary solubility study:

(b) the test material is a surfactant and you do not report the critical micelle concentration.

13 Test solutions preparation methods:

(c) you have performed the test at nominal concentrations 10, 20, 50, 100, 200, 500 and 1000 mg/L.

14 Based on the above, there are critical methodological deficiencies resulting in the rejection of the study results. More, specifically in the absence of analytical monitoring you have not demonstrated that the substance was stable in test solution.

15 Furthermore, the Substance is difficult to test since it is a surfactant and there are critical methodological deficiencies resulting in the rejection of the study results. More, specifically you have not determined the critical micelle concentration of the Substance in test solution. Therefore, you have not demonstrated that the exposure concentrations were below the CMC and that the test organisms were exposed to the freely dissolved chemical species and not the micelle form, which is considered to be biologically unavailable, at the used tested doses.

16 Therefore, the requirements of the OECD TG 202 are not met.

17 In the comments to the draft decision submitted by one of the members, reference is made to Annex VII, Section 9.1.1., Column 1, and in particular to the possibility for registrants to consider long-term toxicity testing instead of short-term.

18 ECHA confirms that the REACH provision provide this choice for registrants how to comply with the information requirement.

19 You remain responsible for complying with this decision by the set deadline.

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

1.3. Study design and test specifications

21 The Substance is difficult to test due to the surface active properties (ST = 41.95 mN/m). The OECD TG 202 specifies that, for difficult to test substances, you must consider the approach described in the 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 the OECD TG 202. 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. Furthermore, exposure concentrations must be below the critical micelle concentration (CMC). This will ensure that test organisms are exposed to the freely dissolved chemical species and not the micelle which can alter the uptake of the test chemical.

2. Growth inhibition study aquatic plants

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

2.1. Information provided

23 You have provided a study according to the OECD TG 201 on the Substance.

2.2. Assessment of the information provided

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

2.2.1. The provided study does not meet the information requirement

25 To fulfil the information requirement, a study must comply with the OECD TG 201 and with the requirements of the OECD GD 23 if the substance is difficult to test (Article 13(3) of REACH). Therefore, the following specifications must be met:

26 Characterisation of exposure:

(a) the test media prepared specifically for analysis of exposure concentrations during the test is treated identically to those used for testing (*i.e.* inoculated with algae and incubated under identical conditions);

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

27 Reporting of the methodology and results:

(c) the results of algal biomass determined in each flask at least daily during the test period are reported in a tabular form.

28 Validity criteria:

(d) the following criteria must be met:

- exponential growth in the control cultures is observed over the entire duration of the test;
- at least 16-fold increase in biomass is observed in the control cultures by the end of the test;
- the mean coefficient of variation for section-by-section specific growth rates (days 0-1, 1-2 and 2-3, for 72-hour tests) in the control cultures is ≤ 35%;
- the coefficient of variation of average specific growth rates during the whole test period in replicate control cultures is ≤ 7% in tests with Pseudokirchneriella subcapitata.

29 Additional requirements applicable to difficult to test substances regarding:

30 Preliminary solubility study:

(e) if the test material is forming dispersion or emulsions (*e.g.* certain surfactants, aliphatic amines), the dispersibility limit or the critical micelle concentration of the test material in the specific test solution under the test conditions is determined.

31 Test solutions preparation methods

(f) surface-active test chemicals are tested at concentrations below their critical micelle concentration (CMC) in the test medium.

32 Your registration dossier provides an OECD TG 201 study showing the following:

33 Characterisation of exposure:

(a) the test media prepared specifically for analysis of exposure concentrations was not inoculated with algae;

(b) TOC was used for analytical monitoring of exposure concentrations. You report the detection range of the method to be within 2 to 65 mg/L and you have analysed samples

with nominal concentrations of 50, 100, 200 and 250 mg/L, i.e. outside the detection range.

34 Reporting of the methodology and results:

(c) tabulated data on the algal biomass determined daily for control is not reported.

35 Validity criteria:

(d) you have not provided data on the control cultures allowing independent assessment of the validity criteria.

36 Additional requirements applicable to difficult to test substances regarding:

37 Preliminary solubility study:

(e) the test material is a surfactant and you do not report the critical micelle concentration.

38 Test solutions preparation methods:

(f) you have performed the test at nominal concentrations 2.0, 5.0, 10, 20, 50, 100 and 200 mg/L.

39 Based on the above, there are critical methodological deficiencies resulting in the rejection of the study results. More specifically TOC is not considered a substance specific or sensitive method for monitoring exposure concentrations. Additionally, you have applied the method outside its detection range and you have not reported the background TOC content in the samples. On this basis, you have not demonstrated that the measured concentrations were representative of the exposure concentrations. The samples used for analytical measurements were not treated identically to those used for testing since were not-inoculated with algae therefore, the analytical method showed low variability in the results. Due to the non-specificity of this method, analysis performed at the end of the test with inoculated samples are likely to over-estimate the concentration therefore, it is not reliable for substances with unclear stability. Furthermore, although you have provided tabulated data of the algal growth rate, you have not reported data on the controls allowing an independent assessment of the study validity.

40 The Substance is difficult to test since it is a surfactant and there are critical methodological deficiencies resulting in the rejection of the study results. More, specifically you have not determined the critical micelle concentration of the Substance in test solution therefore, you have not demonstrated that the exposure concentrations were below the CMC and that the test organisms were exposed to the freely dissolved chemical species and not the micelle form, which is considered to be biologically unavailable, at the used tested doses.

41 Therefore, the requirements of the OECD TG 201 are not met.

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

43 In the comments to the draft decision submitted by one of the members, you agree with the deficiencies identified above and that there is presently a data gap. In particular, you consider that additional analytical work is needed. However, you do not agree to perform a new study, unless 'the analytical work reveals some issues/problems'.

44 Instead, you propose to conduct an analytical study retrospectively for the existing algae study. You propose to determine the critical micelle concentration (CMC) and to provide evidence that the test solution preparation was adequate and the exposure concentrations were maintained.

45 Additionally, you you express your intention to provide 'the identified missing information' in a future dossier update.

46 We have assessed this information and identified the following issues:

We note that in this decision ECHA gives the reasons for why the available information does not meet the information requirement and, as a consequence, requests you to provide the standard information requirement. With regards to your comments on '*the identified missing information*' you intend to provide in a future dossier update, you do not define the content of the information nor the issues it would address hence the information in your comments is not sufficient for ECHA to make an assessment. With a view to your comments on 'additional analytical information', we further point you at the following.

In order to provide evidence whether the test solution preparation and the exposure concentrations met the requirements of OECD TG 201 and the OECD GD 23 as listed above, the following must be provided:

- evidence that the concentration of the test material has been maintained within 20 % of the nominal concentration throughout the test.

First, it is necessary to demonstrate that the nominal concentrations were below the CMC (points e) and f) above).

Second, in the preliminary study the test solutions must be prepared under conditions equivalent (in terms of test medium, pH, test vessels, preparation procedures, etc.) to those used in the reported study, as given in OECD GD 23.

Third, to demonstrate stability of the test chemical, a reliable analytical method must be used (point b) above) and samples of the test solution should be analysed at the beginning and typically at 24-hour intervals for the duration of the test period, as given in OECD GD 23.

47 In your comments, you have not provided any information on the CMC, but you indicate your intention to determine it.

48 Additionally, you have indicated your intention to demonstrate the Substance stability in relevant medium however you have not provided further information on the test conditions.

49 Finally, you have not indicated the analytical method nor the sampling frequency for the analytical monitoring to demonstrate the stability of the test substance throughout the algae test.

50 Unless these conditions are followed closely as explained above, the preliminary study cannot serve to provide evidence that the exposure concentrations were maintained throughout the test (within ±20 % of the nominal concentration) and that the tested concentrations were below the CMC hence ensuring Substance bioavailability.

51 As this strategy relies essentially on data which is yet to be generated, ECHA points out that no conclusion on the compliance with this information requirement can currently be made.

52 On this basis, the information requirement is not fulfiled.

2.3. Study design and test specifications

53 The OECD TG 201 specifies that, for difficult to test substances, the OECD GD 23 must be followed. As already explained above, the Substance is difficult to test. Therefore, you must fulfil the requirements described in 'Study design' under request 1.

Reasons related to the information under Annex VIII of REACH

3. In vitro cytogenicity study in mammalian cells or In vitro micronucleus study

54 An in vitro cytogenicity study in mammalian cells or an in vitro micro-nucleus study is an information requirement under Annex VIII to REACH (Section 8.4.2.).

3.1. Information provided

55 You have provided an in vitro mammalian chromosomal aberration test conducted with the Substance (2007) (study i.).

3.2. Assessment of the information provided

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

3.2.1. Study not adequate for the information requirement

57 To fulfil the information requirement the study has to be an in vitro chromosomal aberration test or an in vitro micronucleus test, conducted in mammalian cells in accordance with OECD TG 473 or OECD TG 487, respectively (Guidance on IRs and CSA, Table R.7.7–2). Therefore, the following specifications must be:

a) The maximum concentration tested must induce 55+5% of cytotoxicity compared to the negative control, or the precipitation of the tested substance. If no precipitate or limiting cytotoxicity is observed, the highest test concentration must correspond to 10 mM, 2 mg/mL or 2 µl/mL, whichever is the lowest;
b) At least 300 well-spread metaphases must be scored per concentration;
c) One positive control must be included in the study. The positive control substance must produce a statistically significant increase in the response compared with the concurrent negative control;
d) Data on the cytotoxicity and the frequency of cells with structural chromosomal aberration(s) for the treated and control cultures must be reported.

58 The study (i.) is described as an in vitro mammalian chromosomal aberration test. However, the following specifications are not according to the requirements of the OECD TG 473:

a) a maximum tested concentration of 10 mM, 2 mg/mL or 2 µl/mL, or that induced 55+5% of cytotoxicity compared to the negative control, or the precipitation of the tested substance. The highest concentration reported in this study was 700 µg/mL. In addition, you report that cytotoxicity was evident in the initial growth inhibition test. However, at such "cytotoxic" concentrations cell proliferation rates concurrent with the chromosome aberration tests were not reduced.
b) the scoring of at least 300 metaphases per concentration. The provided study reports that only 200 metaphases were scored.
c) a positive control that produced a statistically significant increase in the response compared with the concurrent negative control. The provided study reports that a positive control was used and provided valid results. However, no numerical values or information about statistical significance was provided.
d) data on the cytotoxicity and/or the frequency of cells with structural chromosomal aberration(s) for the treated and control cultures. The provided study reports no numerical data on these investigations.

59 The information provided does not cover key parameter(s) required by the OECD TG 473.

60 In the comments to the draft decision submitted by one of the members, you agree that not all the information required for an assessment is currently in IUCLID. You indicate that the missing information specified in section 3.2.1. (c) and (d) is available and will be given in a dossier update. Furthermore, you mention that the ECHA Guidance of today was not yet available at the time of submission and that the information still passed the completeness check.

61 ECHA acknowledges your agreement with the shortcomings of the study and your intention to provide the identified missing information in a future dossier update. The information in your comments is not sufficient for ECHA to make an assessment, because the information specified in section 3.2.1. (c) and (d) has not yet been provided.

62 Regarding your reference to missing details from the Guidance on IRs and CSA, ECHA notes that under Article 13.3 the information needs to meet the requirements of the relevant test method, and the guidelines already stem from OECD TG 473. Regarding the passing of the completeness check, ECHA highlights that the purpose of the technical completeness check is only to ensure that information has been submitted for the information requirement, however this check does not assess the quality or adequacy of the data, which is the scope of the current compliance check.

63 Regarding section 3.2.1. (a), in the comments to the draft decision you agree that the cytotoxicity criteria are not being met, but you claim that this is sometimes seen with substances with a steep concentration response curve. ECHA notes that the OECD TG 473 provides some guidance on dose selection for substances with potential steep concentration response in paragraph 21. Please note that the last bullet point of paragraph 43 of the OECD TG 473 lists the criteria for the selection of top concentration being consistent with those described in paragraphs 22, 23 and 24 of the OECD TG 473. These paragraphs outline the requirements on the selection of the maximum concentration based on cytotoxicity and approaches to take if no cytotoxicity is seen. You claim that cytotoxicity was evident in the initial growth inhibition test, but you have not provided any data in support of this. In the absence of evidence that the highest dose tested induced the appropriate cytotoxicity, it is not possible to confirm that the acceptability criteria for the study are met.

64 Regarding section 3.2.1. (b), in the comments to the draft decision you consider that the study should be assessed against the test guideline in force when the study was performed. Compliance is assessed against the test method under Article 13.3, which is the OECD TG 473. The study you have provided does not have a comparable statistical power to the current guideline OECD TG 473, therefore the study that you have provided is not fully conclusive and the information provided in your comments does not change the assessment outcome.

65 Finally, in the comments to the draft decision you also mention that the Substance is part of a substance group already assessed by ECHA, where no likely hazards were identified for human health. ECHA's activity referred to as 'Working with Groups' is intended to speed up the identification of chemicals that need regulatory action, and authorities may decide to address groups of structurally related substances rather than single substances. The work is different from grouping and read-across as defined in Section 1.5 of Annex XI to REACH as a general rule for adaptation of standard information required for compliance with REACH. For more information on the 'Working with Groups' please visit: https://echa.europa.eu/working-with-groups.

66 Based on the above, the information provided in your comments does not change the assessment outcome.

67 Therefore, the information requirement is not fulfilled.

3.3. Specification of the study design

To fulfil the information requirement for the Substance, either *in vitro* cytogenicity study in mammalian cells (Annex VIII, Section 8.4.2., test method OECD TG 473) or *in vitro* micronucleus study (Annex VIII, Section 8.4.2., test method OECD TG 487) are considered suitable.

4. In vitro gene mutation study in mammalian cells

68 An in vitro gene mutation study in mammalian cells is an information requirement under Annex VIII to REACH (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.

69 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).

70 The in vitro cytogenicity study in mammalian cells provided in the dossier is rejected for the reasons provided in section 3.

71 The result of the request for information in section 3 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.

4.1. Information provided

72 You have provided an in vitro mammalian cell gene mutation test conducted with the Substance (2009) (study i.).

4.2. Assessment of information provided

73 To fulfil the information requirement, the study must meet the requirements of the OECD TG 476 or the OECD TG 490 (Guidance on IRs and CSA, Table.7.7-2). Therefore, the following specifications must be:

a) The maximum concentration tested must induce 80-90% of cytotoxicity compared to the negative control, or the precipitation of the tested substance. If no precipitate or limiting cytotoxicity is observed, the highest test concentration must correspond to 10 mM, 2 mg/mL or 2 µl/mL, whichever is the lowest.
b) One positive control must be included in the study. The positive control substance must produce a statistically significant increase in the response compared with the concurrent negative control.
c) The response for the concurrent negative control must be inside the historical control range of the laboratory.
d) Data on the cytotoxicity and the mutation frequency for the treated and control cultures must be reported.

74 The study (i.) is described as an in vitro mammalian cell gene mutation test. However, the following specifications are not according to the requirements of the OECD TG 476:

a) a maximum tested concentration of 10 mM, 2 mg/mL or 2 µl/mL, or that induced 80-90% of cytotoxicity compared to the negative control, or the precipitation of the tested substance. In the submitted dossier it was reported that the maximum dose was based on cytotoxicity, however as no cytotoxicity percentages were provided, this claim cannot be independently assessed.
b) one positive control that produced a statistically significant increase in the number of revertant colonies per plate compared with the concurrent negative control. In the submitted dossier it was reported that a positive control was used, however, no numerical values or information about statistical significance was provided. As it is only reported that the positive control was 'valid', this claim cannot be

independently assessed.

c) a negative control with a response inside the historical control range of the laboratory. In the submitted dossier it was reported that a negative control was used but no information about the historical control range was provided. It only said that the negative control was 'valid', which is insufficient information.

d) data on the cytotoxicity and the mutation frequency for the treated and control cultures. In the submitted dossier no numerical data were provided on these investigations.

75 The information provided does not cover key parameter(s) required by the OECD TG 476.

76 In the comments to the draft decision submitted by one of the members, you agree that not all the information required for an assessment is currently in IUCLID. You indicate that the missing information is available and will be given in a dossier update.

77 ECHA acknowledges your agreement with the shortcomings of the study and your intention to provide the information in a future dossier update. The information in your comments is not sufficient for ECHA to make an assessment, because you have not provided any details inyour comments on the nature of the information that you intend to submit to consolidate the reporting of the study i.

78 Therefore, the information would not meet the information requirement.

~~79~~ Consequently, you are required to provide information for this endpoint, if the in vitro cytogenicity study in mammalian cells or an in vitro micronucleus study provides a negative result.

4.3. Specification of the study design

80 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.

5. Short-term toxicity testing on fish

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

5.1. Information provided

82 You have provided a study according to the OECD TG 203 on the Substance.

5.2. Assessment of the information provided

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

5.2.1. The provided study does not meet the information requirement

84 To fulfil the information requirement, a study must comply with OECD TG 203 and the requirements of OECD GD 23 if the substance is difficult to test (Article 13(3) of REACH). Therefore, the following specifications must be met:

85 Technical specifications impacting the sensitivity/reliability of the test:

a) at least 7 fish are used at each test concentration and in the control(s).

86 Characterisation of exposure:

b) analytical monitoring must be conducted. A reliable analytical method for the

quantification of the test material in the test solutions with reported specificity, recovery efficiency, precision, limits of determination (i.e. detection and quantification) and working range must be available.

87 Additional requirements applicable to difficult to test substances regarding:

88 Preliminary solubility study:

c) if the test material is forming dispersion or emulsions (*e.g.* certain surfactants, aliphatic amines), the dispersibility limit or the critical micelle concentration of the test material in the specific test solution under the test conditions is determined.

89 Test solutions preparation methods:

d) surface-active test chemicals are tested at concentrations below their critical micelle concentration (CMC) in the test medium.

90 Your registration dossier provides an OECD TG 203 study showing the following:

91 Technical specifications impacting the sensitivity/reliability of the test:

a) only 3 fishes were used at each test concentration.

92 Characterisation of exposure:

b) no analytical monitoring of exposure was conducted.

93 Additional requirements applicable to difficult to test substances regarding:

94 Preliminary solubility study:

c) the test material is a surfactant and you do not report the critical micelle concentration. Furthermore, you report that turbidity and a oily phase were visible in the stock solution.

95 Test solutions preparation methods:

d) you have performed the test at nominal concentrations 2.2, 22, 220 and 2200 mg/L.

96 Based on the above, there are critical methodological deficiencies resulting in the rejection of the study results. More, specifically you have performed a range-finder test using less fish than recommended in the test guideline therefore, you have compromised the reliability of the study by decreasing its statistical power. Furthermore, you claim that in an attempt to develop analytical methods, you confirmed that the Substance was unstable in the test medium. Nevertheless, you have not performed analytical monitoring of the exposure concentration. Therefore, you have not demonstrated that the effect values can be based on nominal concentrations.

97 The Substance is difficult to test due to its surfactant nature and there are critical methodological deficiencies resulting in the rejection of the study results. More, specifically you have not determined the critical micelle concentration of the Substance in test solution. Therefore, you have not demonstrated that the exposure concentrations were below the CMC and that the test organisms were exposed to the freely dissolved chemical species and not the micelle form, which is considered to be biologically unavailable, at the used tested doses.

98 Therefore, the requirements of the OECD TG 203 are not met.

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

In the comments to the draft decision submitted by one of the members, reference is made to REACH Annex VIII, section 9.1.3, column 1, and the possibility for registrants to consider long-term toxicity testing instead of short-term.

ECHA confirms that the REACH provision provides this choice for registrants how to comply with the information requirement.

Additionally, regarding your reference to animal welfare, please note that minimisation of vertebrate animal testing is not on its own a legal ground for adaptation under the general rules of Annex XI.

100 You remain responsible for complying with this decision by the set deadline.

5.3. Study design and test specifications

101 The OECD TG 203 specifies that, for difficult to test substances, the OECD GD 23 must be followed. As already explained above, the Substance is difficult to test. Therefore, you must fulfil the requirements described in 'Study design' under request 1.

Reasons related to the information under Annex IX of REACH

6. Extended one-generation reproductive toxicity study

102 An extended one-generation reproductive toxicity (EOGRT) study (OECD 443) is an information requirement under Annex IX to REACH (Section 8.7.3.) if the available studies investigating the properties of the test substance after repeated administration indicate adverse effects on reproductive organs or tissues or reveal other concerns in relation with reproductive toxicity.

6.1. Information provided

103 You have provided:

(i) Screening study for reproductive/developmental toxicity in rats with the Substance *(*2013);

(ii) Developmental toxicity study in rats with the Substance *(*2013).

6.2. Assessment of the information provided

104 Your dossier contains studies investigating the properties of the test substance after repeated administration, which indicate adverse effects on reproductive organs or tissues or reveal other concerns in relation with reproductive toxicity, e.g. in study (i.) - reduced survival index of the offspring, in study (ii.) - reduced gravid uterine weights, reduced body weight of offspring.

105 In the comments to the draft decision submitted by one of the members, you say that "From the results of the OECD 421 study, ECHA concluded a reduced survival index of the offspring. This is in contrast to the study director setting the NOAEL for reproductive and developmental toxicity at the highest dose level of 1000 mg/kg bw/day. No further explanation is given on which grounds ECHA concluded this."

106 You have provided the following information in the IUCLID dossier: "Day 4 survival index was significantly lower at 300 and 1000 mg/kg Bwt/day when compared to the control group. This finding was mainly due to the loss of an entire litter from a single dam (Animal No. Ro2741) at 300 mg/kg Bwt/day and also due to litter losses in two dams (Animals No. Ro2751 and Ro2754) at 1000 mg/kg Bwt/day during the lactation period." This is the data that ECHA has used for the assessment, and the opinion of the study director has no bearing on this fact.

107 Further in the comments you state that instead of an EOGRTS, a study according to the "OECD 414 in a second species (the rabbit) would be the right approach to follow up this finding and to investigate potential species differences and the relevance of the finding for humans."

108 The present information indicates a clear concern for reproductive toxicity in rats from two independent studies. Both studies have observed fetal effects at two different timepoints. These effects may be related to the development of the offspring, however an EOGRTS study will further clarify this concern. The PNDT study did not observe severe malformations but a reduced fetal weight. Further investigation of the potential for teratogenicity in a second species will not dismiss this concern. Therefore, ECHA considers that an EOGRTS is the most appropriate follow-up test.

109 In addition, in the comments to the draft decision you state that if it is maintained that an EOGRTS is the most appropriate test, you do not agree with the requirements regarding

the effects to be noted for the highest dose. Please be informed that the purpose of this test is not to investigate systemic toxicity, it is to investigate reproductive toxicity, and therefore the doses need to be sufficiently high. To ensure future compliance of the study, dose setting shall be based on the following:

110 In the OECD TG 443, the specifications for the highest dose level refer to observation of toxicity and provides guidance in order to avoid death or severe suffering: "the highest dose level should be chosen with the aim to induce some systemic toxicity but not death or severe suffering". The focus of the OECD TG 443 study in the REACH annexes is on sexual function and fertility, which should be prioritised in the study design of the OECD TG 443 study. Regarding the highest dose level, it is important to ensure that sufficient severity of toxicity in both female and male animals is achieved to ensure that potential effects on sexual function and fertility in either gender is not overlooked. The highest dose should be as high as possible without causing death or severe suffering in parental P0 generation.

111 As the study should be designed to ensure adequate assessment of the effects on sexual function and fertility, the dose levels should not be reduced to get enough offspring for the assessment of developmental toxicity. Even if the number of offspring would be reduced due to effects on sexual function and fertility, any offspring available at that dose level should be investigated for adverse effects on development as well as those at lower dose levels.

112 Finally, in the comments to the draft decision you claim that the observed reproductive toxicity effects are a result of microbiome alterations and instead of an EOGRTS you propose an alternative step-wise procedure with ex vivo/in vitro tests, followed by in vivo tests. In addition you claim that the intended use of the substance results in dermal exposure.

113 The aim of the reproductive toxicity study is to maximise the systemic exposure to the substance in order to identify potential reproductive toxicity. You claim that the effects observed in the reproductive toxicity studies, i.e. reduced mean gravid uterine weight, lower foetal weights and foetal skeletal malformations are secondary to the antimicrobial effects of the substance. Your argumentation relies on on data which is yet to be generated, therefore no conclusion on the robustness of your argument regarding the secondary nature of the findings can currently be made.

114 In addition, you claim that "exposure of the human gut microbiome at concentrations having an antimicrobial activity on microorganisms and disturbing the human gut flora, can be excluded" since exposure to the Substance will only occur via the dermal route and at low concentrations.

115 ECHA would like to point out that the purpose of the standard information requirements for reproductive toxicity is to identify the potential intrinsic hazards of the Substance. Therefore risk based conclusions can only be made after the intrinsic hazards are known.

116 In relation to the final point, you also requested an extension of the deadline to provide information from 24 to 36 months from the date of adoption of the decision. However, you have not provided sufficient justification that would explain why the deadline set in this decision would not allow you to perform the requested EOGRTS study. ECHA fails to understand how the proposed microbiome studies would demonstrate that the observed effects are not relevant for humans. It is in your discretion of whether to perfom additional mechanistic studies, however it does not remove your obligation to comply with the standard information requirements.

On this basis the information requirement is not fulfilled.

117 Therefore, the concern for reproductive toxicity must be further investigated.

6.3. Specification of the study design

6.3.1. Species and route selection

118 A study according to the test method OECD TG 443 must be performed in rats with oral administration of the Substance (Guidance on IRs and CSA, Section R.7.6.2.3.2.).

6.3.2. Pre-mating exposure duration

119 The length of pre-mating exposure period must be ten weeks to cover the full spermatogenesis and folliculogenesis before the mating, allowing meaningful assessment of the effects on fertility.

120 Ten weeks pre-mating exposure duration is required to obtain results adequate for classification and labelling and/or risk assessment. There is no substance specific information in the dossier supporting shorter premating exposure duration (Guidance on IRs and CSA, Section R.7.6.).

121 Therefore, the requested pre-mating exposure duration is ten weeks.

6.3.3. Dose-level setting

122 The aim of the requested test must be to demonstrate whether the classification criteria of the most severe hazard category for sexual function and fertility (Repr. 1B; H360F) and developmental toxicity (Repr. 1B; H360D) under the CLP Regulation apply for the Substance (OECD TG 443, para. 22; OECD GD 151, para. 28; Annex I Section 1.0.1. of REACH and Recital 7, Regulation 2015/282), and whether the Substance meets the criteria for a Substance of very high concern regarding endocrine disruption according to Art.57(f) of REACH as well as supporting the identification of appropriate risk management measures in the chemical safety assessment.

123 To investigate the properties of the Substance for these purposes, the highest dose level must be set on the basis of clear evidence of an adverse effect on sexual function and fertility, but no deaths (i.e., no more than 10% mortality; Section 3.7.2.4.4 of Annex I to the CLP Regulation) or severe suffering such as persistent pain and distress (OECD GD 19, para. 18) in the P0 animals.

124 In case there are no clear evidence of an adverse effect on sexual function and fertility, the limit dose of at least 1000 mg/kg bw/day or the highest possible dose level not causing severe suffering or deaths in P0 must be used as the highest dose level. A descending sequence of dose levels should be selected to demonstrate any dose-related effect and aiming to establish the lowest dose level as a NOAEL.

125 In summary: Unless limited by the physical/chemical nature of the Substance, the highest dose level in P0 animals must be as follows:

(1) in case of clear evidence of an adverse effect on sexual function and fertility without severe suffering or deaths in P0 animals, the highest dose level in P0 animals must be determined based on such clear evidence, or
(2) (2 in the absence of such clear evidence, the highest dose level in P0 animals must be set to be the highest possible dose not causing severe suffering or death, or
(3) if there is such clear evidence but the highest dose level set on that basis would cause severe suffering or death, the highest dose level in P0 animals must be set to be the highest possible dose not causing severe suffering or death, or
(4) the highest dose level in P0 animals must follow the limit dose concept.

126 You have to provide a justification with your study results demonstrating that the dose level selection meets the conditions described above.

127 Numerical results (i.e. incidences and magnitudes) and description of the severity of effects at all dose levels from the dose range-finding study/ies must be reported to facilitate the assessment of the dose level section and interpretation of the results of the main study.

6.3.4. Cohorts 1A and 1B

128 Cohorts 1A and 1B belong to the basic study design and must be included.

129 Histopathological investigations in Cohorts 1A and 1B

130 In addition to histopathological investigations of cohorts 1A, organs and tissues of Cohort 1B animals processed to block stage, including those of identified target organs, must be subjected to histopathological investigations (according to OECD TG 443, para. 67 and 72) if:

- the results from Cohort 1A are equivocal,
- the test substance is a suspected reproductive toxicant or
- the test substance is a suspected endocrine toxicant.

131 Splenic lymphocyte subpopulation analysis

132 Splenic lymphocyte subpopulation analysis must be conducted in Cohort 1A (OECD TG 443, para. 66; OECD GD 151, Annex Table 1.3).

133 Investigations of sexual maturation

134 To improve the ability to detect rare or low-incidence effects, all F1 animals must be maintained until sexual maturation to ensure that sufficient animals (3/sex/litter/dose) are available for evaluation of balano-preputial separation or vaginal patency (OECD GD 151, para. 12 in conjunction with OECD TG 443, para. 47). For statistical analyses, data on sexual maturation from all evaluated animals/sex/dose must be combined to maximise the statistical power of the study.

6.4. Further expansion of the study design

135 The conditions to include the extension of Cohort 1B are currently not met. Furthermore, no triggers for the inclusion of Cohorts 2A and 2B (developmental neurotoxicity) and Cohort 3 (developmental immunotoxicity) were identified. However, you may expand the study by including the extension of Cohort 1B, Cohorts 2A and 2B and/or Cohort 3 if relevant information becomes available from other studies or during conduct of this study. Inclusion is justified if the available information meets the criteria and conditions which are described in Column 2, Section 8.7.3., Annex IX. You may also expand the study due to other scientific reasons in order to avoid a conduct of a new study. The study design, including any added expansions, must be fully justified and documented. Further detailed guidance on study design and triggers is provided in Guidance on IRs & CSA, Section R.7.6.

7. Long-term toxicity testing on aquatic invertebrates

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

137 You have adapted the standard information requirement(s) mentioned above according to Annex XI, Section 1.2. of REACH (weight of evidence).

7.1. Information provided

138 In support of your adaptation, you have provided the following justification to omit the study: "There is sufficient weight of evidence available from several independent sources of information leading to the conclusion that the substance has not a particular dangerous

property with regard to long-term toxicity to aquatic organisms. The substance is not classified for the environment. Due to the rapid degradation resulting in short exposure time and the low bioaccumulation potential of the substance, exposure to aquatic organisms will be low. Therefore, it is not expected that performance of a long-term toxicity study in daphnia would provide additional ecotoxicological information on this substance with regard to its safety to the environment."

7.2. Assessment of the information provided

139 We have assessed this information and identified the following issues:

7.2.1. The provided adaptation does not meet the criteria of Annex XI, Section 1.2

140 Annex XI, Section 1.2 states that there may be sufficient weight of evidence from several independent sources of information leading to assumption/conclusion that a substance has or has not a particular dangerous (hazardous) property, while information from a single source alone is insufficient to support this notion.

141 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 that the Substance has or has not the (dangerous) property investigated by the required study.

142 Annex XI, section 1.2 requires that adequate and reliable documentation is provided to describe your weight of evidence adaptation.

143 While you have listed various arguments (e.g. lack of environmental classification, rapid degradation and low bioaccumulation) to justify your adaptation, you have not included a justification with an assessment, integration and weighing of the individual sources of information for relevance, reliability, coverage, consistency and results, and subsequently decided whether they together provide sufficient weight to conclude that the Substance has or has not the dangerous property investigated by the required study.

144 Irrespective of the above mentioned deficiencies on the documentation, which in itself could lead to the rejection of the adaptation, ECHA has assessed the provided sources of information, and identified an additional issue:

7.2.1.1. Absence of relevant hazard information

145 Relevant information that can be used to support weight of evidence adaptation for information requirement of Section 9.1.5 at Annex IX includes similar information that is produced by the OECD TG 211. This includes:

1) the reproductive output of Daphnia sp. expressed as the total number of living offspring produced at the end of the test, and
2) the survival of the parent animals during the test, and
3) the time to production of the first brood.

146 The arguments presented in your justification do not provide relevant information on any of the key investigations listed above.

147 The sources of information, as indicated above, lack information on all essential key investigations. This information is essential to assess the long-term toxicity on aquatic invertebrates and cannot be covered by or derived from any of the available sources of

information. In this absence of any information addressing the hazardous properties investigated by the OECD TG 211 in the set of information provided in your weight of evidence approach, no conclusion on the long-term toxicity on aquatic invertebrates of the Substance can be made.

148 Furthermore, it is also pointed out that 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 (Decision of the Board of Appeal in case A-011-2018).

149 Therefore, you have not demonstrated that this information can be omitted.

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

151 In the comments to the draft decision submitted by one of the members, you agree to perform the requested study.

7.3. Study design and test specifications

152 The OECD TG 211 specifies that, for difficult to test substances, the OECD GD 23 must be followed. As already explained above, the Substance is difficult to test. Therefore, you must fulfil the requirements described in 'Study design' under request 1.

8. Long-term toxicity testing on fish

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

154 You have adapted the standard information requirement(s) mentioned above according to Annex XI, Section 1.2. of REACH (weight of evidence).

8.1. Information provided

155 In support of your adaptation, you have provided a similar justification to omit the study as provided to adapt the information requirement stated under request 8 above: "There is sufficient weight of evidence available from several independent sources of information leading to the conclusion that the substance has not a particular dangerous property with regard to long-term toxicity to aquatic organisms. The substance is not classified for the environment. Due to the rapid degradation resulting in short exposure time and the low bioaccumulation potential of the substance, exposure to aquatic organisms will be low. As it is therefore not expected that performance of a long-term toxicity study in fish would provide additional ecotoxicological information on this substance with regard to its safety to the environment and for animal welfare, a study on long-term toxicity to fish is not proposed."

8.2. Assessment of the information provided

156 We have assessed this information and identified the following issues:

8.2.1. The provided adaptation does not meet the criteria of Annex XI, Section 1.2

157 As stated above, Annex XI, Section 1.2 states that there may be sufficient weight of evidence weight of evidence from several independent sources of information leading to assumption/conclusion that a substance has or has not a particular dangerous (hazardous) property, while information from a single source alone is insufficient to support this notion.

158 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 that the Substance has or has not the (dangerous) property investigated by the required study.

159 Annex XI, section 1.2 requires that adequate and reliable documentation is provided to describe your weight of evidence adaptation.

160 While you have listed various arguments (e.g. lack of environmental classification, rapid degradation and low bioaccumulation) to justify you adaptation, you have not included a justification with an assessment, integration and weighing of the individual sources of information for relevance, reliability, coverage, consistency and results, and subsequently decided whether they together provide sufficient weight to conclude that the Substance has or has not the dangerous property investigated by the required study.

161 Irrespective of the above mentioned deficiencies on the documentation, which in itself could lead to the rejection of the adaptation, ECHA has assessed the provided sources of information, and identified an additional issue:

8.2.1.1. Absence of relevant hazard information

162 Relevant information that can be used to support weight of evidence adaptation for information requirement of Section 9.1.1 at Annex IX includes similar information that is produced by the OECD TG 210. This includes:

1) the stage of embryonic development at the start of the test, and
2) hatching of fertilized eggs and survival of embryos, larvae and juvenile fish, and
3) the appearance and behaviour of larvae and juvenile fish, and
4) the weight and length of fish at the end of the test.

163 The arguments presented in your justification do not provide relevant information on any of the key investigations listed above.

164 The sources of information, as indicated above, lack information on all essential key investigations. This information is essential to assess the long-term toxicity on fish and cannot be covered by or derived from any of the available sources of information. In this absence of any information addressing the hazardous properties investigated by the OECD TG 210 in the set of information provided in your weight of evidence approach, no conclusion on the long-term toxicity on fish of the Substance can be made.

165 Furthermore, it is pointed out that Annex IX, Section 9.1., Column 2 does not allow omitting the need to submit information on long-term toxicity on fish under Column 1 (Decision of the Board of Appeal in case A-011-2018).

166 Therefore, you have not demonstrated that this information can be omitted. It is also noted that minimisation of animal testing is not on its own a legal ground for adaptation under the general rules of Annex XI.

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

168 In the comments to the draft decision submitted by one of the members, you agree to perform the requested study.

8.3. Study design and test specifications

169 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.).

170 The OECD TG 210 specifies that, for difficult to test substances, the OECD GD 23 must be followed. As already explained above, the Substance is difficult to test. Therefore, you must fulfil the requirements described in 'Study design' under request 1.

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

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 08 June 2021.

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

ECHA took into account your comments and did not amend the requests or the deadline.

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]
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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].

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