~~Confidential~~

Helsinki, 12 October 2022

Addressees
Registrant(s) of JS_3775-90-4 as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
28 October 2021

Registered substance subject to this decision ("the Substance")
Substance name: 2-tert-butylaminoethyl methacrylate
EC number: 223-228-4

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

DECISION ON A COMPLIANCE CHECK

Under Article 41 of Regulation (EC) No 1907/2006 (REACH), you must submit the information listed below, by the deadline of ***19 January 2026***.

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

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

1. In vivo mammalian alkaline comet assay (triggered by Annex VIII, Section 8.4., column 2); see Request 5 below
2. Justification for an adaptation of a Short-term repeated dose toxicity (28 days) based on the results of the Sub-chronic toxicity study (90 days) requested below (Annex VIII, Section 8.6.1.)
3. Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.; test method: EU B.64/OECD TG 422) by oral route, in rats
4. Hydrolysis as a function of pH (Annex VIII, Section 9.2.2.1.; test method: EU C.7./OECD TG 111)

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

5. In vivo mammalian alkaline comet assay (Annex IX, Section 8.4., column 2; test method: OECD TG 489) in rats, or if justified, other rodent species, oral route, on the following tissues: liver, glandular stomach and duodenum.
6. Sub-chronic toxicity study (90-day) (Annex IX, Section 8.6.2.; test method: OECD TG 408) by oral route, in rats
7. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method: OECD TG 414) by oral route, in one species (rat or rabbit)
8. Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.; test method: EU C.20./OECD TG 211)
9. Long-term toxicity testing on fish (Annex IX, Section 9.1.6.; test method: EU C.47./OECD TG 210)

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

Information required depends on your tonnage band

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

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.

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 exposure-based adaptations

1 You have adapted the following standard information requirements by using substance-tailored exposure-driven testing approach under Annex XI, Section 3:

- Sub-chronic toxicity study (90-day), (Annex IX, Section 8.6.2.)
- Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)

2 ECHA has considered the scientific and regulatory validity of your substance-tailored exposure-driven testing approach in general before assessing the specific standard information requirements in the following sections.

3 You have provided an adaptation in Sections 7.5.1 and 7.8.2 of your dossier, and you conclude that "At this tonnage level there is a limited possibility of human exposure to 2-tert-butylaminoethyl methacrylate within the European Community, as it is neither manufactured nor used within the European Community, it is imported incorporated in polymers with low residual monomer [redacted]%. In addition any residual monomer is of low volatility so making inhalation exposure very unlikely. Therefore we are waiving these required studies on the grounds of lack of potential for human exposure. [….] Repeat dose toxicity is the lead effect with no indications of any specific effects on reproduction and development, there being only limited effects on the offspring clearly mediated via severe maternal toxicity. This together with the low potential for exposure indicate that it is not scientifically justified to carry out any further animal experiments for repeat dose and reproductive toxicity.".

4 ECHA has evaluated the above information under the rules set in Annex XI, Section 3. Substance-tailored exposure-driven testing.

5 As stated in Annex XI, Section 3, testing in accordance with Sections 8.6 and 8.7 of Annex VIII and in accordance with Annexes IX and X may be omitted based on the exposure scenario(s) developed in the CSR, by providing an adequate and scientifically-supported justification based on a thorough and rigorous exposure assessment in accordance with Section 5 of Annex I and by communicating the specific conditions of use through the supply chain. Any one of the following criteria 3.2.(a), (b) or (c) shall be met. In particular:

- 3.2 (a) the manufacturer or importer demonstrates and documents that all the following conditions are fulfilled, where two conditions are that
  - i. the results of the exposure assessment covering all relevant exposures throughout the life cycle of the substance demonstrate the absence of or no significant exposure in all scenarios of the manufacture and all identified uses as referred to in Annex VI section 3.5.;
  - ii. a suitable DNEL can be derived from results of available test data for the Substance taking full account of the increased uncertainty resulting from the omission of the information requirement, and that DNEL is relevant and appropriate both to the information requirement to be omitted and for risk assessment purposes; and
- 3.2 (b) where the substance is not incorporated in an article the manufacturer, or the importer demonstrates and documents for all relevant scenarios that throughout the life cycle strictly controlled conditions as set out in Art 18(4)(a) to (f) apply; and
- 3.2 (c) where the substance is incorporated in an article in which it is permanently

embedded in a matrix or otherwise rigorously contained by technical means, it is demonstrated and documented that all the following conditions are fulfilled, where two conditions are:

i. the substance is not released during its life cycle;
ii. the likelihood that workers or the general public or the environment are exposed to the substance under normal or reasonably foreseeable conditions of use is negligible.

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

0.1.1. Exposure assessment

7 REACH Annex XI 3.2 specifies that in all cases, adequate justification and documentation shall be provided. The justification shall be based on a thorough and rigorous exposure assessment in accordance with section 5 of Annex I. According to ECHA Guidance Chapter R.5: Adaptation of information requirements (version 2.1 December 2011) in order to justify for a certain endpoint the omission of the standard information requirement, a high level of confidence is needed to demonstrate no or no significant exposure or no release.

8 ECHA notes that you have not identified any use for the Substance, nor have you created any exposure scenario in the CSR. The CSR does not contain a chemical risk assessment covering all relevant exposures of the entire life-cycle of the monomer substance subject to this decision. Instead, you state that as polymerisation takes place outside the EU, there is no identified use within the EU and no exposure assessment needs to be addressed.

9 However, you have not provided documentary evidence (e.g. laboratory report, confirmation from your supplier or reference to literature) confirming that the total concentration of the residual unreacted monomer in the polymer is always below [redacted]%.

10 You have neither considered the possibility that the unreacted monomer might be released from the polymer upon degradation, or the polymer might be decomposed to the monomer and result in exposure to man. In this respect, you are also referred to the ECHA Guidance for monomers and polymers (April 2012, Version 2.0), in particular Sections 2.2, 3.2.1 and 4.2, and the judgement of the European Court of Justice in EU Case C 558/07 of 7 July 2009, paragraph 51.

11 Therefore, ECHA concludes that reliable documentation and justification for the premise that there is no exposure to the registered substance is currently missing. In particular, the following requirements of Annex XI, Section 3 of the REACH Regulation are not fulfilled:

a) you have not provided relevant exposure scenario(s) in the chemical safety report (cf. Annex XI, Section 3.1 of the REACH Regulation) with thorough and rigorous exposure assessment in accordance with Annex I, Section 5 of the REACH Regulation covering whole life cycle of the Substance (cf. Annex XI, Section 3.2 of the REACH Regulation);
b) you have not provided relevant life-cycle information and exposure scenarios relating to the unreacted monomer (cf. Annex XI, Section 3.2.(a)(i) of the REACH Regulation);
c) you have not provided any description of exposure scenarios, nor strictly controlled conditions throughout the life cycle (cf. Annex XI, Section 3.2.(b) of the REACH Regulation);
d) you have not demonstrated and documented that the registered substance (the monomer) is not released during its life cycle e.g. via decomposition or degradation (cf. Annex XI, Section 3.2.(c)(i) of the REACH Regulation).
e) you have not demonstrated that the likelihood that the workers or the general public are exposed to the substance under normal or reasonably foreseeable conditions of use is negligible (cf. Annex XI, Section 3.2.(c)(ii) of the REACH

Regulation).

12 Based on above, requirements of Annex XI, Section 3.2(a)(i), 3.2(b) and 3.2(c) of the REACH Regulation are not fulfilled.

13 In your comments to the draft decision, you have attached a CSR, including the description of the use for the Substance, and the corresponding exposure scenario as part of an exposure assessment, and supporting documents in which you have provided information regarding the life-cycle information and exposure scenarios relating to the unreacted of the monomer.

14 The information provided as part of your comments addresses the incompliances identified above. However, the information is currently not available in your registration dossier.

0.1.2. DNEL derivation

15 REACH Annex XI, section 3.2(a)(ii) explicitly states the following

- *"…..that DNEL is relevant and appropriate both to the information requirement to be omitted and for risk assessment purposes."*;
- *"… a DNEL derived from a 28-day repeated dose toxicity study shall not be considered appropriate to omit a 90-day repeated dose toxicity study."*; and
- *"… a DNEL derived from a screening test for reproductive/developmental toxicity shall not be considered appropriate to omit a prenatal developmental toxicity study."*

16 You have derived a DNEL for both the sub-chronic toxicity (90-day) and pre-natal developmental toxicity based on a Screening for reproductive/developmental toxicity study (OECD TG 422) with the source substance EC No. 220-688-8.

17 We have identified the following issue(s) with the derivation of DNEL:

18 The DNEL derivation based on the Screening for reproductive /developmental toxicity study conducted with the source substance is not considered appropriate as

- your read-across adaptation is rejected as explained in Section 0.2. below, and therefore the Screening for reproductive/developmental toxicity study (OECD TG 422) conducted with the source substance is not appropriate to derive DNEL for the Substance for risk assessment purposes;
- the duration of the combined repeated dose and reproduction/developmental screening study (OECD TG 422) serves as an alternative for the short-term repeated dose toxicity (28-day) study. In that study, males were dosed for 28 days. Therefore, the duration of the provided study is not appropriate to derive the relevant and appropriate DNEL for the 90-day repeated dose toxicity study (Section 8.6.2 at Annex IX); and
- the Screening for reproductive/developmental toxicity study (OECD TG 422) is not appropriate to derive the relevant and appropriate DNEL for the pre-natal developmental toxicity study (Annex IX, Section 8.7.2.).

19 Based on above, requirements of Annex XI, Section 3.2(a)(ii) of the REACH Regulation is not fulfilled.

20 In your comments to the draft decision, you have not provided any new information to address the above deficiencies with regard to REACH Annex XI, section 3.2(a)(ii). Therefore the cumulative conditions of Annex XI, Section 3 are not met.

21 Therefore, your adaptation is rejected.

0.2. Assessment of the read-across approach

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

- In vivo mammalian alkaline comet assay (Annex VIII and Annex IX, Section 8.4., column 2)
- Short-term repeated dose toxicity (28 day), (Annex VIII, Section 8.6.1.)
- Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)

23 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.

24 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.

25 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).

0.2.1. Predictions for toxicological properties

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

27 You predict the properties of the Substance from information obtained from the source substance 2-(dimethylamino)ethyl methacrylate, EC No. 220-688-8.

28 You provide the following reasoning for the prediction of toxicological properties:" 2-tert-butylaminoethyl methacrylate and 2-dimethylaminoethyl methacrylate share the common methacrylate functional group, which leads to the common properties such as skin sensitization. Also both are corrosive which is probable related to the amine part of the structure. They both will be metabolised to give methacrylic acid and the corresponding amino alcohol. When these structural similarities are taken into account, this read across is supported by the common functional groups and expected metabolism".

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

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

0.2.1.1. Missing supporting information for the systemic toxicity following repeated exposure

31 Annex XI, Section 1.5 requires that whenever read-across is used adequate and reliable documentation of the applied method must be provided. Such documentation must provide supporting information to scientifically justify the read-across explanation for prediction of properties. The set of supporting information should strengthen the rationale for the read-across in allowing to verify the crucial aspects of the read-across hypothesis and establishing that the properties of the Substance can be predicted from the data on the source substance(s) (Guidance on IRs and CSA R.6, Section R.6.2.2.1.f.).

32 Supporting information must include bridging studies to compare properties of the Substance and source substances.

33 As indicated above, your read-across hypothesis is based on the assumption that the structurally similar substances cause the same type of effect(s). In this context, relevant,

reliable, and adequate information allowing to compare the properties of the Substance and of the source substance(s) is necessary to confirm that both substances cause the same type of effects. Such information can be obtained, for example, from bridging studies of comparable design and duration for the Substance and of the source substance(s).

34 To support your claim that the Substance and source substance have similar properties for the endpoints under consideration, you state in your read-across justification that "*the two substances have very similar acute toxicological properties. Also in the genotoxicity testing both substances show a weak positive response in a single strain of S. Typhimurium and both were positive in the in-vitro cytogenetics, human lymphocyte assay*.".

35 The target and source substances are methacrylate esters. However, the substances differ structurally as the target is an ester with a secondary amino alcohol while the source is an ester with a tertiary amino alcohol.

36 You have considered the impact of the structural differences by comparing the acute and genotoxicity properties of the substances. However, the acute toxicity and genotoxicity properties of the substances do not inform on the systemic toxicity following repeated exposure including short-term repeated dose toxicity (28 day) as well as developmental and reproductive toxicity properties of the Substance and of the source substances. Accordingly, this information is not considered as relevant to support your read-across hypothesis.

37 Therefore, you have not provided supporting information to scientifically justify the read-across explanation for prediction of these properties.

38 In the absence of such information, you have not established that the Substance and the source substance(s) are likely to have similar properties for the systemic toxicity following repeated exposure.

39 Therefore you have not provided sufficient supporting information to scientifically justify the read-across for the Short-term repeated dose toxicity (28 day) and Screening for reproductive/developmental toxicity.

40 In your comments to the draft decision, you recognise with respect to Screening for reproductive/ developmental toxicity that the provided information does not satisfy the provisions for a read-across adaptation. You propose to update the read-across to "*fill the requested requirements*".

41 However, you have not provided any further information to address the above deficiencies of your read-across adaptation. Therefore, the deficiencies remain.

0.2.1.2. Adequacy and reliability of source studies

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.

42 Specific reasons why the study on the source substance does not meet these criteria are explained further below under the applicable information requirement section 5. Therefore, no reliable predictions can be made for this information requirements.

0.2.1.3. Conclusion on the read-across approach

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

Reasons related to the information under Annex VIII of REACH

1. In vivo mammalian alkaline comet assay

Under Annex VIII, Section 8.4, Column 2, the performance of an appropriate *in vivo* somatic cell genotoxicity study must be considered if there is a positive result in any of the *in vitro* genotoxicity studies in Annex VII or VIII.

1.1. Triggering the information requirement

44 Your dossier contains positive results for the *in vitro* cytogenicity test which raise the concern for chromosomal aberration. However, the *in vivo* study submitted in your dossier is inadequate for the reasons described under Request 5.

45 ECHA considers that an appropriate *in vivo* follow up genetic toxicity study is necessary to address the concern(s) identified in vitro.

46 In your comments to the draft decision, you recognise that further testing may be required to establish a reliable conclusion to genotoxicity.

1.2. Specification of the study design

47 The specifications of the study design are addressed under Request 5.

2. Justification for an adaptation of a Short-term repeated dose toxicity (28 days) based on the results of the Sub-chronic toxicity study (90 days)

48 A short-term repeated dose toxicity study (28 days) is an information requirement under Annex VIII, Section 8.6.1. This information may take the form of a study record or a valid adaptation in accordance with either a specific adaptation rule under Column 2 of Annex VIII or a general adaptation rule under Annex XI.

2.1. Information provided

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

(i) A combined repeated dose and reproduction/developmental screening study (OECD TG 422) with the analogue substance (EC No. 220-688-8).

2.2. Assessment of the information provided

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

2.2.1. Read-across adaptation rejected

51 As explained in Section 0.2., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5 is rejected.

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

53 In your comments to the draft decision, you agree to include the requested information in the dossier.

2.3. Specification of the study design

54 Annex VIII, Section 8.6.1., Column 2 provides that an experimental study for this information requirement is not needed if a reliable sub-chronic (90 days) or chronic toxicity study is available.

55 The present decision requests the registrants concerned to generate and submit a reliable sub-chronic toxicity study (90 days) (see request 6). According to Annex VIII, Section 8.6.1., Column 2 and to prevent unnecessary animal testing, a short-term toxicity study (28 days) does not therefore need to be conducted.

56 Because you still must comply with the information requirement in Annex VIII, Section 8.6.1., you are requested to submit a justification for the adaptation provided in Column 2 of that provision.

3. Screening for reproductive/developmental toxicity

57 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.

3.1. Information provided

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

(i) A combined repeated dose and reproduction/developmental screening study (OECD TG 422) with the analogue substance (EC No. 220-688-8).

3.2. Assessment of the information provided

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

3.2.1. Read-across adaptation rejected

60 As explained in Section 0.2., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5 is rejected.

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

3.3. Specification of the study design

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

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

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

4. Hydrolysis as a function of pH

65 Hydrolysis as a function of pH is an information requirement under Annex VIII to REACH (Section 9.2.2.1).

4.1. Information provided

66 You have adapted this information requirement by using a Grouping of substances and read-across approach and provided the following information:

(i) A hydrolysis study (1998) with 2-(dimethylamino)ethyl methacrylate, EC 220-688-8,).

You provide the following reasoning for the prediction of this information requirement: "*The hydrolytical stability of 2-tert-butylaminoethyl methacrylate is based on read across from a structurally strongly related substance N,N-Dimethylaminoethyl Methacrylate. This substance has a very short half-life of 3.3 h at 25 °C and pH 9; a short half-life of 4.5 days at 25 °C and pH 7 and is considered to be stable at 50°C and pH 4".*

4.2. Assessment of the information provided

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

4.2.1. Read-across adaptation rejected

68 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, ecotoxicological and environmental fate 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.

69 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).

70 We have identified the following issue(s) with the prediction of environmental fate properties:

4.2.1.1. Absence of read-across documentation

71 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 substance(s).

72 You have provided robust study summary for study conducted with another substance 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 substance(s).

73 In the absence of such documentation, the properties of the Substance cannot be reliably predicted from the data on the source substance(s).

74 In your comments to the draft decision, you reiterate your adaptation of the information requirement according to Annex XI, Section 1.5. You provide a justification indicating that

"both substances [i.e. source and the Substance] *are highly similar and share a methacrylate functional group and are quickly metabolized."* You claim that the Substance *"hydrolyzes to methacrylic acid (CAS 79- 41-4) and N-tert butyl, N-hydroxyethylamine (CAS No. 4620-70-6)."*

75 The information provided as part of your comments addresses the initially identified deficiency. However, the information is currently not available in your registration dossier.

76 Based on the new information provided in your comments, ECHA has assessed the information and identified these additional issue(s):

77 ECHA understands that you predict the properties of the Substance using a read-across hypothesis which is based on the formation of common (bio)transformation products. The properties of your Substance are predicted to be quantitatively equal to those of the source substance.

4.2.1.2. Missing supporting information on the formation of common compound

78 Annex XI, Section 1.5 requires that whenever read-across is used adequate and reliable documentation of the applied method must be provided. Such documentation must provide supporting information to scientifically justify the read-across explanation for prediction of properties. The set of supporting information should strengthen the rationale for the read-across in allowing to verify the crucial aspects of the read-across hypothesis and establishing that the properties of the Substance can be predicted from the data on the source substance(s) (Guidance on IRs and CSA R.6, Section R.6.2.2.1.f.).

79 Supporting information must include toxicokinetic information on the formation of the common compound, supporting information on the hydrolys rate.

80 As indicated above, your read-across hypothesis is based on the (bio)transformation of the Substance and of the source substance(s) to a common compound(s). In this context, information characterising the rate and extent of the (bio)transformation of the Substance and of the source susbtance(s) is necessary to confirm the formation of the proposed common (bio)transformation product and to assess the impact of the exposure to the parent compounds.

81 However, you have not provided any experimental information about the (bio)transformation of the Substance e.g. toxicokinetic information nor supporting information on the hydrolys rate to support your claims regarding formation of a common compound.

82 In the absence of this information, you have not provided supporting evidence establishing that the proposed common (bio)transformation product is formed as assumed in your read-across hypothesis. Therefore, you have not provided sufficient supporting information to scientifically justify your read-across hypothesis.

4.2.1.3. Adequacy and reliability of study on the source substance

83 Under Annex XI, Section 1.5., the results to be read across must have an adequate and reliable coverage of the key parameters addressed in this case OECD TG 111. Therefore, the following specifications must be met:

84 Technical specifications impacting the sensitivity/reliability of the test

- the test is conducted in the dark;
- the test is performed under sterile conditions;

85 Reporting of the methodology and results

- the analytical method is described including appropriate information on performance parameters (i.e. specificity, recovery efficiency, precision, limits of determination (*i.e.* detection and quantification) and working range);
- the result of the sterility verification at the end of the test is reported;
- the amounts of test material at the end of the test are reported for each pH.

86 Your registration dossier provides an OECD TG 111, preliminary test (tier 1) showing the following:

87 Technical specifications impacting the sensitivity/reliability of the test

- On the test conditions, you have not specified if the test was conducted in the dark and under sterile conditions;

88 Reporting of the methodology and results

- on analytical method, you have not provided any information neither on the test method nor on the performance parameters;
- the result of the sterility verification at the end of the test is not reported.

89 Based on the above there are critical methodological and reporting deficiencies resulting in the rejection of the study results. More, specifically: there is no information on the analytication method, on the conditions of the test nor on the amounts of test material at the end of the test at each pH, therefore the reporting of the study is not sufficient to conduct an independent assessment of its reliability.

90 In your comment to the draft decision, you indicate that the information of the study (i) was purchased from the OECD SIDS Initial Assessment Report for SIAM 14 (Chemical name: 2- Dimethylaminoethyl methacrylate, 2002). You state that the conditions of the test were not specified in the report (i.e. whether the test was performed under dark and sterile conditions). However, you indicate that performance of the test in the dark and under sterile conditions is explicitly mentioned in the OECD TG 111, and on this basis you assume that the guideline procedures were followed. Therefore, you consider this missing information as negligibile for the reliability of the study. You refer to assumptions but you do not provide specific information addressing the issues identified above. Therefore, the information provided in your comments does not change the assessment outcome.

91 Further, you also mention that information on the analytical method is not provided in the report and consequently you cannot provide this missing information. ECHA acknowledges your comments. However as indicated above the information on the analytical method must be reported. This information is needed to validate the analytical method that has been used during the test for monitoring the source substance.

92 Further, you specify that you will request permission to the original report and update the robust study summary with the missing information, and improve the read-across justification.

93 Furthermore, you indicate that in the case you will not be able to provide the requested information, you will perform a study according to OECD TG 111 with the Substance.

94 ECHA acknowledges your intentions to provide further information on the study (i) and your plan to refine your read-across approach. However, as indicated in your comments, this strategy relies essentially on data which is yet to be generated and/or provided, therefore the current incompliance remains.

95 Therefore, the requirements of OECD TG 111 are not met.

96 Hence, the study submitted in your adaptation, as currently reported in your dossier, does not provide an adequate and reliable coverage of the key parameter(s) in the corresponding OECD TG.

97 As explained above, you have not established that relevant properties of the Substance can be predicted from data on the source substance(s). Therefore, your read-across approach under Annex XI, Section 1.5. is rejected and the information requirement is not fulfilled.

Reasons related to the information under Annex IX of REACH

5. In vivo mammalian alkaline comet assay

98 Under Annex IX, Section 8.4, column 2 of REACH, the information requirement for an appropriate *in vivo* somatic cell genotoxicity study is triggered if 1) there is a positive result in any of the *in vitro* genotoxicity studies in Annex VII or VIII and 2) there are no appropriate results already available from an *in vivo* somatic cell genotoxicity study.

5.1. Triggering of the information requirement

99 Your dossier contains positive results for the *in vitro* cytogenicity test (2004) which raise the concern for chromosomal aberrations.

100 Therefore, the information requirement is triggered.

101 ECHA considers that an appropriate in vivo follow up genetic toxicity study is necessary to address the concern(s) identified in vitro.

5.2. Information provided

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

(i) In vivo micronucleus test (1989) with the analogue substance 2-(dimethylamino)ethyl methacrylate, EC No 220-688-8

5.3. Assessment of the information provided

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

104 As explained in Section 0.2., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5 is rejected.

5.3.1. Adequacy and reliability of study on the source substance

105 As explained in the Appendix on Reasons common to several requests, the results to be read across must have an adequate and reliable coverage of the key parameters addressed in the test guideline for the corresponding study that shall normally be performed for a particular information requirement, in this case OECD TG 474/475.

106 Based on the information provided in the dossier, due to the expected rapid metabolism and reactivity of the Substance and the other methacrylate esters such as the analogue substance used in the source study, the substances are readily absorbed by all routes and rapidly hydrolysed by carboxylesterases to methacrylic acid and the respective alcohol.

107 However, there is a concern for chromosomal aberrations induced by the Substance in the initial site of contact tissues, which cannot be evaluated by performing OECD TG 474/475, since these studies only measure effects in the bone marrow (distant tissue). The in vivo comet assay (OECD TG 489) is suitable to follow up the positive in vitro result for gene mutations and chromosomal aberrations.

108 Moreover, it enables the generation of information regarding potential genotoxic effects at the site of contact.

109 Therefore, the in vivo comet assay (OECD TG 489) is the most appropriate follow-up test for the Substance.

110 Therefore, the following specifications of OECD TG 489 must be met:

a) the study includes a minimum of three dose level groups of treated animals, as well as a negative control group and a positive control group;
b) the highest dose studied is the maximum tolerated dose (MTD), i.e. the highest dose that is tolerated without evidence of toxicity (e.g. body weight depression or hematopoietic system cytotoxicity, but not death or evidence of pain, suffering or distress necessitating humane euthanasia);
c) the test substance, or a relevant metabolite, reach the target tissue, and the tissue of interest will be adequately exposed.

111 The study (i) is described as a mammalian erythrocyte micronucleus test according to OECD TG 474.

112 In this study (i), the following specifications are not according to the requirements of the OECD TG 489:

a) one dose level groups of treated animals (i.e., less than three doses/groups) were included, and the dose level was not a limit dose;

b) you did not demonstrate that the highest dose studied was the maximum tolerated dose;

c) As explained above, the Substance is expected to be rapidly hydrolysed, and metabolites readily absorbed by all routes. The exposure to the unmetabolised Substance occurs in the tissues at initial site of contact which are relevant target tissues. Therefore, there is a concern for chromosomal aberrations in the tissues at initial site of contact which cannot be evaluated by performing an OECD TG 474/475, since these studies only measure effects in the bone marrow (distant tissue). Therefore, the tissue of interest is not adequately exposed to the Substance.

113 Based on above, the study submitted in your adaptation, as currently reported in your dossier, does not provide an adequate and reliable coverage of the key parameter(s) of the corresponding OECD TG 489.

114 Therefore, the read-across adaptation is rejected.

115 ECHA considers that an appropriate in vivo follow up genetic toxicity study is necessary to address the concern(s) identified in vitro.

116 In your comments to the draft decision, you recognise that further testing may be required to establish a reliable conclusion to genotoxicity.

5.4. Test selection

117 As indicated above, the Substance may be too short-lived or reactive and systemic availability insufficient to evaluate its genotoxic potential in an OECD TG 474/475 study. According to the ECHA Guidance on information requirements and chemical safety assessment (version 6.0, July 2017) Chapter R.7a, Section R.7.7.6.3, the comet assay (OECD TG 489) is a suitable alternative to follow up positive in vitro results for gene mutations and/or chromosomal aberrations. Moreover, it enables the generation of information regarding potential genotoxic effects at the site(s) of contact. Therefore, the in vivo comet assay is the most appropriate follow-up test for the Substance.

118 In your comments to the draft decision, you recognise that a study according to OECD TG 489 may be used to fill this information requirement.

5.5. Specification of the study design

119 According to the test method OECD TG 489, rats are the preferred species. Other rodent species can be used if scientifically justified.

120 Having considered the anticipated routes of human exposure and adequate exposure of the target tissue(s) performance of the test by the oral route is appropriate.

5.5.1. Germ cells

121 You must consider collecting the male gonadal cells from the seminiferous tubules in addition to the other aforementioned tissues in the comet assay, as it would optimise the use of animals. You can prepare the slides for male gonadal cells and store them for up to 2 months, at room temperature, in dry conditions and protected from light. Following the generation and analysis of data on somatic cells in the comet assay, you should consider analysing the slides prepared with gonadal cells.

122 This type of evidence may be relevant for the overall assessment of possible germ cell mutagenicity including classification and labelling according to the CLP Regulation.

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

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

6.1. Information provided

124 You have adapted this information requirement using substance-tailored exposure-driven testing combined with a Grouping of substances and read-across approach.

125 To support the adaptation, you have provided the following information:

(i) Testing Waiving Proposal for IUCLID May 2013;

(ii) A combined repeated dose and reproduction/developmental screening study (OECD TG 422) with the analogue substance (EC No. 220-688-8).

6.2. Assessment of the information provided

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

6.2.1. Exposure based adaptation in combination with read-across adaptation rejected

127 As explained in Sections 0.1 and 0.2., respectively, your adaptation based on substance-tailored exposure-driven testing under Annex XI, Section 3 as well as grouping of substances and read-across approach under Annex XI, Section 1.5, are rejected.

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

In your comments to the draft decision, you recognise that further testing may be required for this information requirement.

6.3. Specification of the study design

129 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.

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

7. Pre-natal developmental toxicity study in one species

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

7.1. Information provided

132 You have adapted this information requirement using substance-tailored exposure-driven testing combined with a Grouping of substances and read-across approach.

133 To support the adaptation, you have provided the following information:

(i) Testing Waiving Proposal for IUCLID May 2013;

(ii) A combined repeated dose and reproduction/developmental screening study (OECD TG 422) with the analogue substance (EC No. 220-688-8).

7.2. Assessment of the information provided

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

7.2.1. Exposure based adaptation in combination with read-across adaptation rejected

135 As explained in Sections 0.1 and 0.2., respectively, your adaptation based on substance-tailored exposure-driven testing under Annex XI, Section 3 as well as grouping of substances and read-across approach under Annex XI, Section 1.5, are rejected.

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

137 In your comments to the draft decision, you recognise that further testing may be required for this information requirement.

7.3. Specification of the study design

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

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

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

8. Long-term toxicity testing on aquatic invertebrates

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

8.1. Information provided

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

143 "According to REACH Annex IX, endpoint 9.1, column 2, long-term toxicity testing shall be proposed by the registrant if the chemical safety assessment according to Annex I indicates the need to investigate further the effects on aquatic organisms".

144 In addition of that, you state the following: "According to REACH Annex XI, 3.2, testing in accordance with Annex IX can be omitted, based on exposure considerations. 2-tert-butylaminoethyl methacrylate (CAS 3775-90-4) is a monomer for manufacturing acrylic copolymers used as ingredients in personal care and industrial products. Manufacture of both the monomer and the polymers containing it, takes place outside the European Community. Free (unreacted) 2-tert-butylaminoethyl methacrylate is contained in the imported polymers at a fraction of [redacted]%, this is to be considered as a minor impurity present in the polymer. Accordingly, there are no identified uses of 2-tert-butylaminoethyl methacrylate (CAS 3775-90-4) in the EU. The provisions of REACH Annex XI section 3.2 are thus fulfilled by qualitative assessment: Due to absence of identified uses in the EU there is no relevant exposure of workers, consumers, or the environment. Quantitative exposure assessment (CSR chapters 9 and 10) is neither necessary nor possible. Therefore, further studies do not need to be conducted because direct and indirect exposure of the environment is unlikely".

8.2. Assessment of the information provided

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

8.2.1. Annex IX, Section 9.1., Column 2 is not a valid basis to omit the study and your exposure-based adaptation is not valid

146 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).

147 For the sake of completeness, ECHA also evaluated your adaptation under Annex XI, Section 3.2(a)(b)(c) (Substance-tailored exposure-driven testing).

148 Under Annex XI, Section 3, testing in accordance with Annexes IX and X may be omitted based on the exposure scenario(s) developed in the CSR, by providing an adequate and scientifically-supported justification based on a thorough and rigorous exposure assessment in accordance with Section 5 of Annex I and by communicating the specific conditions of use through the supply chain. Any one of the following criteria 3.2.(a), (b) or (c) shall be met. In particular:

- 3.2 (a) the manufacturer or importer demonstrates and documents that all the following conditions are fulfilled, where two conditions are that
  i. the results of the exposure assessment covering all relevant exposures throughout the life cycle of the substance demonstrate the absence of or no significant exposure in all scenarios of the manufacture and all identified uses as referred to in Annex VI section 3.5.;
- 3.2 (b) where the substance is not incorporated in an article the manufacturer, or the importer demonstrates and documents for all relevant scenarios that throughout the

life cycle strictly controlled conditions as set out in Art 18(4)(a) to (f) apply; and

- 3.2 (c) where the substance is incorporated in an article in which it is permanently embedded in a matrix or otherwise rigorously contained by technical means, it is demonstrated and documented that all the following conditions are fulfilled, where two conditions are:
  i. the substance is not released during its life cycle;
  ii. the likelihood that workers or the general public or the environment are exposed to the substance under normal or reasonably foreseeable conditions of use is negligible.

149 As explained above, Column 2 of Annex IX, Section 9.1. does not allow omitting the need to submit information on long-term toxicity to aquatic invertebrates under Column 1. Therefore, your adaptation based on Column 2 of Annex IX, Section 9.1. is rejected.

150 Furthermore, ECHA notes that you have not identified any use for the Substance, nor have you created any exposure scenario in the CSR. The CSR does not contain a chemical risk assessment covering all relevant exposures of the entire life-cycle of the monomer substance subject to this decision.

151 Instead, you state that as polymerisation takes place outside the EU, there is no identified use within the EU and no exposure assessment needs to be addressed. However, you have not provided documentary evidence (e.g. laboratory report, confirmation from your supplier or reference to literature) confirming that the total concentration of the residual unreacted monomer in the polymer is always below [redacted]%.

152 You have neither considered the possibility that the unreacted monomer might be released from the polymer upon degradation, or the polymer might be decomposed to the monomer and result in exposure to man. In this respect, you are also referred to the ECHA Guidance for monomers and polymers (April 2012, Version 2.0), in particular Sections 2.2, 3.2.1 and 4.2, and the judgement of the European Court of Justice in EU Case C 558/07 of 7 July 2009, paragraph 51.

153 Therefore, ECHA concludes that reliable documentation and justification for the premise that there is no exposure to the registered substance is currently missing. In particular, the following requirements of Annex XI, Section 3 of the REACH Regulation are not fulfilled:

a) you have not provided relevant exposure scenario(s) in the chemical safety report (cf. Annex XI, Section 3.1 of the REACH Regulation) with thorough and rigorous exposure assessment in accordance with Annex I, Section 5 of the REACH Regulation covering whole life cycle of the Substance (cf. Annex XI, Section 3.2 of the REACH Regulation);
b) you have not provided relevant life-cycle information and exposure scenarios relating to the unreacted monomer (cf. Annex XI, Section 3.2.(a)(i) of the REACH Regulation);
c) you have not provided any description of exposure scenarios, nor strictly controlled conditions throughout the life cycle (cf. Annex XI, Section 3.2.(b) of the REACH Regulation);
d) you have not demonstrated and documented that the registered substance (the monomer) is not released during its life cycle e.g. via decomposition or degradation (cf. Annex XI, Section 3.2.(c)(i) of the REACH Regulation). You have neither not demonstrated that the likelihood that the environment are exposed to the substance under normal or reasonably foreseeable conditions of use is negligible.

154 In your comments to the draft decision, you have provided a new CSR in which you include the description of the use of the Substance, and the corresponding exposure scenario as part of an exposure assessment.

155 You have also provided documents in which it is stated that the Substance is typically incorporated in the polymer at up to [redacted]% of the mass of the polymer. From those [redacted]%, you state that >[redacted]% is bound into the polymer. Therefore, only <[redacted]% of [redacted]% of the mass of the polymer, i.e. <[redacted]% w/w or <100 ppm is made of the unreacted Substance.

156 Moreover, in the new CSR provided in the comments to the draft decisison you have also provided information on the exposure risk related to the release of the unreacted part of the monomer in the environment, based on the worst case scenario in which the entire volume of the monomer would be released into the environment in case the polymer decomposes. You indicate that the results of the exposure assessment based on the worst-case scenario demonstrate that there is no significant exposure for all the identified uses. The exposures are always well below the derived PNEC (risk characterization ratio is well below 1). Therefore, the likelihood that the workers or the general public are exposed to the substance under normal or reasonable foreseeable conditions of use is negligible since the monomer is only present in a really low concentration in the polymer.

157 ECHA has assessed the information provided in your comments and identified the following:

e) Regarding the exposure assessment (cf. Annex XI, Section 3.2.(a)(i) of the REACH Regulation); in the new CSR you have provided three exposure scenarios including "exposure scenario 2" (i.e. *Widespread use by professional workers - Hairdressing and other professional cosmetic services'*) and "exposure scenario 3" (i.e. *Consumer use - Consumer end use of cosmetic products'*). For both scenarios, you have used SpERC entitled '*Cosmetics Europe 8a.1.b.v2: Wide Dispersive Use in Aerosol products for hair and skin care (Propellants)*'. This SpERC was developed for substances used as propellants in personal care spray products (and other "leave-on" products that are not washed off immediately) that evaporate completely into the air. It assumes that 100% of the substance is released into the air (release factor to air: 100%). However, based on the data in the dossier the Substance and the polymers are clearly not volatile, therefore they cannot be used as propellants. Furthermore, based on the uses described in the CSR, it seems that SpERC '*Cosmetics Europe 8a.1.**c**.v2: Wide Dispersive Use in Aerosol products for hair and skin care (**Non-**Propellants)*' is the most appropriate for the Substance. This Sperc is applicable to non-volatile constituents in personal care spray products that will deposit on the skin surface and will be transferred to the waste water system in the next washing event. Which assumes that 100% of the substance is released into the water. This implies that SpERC 'Cosmetics Europe 8a.1.b.v2' is not applicable to the Substance.

f) Regarding the condition set out under Annex XI, Section 3.2.(b) of the REACH Regulation, ECHA acknowledges that you have provided all the documents and evidences confirming that the total concentration of the residual unreacted monomer in the polymer is always below [redacted]%. This information provided as part of your comments addresses the incompliances identified above. However, the information is currently not available in your registration dossier.

g) Regarding the information related to the the release of the Substance during its life cycle e.g. via decomposition or degradation (cf. Annex XI, Section 3.2.(c)(i) of the REACH Regulation), and the risk of exposure of the workers or the general public or the environment. As indicated above, based on the assessment provided in your comments you indicate that in a worst case scenario i.e. in which the entire volume of the monomer (100%) would be released into the environment, the exposures are always well below the derived PNEC (risk characterization ratio is well below 1), and therefore the risk of exposure is negligible. However, as indicated above under point (e), you have not used the relevant SpERC. Therefore, there are uncertainties regarding the risk charatecrisation ratio and the low risk of exposure. A new calculation of the risk charatecrisation ratio (including PEC water) using the

most appropriate SpERC i.e. '*Cosmetics Europe 8a.1.**c**.v2: Wide Dispersive Use in Aerosol products for hair and skin care (**Non-**Propellants)*' needs to be considered in order to demonstrate that the exposures are always well below the derived PNEC (risk characterization ratio is well below 1), and therefore the risk of exposure is negligible.

158 Based on above, requirements of Annex XI, Section 3.2(a)(i), 3.2(b) and 3.2(c) of the REACH Regulation are not fulfilled. Therefore your adaptation is rejected.

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

8.3. Study design and test specifications

160 The Substance might be difficult to test due to potential rapid hydrolysis (under section 2.3 of the IUCLID dossier it is indicated that the Substance is expected to hydrolyse). While the submitted hydrolysis study indicating a half-life of 4.5 days is currently incompliant, the outcome of the study requested under request 4 must be used to assess whether the Substance is difficult to test due to rapid hydrolysis (i.e. resulting in a loss of 20% of the initial concentration of a test chemical), prior conducting this study.

161 OECD TG 211 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.

162 Considering the potential rapid hydrolysis of the parent substance, it may be difficult to achieve and maintain the desired exposure concentrations of the Substance (or its hydrolysis products if relevant).

163 Therefore, the selection of the appropriate exposure systems must be dictated by the goal of maintaining test chemical concentrations as close to nominal as possible. Furthermore, you must monitor the test concentration(s) of the Substance, or its hydrolysis products, throughout the exposure duration and report the results.

164 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 211. 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.

165 In case the hydrolysis half-life is less than 3 days, it is important to take into account the relative toxicities of the parent test chemical and degradation products in order to determine the appropriate test design and test media preparation methods for the Substance.

9. Long-term toxicity testing on fish

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

9.1. Information provided

167 You have adapted this information requirement by using Column 2 of Annex IX, Section 9.2. and Annex XI, Section 3. To support the adaptation, you have provided the same

justification as for long-term toxicity testing on aquatic invertebrates (i.e. Request 8 above).

9.2. Assessment of the information provided

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

169 As already explained under Request 8, the requirements of Annex XI, Section 3.2(a)(i), 3.2(b) and 3.2(c) of the REACH Regulation are not fulfilled. 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. Therefore your adaptation is rejected.

170 In your comments to the draft decision, you have provided the same information as for as for long-term toxicity testing on aquatic invertebrates (i.e. Request 8 above).

171 ECHA acknowledges your comments, however for the same reasons as explained under Request 8, the information requirement is still not fulfilled.

9.3. Study design and test specifications

172 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.).

173 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 8.

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 did not amend the request(s).

In your comments to the draft decision, you propose to combine studies according to OECD TG 422, OECD TG 408 and OECD TG 489 into one larger study "*to help reduce animal testing as well as increase the level of information*". Therefore, you request an extension of the deadline to provide information from 24 to 30 months from the date of adoption of the decision.

Since you have not provided a detailed description of the design of the combined study you are proposing to perform, ECHA cannot comment on the validity of the proposed approach. ECHA highlights that it is your responsibility to ensure that the design of the individual studies is not compromised and that the information requirements for Screening for reproductive/ developmental toxicity, Sub-chronic toxicity study (90-day) and *in vivo* mammalian alkaline comet assay, as requested in this decision, are fulfilled and the information obtained is adequate for hazard assessment, classification and labelling and/or risk assessment.

Regarding the request of deadline extension, ECHA notes that the deadline of the decision is generally 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.

Therefore, ECHA has extended the deadline from 24 months to 36 months.

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[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

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

(1) Selection of the Test material(s)
The Test Material used to generate the new data must be selected taking into account the following:
- the variation in compositions reported by all members of the joint submission,
- the boundary composition(s) of the Substance,
- the impact of each constituent/ impurity on the test results for the endpoint to be assessed. For example, if a constituent/ impurity of the Substance is known to have an impact on (eco)toxicity, the selected Test Material must contain that constituent/ impurity.

(2) Information on the Test Material needed in the updated dossier
- You must report the composition of the Test Material selected for each study, under the "Test material information" section, for each respective endpoint study record in IUCLID.
- The reported composition must include all constituents of each Test Material and their concentration values and other parameters relevant for the property to be tested.

This information is needed to assess whether the Test Material is relevant for the Substance and whether it is suitable for use by all members of the joint submission.

Technical instructions on how to report the above is available in the manual on How to prepare registration and PPORD dossiers[3].

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