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Helsinki, 25 May 2023

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

Date of submission of the dossier subject to this decision
15/05/2018

Registered substance subject to this decision ("the Substance")
Substance name: Ethyldimethyl[2-[(2-methyl-1-oxoallyl)oxy]ethyl]ammonium ethyl sulphate
EC number: 236-195-6

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

DECISION ON A COMPLIANCE CHECK

Under Article 41 of Regulation (EC) No 1907/2006 (REACH), you must submit the information listed below, by the deadline of ***1 September 2025***.

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 methods):

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

3. Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.; test method: EU C.3./OECD TG 201 or EU C.26./OECD TG 221).

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

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

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

6. Short-term repeated dose toxicity (28 days; Annex VIII, Section 8.6.1.) to be combined with the Screening for reproductive/developmental toxicity below;

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

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 registrant with the Registration number 01-2120769672-43-0001 ('Annex VII opt-out registrant') is not requested to provide the information under requests 1, 2 and 3 (Skin sensitisation, Short-term toxicity on aquatic invertebrates and Growth inhibition on aquatic plants), because it has opted out from the joint subsmission for those information requirements for which it has provided adequate information.

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.

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

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

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

Appendix 1: Reasons for the decision

Contents

0. Reasons common to several requests

0.1. Assessment of the read-across approach

1 You have provided experimental data on [2-(methacryloyloxy)ethyl]trimethylammonium chloride EC No. 225-733-5, diallyldimethylammonium chloride EC No. 230-993-8 and trimethyl-3-[(1-oxoallyl)amino]propylammonium chloride EC No. 256-181-3, for the following standard information requirements:

- Skin sensitisation (Annex VII, Section 8.3.);
- In vitro cytogenicity study in mammalian cells or in vitro micronucleus study (Annex VIII, Section 8.4.2.);
- In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.)
- Short-term repeated dose toxicity (28 day), (Annex VIII, Section 8.6.1.);
- Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.);
- Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.)
- Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.)

2 While you have not identified this information as a read-across approach, the test materials used are different than the Substance. Therefore, the studies conducted with these substances (hereafter referred to as "source substance(s)") will be evaluated as a read-across adaptation under Annex XI, Section 1.5 of REACH.

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

4 Annex XI, Section 1.5. specifies two conditions which must be fulfilled whenever a read-across approach is used. Firstly, there needs to be structural similarity between substances which results in a likelihood that the substances have similar physicochemical, toxicological and ecotoxicological properties so that the substances may be considered as a group or category. Secondly, it is required that the relevant properties of a substance within the group may be predicted from data for reference substance(s) within the group.

5 Additional information on what is necessary when justifying a read-across approach can be found in the Guidance on IRs and CSA, Chapter R.6. and related documents (RAAF, 2017; RAAF UVCB, 2017).

0.1.1. Predictions for (eco)toxicological properties

6 You predict the properties of the Substance from information obtained from the following source substance(s):

- [2-(methacryloyloxy)ethyl]trimethylammonium chloride EC No. 225-733-5;
- diallyldimethylammonium chloride EC No. 230-993-8;
- trimethyl-3-[(1-oxoallyl)amino]propylammonium chloride EC No. 256-181-3.

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

0.1.2. Absence of read-across documentation

8 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 information on the source substances.

9 You have provided robust study summaries for studies conducted with other substances than the Substance in order to comply with the REACH information requirements. However, you have not provided documentation as to why this information is relevant for the Substance and thus why the properties of the Substance may be predicted from information on the source substances.

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

0.1.3. Adequacy and reliability of source studies

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

(1) be adequate for the purpose of classification and labelling and/or risk assessment;
(2) have adequate and reliable coverage of the key parameters addressed in the corresponding study that shall normally be performed for a particular information requirement;

12 Specific reasons why the studies on the source substances do not meet these criteria are explained further below under the applicable information requirement sections 1.2.1.1, 6.2.1.1 and 6.2.1.2. Therefore, no reliable predictions can be made for these information requirements.

0.1.4. Information provided in the comments to the draft decision

13 In the comments to the draft decision, you indicate that you will submit an updated 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 0.1.2). The additional information provided for the skin sensitisation endpoint is addressed under the Request 1.

0.2. Conclusion on the read-across approach

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

Reasons related to the information under Annex VII of REACH

1. Skin sensitisation

15 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

16 For the information requirement you have provided an *in vivo* Guinea Pig Maximisation Test (2014) with the analogue substance 2-(methacryloyloxy)ethyl]trimethylammonium chloride, EC No. 225-733-5.

17 In your comments to the draft decision, you refer to three skin sensitisation tests ([redacted]) conducted with structurally similar substances EC No. 256-176-6, EC No. 225-733-5, and EC No. 256-283-8.

18 As the study (EC No. 225-733-5) you provided in the dossier and the information on skin sensitisation tests (EC 256-176-6, EC 225-733-5, and EC 256-283-8) provided in the comments are conducted with a test material that is different than the Substance, ECHA understands that you have adapted this information requirement by using a Grouping of substances and read-across approach.

1.2. Assessment of the information provided

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

1.2.1. Read-across adaptation rejected

20 As explained in Sections 0.1.2. and 0.1.3., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5. is rejected. In addition, ECHA identified endpoint-specific issue(s) addressed below.

21 In the comments to the draft decision you provided further information to justify your read-across approach for skin sensitisation and indicated that you will update your registration dossier respectively.

22 However, you have not provided an updated read-across justification in your registration dossier.

1.2.2. Assessment whether the Substance causes skin sensitisation

1.2.2.1. The source study does not meet the information requirement

23 Under Annex XI, Section 1.5., the study to be read across must have an adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3), in this case EU Method B.6/OECD TG 406. Therefore, the following specifications must be met: the challenge dose is the highest non-irritation concentration.

24 The study provided in the registration dossier is described as a Guinea Pig Maximisation Test.

25 However, the following specifications are not according to the requirements of OECD TG 406: the concentration chosen for the challenge exposure appears not to be the highest non-irritating concentration, as the concentration used for topical challenge was only 0.1% and the source substance is not a skin irritant.

26 In the comments to the draft decision, you state that the study is a recent GLP study conducted with the analogous substance. However, only specifying the study as a GLP study does not address the issue on reliable coverage of the key parameters addressed by the OECD TG 406 (section 1.2.2.1 above). Based on the above, the study does not provide an adequate and reliable coverage of the key parameters addressed by the OECD TG 406 and this study is not an adequate basis for your read-across predictions.

1.2.2.2. Missing robust study summaries

27 Annex XI, Section 1.5. requires that whenever read-across is used adequate and reliable documentation of the applied method must be provided. Such documentation must include robust study summary for each source study used in the adaptation.

28 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)).

29 In the comments to the draft decision, you refer to three skin sensitisation tests ([redacted]) conducted with structurally similar substances EC 256-176-6, EC 225-733-5, and EC 256-283-8 and indicated that the studies are GLP compliant.

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

1.2.2.3. No assessment of potency

31 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).

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

33 Based on above, the information requirement is not fulfilled.

1.3. Specification of the study design

34 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.

35 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.

1.4. Information regarding data sharing

36 The Annex VII opt-out registrant's registration dossier for the Substance contains studies 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) (2018) which are adequate for this information requirement. In accordance with Title III of the REACH Regulation, you may request it from the other registrants and then make every effort to reach an agreement on the sharing of data and costs (Guidance on data-sharing[2]).

2. Short-term toxicity testing on aquatic invertebrates

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

2.1. Information provided

38 For the information requirement you have provided a short-term toxicity study in aquatic invertebrates (1996) with the analogue substance [2-(methacryloyloxy)ethyl]trimethylammonium chloride, EC No. 225-733-5.

39 As the study you provided is conducted with a test material that is different than the Substance, ECHA understands that you have adapted this information requirement by using a Grouping of substances and read-across approach.

2.2. Assessment of the information provided

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

2.2.1. Read-across adaptation rejected

41 For the reasons explained in Section 0.1.2., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5. is rejected.

42 In the comments to the draft decision, you indicate that you intend to submit the justification for your read-across adaptation. As explained in section 0.1.4, you have not provided any new information addressing the deficiencies identified in your read-across adaptation.

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

2.3. Information regarding data sharing

44 The Annex VII opt-out registrant's registration for the Substance contains a short-term toxicity study in aquatic invertebrates (2018) which is adequate for this information requirement. In accordance with Title III of the REACH Regulation, you may request it from the other registrants and then make every effort to reach an agreement on the sharing of data and costs (Guidance on data-sharing).

3. Growth inhibition study aquatic plants

[2] https://echa.europa.eu/regulations/reach/registration/data-sharing

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

3.1. Information provided

46 For the information requirement you have provided a study on effects on algae growth (1994) with the analogue substance [2-(methacryloyloxy)ethyl]trimethylammonium chloride, EC No. 225-733-5.

47 As the study you provided is conducted with a test material that is different than the Substance, ECHA understands that you have adapted this information requirement by using a Grouping of substances and read-across approach.

3.2. Assessment of the information provided

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

3.2.1. Read-across adaptation rejected

49 As explained in Section 0.1.2., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5. is rejected.

50 In the comments to the draft decision, you indicate that you intend to submit the justification for your read-across adaptation. As explained in section 0.1.4, you have not provided any new information addressing the deficiencies identified in your read-across adaptation.

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

3.3. Specification of the study design

52 To fulfil the information requirement for the Substance, either Freshwater Alga and Cyanobacteria, Growth Inhibition Test (Annex VII, Section 9.2.2, test method OECD TG 201) or Lemna sp. Growth Inhibition Test (Annex VII, Section 9.2.2, test method OECD TG 221) are considered suitable.

3.4. Information regarding data sharing

53 The Annex VII opt-out registrant's registration for the Substance contains a Lemna sp. Growth inhibition test (2018) which is adequate for this information requirement. In accordance with Title III of the REACH Regulation, you may request it from the other registrants and then make every effort to reach an agreement on the sharing of data and costs (Guidance on data-sharing).

Reasons related to the information under Annex VIII of REACH

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

54 An in vitro cytogenicity study in mammalian cells or an in vitro micronucleus study is an information requirement under Annex VIII, Section 8.4.2.

4.1. Information provided

55 For the information requirement you have provided an *in vitro* cytogenicity study in mammalian cells (1995) with the analogue substance 2-(methacryloyloxy)ethyl]trimethylammonium chloride, EC No. 225-733-5.

56 As the study you provided is conducted with a test material that is different than the Substance, ECHA understands that you have adapted this information requirement by using a Grouping of substances and read-across approach.

4.2. Assessment of the information provided

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

4.2.1. Read-across adaptation rejected

58 As explained in Section 0.1.2., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5. is rejected.

59 In the comments to the draft decision, you indicate that you intend to submit the justification for your read-across adaptation. As explained in section 0.1.4, you have not provided any new information addressing the deficiencies identified in your read-across adaptation.

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

4.3. Specification of the study design

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

5. In vitro gene mutation study in mammalian cells

62 An in vitro gene mutation study in mammalian cells is an information requirement under Annex VIII, Section 8.4.3., in case of a negative result in the in vitro gene mutation test in bacteria and the in vitro cytogenicity test.

5.1. Triggering of the information requirement

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

64 The in vitro cytogenicity study in mammalian cells provided in the dossier is rejected for the reasons provided in request 4.

65 The result of request 4 will determine whether the present requirement for an in vitro mammalian cell gene mutation study in accordance with Annex VIII, Section 8.4.3 is triggered.

66 Consequently, you are required to provide information for this information requirement, if the in vitro cytogenicity study in mammalian cells provides a negative result.

5.2. Information provided

67 For the information requirement you have provided an *in vitro* gene mutation study in mammalian cells (1997) with the analogue substance [2-(methacryloyloxy)ethyl]trimethylammonium chloride, EC No. 225-733-5.

68 As the study you provided is conducted with a test material that is different than the Substance, ECHA understands that you have adapted this information requirement by using a Grouping of substances and read-across approach.

5.3. Assessment of the information provided

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

5.3.1. Read-across adaptation rejected

70 As explained in Section 0.1.2., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5. is rejected.

71 In the comments to the draft decision, you indicate that you intend to submit the justification for your read-across adaptation. As explained in section 0.1.4, you have not provided any new information addressing the deficiencies identified in your read-across adaptation.

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

5.4. Specification of the study design

73 To fulfil the information requirement for the Substance, either the in vitro mammalian cell gene mutation tests using the hprt and xprt genes (OECD TG 476) or the thymidine kinase gene (OECD TG 490) are considered suitable.

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

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

6.1. Information provided

75 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;

76 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 [2-(methacryloyloxy)ethyl]trimethylammonium chloride, EC No. 225-733-5;

(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.

77 As the studies you provided are conducted with test materials that are different than the Substance, ECHA understands that you have adapted this information requirement by using a Grouping of substances and read-across approach. In addition, as you have provided a 90-day repeated dose toxicity study as a key study, ECHA understands that your intention is to invoke also an adaptation in Annex VIII, Section 8.6.1., Column 2.

6.2. Assessment of the information provided

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

6.2.1. Read-across adaptation rejected

79 As explained in Sections 0.1.2. and 0.1.3., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5. is rejected.

80 In the comments to the draft decision, you indicate that you intend to submit the justification for your read-across adaptation. As explained in section 0.1.4, you have not provided any new information addressing the deficiencies identified in your read-across adaptation.

81 In addition, ECHA identified endpoint-specific issue(s) addressed below.

6.2.1.1. No adequate and reliable coverage of the key parameters in the 90-day repeated dose toxicity study

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

83 Under Annex XI, Section 1.5., the study to be read across must have an adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3).

84 The study (i) was conducted in dogs, therefore, in order to be considered reliable and to be used in the context of an adaptation according to Annex VIII, Section 8.6.1, Column 2, the study needs to be performed in accordance with the specifications of OECD TG 409, and provide information equivalent to the information obtained from a study performed according to OECD TG 409. Therefore, the following specifications must be met:

a. clinical signs observed daily, and ophthalmological examination made prior to the administration of the substance and at the termination of the study;
b. haematological and clinical biochemistry tests as specified in paragraphs 24-29 of the test guideline;
c. terminal organ and body weights;
d. gross pathology as specified in paragraphs 30-31 of the test guideline.

85 The study (i) is described as a 90-day repeated dose toxicity study in dogs.

86 However, the following specifications are not according to the requirements of the OECD TG 409:

a. data on clinical signs and ophthalmological examination are missing: nature, severity and duration;
b. data on haematology and clinical biochemistry findings are missing: incidence and severity with relevant base-line values; in particular, the following investigations are missing: erythrocyte and platelet counts, and a measure of clotting potential;
c. data on terminal organ weights, in particular for the following organs: parathyroids, thymus, epididymides, uterus, and all organ/body weight ratios are missing;
d. data on gross pathology findings are missing: incidence and severity.

87 Based on the above, the provided 90-day study does not have an adequate and reliable coverage of the required key parameters and is not an adequate basis for your read-across prediction. Therefore your adaptation according to Annex XI, Section 1.5. in conjunction with Annex VIII, Section 8.6.1, Column 2, Paragraph 1, Indent 1 is rejected.

6.2.1.2. No adequate and reliable coverage of the key parameters in short-term repeated dose toxicity studies (28-day)

88 Under Annex XI, Section 1.5., the study to be read across must have an adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3), in this case OECD TG 407. Therefore, the following specifications must be met:

a. nature, severity, and duration of clinical signs observed daily and functional observations during the fourth exposure week, i.e. sensory activity, grip strength and motor activity assessments;
b. haematological and clinical biochemistry tests as specified in paragraphs 32-39 of the test guideline;
c. terminal organ and body weights;
d. gross pathology, including incidence and severity, as specified in paragraphs 40-46 of the test guideline;
e. full histopathology, including incidence and severity, as specified in paragraphs 47-49 of the test guideline.

89 The studies (ii) and (iii) are described as 28-day repeated dose toxicity studies.

90 However, the following specifications are not according to the requirements of the OECD TG 407:

a. data on clinical signs and functional observations are missing: nature, severity and duration (study ii);
b. data on haematology and clinical biochemistry findings are missing: incidence and severity with relevant base-line values; in particular, the following investigations are missing for study (ii): reticulocytes, total and differential leucocyte count, platelet count and a measure of blood clotting time/potential; and for study (iii): haematocrit, haemoglobin concentrations, erythrocyte count, reticulocytes, total and differential leucocyte count, platelet count and a measure of blood clotting time/potential;
c. data on terminal organ weights and organ/body weight ratios are missing (study ii and iii);
d. data on gross pathology findings: incidence and severity are missing (study ii and iii);
e. data on histopathology findings are missing: incidence and severity (study ii and

iii).

91 Based on the above, the studies ii. and iii. do not provide an adequate and reliable coverage of the key parameter(s) addressed by the OECD TG 407 and these studies are not an adequate basis for your read-across predictions.

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

6.3. Specification of the study design

93 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) is preferred to ensure that unnecessary animal testing is avoided. Such an approach offers the possibility to avoid carrying out a 28-day study according to OECD TG 407, because the OECD TG 422 can at the same time fulfil the information requirement of REACH Annex VIII, Section 8.6.1 and that of REACH Annex VIII, Section 8.7.1. (Guidance on IRs and CSA, Section R.7.6.2.3.2.).

94 For information on the study design see the request for OECD TG 422 below.

7. Screening for reproductive/developmental toxicity

95 A screening for reproductive/developmental toxicity study (OECD 421 or OECD 422) is an information requirement under Annex VIII, Section 8.7.1., if there is no evidence from analogue substances, QSAR or in vitro methods that the substance may be a developmental toxicant.

7.1. Information provided

96 For the information requirement you have provided a reproduction/developmental toxicity screening study (2008) with the analogue substance 3-(acryloylamino)-N,N,N-trimethylpropan-1-aminium chloride, EC No. 256-181-3.

97 As the study you provided is conducted with a test material that is different than the Substance, ECHA understands that you have adapted this information requirement by using a Grouping of substances and read-across approach.

7.2. Assessment of the information provided

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

7.2.1. Read-across adaptation rejected

99 As explained in Section 0.1.2., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5. is rejected.

100 In the comments to the draft decision, you indicate that you intend to submit the justification for your read-across adaptation. As explained in section 0.1.4, you have not provided any new information addressing the deficiencies identified in your read-across adaptation.

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

7.3. Specification of the study design

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

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

104 Therefore, the study must be conducted in rats 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

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) but extended the deadline.

You indicated in your comments your intention to submit additional information in a dossier update by 31 July 2022. However, no such information or dossier update was submitted.

In its comments, one registrant requested an extension of the deadline. 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 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]

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[3].

(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

(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 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[4].

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