~~Confidential~~

Helsinki, 25 May 2023

Addressees
Registrant of JS_ADAMBC as listed in Appendix 3 of this decision

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

Registered substance subject to this decision ("the Substance")
Substance name: Benzyldimethyl[2-[(1-oxoallyl)oxy]ethyl]ammonium chloride
EC number: 256-283-8

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 12 by the deadline of ***2 June 2025*** and all other information listed below by ***1 September 2027***.

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

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

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

5. 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);

6. 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);

7. Simulation testing on ultimate degradation in surface water also requested below (triggered by Annex VIII, Section 9.2.);

8. Soil simulation testing also requested below (triggered by Annex VIII, Section 9.2.);

9. Sediment simulation testing also requested below (triggered by Annex VIII, Section 9.2.);

10. Identification of degradation products also requested below (triggered by Annex VIII, Section 9.2);

11. Bioaccumulation in aquatic species also requested below (triggered by Annex VIII, Section 9.3., Column 2)

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

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

13. 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);

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

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

16. Simulation testing on ultimate degradation in surface water (Annex IX, Section 9.2.1.2.; test method: EU C.25./OECD TG 309) at a temperature of 12°C. Non-extractable residues (NER) must be quantified and a scientific justification of the selected extraction procedures and solvents must be provided;

17. Soil simulation testing (Annex IX, Section 9.2.1.3.; test method: EU C.23./OECD TG 307) at a temperature of 12°C. Non-extractable residues (NER) must be quantified and a scientific justification of the selected extraction procedures and solvents must be provided;

18. Sediment simulation testing (Annex IX, Section 9.2.1.4.; test method: EU C.24./OECD TG 308) at a temperature of 12°C. Non-extractable residues (NER) must be quantified and a scientific justification of the selected extraction procedures and solvents must be provided;

19. Identification of degradation products (Annex IX, 9.2.3.; test method: EU C.25./OECD TG 309; EU C.23./OECD TG 307 or EU C.24./OECD TG 308);

20. Bioaccumulation in aquatic species (Annex IX, Section 9.3.2; test method: EU C.13./OECD TG 305, aqueous exposure);

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

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

In the requests above, the same study has been requested under different Annexes. This is because some information requirements may be triggered at lower tonnage band(s). In such cases, only the reasons why the information requirement is triggered are provided for the lower tonnage band(s). For the highest tonnage band, the reasons why the standard information requirement is not met and the specification of the study design are provided. Only one study is to be conducted; all registrants concerned must make every effort to reach an agreement as to who is to carry out the study on behalf of the others under Article 53 of REACH.

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. In addition, the studies relating to biodegradation and bioaccumulation are necessary for the PBT assessment. However, to determine the testing needed to reach the conclusion on the persistency and bioaccumulation of the Substance you should consider the sequence in which these tests are performed and other conditions described in this Appendix.

Appeal

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

Failure to comply

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

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

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

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

Appendix 1: Reasons for the decision

Contents

0. Reasons common to several requests

0.1. Assessment of the read-across approach

1 You have adapted the following standard information requirements by using grouping and read-across approach under Annex XI, Section 1.5:

- 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.);
- Sub-chronic toxicity study (90-day), (Annex IX, Section 8.6.2.).

2 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.

3 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.

4 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. Scope of the grouping of substances (category)

5 You provide a read-across justification document in IUCLID under "Linked Categories".

6 For the purpose of this decision, the following abbreviations are used for 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.

7 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*".

8 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*".

9 We have identified the following issue(s) with the proposed grouping and with the prediction(s) of toxicological properties.

0.1.1.1. Documentation of the grouping and read-across adaptation

10 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.

11 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* [redacted]".

12 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.

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

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

(i) The applicability domain of the category: 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) The composition of the category members: 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) The read-across hypothesis: 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).

15 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.

0.1.1.2. Adequacy and reliability of source studies

16 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.

17 Specific reasons why the studies on the source substances do not meet these criteria are explained further below under the applicable information requirement section 5.2.1.1. Therefore, no reliable predictions can be made for these information requirements.

0.1.2. Information provided in the comments to the draft decision

18 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 0.1.1.1).

0.1.3. Conclusion on the read-across approach

19 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 approaches under Annex XI, Section 1.5. are rejected.

0.2. Exposure based adaptations – Information in the comments

20 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:

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

22 Long-term toxicity testing on fish (Annex IX, Section 9.1.6.1.)

23 However, the information in your comments is not sufficient for ECHA to make an assessment, because while you have described your intentions, you have not provided any information to substantiate your claim.

Reasons related to the information under Annex VII of REACH

1. Skin sensitisation

24 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

You have provided a skin sensitisation test in guinea pigs (2016) with the Substance (study i).

1.2. Assessment of the information provided

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

1.2.1. Assessment whether the Susbtance causes skin sensitisation

1.2.1.1. The provided study does not meet the information requirement

26 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) justification for the dose level selection (induction and challenge), including the results of the dose range finding study;
b) a table of individual results (individual animal approach) or mean/median results (pooled treatment group approach) for the treatment and control groups.

27 The study (i) is described as a Guinea Pig Maximization Test.

28 However, the following specifications are not according to the requirements of OECD TG 406:

a) no results of the dose range finding study was provided;
b) the results have not been reported by identifying whether the reactions are observed in treatment or control groups.

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

30 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 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

31 - the study covers all the key parametes required by OECD TG 406.

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

33 However, you have not provided any results from dose range finding study/ies to substantiate your claims that the dose level selection was established according to the test guideline. 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. In addition, you have not provided any results identifying whether the reactions are observed in treatment or control groups.

1.2.2. No assessment of potency

34 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).

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

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

1.3. Specification of the study design

37 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.

38 In case no conclusion on the skin sensitisation potency can be made for the Substance based on the existing data or 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

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

2.1. Information provided

40 You have provided an *in vitro* gene mutation study (1992) with the Substance.

2.2. Assessment of the information provided

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

2.2.1. The provided study does not meet the information requirement

42 To fulfil the information requirement, a study must comply with 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).

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

44 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 (i.e., the *E. coli* WP2 uvrA, or *E. coli* WP2 uvrA (pKM101), or *S. typhimurium* TA102 strainsare missing).

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

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

2.3. Specification of the study design

47 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.

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

3. Short-term toxicity testing on aquatic invertebrates

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

3.1. Information provided

49 You have provided a short-term toxicity to aquatic invertebrates study (1993) with the Substance.

3.2. Assessment of the information provided

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

3.2.1. The provided study does not meet the information requirement

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

a) analytical monitoring must be conducted. A reliable analytical method for the quantification of the test material in the test solutions with reported specificity, recovery efficiency, precision, limits of determination (i.e. detection and quantification) and working range must be available;
b) the effect values can only be based on nominal or measured initial concentration if the concentration of the test material has been satisfactorily maintained within 20 % of the nominal or measured initial concentration throughout the test (see also Guidance on IRs and CSA, Section R.7.8.4.1).

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

a) no analytical monitoring of exposure was conducted;

b) the reported effect values are based on nominal concentrations. However, no measured concentrations of the test material are available that demonstrate exposure concentrations were within ± 20 % of the nominal or measured initial concentration.

53 Based on the above, there are critical methodological deficiencies resulting in the rejection of the study results. More, specifically, in the lack of analytical monitoring we cannot verify if the exposure concentrations remained stable throughout the study. Therefore the results based on nominal concentrations are not reliable.

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

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

3.3. Study design and test specifications

56 The Substance is difficult to test due to the instability as indidcated by its hydrolytic half-lives of <24 hours (i.e. 10.6 hours at pH 9). OECD TG 202 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. 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 202. In case a dose-response relationship cannot be established (no observed effects), you must demonstrate that the approach used to prepare test solutions was adequate to maximise the concentration of the Substance in the test solution.

4. Growth inhibition study aquatic plants

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

4.1. Information provided

58 You have provided a toxicity to aquatic algae study (2010) with the Substance.

4.2. Assessment of the information provided

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

4.2.1. The provided study does not meet the information requirement

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

a) the test media prepared specifically for analysis of exposure concentrations during the test is treated identically to those used for testing (*i.e.* inoculated with algae and incubated under identical conditions);
b) for volatile, unstable or strongly adsorbing test substances, additional samplings for analysis at 24 hour intervals is required.

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

a) the exposure concentrations were determined in samples not inoculated with algae and you have expressed the effect values based on these measured concentrations. The concentrations of the test material were also determined in samples inoculated with algae. Those were lower than the ones of non-inoculated samples and not used as basis to determine the effect values;
b) the Substance is unstable and no additional sampling for analysis at 24 h interval was conducted.

62 Based on the above, there are critical methodological deficiencies resulting in the rejection of the study results. More specifically, effect values are based on inadequately determined mean measured concentrations and the sampling frequency for analytical monitoring was not appropriate to take into account decline of test material concentration. Moreover, if determined in samples inoculated with algae, the test material was not detectable (<LOD) at concentrations relevant to determine NOErC. Taken together, the results of this study are not reliable.

63 Therefore, the requirements of OECD TG 201 are not met and the information requirement is not fulfilled.

4.3. Study design and test specifications

64 OECD TG 201 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 and test specifications' under Request 3.

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

Reasons related to the information under Annex VIII of REACH

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

66 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.

5.1. Information provided

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

(i) an *in vitro* mammalian chromosome aberration test (1990) with the analogue substance dimethylaminoethylacrylate methylchloride, EC No. 256-176-6.

5.2. Assessment of the information provided

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

5.2.1. Read-across adaptation rejected

69 As explained in Section 0.1.1.1, 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. As explained in section 0.1.2, you have not provided any new information addressing the deficiencies identified in your read-across adaptation.

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

5.3. Specification of the study design

72 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.

6. In vitro gene mutation study in mammalian cells

73 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.

6.1. Information provided

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

(i) an *in vitro* gene mutation study in mammalian cells (1997) with the analogue substance dimethylaminoethylacrylate methylchloride, EC No. 256-176-6.

6.2. Assessment of the information provided

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

6.2.1. Read-across adaptation rejected

76 As explained in Section 0.1.1.1., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5 is rejected.

77 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. As explained in section 0.1.2, you have not provided any new information addressing the deficiencies identified in your read-across adaptation.

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

6.3. Specification of the study design

79 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.

7. Simulation testing on ultimate degradation in surface water

80 Further degradation testing must be considered if the chemical safety assessment (CSA) according to Annex I indicates the need to investigate further the degradation of the substance (Annex VIII, Section 9.2., Column 2).

7.1. Triggering of the information requirement

81 This information requirement is triggered in case the chemical safety assessment (CSA) indicates the need for further degradation investigation (Annex I, Section 4; Annex XIII, Section 2.1), such as if the substance is a potential PBT/vPvB substance (Guidance on IRs and CSA, Section R.11.4.). This is the case if the Substance itself or any of its constituent or impurity present in concentration ≥ 0.1% (w/w) or relevant transformation/degradation product meets the following criteria:

- it is potentially persistent or very persistent (P/vP) as:
  - it is not readily biodegradable (*i.e.* <60/70% degradation in an OECD 301 A-F), and
- it is potentially bioaccumulative or very bioaccumulative (B/vB) as:
  - for some groups of substances (e.g. organometals, ionisable substances, surfactants) other partitioning mechanisms may drive bioaccumulation (e.g. binding to protein/cell membranes) and high potential for bioaccumulation cannot be excluded solely based on its potential to partition to lipid.

82 Your registration dossier provides the following:

- the Substance is not readily biodegradable (23% degradation after 28 days in ISO 7827 test, which is comparable to an OECD 301A or E (Guidance on IR and CSA R7.7.9.-1);

- the Substance is ionisable and therefore high potential for bioaccumulation cannot be excluded based on available information.

83 Furthermore:

- it is not possible to conclude on the bioaccumulation potential of the Substance (see Request 20 of this decision), and
- it is not possible to conclude on the toxicity of the Substance (see Request 12, 14, 15, and 21 of this decision).

84 Based on the above, the available information on the Substance indicates that it is a potential PBT/vPvB substance.

85 In your comments to the draft decision, you claimed that the Substance is neither PBT nor vPvB and not ionisable. You indicate the following :" Quaternary ammonium salts, such as the Substance, are not ionisable; they are permanently ionic. An ionisable group is any uncharged group in a molecular entity that is capable of dissociating by yielding an ion (usually an H+ ion) or an electron and itself becoming oppositely charged. They are functional groups that act as proton-donors or proton acceptors. Ionisable organic chemicals (IOCs) are subject to change in speciation state depending on their proton affinity, as expressed by the acidity/basicity constant (pKa/pKb), and the pH of their endogenous environment. Quaternary ammonium cations are positively charged ions of the structure NR+4, R being an alkyl group or an aryl group. Unlike the ammonium ion (NH+4) and the primary, secondary, or tertiary ammonium cations, quaternary ammonium cations are permanently charged, independent of the pH of their solution. Quaternary ammonium cations are unreactive toward even strong electrophiles, oxidants, and acids. They also are stable toward most nucleophiles. Quaternary ammonium salts are simply salts of quaternary ammonium cations"

86 As mentioned in your comment as summarised above, the quaternary ammonium salts including the Substance are permanently charged (i.e. positively charged) and this regardless of the pH. This indicates that the Substance is considered as an ionic substance under relevant environmental conditions (i.e pH 4.5 to 8.5). Considering those properties of the Substance, it cannot be ruled out that the bioaccumulation properties of the Substance could be driven by other mechanisms (e.g. binding to protein/cell membranes) and therefore the high potential for bioaccumulation cannot be excluded solely based on its potential to partition to lipid. On this basis, as you have not provided specific information addressing the issues identified above, the information provided in your comments does not change the assessment outcome.

87 The examination of the available information or adaptations, as well as the selection of the requested test and the test design are addressed respectively in Request 16.

8. Soil simulation testing

88 Further degradation testing must be considered if the chemical safety assessment (CSA) according to Annex I indicates the need to investigate further the degradation of the substance (Annex VIII, Section 9.2., Column 2).

8.1. Triggering of the information requirement

89 This information requirement is triggered in case the chemical safety assessment (CSA) indicates the need for further degradation investigation (Annex I, Section 4; Annex XIII,

Section 2.1), such as if the substance is a potential PBT/vPvB substance (Guidance on IRs and CSA, Section R.11.4.).

90 As explained in Request 7, the Substance is a potential PBT/vPvB substance. In your comments to the draft decision, you claimed that the Substance is neither PBT nor vPvB and not ionisable.

91 However, as explained in Request 7, the information provided in your comments does not change the assessment outcome.

92 Therefore, the chemical safety assessment (CSA) indicates the need for further degradation investigation. Based on the adsorptive properties of the Substance, soil represents a relevant environmental compartment.

93 The examination of the available information or adaptations, as well as the selection of the requested test and the test design are addressed respectively in Request 17.

9. Sediment simulation testing

94 Further degradation testing must be considered if the chemical safety assessment (CSA) according to Annex I indicates the need to investigate further the degradation of the substance (Annex VIII, Section 9.2., Column 2).

9.1. Triggering of the information requirement

95 This information requirement is triggered in case the chemical safety assessment (CSA) indicates the need for further degradation investigation (Annex I, Section 4; Annex XIII, Section 2.1), such as if the substance is a potential PBT/vPvB substance (Guidance on IRs and CSA, Section R.11.4.).

96 As explained in request 7, the Substance is a potential PBT/vPvB substance.

97 In your comments to the draft decision, you claimed that the Substance is neither PBT nor vPvB and not ionisable.

98 However, as explained in Request 7, the information provided in your comments does not change the assessment outcome.

99 Therefore, the chemical safety assessment (CSA) indicates the need for further degradation investigation. Based on the adsorptive properties of the Substance, sediment represents a relevant environmental compartment.

100 The examination of the available information or adaptations, as well as the selection of the requested test and the test design are addressed respectively in Request 18.

10. Identification of degradation products

101 Further degradation testing must be considered if the chemical safety assessment (CSA) according to Annex I indicates the need to investigate further the degradation of the substance (Annex VIII, Section 9.2., Column 2).

10.1. Triggering of the information requirement

102 This information requirement is triggered in case the chemical safety assessment (CSA) indicates the need for further degradation investigation (Annex I, Section 4; Annex XIII, Section 2.1), such as if the substance is a potential PBT/vPvB substance (Guidance on IRs and CSA, Section R.11.4.).

103 As explained in request 7, the Substance is a potential PBT/vPvB substance. In your comments to the draft decision, you claimed that the Substance is neither PBT nor vPvB and not ionisable.

104 However, as explained in Request 7, the information provided in your comments does not change the assessment outcome.

105 Therefore, the chemical safety assessment (CSA) indicates the need for further degradation investigation.

106 The examination of the available information or adaptations, as well as further information on the selection of the approach to generate this information are addressed in Request 19.

11. Bioaccumulation in aquatic species

107 Under Annex VIII, Section 9.3., Column 2, further information on bioaccumulation or further testing as described in Annex IX must be generated if the chemical safety assessment (CSA) in accordance with Annex I indicates the need to investigate further the bioaccumulation properties of the substance.

11.1. Triggering of the information requirement

108 This information requirement is triggered in case the chemical safety assessment (CSA) indicates the need for further investigation on bioaccumulation in aquatic species (Annex I, Section 4; Annex XIII, Section 2.1), such as if the substance is a potential PBT/vPvB substance (Guidance on IRs and CSA, Section R.11.4.).

109 As already explained in Request 7, the Substance is a potential PBT/vPvB substance. In your comments to the draft decision, you claimed that the Substance is neither PBT nor vPvB and not ionisable.

110 However, as explained in Request 7, the information provided in your comments does not change the assessment outcome.

111 Therefore, the chemical safety assessment (CSA) indicates the need for further investigation on bioaccumulation in aquatic species.

112 The examination of the available information or adaptations, as well as the selection of the requested test and the test design are addressed in Request 20.

Reasons related to the information under Annex IX of REACH

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

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

12.1. Information provided

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

(i) a sub-chronic repetead dose toxicity study (1976) with the analogue substance dimethylbis(prop-2-en-1-yl)azanium chloride, EC No. 230-993-8.

12.2. Assessment of the information provided

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

12.2.1. Read-across adaptation rejected

116 As explained in Section 0.1.1.1., 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.

12.2.1.1. Source study not adequate for the information requirement

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

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

119 This study has been conducted using a non-rodent species, i.e., dogs, in order to investigate the sub-chronic toxicity of the analogue substance. Since Annex IX, Section 8.6.2., Column 1, requires that the sub-chronic toxicity study (90-day) must be conducted in a rodent species, study (i) is not an adequate basis for your read-across prediction and is therefore, rejected.

120 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. As explained in section 0.1.2, you have not provided any new information addressing the deficiencies identified in your read-across adaptation.

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

12.3. Specification of the study design

122 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.

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

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

13. Pre-natal developmental toxicity study in one species

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

13.1. Information provided

126 For the information requirement you have provided the following justification: "*At 1000 mg/kg (the highest dose) an analagous quaternary ammonium substance 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*."

127 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.

13.2. Assessment of the information provided

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

13.2.1. Low toxicological activity not demonstrated

129 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, two of them being:

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

130 ECHA notes that:

- the Substance shows toxicity. In IUCLID Section 7.2.1, the acute oral toxicity study performed with the Substance reports effects such as ataxia, reduced muscle tone and hypokinesia, dyspnoea and mydriasis;
- the registration dossier does not contain any toxicokinetic data with the Substance in order to show that systemic absorption does not take place. However, the acute toxicity studies shows that systemic absorption occurs orally.

131 In the comments to the draft decision, you refer to the acute oral toxicity study and self-classification as Acute Tox 4, and explain that the oral route is not a relevant route of exposure in the industrial setting. In addition, you explain that the substance demonstrated no effects in an acute dermal toxicity test and is not volatile which excludes exposure through the inhalation route. However, you have not addressed the deficiencies identified above as the provided information does not address the Annex IX, Section 8.7, column 2 requirements for

- no toxicity in any of the tests available while signs of toxicity have been reported in the acute oral toxicity study conducted on the Substance; and
- lack of toxicokinetic data that no systemic absorption occurs via relevant routes of exposure.

132 While you explain that oral route is not a relevant route of exposure, the column 2 requirement above indicates "no toxicity in any of the tests available" and does not refer to particular relevance of route of exposure.

13.2.2. Read-across adaptation rejected

133 As explained in Section 0.1.1.1., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5. is rejected.

134 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. As explained in section 0.1.2, you have not provided any new information addressing the deficiencies identified in your read-across adaptation.

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

13.3. Specification of the study design

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

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

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

14. Long-term toxicity testing on aquatic invertebrates

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

14.1. Information provided

140 You have adapted this information requirement and to support the adaptation, you have provided following information: "*Substance is not acutely toxic to daphnia. Emissions to water are not to be expected. The Chemical Safety Assessment does not indicate the need to investigate further effects on aquatic organisms*."

141 ECHA understands that you intend to apply Column 2 of Annex IX, Section 9.1.

14.2. Assessment of the information provided

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

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

143 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).

144 In the comments to the draft decision, you indicate that 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. However, as already explained under Section 0.2, based on the

information provided in your comments there is currently no information to assess whether your adaptation fulfils the requirement.

145 Your adaptation is therefore rejected.

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

147 OECD TG 211 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 and test specifications' under Request 3.

15. Long-term toxicity testing on fish

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

15.1. Information provided

149 You have adapted this information requirement and to support the adaptation, you have provided following information: "*Substance is not acutely toxic to fish. The Chemical Safety Assessment does not indicate the need to investigate further effects on aquatic organisms*."

150 ECHA understands that you intend to apply Column 2 of Annex IX, Section 9.1.

15.2. Assessment of the information provided

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

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

152 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).

153 In the comments to the draft decision, you indicate that 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. However, as already explained under Section 0.2, based on the information provided in your comments there is currently no information to assess whether your adaptataion fulfil the requierement.

154 Your adaptation is therefore rejected.

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

15.3. Study design and test specifications

156 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.).

157 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 and test specifications' under Request 3.

16. Simulation testing on ultimate degradation in surface water

158 Simulation testing on ultimate degradation in surface water is an information requirement under Annex IX to REACH (Section 9.2.1.2.).

16.1. Information provided

159 You have adapted this information requirement and you have provided following justification: "*The Chemical Safety Assessment does not indicate the need for further investigation of the degradation*."

160 ECHA understands that you intend to apply Column 2 of Annex IX, Section 9.2..

16.2. Assessment of information provided

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

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

162 Annex IX, Section 9.2., Column 2 provides that "further" biodegradation testing must be proposed if the chemical safety assessment according to Annex I indicates the need to investigate further the degradation of the substance and its degradation products. That provision allows a registrant to propose, or ECHA to require, biotic degradation testing not covered by the information on degradation listed under Annex IX, section 9.2., Column 1. Therefore, this provision cannot be used as a justification for omitting the submission of information on simulation testing on ultimate degradation in surface water required under Annex IX, Section 9.2.1.2, Column 1.

163 Therefore, your adaption is rejected.

On this basis, the information requirement is not fulfilled.

16.3. Study design and test specifications

164 Simulation degradation studies must include two types of investigations (Guidance on IRs and CSA, Section R.7.9.4.1.):

1) a degradation pathway study where transformation/degradation products are quantified and, if relevant, are identified, and
2) a kinetic study where the degradation rate constants (and degradation half-lives) of the parent substance and of relevant transformation/degradation products are experimentally determined.

165 You must perform the test, by following the pelagic test option with natural surface water containing approximately 15 mg dw/L of suspended solids (acceptable concentration between 10 and 20 mg dw/L) (Guidance on IRs and CSA, Section R.11.4.1.1.3.).

166 The required test temperature is 12°C, which corresponds to the average environmental temperature for the EU (Guidance on IRs and CSA, Table R.16-8) and is in line with the applicable test conditions of the OECD TG 309.

167 As specified in Guidance on IRs and CSA, Section R.7.9.4.1., the organic carbon (OC) concentration in surface water simulation tests is typically 2 to 3 orders of magnitude higher than the test material concentration and the formation of non-extractable residues (NERs) may be significant in surface water tests. Therefore, non-extractable residues (NER) must be quantified. The reporting of results must include a scientific justification of the used extraction procedures and solvents. By default, total NER is regarded as non-degraded

Substance. However, if reasonably justified and analytically demonstrated a certain part of NER may be differentiated and quantified as irreversibly bound or as degraded to biogenic NER, such fractions could be regarded as removed when calculating the degradation half-life(s) (Guidance on IRs and CSA, Section R.11.4.1.1.3.). Further recommendations may be found in the background note on options to address non-extractable residues in regulatory persistence assessment available on the ECHA website.

168 Relevant transformation/degradation products are at least those detected at ≥ 10% of the applied dose at any sampling time or those that are continuously increasing during the study even if their concentrations do not exceed 10% of the applied dose, as this may indicate persistence (OECD TG 309; Guidance on IRs and CSA, Section R.11.4.1.).

17. Soil simulation testing

169 Soil simulation testing is an information requirement under Annex IX to REACH (Section 9.2.1.3.) for substances with a high potential for adsorption to soil.

170 As explained in Request 8, the Substance has high potential for adsorption to soil.

17.1. Information provided

171 You have adapted this information requirement and you have provided following justification: "*Substance is used strictly as an intermediate in the manufacture of polymers. Emissions to soil are not to be expected*."

172 ECHA understands that you intend to apply Column 2 of Annex IX, Section 9.2.1.3.

17.2. Assessment of information provided

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

17.2.1. The provided adaptation does not meet the criteria of Annex IX, Section 9.2.1.3., Column 2

174 Under Annex IX, Section 9.2.1.3., Column 2, second indent, the study may be omitted if direct and indirect exposure of soil is unlikely. Therefore, it must be demonstrated that there is no release to the environment at any stage in the life cycle of the substance (Guidance on IRs and CSA, Section R.7.10.4.5.).

175 In your chemical safety assessment, you report the following uses:

- Monomer for polymerisation, ERC 6a use of intermediate

176 On exposure assessment, your further describe e.g.:"*Only short term emissions to wastewater during limited maintenance and cleaning activities or in the event of an accidental spill*" and "*Contaminated water such as wash water from reactors or from maintenance operations should be returned to the process or, if impracticable, sent to a wastewater treatment plant*".

177 Based on the above, releases to a wastewater treatment plant/STP are possible. On this basis, exposure to the aquatic environment (via STP effluent) or to soil (via application of STP sludge to agricultural soil) cannot be ruled out.
The information provided in your dossier indicates releases to the environment and contradict your statement of unlikely direct and indirect exposure.

178 Therefore your adaptation is rejected.

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

17.3. Study design and test specifications

180 Simulation degradation studies must include two types of investigations (Guidance on IRs and CSA, Section R.7.9.4.1):

1) a degradation pathway study where transformation/degradation products are quantified and, if relevant, are identified, and
2) a kinetic study where the degradation rate constants (and degradation half-lives) of the parent substance and of relevant transformation/degradation products are experimentally determined.

181 In accordance with the specifications of OECD TG 307, you must perform the test using at least four soils representing a range of relevant soils (i.e. varying in their organic content, pH, clay content and microbial biomass).

182 The required test temperature is 12°C, which corresponds to the average environmental temperature for the EU (Guidance on IRs and CSA, Table R.16-8) and is in line with the applicable test conditions of the OECD TG 309.

183 In accordance with the specifications of OECD TG 307, non-extractable residues (NER) must be quantified. The reporting of results must include a scientific justification of the used extraction procedures and solvents (Guidance on IRs and CSA, Section R.7.9.4.1.). By default, total NER is regarded as non-degraded Substance. However, if reasonably justified and analytically demonstrated a certain part of NER may be differentiated and quantified as irreversibly bound or as degraded to biogenic NER, such fractions could be regarded as removed when calculating the degradation half-life(s) (Guidance on IRs and CSA, Section R.11.4.1.1.3.). Further recommendations may be found in the background note on options to address non-extractable residues in regulatory persistence assessment available on the ECHA website.

184 Relevant transformation/degradation products are at least those detected at ≥ 10% of the applied dose at any sampling time or those that are continuously increasing during the study even if their concentrations do not exceed 10% of the applied dose, as this may indicate persistence (OECD TG 307; Guidance on IRs and CSA, Section R.11.4.1.).

18. Sediment simulation testing

185 Sediment simulation testing is an information requirement under Annex IX to REACH (Section 9.2.1.4.) for substances with a high potential for adsorption to sediment.

186 As explained under Request 8, the Substance has a high potential for adsorption to sediment.

18.1. Information provided

187 You have adapted this information requirement and you have provided following justification: "*The Chemical Safety Assessment does not indicate the need for further investigation of the degradation*."

188 ECHA understands that you intend to apply Column 2 of Annex IX, Section 9.2.

18.2. Assessment of information provided

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

190 Annex IX, Section 9.2., Column 2 provides that "further" biodegradation testing must be proposed if the chemical safety assessment according to Annex I indicates the need to investigate further the degradation of the substance and its degradation products. That provision allows a registrant to propose, or ECHA to require, biotic degradation testing not covered by the information on degradation listed under Annex IX, section 9.2., Column 1. Therefore, this provision cannot be used as a justification for omitting the submission of information on Sediment simulation testing required under Annex IX, Section 9.2.1.4, Column 1.

191 Therefore, your adaption is rejected and the information requirement is not fulfilled.

18.3. Study design and test specifications

192 Simulation degradation studies must include two types of investigations (Guidance on IRs and CSA, Section R.7.9.4.1.):

1) a degradation pathway study where transformation/degradation products are quantified and, if relevant, are identified, and
2) a kinetic study where the degradation rate constants (and degradation half-lives) of the parent substance and of relevant transformation/degradation products are experimentally determined.

193 In accordance with the specifications of OECD TG 308, you must perform the test using two sediments. One sediment should have a high organic carbon content (2.5-7.5%) and a fine texture, the other sediment should have a low organic carbon content (0.5-2.5%) and a coarse texture. If the Substance may also reach marine waters, at least one of the water-sediment systems should be of marine origin.

194 The required test temperature is 12°C, which corresponds to the average environmental temperature for the EU (Guidance on IRs and CSA, Table R.16-8) and is in line with the applicable test conditions of the OECD TG 309.

195 In accordance with the specifications of OECD TG 308, non-extractable residues (NER) must be quantified. The reporting of results must include a scientific justification of the used extraction procedures and solvents (Guidance on IRs and CSA, Section R.7.9.4.1.). By default, total NER is regarded as non-degraded Substance. However, if reasonably justified and analytically demonstrated a certain part of NER may be differentiated and quantified as irreversibly bound or as degraded to biogenic NER, such fractions could be regarded as removed when calculating the degradation half-life(s) (Guidance on IRs and CSA, Section R.11.4.1.1.3.). Further recommendations may be found in the background note on options to address non-extractable residues in regulatory persistence assessment available on the ECHA website.

196 Relevant transformation/degradation products are at least those detected at ≥ 10% of the applied dose at any sampling time or those that are continuously increasing during the study even if their concentrations do not exceed 10% of the applied dose, as this may indicate persistence (OECD TG 308; Guidance on IRs and CSA, Section R.11.4.1.).

19. Identification of degradation products

197 Identification of degradation products is an information requirement under Annex IX to REACH (Section 9.2.3.).

198 You have provided information on the identity of the hydrolysis products, but no information on the identity of further transformation/biodegradation products for the Substance.

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

19.1. Study design and test specifications

200 Simulation degradation studies must include two types of investigations (Guidance on IRs and CSA, Section R.7.9.4.1.):

(1) a degradation pathway study where transformation/degradation products are quantified and, if relevant, are identified, and
(2) a kinetic study where the degradation rate constants (and degradation half-lives) of the parent substance and of relevant transformation/degradation products are experimentally determined.

201 Identity, stability, behaviour, and molar quantity of the degradation/transformation products relative to the Substance must be evaluated and reported. In addition, identified transformation/degradation products must be considered in the CSA including PBT assessment.

202 You must obtain this information from the degradation studies requested in requests 16, 17 or 18.

203 To determine the degradation rate of the Substance, the requested study according to OECD TG 309 (request 16) must be conducted at 12°C and at a test concentration < 100 µg/L. However, to overcome potential analytical limitations with the identification and quantification of major transformation/degradation products, you may consider running a parallel test at higher temperature (but within the frame provided by the test guideline, e.g. 20°C) and at higher application rate (i.e. > 100 µg/L).

204 To determine the degradation rate of the Substance, the requested studies according to OECD TG 308 and 307 (requests 17 and 18) must be conducted at 12°C and at a test material application rates reflecting realistic assumptions. However, to overcome potential analytical limitations with the identification and quantification of major transformation/degradation products, you may consider running a parallel test at higher temperature (but within the frame provided by the test guideline) and at higher application rate (e.g. 10 times).

20. Bioaccumulation in aquatic species

205 Bioaccumulation in aquatic species is an information requirement under Annex IX to REACH (Section 9.3.2.).

20.1. Information provided

206 You have adapted this information requirement by using Column 2 of Annex IX, Section 9.3.2. To support the adaptation, you have provided following justification:

(i) "The substance has a low potential for bioaccumulation (log Kow < 0)";
(ii) "Substance is used strictly as an intermediate in the manufacture of polymers. Emissions to water are not to be expected."

207 ECHA understands that you intend to apply Column 2 of Annex IX, Section 9.3.2. first and second indent.

20.2. Assessment of information provided

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

20.2.1. The log Kow is not a valid descriptor of the bioaccumulation potential of the Substance

209 Under Section 9.3.2., Column 2, first indent of Annex IX to REACH, the study may be omitted if the substance has a low potential for bioaccumulation and/or a low potential to cross biological membranes.

210 A low logKow (i.e. log Kow < 3) on its own may be used to show low potential for bioaccumulation only if the potential for bioaccumulation of the substance is solely driven by lipophilicity. This excludes, for example, situations where the substance is surface active or ionisable at environmental pH (pH 4 – 9).

211 Your registration dossier provides an adaptation stating that the log Kow is < 0 without further explanation and the Substance is ionisable.

212 Therefore, logKow is not a valid descriptor of the bioaccumulation potential of the Substance and your adaptation is rejected.

20.2.2. The provided adaptation does not meet the criteria of Annex IX, Section 9.3.2., Column 2

213 As explained under request 17 above, you have not demonstrated that exposure to the environment can be ruled out. Therefore, your adaptation is rejected.

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

20.3. Study design and test specifications

215 Bioaccumulation in fish: aqueous and dietary exposure (Method EU C.13 / OECD TG 305) is the preferred test to investigate bioaccumulation (Guidance on IRs and CSA, Section R.7.10.3.1.). Exposure via the aqueous route (OECD TG 305-I) must be conducted unless it can be demonstrated that:

- a stable and fully dissolved concentration of the test material in water cannot be maintained within ± 20% of the mean measured value, and/or
- the highest achievable concentration is less than an order of magnitude above the limit of quantification (LoQ) of a sensitive analytical method.

216 This test set-up is preferred as it allows for a direct comparison with the B and vB criteria of Annex XIII of REACH.

217 You may only conduct the study using the dietary exposure route (OECD 305-III) if you justify and document that testing through aquatic exposure is not technically possible as indicated above. You must then estimate the corresponding BCF value from the dietary test data according to Annex 8 of the OECD 305 TG and OECD Guidance Document on Aspects of OECD TG 305 on Fish Bioaccumulation (ENV/JM/MONO(2017)16).

Reasons related to the information under Annex X of REACH

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

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

21.1. Information provided

219 For the information requirement you have provided the following justification: "*At 1000 mg/kg (the highest dose) an analagous quaternary ammonium substance 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.*"

220 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.

21.2. Assessment of the information provided

221 Your adaptation is rejected for the same reasons explained under request 13 above. In addition, for the reasons explained under request 13 above, the information provided in your comments does not change the outcome of ECHA's assessment.

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

21.3. Specification of the study design

223 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 13).

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

225 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 is 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).

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

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.

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]

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

(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[3].

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

2. General recommendations for conducting and reporting new tests

2.1. Strategy for the PBT/vPvB assessment

Under Annex XIII, the information must be based on data obtained under conditions relevant for the PBT/vPvB assessment. You must assess the PBT properties of each relevant constituent of the Substance present in concentrations at or above 0.1% (w/w) and of all relevant transformation/degradation products. Alternatively, you would have to justify why you consider these not relevant for the PBT/vPvB assessment.

You are advised to consult Guidance on IRs & CSA, Sections R.7.9, R.7.10 and R.11 on PBT assessment to determine the sequence of the tests needed to reach the conclusion on PBT/vPvB. The guidance provides advice on 1) integrated testing strategies (ITS) for the P, B and T assessments and 2) the interpretation of results in concluding whether the Substance fulfils the PBT/vPvB criteria of Annex XIII.

In particular, you are advised to first conclude whether the Substance fulfils the Annex XIII criteria for P and vP, and then continue with the assessment for bioaccumulation. When determining the sequence of simulation degradation testing you are advised to consider the intrinsic properties of the Substance, its identified uses and release patterns as these could significantly influence the environmental fate of the Substance. You must revise your PBT assessment when the new information is available.

2.2. 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 in Appendix 1.