~~Confidential~~

Helsinki, 07 November 2023

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

Date of submission of the dossier subject to this decision
11 March 2014

Registered substance subject to this decision ("the Substance")
Substance name: Propanoic acid, 2-hydroxy-, C12-13-branched-alkyl esters
EC/List number: 939-514-3

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

2. Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: EU C.4. A/B/C/D/E/F/OECD TG 301A/B/C/D/E/F or EU C.29./OECD TG 310) on relevant constituent(s)/fraction(s) of the Substance, as described under the corresponding appendix on reasons for the request.

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

3. Justification for an adaptation of the short-term repeated dose toxicity study (28 days) (Annex VIII, Section 8.6.1., Column 2) based on the request 6 below.

   If the sub-chronic toxicity study (90 days) is not requested:

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

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

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

7. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method: OECD TG 414) by oral route, in one species (rat or rabbit);

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 request(s) are explained in Appendix 1.

Information required depends on your tonnage band

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

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

How to comply with your information requirements

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

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

Appeal

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

Failure to comply

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

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

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

[1] As this is an electronic document, it is not physically signed. This communication has been approved according to ECHA's internal decision-approval process.

Appendix 1: Reasons for the request(s)

Reasons common to several requests 4

Reasons related to the information under Annex VII of REACH 8

1. Growth inhibition study aquatic plants 8
2. Ready biodegradability 9

Reasons related to the information under Annex VIII of REACH 12

3. Short-term repeated dose toxicity (28 days) 12
4. Screening for reproductive/developmental toxicity 14
5. Short-term toxicity testing on fish 17

Reasons related to the information under Annex IX of REACH 19

6. Sub-chronic toxicity study (90-day) 19
7. Pre-natal developmental toxicity study in one species 21
8. Long-term toxicity testing on fish 24

References 25

Reasons common to several requests

0.1. Weight of evidence adaptation rejected

0.1.1. Information provided

1 You have adapted the following standard information requirements by using weight of evidence adaptations in accordance with Annex XI, Section 1.2.:

- Short-term repeated dose toxicity (28 day) (Annex VIII, Section 8.6.1.)
- Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)
- Sub-chronic toxicity study (90-day) (Annex IX, Section 8.6.2.)
- Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)

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

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

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

0.1.2. Use of information on analogue substances

5 You intend to predict the relevant properties of the Substance from data obtained with source substances in a read-across approach as part of your weight of evidence adaptation.

6 For this information to reliably contribute to the weight of evidence approach, it would have to meet the requirements for Grouping of substances and read-across approaches (Annex XI, Section 1.5.).

7 Annex XI, Section 1.5. specifies two conditions which must be fulfilled whenever a read-across approach is used.

8 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.

9 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.

10 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).

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

12 You provide the following reasoning for the prediction of toxicological properties:

13 You consider that the Substance, Propanoic acid, 2-hydroxy-, C12-13-branched-alkyl esters, will hydrolyse in the gastro-intestinal tract to form free Alcohols C12-13-branched and lactic acid. Therefore you consider that "Alcohols, C12-13-branched and linear, Lactic acid and additional structurally similar substances of the breakdown products are suitable substances for read-across". Your weight of evidence adataptions also include information on esters of lactic acid similar to the Substance.

14 More specifically, you predict the properties of the Substance from the following analogue substances:

- Propanoic acid, 2-hydroxy-, 2-ethylhexyl ester, EC No. 228-503-2 (source substance 1);
- Tetradecyl 2-hydroxypropionate, EC No. 215-350-1 (source substance 2) ;
- 2-Hydroxypropanoic acid (Lactic acid), EC 200-018-0 (source substance 3);
- Hexan-1-ol, EC No. 203-852-3 (source substance 4);
- Alcohols, C7-11-branched and linear, EC No. 287-623-3 (source substance 5);
- Dodecan-1-ol, EC No. 203-982-0 (source substance 6);
- Alcohols, C12-13-branched and linear, EC No. 278-306-0 (souce substance 7);
- Octadecan-1-ol, EC No. 204-017-6 (source substance 8);
- Docosan-1-ol, EC No. 211-546-6 (source substance 9).

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

0.1.2.1. Assessment of the information provided

0.1.2.1.1. Incomplete characterisation of the source substances 5 and 7

16 Annex XI, Section 1.5. provides that "substances whose physicochemical, toxicological and ecotoxicological properties are likely to be similar or follow a regular pattern as a result of structural similarity may be considered as group."

17 Therefore, qualitative and quantitative information on the compositions of the Substance and of the source substance(s) must be provided to allow assessing whether the attempted predictions are compromised by the composition and/or impurities.

18 In your read-across justification you report that the source substances 5 and 7 are composed of a set of constituents with branched and linear carbon chain length ranging from C7 to 11 and from C12 to C13, respectively.

19 You do not further characterise the length and position of the branching in the structures of the constituents of these substances.

20 Without this information, it is not possible to determine the extent of the similarity between the source substances 5 and 7 and the free alcohols formed from the hydrolysis of the Substance.

21 Therefore the reliability of the contribution of the information obtained from source substances 5 and 7 to the weight of evidence adaptations cannot be established.

0.1.2.1.2. Missing supporting information to compare the properties of the substances

22 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 substances (Guidance on IRs and CSA R.6, Section R.6.2.2.1.f.).

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

24 In your read-across justification document you indicate that "due to the anticipated enzymatic ester hydrolysis of Propanoic acid, 2-hydroxy-, C12-13- branched-alkyl esters, Alcohols, C12-13-branched and linear, Lactic acid and additional structurally similar substances of the breakdown products are suitable substances for read across." You further consider that esters of lactic acid similar to the Substance also constitute suitable source substances.

25 You have provided supporting evidence to characterise the rapid hydrolysis of the ester bond of the Substance in simulated intestinal fluids leading to the formation of free Alcohols C12-13-branched and lactic acid.

26 In order to support your predictions from these source substances, you point out structural similarities, similarity in physico-chemical properties, similarity in the metabolic pathways. You also refer to similarities in "the levels and mode of human related effects" with an emphasis on toxicokinetic behaviour and conclude that the Substance and the source substances "are similar with regard to the assessment of health effects".

27 Your read-across hypothesis is based on the assumption that the properties of the Substance can then be predicted from esters which are structurally similar to the Substance, from the hydrolysis products formed from the Substance, i.e. Alcohols C12-13-branched and lactic acid, and from substance structurally similar to the free alcohols formed from the hydrolysis of the Substance.

28 The esters which are structurally similar to the Substance, i.e. source substances 1 and 2, are anticipated to hydrolyse and release free alcohols with branched C8 and C14 carbon chain length, respectively.

29 The carbon chain lengths of the source substances 4, 6, 8 and 9, are 6, 12, 18 and 22, respectively.

30 This means that the carbon chain length of the source substances 1, 2, 4, 8 and 9 are either of shorter or longer than the carbon chain length of the free alcohols formed from the hydrolysis of the Substance, Alcohols C12-13-branched.

31 The carbon chain length of the source substance 6 matches the carbon chain length of some of the free alcohols formed from the hydrolysis of the Substance, i.e C12. However the source substance 6 corresponds to a linear C12 alcohol whereas the Substance hydrolyses to branched C12 alcohols.

32 While you refer to similarities in physico-chemical properties, and to similarities in metabolic pathways for the alcohol components of the read-across adaptations, you have not provided information, such as bridging studies, establishing that these alcohol components and the alcohols formed from the hydrolysis of the Substance are likely to have similar toxicological properties despite the variation in carbon chain length and/or their branching/linear structures. Similarity in physico-chemical properties and in metabolic pathways does not necessarily translate in similarity in toxicological properties.

33 In the absence of such information, you have not established that the free alcohols formed from the hydrolysis of the Substance and the source substances 1, 2, 4, 6, 8 and 9 are

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

0.1.2.1.3. Missing robust study summaries

34 Annex XI, Section 1.2. requires that whenever weight of evidence is used adequate and reliable documentation of the applied method must be provided. Such documentation must include a robust study summary for each source of information used in the adaptations.

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

36 In addition, for weight of evidence adaptations, the robust study summary must clearly indicate which key parameters of the study normally required for the information requirement are investigated in the study.

37 The following sources of information have been included in your weight of evidence adaptations to address:

38 The short-term repeated dose toxicity and sub-chronic toxicity of the Substance:

(i) a publication on the safety assessment of lactic acid (1998) (source substance 3);

39 The pre-natal developmental toxicity of the Substance:

(ii) a publication on the developmental toxicity data from structurally related long-chain alcohols (1995) including the source substance 7.

40 You have provided only the name of these studies and information on the identity of substances investigated.

41 However you have not provided detailed information on the methods, results and conclusions, allowing for an independent assessment of each source of information and contributing to the overall weight of evidence for the information requirement under consideration.

42 In the absence of robust study summary, the coverage of the key parameters associated with the information requirements for which these these sources are used and the reliability of their contribution on these parameters to your weight of evidence adaptations cannot be evaluated.

43 ECHA concludes that you have failed to provide a robust study summary for these specific source studies used in the adaptation as required by Annex XI, Section 1.2.

44 Consequently, these sources of information that are lacking robust study summaries cannot be considered as contributing to the overall weight of evidence for the information requirement under consideration.

45 Additional deficiencies that are specific for each of the information requirements individually are addressed under requests 3, 4, 6 and 7.

Reasons related to the information under Annex VII of REACH

1. Growth inhibition study aquatic plants

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

1.1. Information provided

47 You have provided:

(i) Growth inhibition study on aquatic plants/algae (2008) with the Substance;

1.2. Assessment of the information provided

1.2.1. The provided study does not meet the specifications of the test guideline(s)

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

49 Key parameter measured

a) the concentrations of the test material leading to a 50 % and 0% (or 10%) inhibition of growth at the end of the test are estimated. Growth must be expressed as the logarithmic increase in biomass (average specific growth rate) during the exposure period;

50 Characterisation of exposure

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

c) for some substances (e.g. adsorbing substances), the results may only be expressed based on nominal concentrations if the decrease in measured concentrations of the test substance during the test is not accompanied by a decrease in growth inhibition. If a reduction in growth inhibition is observed, a suitable model describing the decline of the concentration of the test material must be used;

51 Reporting of the methodology and results

d) adequate information on the analytical method (including performance parameters of the method) and on the results of the analytical determination of exposure concentrations is provided;

52 In study (i):

53 Key parameter measured

a) The long-term toxicity response variable EC10/NOEC and its associated confidence intervals were not measured.

54 Characterisation of exposure

b) no analytical monitoring of exposure was conducted;

55 Reporting of the methodology and results

c) The results of the analytically determined exposure concentrations are not provided;

56 Based on the above,the key parameter of OECD TG 201 is not covered.

57 Furthermore, there are critical methodological deficiencies resulting in the rejection of the study results. More specifically, the exposure concentrations were not measured.

58 Based on the above, ECHA cannot verify if study (i) is valid.

59 On this basis, the specifications of OECD TG 201 are not met.

60 Therefore, the information requirement is not fulfilled.

1.3. Study design

61 The Substance is difficult to test due to the adsorptive properties (Log K_{ow} 5.7). OECD TG 201 specifies that, for difficult to test substances, you must consider the approach described in OECD GD 23 or other approaches, if more appropriate for your substance. In all cases, the approach selected must be justified and documented. Due to the properties of Substance, it may be difficult to achieve and maintain the desired exposure concentrations.

62 Therefore, you must monitor the test concentration(s) of the Substance throughout the exposure duration and report the results. If it is not possible to demonstrate the stability of exposure concentrations (i.e. measured concentration(s) not within 80-120% of the nominal concentration(s)), you must express the effect concentration based on measured values as described in OECD TG 201.

63 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.

64 For multi-constituents/UVCBs, the analytical method must be adequate to monitor qualitative and quantitative changes in exposure to the dissolved fraction of the test material during the test (e.g. by comparing mass spectral full-scan GC or HPLC chromatogram peak areas or by using targeted measures of key constituents or groups of constituents).

65 If you decide to use the Water Accommodated Fraction (WAF) approach, in addition to the above, you must:

- use loading rates that are sufficiently low to be in the solubility range of most constituents (or that are consistent with the PEC value). This condition is mandatory to provide relevant information for the hazard and risk assessment (Guidance on IRs and CSA, Appendix R.7.8.1-1, Table R.7.8-3);
- provide a full description of the method used to prepare the WAF (including, among others, loading rates, details on the mixing procedure, method to separate any remaining non-dissolved test material including a justification for the separation technique);
- prepare WAFs separately for each dose level (*i.e.* loading rate) and in a consistent manner.

66 In the comments to the draft decision you agree with the request.

2. Ready biodegradability

67 Ready biodegradability is an information requirement in Annex VII to REACH (Section 9.2.1.1.).

2.1. Information provided

68 You have provided:

(i) a ready biodegradability study (1997) with the Substance;

2.2. Assessment of the information provided

2.2.1. Ready biodegradation tests are normally intended for pure substances

69 The revised introduction to the OECD Guidelines For Testing Of Chemicals, Section 3 Part I states that ready biodegradability tests are intended for pure substances but may also be relevant, on a case-by-case basis, to mixtures of structurally similar chemicals (i.e. which are composed of constituents expected to show similar degradation kinetics).

70 However, such tests are not generally applicable for complex mixtures or substances (i.e. UVCB or multi-constituent substances) containing different types of constituents. For complex substances, a single ready biodegradability test does not allow to conclude on the ready biodegradability of all constituents and therefore, does not fulfil the information requirement.

71 In this case, the ready biodegradability test must be performed on relevant constituent(s)/fraction(s) of the Substance.

72 You have provided a study conducted on the Substance as a whole.

73 In Section 1.1. of your dossier you describe the Substance as UVCB. In Section 1.2, you describe the substance as a mixture of alkyl esters (propanoic acid, 2-hydroxy-, C13-alkyl-branched esters and propanoic acid, 2-hydroxy-, C12-alkyl-branched esters), alcohols (Alcohols, C12-13-branched and linear) and oxopropane-2-yl fractions (1-(tridecyl-branched-oxy)-1-oxopropan-2-yl 2-hydroxypropanoate and 1-(dodecyl-branched-oxy)-1-oxopropan-2-yl 2-hydroxypropanoate).

74 The Substance is a complex substance and contains constituents with significant structural differences described above. Therefore, the provided study does not provide unequivocal conclusion that all constituents can safely be regarded as readily biodegradable.

75 Therefore, the information requirement is not fulfilled.

76 In the comments to the draft decision you indicate that available information already confirms that all constituents of the Substance are ready biodegradable.

77 You clarify that "While the substance is a complex substance, the components fall into 3 categories: alcohols, lactates of the alcohols and di-lactates of the alcohols".

78 In your comments to the draft decision you provide the following supporting information demonstrating that all constituents of the Substance are readily biodegradable:

- BIOWIN 2, 3 and 6 model predictions on multiple constituents of the Substance, belonging to alcohols, lactates of the alcohols and di-lactates of the alcohols categories, consistently indicating ready biodegradability;
- Robust study summary of a ready biodegradability study (1993) with analogue substance CAS 85586-10-3 (a starting material of reaction), demonstrating readily biodegradability;
- Reference to ready biodegradability and nature of lactic acid (another starting material of reaction), "a naturally occurring substrate found in animal and bacterial cells which have enzymes capable of metabolizing the substance".

79 ECHA has assessed the information provided in your comments and consider it appropriate to potentially fulfil this information requirement.

80 However, as the information is currently not available in the registration dossier, the data gap remains.

81 You may consider submitting this information in an updated registration dossier by the deadline set out in the decision.

2.3. Study design

82 To fulfil the information requirement, the test method(s) according to OECD TG 301A/B/C/D/E/F or OECD TG 310 are in general appropriate. You can choose any of these methods, but you must ensure that the Substance is within the applicability domain of the test method chosen.

83 For the reasons provided above, testing on the Substance as a whole does not fulfil the information requirement. For the generation of information on ready biodegradability, you must consider the level of information required for the purposes of classification and labelling and, if applicable to your registration, the PBT/vPvB assessment and the exposure assessment/risk characterisation.

84 In order to conclude on which of constituents of the Substance are and which are not readily biodegradable, you may have to consider conducting more than one study using selected individual constituents and/or fractions. If you choose to test one (or more) fraction(s) of the Substance, you must provide a justification that their constituents within chosen fraction(s) are similar enough so that similar degradation kinetics can be assumed.

85 If you decide to conduct a single study in order to prove that all constituents of the Substance are readily biodegradable, you must provide a justification that the selected constituent/fraction can be considered a reasonable worst-case for the Substance as a whole in terms of degradation kinetics.

86 Justification for selection of relevant constituent and/or fractions for the testing, must consider degradation kinetics of constituents of the Substance based, as minimum, on the similarity/differences of the chemical structures and the physico-chemical properties of constituents of the Substance. For that purpose, tools and approaches mentioned in Guidance on IRs and CSA, Sections R.7b and R.11 should be considered.

Reasons related to the information under Annex VIII of REACH

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

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

3.1. Information provided

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

(i) a repeated dose toxicity study (90 days) (1985) with the source substance 2;
(ii) a repeated dose toxicity study (90 days) (1966) with the source substance 4
(iii) a repeated dose toxicity study (28 days) (1992) with the source substance 6;
(iv) a publication on the safety assessment of lactic acid (1998) (source substance 3).

3.2. Assessment of the information provided

89 In addition to the deficiencies identified in Section 0.1., ECHA identified endpoint specific issue(s) addressed below.

90 Information that can be used to support weight of evidence adaptation for the information requirement of Annex VIII, Section 8.6.1. includes similar information that is produced by the OECD TG 407. The OECD TG 407 requires to investigate the following key parameters: 1) in-life observations, 2) blood chemistry, 3) organ and tissue toxicity.

3.2.1. In-life observations

91 In-life observations must include information on survival, body weight development, clinical signs, functional observations, food/water consumption and other potential aspects of in life observations on the relevant physiological systems (circulatory, digestive/excretory, integumentary, musculoskeletal, nervous, renal/urinary, and respiratory).

3.2.1.1. Relevance of the information provided

92 The source of information (i) provides relevant information on survival, body weight development and clinical observations only.

93 The source of information (ii) provides relevant information on survival, body weight development only.

94 The source of information (iii) provides relevant information on survival, body weight development, clinical observations, food consumption.

95 For the reasons presented in Section 0.1.2.1.3 above, the source of information (iv) does not provide relevant information on in life observations.

3.2.1.2. Reliability of the contribution of the information to the weight of evidence

96 The reliability of the contribution of the sources of information (i)-(iii) is affected by the deficiencies presented in section 0.1.2.1.2 above.

97 Therefore, none of the studies can be considered a source of information that could reliably contribute to the conclusion on in life observations investigated by the required study.

3.2.2. Blood chemistry

98 Information on blood chemistry must include haematological (full-scale) and clinical chemistry analysis (full-scale), and other potential aspects related to blood chemistry to address relevant physiological systems (circulatory digestive/excretory, endocrine, immune, musculoskeletal, and renal/urinary)

3.2.2.1. Relevance of the information provided

99 The source of information (i) provides relevant information on haematological and clinical chemistry and urinalysis only.

100 The source of information (ii) provides relevant information on a limited set of haematological examinations and urinalysis only.

101 The source of information (iii) provides relevant information on haematological, clinical and blood chemistry.

102 For the reasons presented in Section 0.1.2.1.3 above, the source of information (iv) does not provide relevant information on blood chemistry.

3.2.2.2. Reliability of the contribution of the information to the weight of evidence

103 The reliability of the contribution of the sources of information (i)-(iii) is affected by the deficiencies presented in section 0.1.1.2 above.

104 Therefore, none of the studies can be considered a source of information that could reliably contribute to the conclusion on blood chemistry investigated by the required study.

3.2.3. Organ and tissue toxicity

105 Organ and tissue toxicity must include information on terminal observations on organ weights, gross pathology and histopathology (full-scale and other potential aspects related to organ and tissue toxicity to address relevant physiological systems (circulatory, digestive/excretory, endocrine, immune, integumentary, musculoskeletal, nervous, renal/urinary system, reproductive, and respiratory).

3.2.3.1. Relevance of the information provided

106 The sources of information (i)-(iii) provide relevant information on a set of organ weights, gross pathology and histopathology only. More specifically, none of the sources of information provide information on gross pathology and histopathology of epididymides, prostate and seminal vesicle, thymus and vagina.

107 For the reasons presented in Section 0.1.2.1.3 above, the source of information (iv) does not provide relevant information on organ and tissue toxicity..

3.2.3.2. Reliability of the contribution of the information to the weight of evidence

108 The reliability of the contribution of the sources of information (i)-(iii) is affected by the deficiencies presented in section 0.1.2.1.2 above.

109 Therefore, none of the studies can be considered a source of information that could reliably contribute to the conclusion on organ and tissue toxicity investigated by the required study.

3.2.4. Conclusion

110 In summary, you have provided information on in-life observations, blood chemistry and on some elements of organ and tissue toxicity only. Specifically, none of the studies

investigate gross pathology and histopathology of epididymides, prostate and seminal vesicle, thymus and vagina.

111 Furthermore, for the elements covered, the corresponding sources of information have deficiencies affecting their reliability that prevent reaching conclusion on any of the aspects investigated.

112 Therefore, it is not possible to conclude, based on any source of information alone or considered together, on the information requirement for a short-term repeated dose toxicity study.

113 Based on the above, your adaptation is rejected and the information requirement is not fulfilled.

3.3. Study design

114 The OECD TG 407 is an appropriate guideline for fulfilling this information requirement.

115 Following the criteria provided in Annex VIII, Section 8.6.1., Column 2, and considering the Guidance on IRs and CSA, Section R.7.5.6.3.1., the oral route is the most appropriate route of administration to investigate repeated dose toxicity of the Substance.

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

117 The information requirement for the screening study for reproductive/developmental toxicity is not fulfilled for the reasons explained under request 4.

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

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

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

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

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

122 Therefore, you are requested to either submit:

- a justification for the adaptation according to Annex VIII, Section 8.6.1., Column 2, based on request 6; or
- a 28-day study to be combined with the screening for reproductive/developmental toxicity in case the 90-day study is not requested in the adopted decision.

123 In the comments to the draft decision you agree with the request.

4. Screening for reproductive/developmental toxicity

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

4.1. Information provided

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

(i) a repeated dose toxicity study (1966) with the source substance 4;
(ii) a combined repeat dose and reproductive/developmental toxicity screening test (1992) with the source substance 6;
(iii) a combined repeat dose and reproductive/developmental toxicity screening test (1992) with the source substance 8;
(iv) a one-generation reproductive toxicity (2002) with the source substance 9;
(v) a repeated dose toxicity study (28 days) (1992) with the source substance 6.

4.2. Assessment of the information provided

126 In addition to the deficiencies identified in Section 0.1., ECHA identified endpoint specific issue(s) addressed below.

127 Information that can be used to support weight of evidence adaptation for the information requirement of Annex VIII, Section 8.7.1. includes similar information that is produced by the OECD TGs 421/422OECD TGs 421/422 require to investigate the following key parameters: 1) sexual function and fertility, 2) toxicity to offspring, and 3) systemic toxicity.

4.2.1. Sexual function and fertility

128 Sexual function and fertility on both sexes must include information on mating, fertility, gestation (length), maintenance of pregnancy (abortions, total resorptions), parturition, lactation, organ weights and histopathology of reproductive organs and tissues, litter sizes, nursing performance and other potential aspects of sexual function and fertility.

4.2.1.1. Relevance of the information provided

129 The source of information (i) provides relevant information on organ weights and histopathology of reproductive organs and tissues only. The sources of information (ii)-(v) provide relevant information on all the elements of this key parameter.

4.2.1.2. Reliability of the contribution of the information to the weight of evidence

130 However, the reliability of the contribution of all the sources of information is affected by the deficiencies presented in section 0.1.2.1.2 above.

131 Therefore, none of the studies can be considered a source of information that could reliably contribute to the conclusion on sexual function and fertility investigated by the required study.

4.2.2. Toxicity to offspring

132 Information on pre- and perinatal developmental toxicity reflected by litter sizes, postimplantation loss (resorptions and dead foetuses), stillborns, and external malformations, postnatal developmental toxicity reflected by survival, clinical signs and body weights of the pups (or litters), and other potential aspects related to pre-, peri- and postnatal developmental toxicity observed up to postnatal day 13.

4.2.2.1. Relevance of the information provided

133 The sources of information (i) and (v) do not provide relevant information on toxicity to the offspring. The sources of information (ii)-(iv) provide relevant information on all the elements of this key parameter.

4.2.2.2. Reliability of the contribution of the information to the weight of evidence

134 However, the reliability of the contribution of the sources of information (ii)-(iv) is affected by the deficiencies presented in section 0.1.2.1.2 above.

135 Therefore, none of the studies can be considered a source of information that could reliably contribute to the conclusion on sexual function and fertility investigated by the required study.

4.2.3. Systemic toxicity

136 Information on systemic toxicity include clinical signs, survival, body weights, food consumption, haematology, clinical chemistry, organ weights and histopathology of non-reproductive organs and other potential aspects of systemic toxicity in the parental generation up to postnatal day 13.

4.2.3.1. Relevance of the information provided

137 The sources of information (i) and (v) provide information on clinical signs, survival, body weights, food consumption, haematology, clinical chemistry, organ weights and histopathology of non-reproductive organs and other potential aspects of systemic toxicity in males and non-pregnant females only. This means that the sources of information (i) and (v) do not inform on the systemic toxicity of the test item after administration to females during the course of pregnancy and during the lactation phase until post-natal dat 13.

138 The sources of information (ii)-(iv) provide relevant information on all the elements of this key parameter.

4.2.3.2. Reliability of the contribution of the information to the weight of evidence

139 However, the reliability of the contribution of all the sources of information is affected by the deficiencies presented in section 0.1.2.1.2 above.

140 Therefore, none of the studies can be considered a source of information that could reliably contribute to the conclusion on sexual function and fertility investigated by the required study.

4.2.4. Conclusion

141 While you have provided information on sexual function and fertility, toxicity to offspring, and systemic toxicity, the corresponding sources of information have deficiencies affecting their reliability which prevents reaching any conclusion on the key parameters investigated

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

143 Based on the above, your adaptation is rejected and the information requirement is not fulfilled.

4.3. Study design

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

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

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

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

148 In case the adopted decision no longer contains a request for a sub-chronic (90 days) study (e.g. as a result of an overall tonnage band change of the joint submission) and the the 28-day study must be performed, a screening study for reproductive/developmental toxicity performed according to the OECD TG 422 is required, as it will fulfil both information requirements.

149 In the comments to the draft decision you agree with the request.

5. Short-term toxicity testing on fish

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

5.1. Information provided

151 You have provided:

(i) a short-term toxicity study on fish (2008) with the Substance;

5.2. Assessment of the information provided

5.2.1. The provided study does not meet the specifications of the test guideline(s)

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

Validity criteria

a) the analytical measurement of test concentrations is conducted;

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;

153 In study (i):

Validity criteria

a) no analytical measurement of test concentrations was conducted;

Characterisation of exposure

b) no analytical monitoring of exposure was conducted;

154 In the comments to the draft decision, you agree with the deficiencies identified above however, you consider that a new study should not be requested.

155 You claim that, as this study was a limit test at 100 mg/L loading concentration, the fish were exposed to the maximum possible concentration. Consequently, you consider that the results of a new study would not differ, i.e. absence of mortality would be expected, from those observed in the study provided.

156 ECHA has assessed your comments and disagrees with your conclusions.

157 The Substance is difficult to test, as already explained in this decision.

158 ECHA further notes that in section 6.1 of your dossier you claim that "*It might be possible that a component of the UVCB substance tends to [form] micro-micelles with increasing loading rates*". Therefore, it is not possible to assess if the Substance was bioavailable during the exposure period.

159 Furthermore, the results of the long-term toxicity to aquatic invertebrates reported in section 6.1.4 of your dossier indicate that the effective concentration of the Substance in medium can be ca. 2 orders of magnitude lower than the nominal concentration. Therefore, in the absence of analytical monitoring, it is not possible to assess at what concentration fish were effectively exposed.

160 On this basis, the specifications of OECD TG 203, including the validity criteria, are not met and the limit test with the Substance without analytical monitoring (study i), does not inform on the acute toxic potential of the Substance on fish.

161 Therefore, the information requirement is not fulfilled.

162 In addition, in your comments to the draft decision you note that a long-term toxicity study on fish is also requested in this decision, under Request 8.With regards to the parallel Request 8, REACH Annex VII section 9.1.1 column 2 specifies that the short-term toxicity study does not need to be conducted if a long-term aquatic toxicity study on invertebrates is available. At present no long-term toxicity study on aquatic invertebrates is provided in the IUCLID dossier, therefore you remain responsible for complying with this decision by the set deadline.

5.3. Study design

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

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

6.1. Information provided

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

(i) a repeated dose toxicity study (90 days) (1985) with the source substance 2;
(ii) a repeated dose toxicity study (90 days) (1966) with the source substance 4
(iii) a repeated dose toxicity study (28 days) (1992) with the source substance 6;
(iv) a publication on the safety assessment of lactic acid (1998) (source substance 3).

6.2. Assessment of the information provided

166 In addition to the deficiencies identified in Section 0.1., ECHA identified endpoint specific issue(s) addressed below.

167 Information that can be used to support weight of evidence adaptation for the information requirement of Annex IX, Section 8.6.2. includes similar information that is produced by the OECD TG 408. The OECD TG 408 requires to investigate the following key parameters: 1) in-life observations, 2) blood chemistry, 3) organ and tissue toxicity.

6.2.1. In-life observations

168 In-life observations must include information on survival, body weight development, clinical signs, functional observations, food/water consumption and other potential aspects of in life observations on the relevant physiological systems (circulatory, digestive/excretory, integumentary, musculoskeletal, nervous, renal/urinary, and respiratory).

6.2.1.1. Relevance of the information provided

169 The source of information (i) provides relevant information on survival, body weight development and clinical observations only.

170 The source of information (ii) provides relevant information on survival, body weight development only.

171 The source of information (iii) provides relevant information on survival, body weight development, clinical observations, food consumption.

172 For the reasons presented in Section 0.1.2.1.3 above, the source of information (iv) does not provide relevant information on in life observations..

6.2.1.2. Reliability of the contribution of the information to the weight of evidence

173 The reliability of the contribution of the sources of information (i)-(iii) is affected by the deficiencies presented in section 0.1.1.2 above.

174 Furthermore, investigations/specifications in a sub-chronic toxicity study (OECD TG 408) include dosing of the Substance daily for a minimum of 90 days to 10 animals per sex per group.

175 According to the information provided in your dossier, the study (iii) has an exposure duration of 28 days and only 5 animals were used per sex per dose.

176 This means that the exposure duration in study (iii) is shorter than the minimum exposure duration expected from a study conducted according to the OECD TG 408. This condition of exposure is essential because the effects observed over the required period of exposure of 90-days might be considerably more pronounced than over a shorter study duration. Furthermore, as a result of the reduced number of animals used in study (iii) compared to the requirements of the OECD TG 408, the statistical power of the results obtained from study (iii) is reduced. Therefore, the reliability of the contribution of the results from the study (iii) is limited.

177 Therefore, none of the studies can be considered a source of information that could reliably contribute to the conclusion on in life observations investigated by the required study.

6.2.2. Blood chemistry

178 Information on blood chemistry must include haematological (full-scale) and clinical chemistry analysis (full-scale), and other potential aspects related to blood chemistry to address relevant physiological systems (circulatory digestive/excretory, endocrine, immune, musculoskeletal, and renal/urinary)

6.2.2.1. Relevance of the information provided

179 The source of information (i) provides relevant information on haematological and clinical chemistry and urinalysis.

180 The source of information (ii) provides relevant information on a limited set of haematological examinations and urinalysis.

181 The source of information (iii) provides relevant information on haematological and clinical chemistry.

182 For the reasons presented in Section 0.1.2.1.3 above, the source of information (iv) does not provide relevant information on blood chemistry.

6.2.2.2. Reliability of the contribution of the information to the weight of evidence

183 The reliability of the contribution of the sources of information (i)-(iii) is affected by the deficiencies presented in section 0.1.2.1.2 above.

184 Furthermore, the limitations relating to the exposure duration and the number of animals identified in section 6.2.1.2 above for study (iii) also apply to this key element.

185 Therefore, none of the studies can be considered a source of information that could reliably contribute to the conclusion on blood chemistry investigated by the required study.

6.2.3. Organ and tissue toxicity

186 Organ and tissue toxicity must include information on terminal observations on organ weights, gross pathology and histopathology (full-scale and other potential aspects related to organ and tissue toxicity to address relevant physiological systems (circulatory, digestive/excretory, endocrine, immune, integumentary, musculoskeletal, nervous, renal/urinary system, reproductive, and respiratory).

6.2.3.1. Relevance of the information provided

187 The sources of information (i)-(iii) provide relevant information on organ weights, gross pathology and histopathology for a limited set of organs compared to the requirements of the OECD TG 408. More specifically, none of the sources of information provide information on gross pathology and histopathology of epididymides, prostate and seminal vesicle, thymus, aorta pituitary, vagina, cervix and mammary gland.

188 For the reasons presented in Section 0.1.2.1.3 above, the source of information (iv) does not provide relevant information on organ and tissue toxicity.

6.2.3.2. Reliability of the contribution of the information to the weight of evidence

189 The reliability of the contribution of the sources of information (i)-(iii) is affected by the deficiencies presented in section 0.1.2.1.2 above.

190 Furthermore, the limitations relating to the exposure duration and the number of animals identified in section 6.2.1.2 above for study (iii) also apply to this key element.

191 Therefore, none of the studies can be considered a source of information that could reliably contribute to the conclusion on organ and tissue toxicity investigated by the required study.

6.2.4. Conclusion

192 In summary, you have provided information on in-life observations, blood chemistry and on some elements of organ and tissue toxicity only. Specifically, none of the studies investigate gross pathology and histopathology of epididymides, prostate and seminal vesicle, thymus, aorta, pituitary, vagina, cervix and mammary gland.

193 Furthermore, for the elements covered, the corresponding sources of information have deficiencies affecting their reliability that prevent reaching conclusion on any of the aspects investigated.

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

195 Based on the above, your adaptation is rejected and the information requirement is not fulfilled.

6.3. Study design

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

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

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

199 In the comments to the draft decision you agree with the request.

7. Pre-natal developmental toxicity study in one species

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

7.1. Information provided

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

(i) a publication on the developmental toxicity data from structurally related long-chain alcohols (1995) including the source substance 7;
(ii) a pre-natal developmental toxicity study (1997) with the source substance 5;
(iii) a combined repeat dose and reproductive/developmental toxicity screening test (1992) with the source substance 6;
(iv) a combined repeat dose and reproductive/developmental toxicity screening test (1992) with the source substance 8;
(v) a pre-natal developmental toxicity study (1997) with the source substance 3.

7.2. Assessment of the information provided

202 In addition to the deficiencies identified in Section 0.1., ECHA identified endpoint specific issue(s) addressed below.

203 Information that can be used to support weight of evidence adaptation for the information requirement of Annex IX, Section 8.6.2. includes similar information that is produced by the OECD TG 414. The OECD TG 414 requires to investigate the following key parameters: 1) prenatal developmental toxicity, 2) maternal toxicity, and 3) maintenance of pregnancy.

7.2.1. Pre-natal developmental toxicity

204 Pre-natal developmental toxicity includes information after pre-natal exposure on embryonic/foetal survivial (number of live foetuses; number of resorptions and dead foetuses, postimplantation loss), growth (body weights and size) and structural malformations and variations (external, visceral and skeletal).

7.2.1.1. Relevance of the information provided

205 For the reasons presented in Section 0.1.2.1.3 above, the source of information (i) does not provide relevant information on pre-developmental toxicity.

206 The sources of information (iii) and (iv) provide relevant information on embryonic/foetal survivial (number of live foetuses; number of resorptions and dead foetuses, postimplantation loss), growth (body weights and size) but do not inform on structural malformations and variations (external, visceral and skeletal).

207 The sources of information (ii) and (v) provide relevant information on pre-natal developmental toxicity.

7.2.1.2. Reliability of the contribution of the information to the weight of evidence

208 The reliability of the contribution of the sources of information (i)-(iv) is affected by the deficiencies presented in section 0.1.2.1.2 above.

209 Furthermore, investigations/specifications in a pre-natal developmental toxicity study (OECD TG 414) include:

a) at least three dose levels are tested (unless conducted at the limit dose) with concurrent controls;
b) at least 20 female animals with implantation sites are included for each test and control group to ensure a statistical power equivalent to OECD TG 414;

210 According to the information provided in your dossier,

a) A single dose level was used in study (v);
b) Less than 20 female animals with implantation sites are included for each test and control group in studies (ii)-(v). As a result of the reduced number of animals used compared to the requirements of the OECD TG 414, the statistical power of

the results obtained from studies (ii)-(v) is reduced.

211 For the reasons presented above, the reliability of the contribution of the results from the studies (ii)-(v) to the weight of evidence with regard to pre-natal developmental toxicity is limited.

212 Therefore, none of the studies can be considered a source of information that could reliably contribute to the conclusion on pre-natal developmental toxicity investigated by the required study.

7.2.2. Maternal toxicity

213 Maternal toxicity includes information after gestational exposure on maternal survival, body weight and clinical signs and other potential aspects of maternal toxicity in dams.

7.2.2.1. Relevance of the information provided

214 For the reasons presented in Section 0.1.2.1.3 above, the source of information (i) does not provide relevant information on maternal toxicity.

215 The sources of information (ii) to (v) provide relevant information maternal toxicity.

7.2.2.2. Reliability of the contribution of the information to the weight of evidence

216 The reliability issues identified under section 7.2.1.2 equally apply to this key parameter. Therefore, none of the studies can be considered a source of information that could reliably contribute to the conclusion on maternal toxicity investigated by the required study.

7.2.3. Maintenance of pregnancy

217 Maintenance of pregnancy includes information on abortions and/or early delivery as a consequence of gestational exposure and other potential aspects of maintenance of pregnancy.

7.2.3.1. Relevance of the information provided

218 For the reasons presented in Section 0.1.2.1.3 above, the source of information (i) does not provide relevant information on maintenance of pregnancy.

219 The sources of information (ii) to (v) provide relevant information maintenance of pregnancy.

7.2.3.2. Reliability of the contribution of the information to the weight of evidence

220 The reliability issues identified under section 7.2.1.2 equally apply to this key parameter.

221 Therefore, none of the studies can be considered a source of information that could reliably contribute to the conclusion on maintenance of pregnancy investigated by the required study.

7.2.4. Conclusion

222 While you have provided information on pre-natal developmental toxicity, maternal toxicity and maintenance of pregnancy, the corresponding sources of information have deficiencies affecting their reliability.

223 Therefore, it is not possible to conclude, based on any source of information alone or considered together, on the information requirement for a pre-natal developmental toxicity study.

224 Based on the above, your adaptation is rejected and the information requirement is not fulfilled.

7.3. Study design

225 A PNDT study according to the test method OECD TG 414 should be performed in rat or rabbit as preferred species.

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

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

228 In the comments to the draft decision you agree with the request.

8. Long-term toxicity testing on fish

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

8.1. Information provided

230 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 information:

(i) Taking all information from experimental studies into account and due to animal welfare reasons, no further long-term test with fish was proposed in accordance to Annex IX, column 2 of Regulation EC (No) 1907/2006.

8.2. Assessment of the information provided

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

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

232 Your adaptation is therefore rejected.

233 Therefore, the information requirement is not fulfilled.

8.3. Study design

234 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.).

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

236 In the comments to the draft decision you agree with the request.

References

The following documents may have been cited in the decision.

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

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

Guidance on data-sharing; ECHA (2017).
Guidance for monomers and polymers; ECHA (2023).
Guidance on intermediates; ECHA (2010).
All Guidance 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 Bioaccumulation in aquatic species, preferably fish (Annex IX, Section 9.3.2.) and simulation testings (Annex IX, Section 9.2) are not addressed in this decision. This is because the results from the ready biodegradability is needed to conclude whether the Substance or relevant constituent(s)/fraction(s) of the Substance is (are) P/vP and to decide whether a bioaccumulation study and simulation testing(s) are needed to conclude on the PBT/vPvB properties of the Substance. In such case, the results of the requested ready biodegradability study will also inform on the most relevant test material to conduct the bioaccumulation and simulation studies. These information requirement(s) may be addressed in a separate decision at a later stage.

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 02 May 2022.

The deadline of the decision is set based on standard practice for carrying out OECD TG tests. It has been exceptionally extended by 12 months from the standard deadline granted by ECHA to take into account currently longer lead times in contract research organisations.

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

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

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

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

Appendix 3: Addressee(s) of this decision and their corresponding information requirements

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

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

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

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

Appendix 4: Conducting and reporting new tests for REACH purposes

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

1.1 Test methods, GLP requirements and reporting

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

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

(3) Under Article 10(a)(vi) and (vii) of REACH, all new data generated as a result of this decision must be reported as study summaries, or as robust study summaries, if required under Annex I of REACH. See ECHA Practical Guide on How to report robust study summaries (https://echa.europa.eu/practical-guides).

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

1.2 Test material

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

(1) Selection of the Test material(s)

The Test Material used to generate the new data must be selected taking into account the following:

- the variation in compositions reported by all members of the joint submission,
- the boundary composition(s) of the Substance,
- the impact of each constituent/group of constituents on the test results for the endpoint to be assessed. For example, if a constituent/group of constituents of the Substance is known to have an impact on (eco)toxicity, the selected Test Material must contain that constituent/group of constituents.

(2) Information on the Test Material needed in the updated dossier

- You must report the composition of the Test Material selected for each study, under the "Test material information" section, for each respective endpoint study record in IUCLID.
- The reported composition must include the careful identification and description of the characteristics of the Tests Materials in accordance with OECD GLP (ENV/MC/CHEM(98)16) and EU Test Methods Regulation (EU) 440/2008 (Note, Annex), namely all the constituents must be identified as far as possible as well as their concentration. Also any constituents that have harmonised classification and labelling according to the CLP Regulation must be identified and quantified using the appropriate analytical methods.

With that detailed information, ECHA can confirm whether the Test Material is relevant for the Substance and whether it is suitable for use by all members of the joint submission.

Technical instructions on how to report the above is available in the manual on How to prepare registration and PPORD dossiers (https://echa.europa.eu/manuals).

2. General recommendations for conducting and reporting new tests

2.1 Environmental testing for substances containing multiple constituents

Your Substance contains multiple constituents and, as indicated in Guidance on IRs & CSA, Section R.11.4.2.2, you are advised to consider the following approaches for persistency, bioaccumulation and aquatic toxicity testing:

- the "known constituents approach" (by assessing specific constituents), or
- the "fraction/block approach", (performed on the basis of fractions/blocks of constituents), or
- the "whole substance approach", or
- various combinations of the approaches described above

Selection of the appropriate approach must take into account the possibility to characterise the Substance (i.e. knowledge of its constituents and/or fractions and any differences in their properties) and the possibility to isolate or synthesize its relevant constituents and/or fractions.

References to Guidance on REACH and other supporting documents can be found under Appendix 1.