~~Confidential~~

Helsinki, 25 May 2023

Addressees
Registrant(s) of JS_MADAMMC as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
22 March 2016

Registered substance subject to this decision ("the Substance")
Substance name: [2-(methacryloyloxy)ethyl]trimethylammonium chloride
EC number: 225-733-5

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

DECISION ON A COMPLIANCE CHECK

Under Article 41 of Regulation (EC) No 1907/2006 (REACH), you must submit the information listed below under request 4 by the deadline of ***1 September 2025*** and all other information listed below by ***31 August 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. Skin sensitisation (Annex VII, Section 8.3.; test method:

   i. *in vitro/in chemico* skin sensitisation information on molecular interactions with skin proteins (OECD TG 442C), inflammatory response in keratinocytes (OECD TG 442D) and activation of dendritic cells (EU B.71/OECD TG 442E)(Annex VII, Section 8.3.1.); and

   ii. Only if the *in vitro/in chemico* test methods specified under point 1.i. are not applicable for the Substance or the results obtained are not adequate for classification and risk assessment, *in vivo* skin sensitisation (Annex VII, Section 8.3.2.; test method: EU B.42./OECD TG 429);

2. In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.; test method: Bacterial reverse mutation test OECD TG 471 (2020)) using one of the following strains: E. coli WP2 uvrA, or E. coli WP2 uvrA (pKM101), or S. typhimurium TA102;

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

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

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

5. 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);

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

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

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

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

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

Information required depends on your tonnage band

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

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

How to comply with your information requirements

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

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

Appeal

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

Failure to comply

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

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

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

Appendix 1: Reasons for the decision

Contents

0. Reasons common to several requests

0.1. Exposure based adaptations – Information in the comments

1 In the comments to the draft decision, you indicate that there is no exposure to humans or the environment since the manufacture and use of the Substance takes place under strictly controlled conditions and that you intend to provide this information in an updated registration dossier. You intend to submit an adaptation in accordance with Article XI, Section 3 of REACH to demonstrate lack of risk to humans health and environment for the following standard information requirements:

- Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.)
- Long-term toxicity testing on fish (Annex IX, Section 9.1.6.1.)

2 However, while you describe your intentions, the information in your comments is not sufficient for ECHA to make an assessment. Therefore, your adaptation is rejected.

Reasons related to the information under Annex VII of REACH

1. Skin sensitisation

3 Skin sensitisation is an information requirement under Annex VII, Section 8.3. Under Section 8.3., Column 1, the registrants must submit information allowing (1) a conclusion whether the substance is a skin sensitiser and (2) whether it can be presumed to have the potential to produce significant sensitisation in humans (Cat. 1A).

1.1. Information provided

4 You have provided an in vivo Guinea Pig Maximisation Test (2014) with the Substance (study i).

1.2. Assessment of the information provided

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

1.2.1. Assessment whether the Substance causes skin sensitisation

1.2.1.1. The provided study does not meet the information requirement

6 To fulfil the information requirement, and to enable concluding whether the Substance causes skin sensitisation, a study must comply with the EU Method B.6/OECD TG 406 (Article 13(3) of REACH). Therefore, the following specifications must be met:

a) the challenge dose is the highest non-irritation concentration.

7 The study (i) is described as a Guinea Pig Maximisation Test. However, the following specifications are not according to the requirements of the OECD TG 406:

a) the concentration chosen for the challenge exposure appear not to be the highest non-irritating concentration, as the concentration used for topical challenge was only 0.1% and the Substance is not a skin irritant.

8 The information provided does not cover the key parameter(s) required by the OECD TG 406 and does not allow to make a conclusion whether the Substance causes skin sensitisation.

1.2.2. No assessment of potency

9 To be considered compliant and enable a conclusion in cases where the substance is considered to cause skin sensitisation, the information provided must also allow a conclusion whether it can be presumed to have the potential to produce significant sensitisation in humans (Cat. 1A).

10 As the currently available data do not allow to conclude whether the Substance causes skin sensitisation (see Section 1.2.1.1 above), this condition cannot be assessed.

11 In the comments to the draft decision you disagree with the assessment and the requested test. You indicate that:

- the study was conducted in accordance with GLP,

- the dose levels were established according to the procedure included in the Guideline and 0.1% concentration in aqua ad iniectabilia was used for the challenge since this was the highest non-irritant dose in topical application on depilated skin, and
- the study covers all the key parametes required by OECD TG 406.

12 Based on this you conclude that the study allows conclusion that the Substance does not cause skin sensitisation.

13 However, you have not provided any information from e.g. results of the dose range finding study/ies to substantiate your claim that 0.1% concentration used in the challenge was the highest non-irritant dose in topical application on depilated skin. Indeed, if the study was conducted in accordance with GLP and the dose levels established according to the test guideline, this information should be available.

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

1.3. Specification of the study design

15 To fulfil the information requirement for the Substance, information on molecular interaction with skin proteins and inflammatory response in keratinocytes and activation of dendritic cells (OECD TG 442C and OECD TG 442D and EU B.71/OECD TG 442E) must be provided. Furthermore an appropriate risk assessment is required if a classification of the Substance as a skin sensitiser (Cat 1A or 1B) is warranted.

16 In case no conclusion on the skin sensitisation potency can be made for the Substance based on the newly generated in vitro/in chemico data, in vivo skin sensitisation study must be performed and the murine local lymph node assay (EU Method B.42/OECD TG 429) is considered as the appropriate study for the potency estimation.

2. In vitro gene mutation study in bacteria

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

2.1. Information provided

18 You have provided an in vitro gene mutation study in bacteria (1992) with the Substance (study i).

2.2. Assessment of the information provided

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

2.2.1. The provided study does not meet the information requirement

20 To fulfil the information requirement, a study must comply with the OECD TG 471 (Article 13(3) of REACH). Therefore, the following specifications must be met:

a) the test is performed with 5 strains: four strains of *S. typhimurium* (TA98; TA100; TA1535; TA1537 or TA97a or TA97) and one strain which is either *S. typhimurium* TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101).

21 The study (i) is described as an in vitro gene mutation study in bacteria.

22 However, the following specifications are not according to the requirements of the OECD TG 471:

a) the test was performed with the strains *S. typhimurium* TA 1535, TA 1537, TA 98, TA 100 and TA 1538. This means that the strains *E. coli* WP2 uvrA, or *E. coli* WP2 uvrA (pKM101), or *S. typhimurium* TA102 are missing.

23 The information provided does not cover the key parameter(s) required by the OECD TG 471.

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

2.3. Specification of the study design

25 To fulfil the information requirement for the Substance, the in vitro gene mutation study in bacteria (OECD TG 471, 2020) should be performed using one of the following strains: E. coli WP2 uvrA, or E. coli WP2 uvrA (pKM101), or S. typhimurium TA102.

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

3. Growth inhibition study aquatic plants

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

3.1. Information provided

28 You have provided a study on toxicity to aquatic algae (1994) with the Substance.

3.2. Assessment of the information provided

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

3.2.1. The provided study does not meet the information requirement

30 To fulfil the information requirement, a study must comply with OECD TG 201 (Article 13(3) of REACH). Therefore, the following specifications must be met:

a) analytical monitoring must be conducted. Alternatively, a justification why the analytical monitoring of exposure concentrations is not technically feasible must be provided;
b) the results can be based on nominal or measured initial concentration only if the concentration of the test material has been maintained within ±20 % of the nominal or measured initial concentration throughout the test.

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

a) no analytical monitoring of exposure was conducted;
b) the results are based on nominal values but no evidence provided that the exposure concentration was maintained within ±20 % of the nominal or measured initial concentration throughout the test.

32 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 it cannot be verified that exposure concentrations were maintained during the course of the study. Therefore, the reported effect values based on nominal concentrations are not reliable.

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

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

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

Reasons related to the information under Annex IX of REACH

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

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

4.1. Information provided

37 You provide a justification for your adaptation in IUCLID under "Linked Categories".

38 You identify the following substances as the category members:

- Dimethylaminoethylacrylate methylchloride, EC No. 256-176-6;
- Trimethyl((2-[(2-methylprop-2-enoyl)oxy]ethyl))azanium chloride, EC No. 225-733-5;
- Benzyl-dimethyl-(2-prop-2-enoyloxyethyl)azanium chloride, EC No. 256-283-8;
- Benzyl-dimethyl-[2-(2-methylprop-2-enoyloxy)ethyl]azanium chloride, EC No. 256-288-5;
- Methyl sulfate; trimethyl-(2-prop-2-enoyloxyethyl)azanium, EC No. 236-029-2;
- Methyl sulfate; trimethyl-[2-(2-methylprop-2-enoyloxy)ethyl]azanium, EC No. 229-995-1;
- 3-(acryloylamino)-N,N,N-trimethylpropan-1-aminium chloride, EC No. 256-181-3;
- Dimethylbis(prop-2-en-1-yl)azanium chloride, EC No. 230-993-8.

39 In your technical dossier, you justify the grouping of the substances as: "*Quaternary ammonium cations, also known as quats, are positively charged polyatomic ions of the structure NR4+, R being an alkyl group. Unlike the ammonium ion (NH4+) and the primary, secondary, or tertiary ammonium cations, the quaternary ammonium cations are permanently charged, independent of the pH of their solution. Quaternary ammonium salts or quaternary ammonium compounds are salts of quaternary ammonium cations with an anion. The tertiary amine moiety is caustic and lacks stability. In order to alleviate these characteristics, the tertiary amine is reacted with either methyl chloride, dimethyl sulphate or benzyl chloride to produce a more stable and less caustic quaternary amine salt". You further specify that "Quaternary ammonium salts of the esters of acrylic and methacrylic acid and dimethylaminopropyl acrylamide as well as diallyldimethylammonium chloride represent a category for the manufacture of cationic polyelectrolytes and, therefore, for purposes of the REACH registration*".

40 You provide the following reasoning for the prediction of (eco)toxicological properties: "*The toxicity and physical chemical properties of these quaternary ammonium salts are very similar, as would be expected*".

41 In order to support your adaptation, for the information requirement you have provided the following key study:

(i) a 90-day repeated dose toxicity study (1976) with the substance dimethylbis(prop-2-en-1-yl)azanium chloride, EC No. 230-993-8.

42 In addition, you have provided the following 28-day repeated dose toxicity studies as supporting information:

(ii) a 28-day repeated dose toxicity study (2000), with the Substance;

(iii) a 28-day repeated dose toxicity study (2008) with the substance 3-(acryloylamino)-N,N,N-trimethylpropan-1-aminium chloride, EC No. 256-181-3.

4.2. Assessment of the information provided

43 We have identified the following issue(s) with the proposed grouping and with the prediction(s) of toxicological properties. In addition, ECHA identified endpoint specific issue(s) addressed below.

4.2.1. Documentation of the grouping and read-across adaptation

44 Annex XI, Section 1.5 requires that whenever grouping and read-across is used adequate and reliable documentation of the applied method must be provided. Such documentation shall include an explanation why the properties of the registered substance may be predicted from other substances in the group and supporting information to scientifically justify such explanation for prediction of properties.

45 According ot the information provided in your dossier, your grouping is based on elements of structural similarity between the substances and their use "for the manufacture of cationic polyelectrolytes".

46 You refer to similarities in the toxicity and physical chemical properties of these quaternary ammonium salts as the basis for the prediction of the properties of the substances within the group.

47 You have provided robust study summaries for studies conducted with other substances than the Substance in order to comply with the REACH information requirements.

48 However, you have not provided information on the following aspects of your adaptation:

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

(ii) <u>The composition of the category members:</u> Annex XI, Section 1.5 of the REACH Regulation 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."

Therefore, qualitative and quantitative information on the compositions of the category members must be provided to confirm the category membership and to allow assessing whether the attempted predictions are compromised by the composition and/or impurities.

(iii) <u>The read-across hypothesis</u>: Annex XI, Section 1.5 requires that whenever read-across is used adequate and reliable documentation of the applied

method must be provided. Such documentation must include an explanation why the properties of the Substance may be predicted from other substances in the group, i.e. a read-across hypothesis. This hypothesis should be based on recognition of the structural similarities and differences between the substances (Guidance on IRs and CSA, Section R.6.). It should explain why the differences in the chemical structures should not influence the toxicological properties or should do so in a regular pattern, taking into account that variations in chemical structure can affect both toxicokinetics (uptake and bioavailability) and toxicodynamics (e.g. interactions with receptors and enzymes) of substances (Guidance on IRs and CSA, Section R.6.2.1.3).

49 In the absence of such documentation, the properties of the Substance cannot be reliably predicted from the data on the source substances within the group.

4.2.2. Source studies not adequate for the information requirement

50 Under Annex XI, Section 1.5., the results to be read across must have an adequate and reliable coverage of the key parameters and cover an exposure duration comparable to or longer than the one specified in the test guideline for the corresponding study that shall normally be performed for a particular information requirement, in this case OECD TG 408.

51 According to Annex IX, Section 8.6.2., Column 1, the sub-chronic toxicity study (90-day) should be conducted in a rodent species.

52 The study (i) is described as a 90-day repeated dose toxicity study in dogs. This study has been conducted using a non-rodent species, i.e., dogs, in order to investigate the repeated dose toxicity of the analogue substance.

53 The studies (ii) and (iii) investigate short-term toxicity and are described as 28-day repeated dose toxicity studies. Therefore, the studies do not cover the specifications for the corresponding parameters of the OECD TG 408, such as:

a) an exposure duration of at least 90 days. The exposure duration in studies (ii) and (iii) was of 28 days for each study;

b) at least 10 male and 10 female animals for each test and control group. Five male and female animals for each test and control group were used in study (iii) and five male and female animals for the low and mid dose levels were used in study (ii).

54 Based on the above, the provided studies (i), (ii) and (iii) do not have an adequate and reliable coverage of the required key parameters and are not an adequate basis for your read-across prediction. Therefore your adaptation according to Annex XI, Section 1.5. is rejected.

55 In the comments to the draft decision, you indicate that you will submit a read-across justification and that you intend to provide this information in an updated registration dossier. However, the information in your comments is not sufficient for ECHA to make an assessment. While you have described your intentions, you have not provided any new information addressing the deficiencies identified in your read-across adaptation (section 4.2.1 and 4.2.2).

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

4.3. Specification of the study design

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

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

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

5. Pre-natal developmental toxicity study in one species

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

5.1. Information provided

61 For the information requirement you have provided the following justification: "At 1000 mg/kg (the highest dose) an analogous quaternary ammonium substance (APTAC, EC 256-181-3) demonstrated no adverse effects on reproductive parameters (litter size, sex ratio and lactation) or any toxicological endpoints (parental and offspring) in a reproductive/developmental screening study."

62 ECHA understands that you seek to adapt this information requirement under Annex IX, Section 8.7., Column 2, Indent 3. In addition, as far as you refer to data on an analogue substance, ECHA understands that you also seek to adapt this information requirement by using a Grouping of substances and read-across approach.

5.2. Assessment of the information provided

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

5.2.1. Low toxicological activity not demonstrated

64 Under Annex IX, Section 8.7., Column 2, the study does not need to be conducted if the Substance is of low toxicological activity. This needs to be demonstrated with three concomitant criteria, one of them being that it can be proven from toxicokinetic data that no systemic absorption occurs via relevant routes of exposure.

65 ECHA notes that the registration dossier does not contain any toxicokinetic data with the Substance in order to show that systemic absorption does not take place.

66 In the comments to the draft decision, you refer to:

- lack of systemic absorption via the inhalation route since the susbtance is not volatile;
- lack of significant dermal aborption observed in the acute dermal toxicity test; and
- no exposure to humans or the environment due to the manufacture and use of the substance.

67 However, the above does not address the deficiency identified in relation to lack of toxicokinetic data with the Substance in order to show that systemic absorption does not take place (section 5.2.1).

5.2.2. Documentation of the grouping and read-across adaptation

68 Furthermore, in the provided justification, you refer to a study conducted with the analogue substance APTAC, EC No. 256-181-3.

69 For the reasons explained in Section 4.2.1, your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5. is rejected.

70 In the comments to the draft decision, you indicate that you will submit a read-across justification and that you intend to provide this information in an updated registration dossier. However, the information in your comments is not sufficient for ECHA to make an assessment. While you have described your intentions, you have not provided any new information addressing the deficiencies identified in your read-across adaptation (section 4.2.1).

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

5.3. Specification of the study design

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

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

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

6. Long-term toxicity testing on aquatic invertebrates

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

6.1. Information provided

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

"The substance is not acutely toxic to invertebrates and is readily biodegradable. The Chemical Safety Assessment therefore does not indicate the need to investigate further effects on aquatic organisms (Annex IX, 9.1, column 2)."

6.2. Assessment of the information provided

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

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

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

79 In your comment to draft decision, you indicate that you intent to submit an adaptation in accordance with Article XI, Section 3 of REACH. However, as already explained under Section 0.1., since you do not provide in your comments any information substantiating your proposed adaptation, ECHA is not in a position to assess whether your adaptataion fulfills the requirements.

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

7. Long-term toxicity testing on fish

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

7.1. Information provided

82 You have provided the following justification to adapt this information requirement:

"Substance is not acutely toxic to fish. The Chemical Safety Assessment does not indicate the need to investigate further effects on aquatic organisms."

83 ECHA understands that you seek to adapt this information requirement under Column 2 of Annex IX, Section 9.1.

7.2. Assessment of the information provided

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

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

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

86 In your comment to draft decision, you indicate that you intent to submit an adaptation in accordance with Article XI, Section 3 of REACH. However, as already explained above under Section 0.1., since you do not provide in your comments any information substantiating your proposed adaptation, ECHA is not in a position to assess whether your adaptataion fulfills the requirements.

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

7.3. Study design and test specifications

88 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.).

Reasons related to the information under Annex X of REACH

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

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

8.1. Information provided

90 For the information requirement you have provided the following justification: "At 1000 mg/kg (the highest dose) an analogous quaternary ammonium substance (APTAC, EC 256-181-3) demonstrated no adverse effects on reproductive parameters (litter size, sex ratio and lactation) or any toxicological endpoints (parental and offspring) in a reproductive/developmental screening study."

91 ECHA understands that you seek to adapt this information requirement under Annex IX, Section 8.7., Column 2, Indent 3. In addition, as far as you refer to data on an analogue substance, ECHA understands that you also seek to adapt this information requirement by using a Grouping of substances and read-across approach.

8.2. Assessment of the information provided

92 Your adaptation is rejected for the same reasons explained under request 5 above. In addition, for the reasons explained under request 5 the information provided in your comments does not change the outcome of ECHA's assessment.

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

8.3. Specification of the study design

94 A PNDT study according to the test method OECD TG 414 should be performed in rabbit or rat as preferred second species, depending on the species tested in the first PNDT study (request 5 in this decision).

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

96 Based on the above, the study must be conducted in rabbit or rat with oral administration of the Substance.

References

The following documents may have been cited in the decision.

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

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

Guidance on data-sharing; ECHA (2017).

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

Read-across assessment framework (RAAF)

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

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

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

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

Appendix 2: Procedure

The information requirement for an Extended one-generation reproductive toxicity study (EOGRTS; Annexes IX or X, Section 8.7.3.) is not addressed in this decision. This may be addressed in a separate decision once the information from the Sub-chronic toxicity study (90-day) requested in the present decision is provided; due to the fact that the results from the 90-day study are needed for the design of the EOGRTS. Similarly the information requirement for a Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.) is not addressed in this decision, as the EOGRTS will cover the same parameters.

This decision does not prevent ECHA from initiating further compliance checks at a later stage on the registrations present.

ECHA followed the procedure detailed in Articles 50 and 51 of REACH.

The compliance check was initiated on 04 October 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 request(s).

The deadlines of the decision are set based on standard practice for carrying out OECD TG tests. Deadlines have 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.

You indicated in your comments your intention to submit updated information by the end of July 2022. However, no such information was submitted.

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]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

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

Appendix 4: Conducting and reporting new tests for REACH purposes

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

1.1. Test methods, GLP requirements and reporting

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

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

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

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

1.2. Test material

97 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.

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