~~Confidential~~

Helsinki, 10 October 2022

Addressees
Registrants of JS_107-10-8_Propylamine as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
10/07/2013

Registered substance subject to this decision ("the Substance")
Substance name: Propylamine
EC number: 203-462-3

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

DECISION ON A COMPLIANCE CHECK

Under Article 41 of Regulation (EC) No 1907/2006 (REACH), you must submit the information listed below, by the deadline of ***15 January 2025***.

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

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

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

2. Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: EU C.4. C/D/E/F/OECD TG 301B/C/D/F or EU C.29./OECD TG 310)

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

3. 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)

4. 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)

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

6. Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.; test method: EU B.64/OECD TG 422) by oral route, in rats. Due to reasons explained in Section 6., the test sample must be chosen to minimise gastrointestinal irritation and to allow investigation of intrinsic properties at adequate dose levels. This could be achieved by testing a neutral salt of the Substance.

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

Information required depends on your tonnage band

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

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

How to comply with your information requirements

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

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

Appeal

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

Failure to comply

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

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

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 gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.)
- In vitro cytogenicity study in mammalian cells or in vitro micronucleus study (Annex VIII, Section 8.4.2.)
- Short-term repeated dose toxicity (28 day), (Annex VIII, Section 8.6.1.)
- Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)
- Ready biodegradability (Annex VII, Section 9.2.1.1.)

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. Predictions for toxicological and fate properties

5 You have not provided any read-across justification document for toxicological properties in your registration dossier.

6 You predict the properties of the Substance from information obtained from the following source substances:

Source substance 1	Methylamine, EC No. 200-820-0.
Source substance 2	Methylamine hydrochloride, EC No. 209-795-0
Source substance 3	Ethylamine, EC No. 200-834-7.
Source substance 4	Isopropylamine, EC No. 200-860-9.
Source substance 5	Butylamine, EC No. 203-699-2.
Source substance 6	Mono-n-butylamine hydrochloride, EC No. 223-369-1.

Justification provided for toxicological endpoints

7 You have not provided any reasoning for the prediction of toxicological properties.

8 In the absence of supporting justication, ECHA presumes that you intend to predict the properties of the Substance using a read-across hypothesis which assumes that different compounds have the same type of effects. The properties of your Substance are predicted to be quantitatively equal to those of the source substance.

Justification provided for ready biodegradability

9 You provide the following reasoning for the prediction of ready biodegradability: "[the] *chemical structure* [of the selected analogue substances] *is very similar to that of the target 1-propylamine and they contain the same basic structure and functional group. They only differ in the length of the C-chain*".

10 ECHA understands that you predict the properties of the Substance using a read-across hypothesis which assumes that different compounds have the same type of effects. The properties of your Substance are predicted to be quantitatively equal to those of the source substance.

11 We have identified the following issue(s) with the prediction(s) of toxicological and fate properties:

0.1.1.1. *Absence of read-across documentation for the prediction of toxicological properties*

12 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 a justification for the read-across including a hypothesis, explanation of the rationale for the prediction of properties and robust study summary(ies) of the study(ies) on the source substance(s) (Guidance on IRs and CSA, Section R.6.2.6.1.).

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. However, you have not provided documentation as to why this information is relevant for the Substance.

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

0.1.1.2. *Adequacy and reliability of source studies*

15 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 test method referred to in Article 13(3);
(3) cover an exposure duration comparable to or longer than the corresponding test method referred to in Article 13(3) if exposure duration is a relevant parameter.

16 Specific reasons why the studies on the source substances do not meet these criteria are explained further below under the applicable information requirement sections 2, 5 and 6. Therefore, no reliable predictions can be made for these information requirements.

0.1.2. Conclusion on the read-across approach

17 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 VII of REACH

1. Growth inhibition study aquatic plants

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

1.1. Information provided

19 You have adapted this standard information requirement according to Annex XI, Section 1.2. of REACH (weight of evidence). In support of your adaptation, you have provided the following sources of information:

(i) a non-guideline algal growth toxicity study on methylamine hydrochloride with EC 209-795-0 (1959)
(ii) a non-guideline algal cell proliferation inhibition on ethylamine with EC 200-834-7 (1978)
(iii) a non-guideline algal growth inhibition test on butylamine with EC 203-699-2 (1977)
(iv) a study on algal cell proliferation inhibition according to EU Method C.3. test on Octan-1-amine with EC 203-916-0 (1997)
(v) a trend analysis to intrapolate the 72h-NOEC for the Substance using the results of studies (i) to (iv) above.

20 ECHA understands that your weight of evidence approach rely on grouping and read-across approach under Annex XI, Section 1.5. As you rely on a trend analysis to predict the properties of the Substance, ECHA understands that the selected substance follow a regular pattern as result of structural similarity and that you consider those as a group or 'category' of substances.

1.2. Assessment of information provided

21 Annex XI, Section 1.2 states that there may be sufficient weight of evidence weight of evidence from several independent sources of information leading to assumption/conclusion that a substance has or has not a particular dangerous (hazardous) property, while information from a single source alone is insufficient to support this notion.

22 According to ECHA Guidance R.4, a weight of evidence adaptation involves an assessment of the relative values/weights of the different sources of information submitted. The weight given is based on the reliability of the data, consistency of results/data, nature and severity of effects, and relevance and coverage of the information for the given regulatory information requirement. Subsequently, relevance, reliability, coverage, consistency and results of these sources of information must be balanced in order to decide whether they together provide sufficient weight to conclude that the Substance has or has not the (dangerous) property investigated by the required study.

23 Annex XI, section 1.2 requires that adequate and reliable documentation is provided to describe your weight of evidence adaptation.

24 You have not submitted any explanation why the sources of information provide sufficient weight of evidence leading to the conclusion/assumption that the Substance has or has not a particular dangerous property investigated by the required study.

25 In spite of this critical deficiency, ECHA has nevertheless assessed the validity of your adaptation and identified the following issues.

26 To fulfil the information requirement, normally a study performed according to OECD TG 201 must be provided. OECD TG 201 requires the study to investigate the following key parameters:

- The concentrations of the test material leading to a 50 % and 0% (or 10%) inhibition of growth after 72 hours. Growth must be expressed as the logarithmic increase in biomass (average specific growth rate) during the exposure period.

1.2.1. Assessment of the information provided with regard the above key parameter

27 For study (iv), you report an ErC50 and ErC10 values which are relevant to the key parameters as defined in OECD TG 201. The effect values reported for study (i) to (iii) above are expressed as "*toxicity threshold*" values after 96 hours for study (i) and 8 days for study (ii) and (iii), respectively. For study (i) and (ii), you have provided no further information on the basis of the effect (i.e., biomass or specific growth rate). For study (iii), you specify that the effect value is based on "*photometric extinction*" which you claim is "*equivalent to growth rate*". However, photometric extinction is used to determine change in biomass and does not provide a direct estimate of growth rate.

28 Based on the information you provided, it is unlcear whether studies (i) to (iii) provide a coverage of the above key parameters as the basis for the effect is not specified or is unclear. Furthermore, assuming that the effect values are reported based on reduction of growth rate, these studies only provide information in relation to NOEC (or similar parameter) and can, at best, only be regarded as providing a partial coverage of the key parameters that need to be covered.

1.2.2. Assessment of the reliability of the supporting information

Section 0, above, already explains the conditions underlying grouping and read-across adaptation under Annex XI, Section 1.5. This includes the requirement to fulfill two conditions. Firstly, there needs to be structural similarity between substances. Secondly, the relevant properties of a substance within the group may be predicted from data for reference substance(s) within the group.

1.2.2.1. *Scope of the grouping of substances (category)*

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

30 For the purpose of this decision, the following namings are used for the category members:

- Methylammonium chloride, EC No. 209-795-0
- 1-Ethylamine EC No. 200-834-7
- 1-Butylamine EC No. 203-699-2
- 1-Octylamine EC No. 203-916-0

31 You justify the grouping of the substances as "[the] chemical structure is very similar to that of the target 1-propylamine and they contain the same basic structure and functional group".

32 You define the the structural basis for the grouping as substances containing a C-chain and a NH2-group as functional group. ECHA understands that this is the applicability domain of the grouping and will assess your predictions on this basis.

33 We have identified the following issue(s) with the proposed scope of the grouping:.

1.2.2.1.1. Applicability domain of the category

34 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.

35 You describe the applicability domain of the substances covered by the grouping as substances containing a C-chain and a NH2-group as functional group.

36 This applicability domain is vague and therefore does not introduce unambiguous inclusion/exclusion criteria which 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.

37 Despite of the above issue, ECHA understands that this is the applicability domain of the grouping and your predictions are assessed on this basis.

1.2.2.2. *Predictions of growth inhibition on algae*

38 You provide the following reasoning for the prediction of toxicological properties: "all primary amines show a similar chemical structure, the increasing toxic effect (from C1 to C8 bodies) of the five chemicals is doubtlessly based on the escalating bioaccumulative potential with a longer C-chain".

39 ECHA understands that your read-across hypothesis assumes that different compounds have the same type of effects. You predict the properties of the Substance based on an identified trend within the group.

40 We have identified the following issue with the prediction(s) of growth inhibition on algae:

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

42 Key parameter to be measured

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

43 Characterisation of exposure

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

44 Reporting of the methodology and results

c) adequate information on purity and composition is provided in order to allow a verification of the test material identity;

d) the test design is reported (*e.g.*, number of replicates, number of test concentrations and geometric progression used);

e) the test conditions are reported (*e.g.*, composition of the test medium, biomass

density at the beginning of the test);

f) the method for determination of biomass and evidence of correlation between the measured parameter and dry weight are reported. Algal biomass is normally determined based on dry weight per volume, or alternatively as cell counts or biovolume using microscopy or an electric particle counter. If an alternative method is used (*e.g.* flow cytometry, *in vitro* or *in vivo* fluorescence, or optical density), a satisfactory correlation with biomass must be demonstrated over the range of biomass occurring in the test;

g) the results of algal biomass determined in each flask at least daily during the test period are reported in a tabular form.

45 Your registration dossier provides studies showing the following:

46 Key parameter to be measured

a) the effect values reported for study (i) to (iii) are only expressed as "t*oxicity threshold"* values (*i.e.*, equivalent to ErC3 according to you) after 96 hours for study (i) and 8 days for studies (ii) and (iii), respectively. For study (iii), the effect value is expressed on the basis of "*photometric extinction*" which you claim is "*equivalent to growth rate*". However, this parameter only provides an estimate of biomass and not growth rate. Furthermore, for studies (i) and (ii) the basis of effect is not specified. Finally, for study (iv), you only report information on the 72h-NOEC and the basis of effect is not specified;

Characterisation of exposure

b) no analytical monitoring of exposure was conducted in studies (i) and (iv). For studies (ii) and (iii), you state that this information is not specified. You have provided no justification as to why analytical monitoring is not technically feasible;

47 Reporting of the methodology and results

c) for studies (i) to (iii), you provide only a generic description of the test material. You have not provided information on the purity and composition of the corresponding test materials;

d) on the test design, you have not specified the number of replicates, the number of test concentrations and geometric progression used for both studies (i) to (iii);

e) on the test conditions, you have not specified the composition of the test medium and the biomass density at the beginning of the test for studies (i) to (iii);

f) for studies (i) to (iii), the method used to determine algal biomass is not specified;

g) tabulated data on the algal biomass determined daily for each treatment group and control are not reported for studies (i) to (iv).

48 Based on the above,

- the key parameters of OECD TG 201 is not covered for studies (i) to (iv) as these studies does not provide information on ErC50. Furthermore, the basis of the reported effect values all studies is unclear.
- there are critical methodological deficiencies resulting in the rejection of the study results. More specifically, no analytical monitoring of exposure concentrations was reported in any of studies (i) to (iv). Therefore, you have not demonstrated that exposure was satisfactorily maintained over the duration of these tests.
- the reporting of studies (i) to (iv) is not sufficient to conduct an independent assessment of their reliability. In particular,

- you have not provided adequate information on the test materials used in studies (i) to (iii). In the absence of composition information on the test material, the identity of the test material and its impurities cannot be assessed, and you have not demonstrated that the test material is representative for the substance that was intended to be tested;
- you have not provided adequate information (i.e., raw biomass data) to verify whether validity criteria equivalent to those specified in OECD TG 201 were met. Without this information, it is also not possible to verify the interpretation of the studies;
- you have not provided adequate information on the study design and the test conditions in studies (i) to (iii). Therefore, it is not possible to verify whether these studies were conducted under conditions that are consistent with the specifications of the OECD TG 201;
- you have not provided adequate information on the method used to determine algal biomass in studies (i) to (iii). Therefore, the reliability of the reported effect values cannot be verified.

49 Therefore, the requirements of the OECD TG 201 are not met for any of the above studies.

50 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.

1.2.3. Conclusion on the weight of evidence adaptation

51 As a conclusion, as indicated above, it remains unclear if the sources of information supporting your weight of evidence provide, at least, a partial coverage of the key parameters normally investigated for this information requirement. Furthermore, essential parts of information of the dangerous property is lacking (i.e. concentration leading to a 50% reduction og growth rate by the end of the exposure period). Finally, the reliability of the sources of information is so severely affected by the issues identified above that no conclusion on the properties of the Substance can be reached.

52 Accordingly, it is not possible to conclude, based on any source of information alone or considered together, whether your Substance has or has not the particular dangerous properties foreseen to be investigated in an OECD TG 201 study.

53 Therefore, your adaptation is rejected and the information requirement is not fulfilled.

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

2. Ready biodegradability

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

2.1. Information provided

56 You have provided:

(i) a study according to DIN 38409, part 51 and part 41 with the Substance (1983)

57 You have also submitted further studies relying on an adaptation according to Annex XI, Section 1.5. of REACH ('Grouping of substances and read-across approach'):

(ii) a study according to OECD TG 301C on ethylamine with EC 200-834-7 (1988);
(iii) a study similar to OECD TG 301C on butylamine with EC 203-699-2 (1992);

2.2. Assessment of the information provided

2.2.1. The provided studies on the Substance and the selected analogues substances do not meet the information requirement

58 To fulfil the information requirement, a study must comply with the OECD TG 301 or 310 (Article 13(3) of REACH). Therefore, for a study according to OECD TG 301, the following requirements must be met:

59 Technical specifications impacting the sensitivity/reliability of the test

a) For OECD TG 301C, the concentration of the inoculum is set to reach a bacterial cell density of 10^7 to 10^8 cells/L in the test vessel. The suspended solid concentration is 30 mg/L;

b) Determination is carried out at least in duplicate;

60 Reporting of the methodology and results

c) adequate information on purity and composition is provided in order to allow a verification of the test material identity;

d) the test design is described (e.g., number of replicates);

e) the results of measurements at each sampling point in each replicate is reported in a tabular form;

f) the ThOD is described and justified;

g) for nitrogen-containing test materials, correction for nitrification is applied on the theoretical oxygen demand (*i.e.* $ThOD_{NO3}$) unless it can be demonstrated that nitrification did not occur (*e.g.* by monitoring changes in concentrations in nitrite and nitrate).

61 Your registration dossier provides studies showing the following:

62 Technical specifications impacting the sensitivity/reliability of the test

a) The concentration of the inoculum is described as 30 mg/l suspended solids in study (ii) and (iii) but no information on inoculum density in cells/L is provided. No information on inoculum density is provided for study (i);

b) For study (ii), you specify "*Number of culture flasks/concentration: 1*";

63 Reporting of the methodology and results

c) for studies (i) to (iii), you provide only a generic description of the test material. You have not provided information on the purity and composition of the corresponding test materials;

d) for studies (i) and (iii), you have not specified the number of replicates;

e) the results of measurements at each sampling point in each replicate is not reported for studies (i) to (iii);

f) the ThOD is not described for studies (i) to (iii);

g) the test material in studies (i) to (iii) corresponds to a nitrogen-containing substance and it is unclear if a correction for nitrification of the theoretical oxygen demand was applied. You have provided no justification that nitrification did not occur during the test.

64 Based on the above,

- there are critical methodological deficiencies resulting in the rejection of the study

results from study (ii) as this study was not conducted at least in duplicate;

- the reporting of the studies (i) to (iii) is not sufficient to conduct an independent assessment of their reliability. In particular,
    - you have not provided adequate information on the test materials used in studies (i) to (iii). In the absence of composition information on the test material, the identity of the test material and its impurities cannot be assessed, and you have not demonstrated that the test material is representative for the substance that was intended to be tested.

      In your comments on the draft decision, you state that for study (ii), the test material is clearly identified in the full study report. You clarify that the study was conducted on "*ethylamine hydrochloride (C2H5NH2.HCl), which was used instead of ethylamine* […] *for safety reasons*". You also specified that "*the test substance had a high purity of 99.6%*".

    - you have not provided adequate information on inoculum density for studies (i) to (iii). Therefore, it is not possible to verify if the inoculum to test material ratio was consistent with the specifications of the corresponding test method.

      In your comments on the draft decision, you have not provided further information on inoculum density. ECHA emphasizes that the limit values for the inoculum density in mg/L (e.g., for sludge or soil) or mL/L (e.g., for surface water or effluent) are set to ensure that the introduction of exogeneous organic matter in the test system is within an acceptable range. Such parameter does not provide a direct estimate of bacterial biomass (as the density of bacteria in, for e.g., a sludge sample or a secondary effluent may vary by orders of magnitude). Accordingly, Appendix R.7.9-1 of ECHA Guidance on IRs and CSA specifies inoculum conditions as cell density (cells/mL) present in a relevant media (e.g. surface waters, unchlorinated sewage treatment works, activated sludge).

    - you have not provided adequate information on the test design for studies (i) to (iii);

      In your comments on the draft decision, you clarified that study (ii) was conducted in triplicates.

    - you have not provided adequate reporting of the test results for studies (i) to (iii). Therefore, it is not possible to verify whether the validity criteria of the corresponding test guideline were met. Without this information, it is also not possible to verify the interpretation of the study results;

      In your comments on the draft decision, you provided the missing information for study (ii)

    - you have not described the ThOD calculation and you have not specified whether a correction for nitrification was applied to calculated the percentage degradation. In the absence of this information, it is not possible to verify the interpretation of the results of studies (i) to (iii).

      In your comments on the draft decision, you provided the missing information on ThOD calculation for study (ii). Furthermore, you provided additional information showing that no significant nitrate formation was

observed by the end of this study.

65 Therefore, as you have not provided adequate information to demonstrate that inoculum density was within the range specified in the corresponding test guideline, the requirements of OECD 301 are not met by any of the reported studies.

2.2.2. Read-across adaptation rejected

66 In relation to studies (ii) and (iii), as explained in Section 0.1., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5 is rejected.

67 Based on all the above reasons, the information requirement is not fulfilled.

68 In your comments on the draft decision, you specify that "*the previously submitted information for this endpoint will not be considered further in the evaluation of the Substance and are therefore not commented*".

69 Instead you now intend to fulfil the information requirement using the following information:

iv. a study according to OECD TG 301C on the analogue substance Ethylamine hydrochloride (CAS 557-66-4) (1988). ECHA understands that you refer to the same study already specified under (ii) above,
v. CATALOGIC 301C v11.16 and CATALOGIC 301F v14.17 of OASIS Catalogic v.5.14.1.5

70 ECHA has assessed the information provided as part of your comments to the draft decision and identified the following issues:

2.2.3. Study (ii) remains incompliant

71 For the reasons already specified under Section 2.2.2. the provided study does not meet the information requirement.

2.2.4. (Q)SAR results only are not sufficient to fulfil the information requirement under Annex VII, Section 9.2.1.1.

72 Guidance on IRs and CSA, Section R.7.9.5.1. specifies that (Q)SARs for predicting ready biodegradation (e.g. CATALOGIC software suite) are not yet sufficiently accurate to predict rapid degradation. However, when no useful information on degradability is available (either experimentally derived or estimated), (Q)SAR predictions can be used as supporting evidence of that the substance is not rapidly degradable.

73 You provide (Q)SARs predictions as part of your comments on the draft decision. You have used this information to conclude that the Substance is readily biodegradable. You have provided no other reliable source of information to support the prediction. As explained above, (Q)SARs predictions alone is not adequate to conclude on the persistence of the Substance. Therefore, this information does not fulfil the information requirement.

74 Therefore, your adaptations are rejected. You remain responsible for complying with this decision by the set deadline.

Reasons related to the information under Annex VIII of REACH

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

75 An in vitro cytogenicity study in mammalian cells or an in vitro micro-nucleus study is an information requirement under Annex VIII to REACH (Section 8.4.2.).

3.1. Information provided

(i) *In vivo* micronucleus study (1995) with an analogue substance Mono-n-butylamine hydrochloride, EC No. 223-369-1.

76 Although you have not explicitly indicated it in your registration dossier, ECHA understands that you intend to adapt this information requirement under Column 2 of Annex VIII, Section 8.4.2., by using a study on an analogue substance.

3.2. Assessment of the information provided

3.2.1. Read-across adaptation rejected

77 As explained in Section 0.1., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5 is rejected.

78 As a result, the study (i) you submitted cannot be taken into account in support of the adaptation of this information requirement under Column 2 of Annex VIII, Section 8.4.2.

79 Therefore, the information requirement is not fulfilled.

80 In your comments to the draft decision, you do not provide any comments on this request.

3.3. Specification of the study design

81 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.

4. In vitro gene mutation study in mammalian cells

82 An in vitro gene mutation study in mammalian cells is an information requirement under Annex VIII to REACH (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.

4.1. Triggering for in vitro gene mutation study in mammalian cells

83 Your dossier contains (I) a negative result for in vitro gene mutation study in bacteria and (II) inadequate data for an in vitro cytogenicity study in mammalian cells or in vitro micronucleus study.

84 The information for the in vitro cytogenicity study in mammalian cells or in vitro micronucleus study provided in the dossier is rejected for the reasons provided in section 3.

85 The result of the request for information under Request 3 will determine whether the present requirement for an in vitro mammalian cell gene mutation study in accordance with Annex VIII, Section 8.4.3 is triggered.

86 Consequently, you are required to provide information for this endpoint, if the the in vitro cytogenicity study in mammalian cells or an in vitro micronucleus study provides a negative result.

4.2. Information provided on in vitro gene mutation study in mammalian cells

87 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) *In vitro* mammalian cell gene mutation test (2010) with Isopropylamine, EC No. 200-860-9.

4.3. Assessment of information provided

4.3.1. Read-across adaptation is rejected

88 As explained in Section 0.1., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5 is rejected.

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

4.4. Specification of the study design

90 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.

91 In your comments to the draft decision, you do not provide any comments on this request.

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

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

5.1. Information provided

93 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) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (2006) with Methylamine hydrochloride, EC No. 209-795-0.
(ii) 24 weeks repeated dose toxicity study (1984) with Ethylamine, EC No. 200-834-7.
(iii) Subchronic 90 days repeated dose toxicity study (1988) with Isopropylamine, EC No. 200-860-9.
(iv) 14 days repeated dose toxicity study (1986) with Methylamine, EC No. 200-820-0.
(v) Prenatal developmental toxicity study (2002) with Butylamine, EC No. 203-699-2.

94 In your comments on the draft decision, you propose to adapt this information requirement by using substance-tailored exposure-driven testing. Your comments are addressed under Section 6. below.

5.2. Assessment of information provided

5.2.1. Read-across adaptation is rejected

95 In relation to all the studies povided, as explained in Section 0.1., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5 is rejected.

5.2.2. Studies (ii) to (v) do not comply with the applicable test guideline

96 As explained in Section 0.1., the results to be read across must have an adequate and reliable coverage of the key parameters addressed, and cover an exposure duration comparable to or longer than the one specified in the corresponding test method referred to in Article 13(3), in this case OECD TG 412. Therefore, the following specifications must be met:

a) at least 5 male and 5 female animals for each concentration and control group;
b) dosing of the test material for a minimum of 6h/day, on a 5 day per week basis for a period at least 28 day;
c) at least twice weekly body weight measurements and at least weekly food consumption measurements;
d) clinical observations, before, during, and after each exposure period as well as during the post-exposure periods;
e) haematological and clinical biochemistry tests as specified in paragraphs 48-49 of the test guideline;
f) terminal organ and body weights;
g) full histopathology as specified in paragraphs 57 of the test guideline;
h) bronchoalveolar lavage (BAL) as specified in paragraph 50 of the test guideline (also in satellite groups if applicable).

97 The study (ii) is described as a 24-week repeated dose toxicity study. However, the following specifications are not according to the requirements of OECD TG 412:

c) food consumption was not measured
e) clinical biochemistry as only limited parameters were measured
f) terminal organ weights as only the weights of the lungs, liver, kidney and heart were recorded;
g) full histopathology as only limited number of organs and tissues were examined;
h) BAL was not performed.

98 The study (iii) is described as a sub-chronic 90-d repeated dose toxicity study. However, the following specifications are not according to the requirements of OECD TG 412:

c) food consumption was not measured;
d) clinical observations;
e) haematological and clinical biochemistry tests;
f) terminal organ weights;
g) full histopathology;
h) BAL was not performed.

99 The reporting of specifications (d) to (g) does not allow an independent assessment whether these parameters were examined as required in the test guideline.

100 The study (iv) is described as a 2 weeks repeated dose toxicity study. However, the following specifications are not according to the requirements of OECD TG 412:

a) the study was not performed in both sexes as only male rats were used;
b) dosing period of 28 days as the treatment lasted only 2 weeks;
c) food consumption was not measured;
e) clinical biochemistry as only limited parameters were measured;
f) terminal organ weights as only the weights of the heart, lungs, liver, spleen, kidneys, testes and thymus were recorded;

h) BAL was not performed.

101 The study (v) is described as a subacute toxicity study performed according to OECD TG 414. However, the following specifications are not according to the requirements of OECD TG 412:

a) the study was not performed in both sexes as only pregnant female rats were used;
b) dosing period of 28 days as the treatment lasted only 14 days;
c) food consumption was not measured;
e) haematological and clinical biochemistry tests were not performed;
f) terminal organ weights as only ovary, uterus and placenta were examined;
g) full histopathology as only 4 sections of the nasal cavity were examined;
h) BAL was not performed.

102 Based on the above, the studies (ii)-(v) do not provide an adequate and reliable coverage of the key parameter(s) addressed by the OECD TG 412 and these studies are not an adequate basis for your read-across predictions.

103 Therefore, the information you provided do not fulfil the information requirement.

5.3. Specification of the study design

104 When there is no information available neither for the 28-day repeated dose toxicity endpoint (OECD TG 412), nor for the screening study for reproductive/developmental toxicity (OECD TG 421 or TG 422), the conduct of a combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (OECD TG 422) is preferred to ensure that unnecessary animal testing is avoided. Such an approach offers the possibility to avoid carrying out a 28-day study according to OECD TG 412, because the OECD TG 422 can at the same time fulfil the information requirement of REACH Annex VIII, 8.6.1 and that of REACH Annex VIII, 8.7.1. (Guidance on IRs and CSA, Section R.7.6.2.3.2.).

105 For information on the study design, we refer you to the request for OECD TG 422 in Section 6, below.

6. Screening for reproductive/developmental toxicity

106 A screening for reproductive/developmental toxicity study (OECD 421 or OECD 422) is an information requirement under Annex VIII to REACH (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.

6.1. Information provided

107 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) Combined repeated dose toxicity study with reproduction/developmental toxicity screening test (2006) with Methylamine hydrochloride, EC No. 209-795-0.
(ii) One-generation reproduction toxicity study (1988) with Isopropylamine, EC No. 200-860-9.

108 In your comments on the draft decision, you propose to adapt this information requirement by using substance-tailored exposure-driven testing in accordance with Annex XI 3.2.(b). To support the adapation, you provided the following justification:

109 Process description: *"At room temperature, propylamine is a highly volatile flammable liquid with a pungent, strong ammonia like odor. The industrial method used for the*

production of propylamine is the reaction of ammonia, hydrogen and n-propanol at elevated temperature and pressure. Because of the applied reaction conditions and the handling of gaseous compounds the manufacturing facilities are designed as closed systems for higher pressures. Because of the significant health hazards during production, transportation and storage (high pressure, high temperature, strong alkalinity), most stringent safety instructions and protection measures must be adhered to during manufacturing, storage, and shipping. Transfers, buffer/storage tanks, reactors, processing equipment and feeds are operated in fully closed systems. Propylamine is almost exclusively used for the manufacture of other substances. During manufacture and processing operations, worker exposure is controlled by the use of closed systems, industrial hygiene controls, and personal protective equipment. Any risk of accumulation is minimized by natural ventilation and the pungent odor of propylamine in combination with the low odor threshold, which is a warning sign that prevents significant exposure. At processing sites, the exposure of workers is minimized by vapor abstraction. Prior to repair and maintenance work, vessels, pipes and other equipment are purged to remove any residual propylamine. Dedicated systems designed to handle propylamine are used for loading and unloading purposes to prevent any emissions or exposure. The vent gases are either incinerated or cleaned by means of a scrubber. At the production and processing sites, workers wear personal protective equipment which includes gloves, face shields and safety goggles. During repair and maintenance operations, and during drum emptying operations, respiratory protective equipment is additionally used. Additionally, only a small, well-defined and trained group of workers will perform occasionally sampling tasks for quality control under strictly controlled conditions. Consumer exposure to any potentially existing residual propylamine is considered negligible."

110 Rigorous containment measures: "*Propylamine is manufactured and used under strictly controlled conditions over the entire lifecycle. Possible exposure is limited to occasional sampling tasks for quality control. Transport, storage tanks, reactors, processing equipment, and feeds operate in fully closed systems.*"

111 Procedural and control technologies are used to minimise residual emissions/exposure as well as qualitative risk considerations: "*Operational and technical conditions and measures affecting and controlling workers exposure, such as local exhaust ventilation as well as personal protective equipment, such as goggles, chemically resistant gloves, and respiratory protection where potential exposure may occur.*"

112 In addition to the above description of the process, the rigorous containment measures and the procedural and control technologies, you also provide a description of the toxicological profile and classification of the substance. Regarding the toxicological profile you include some considerations of a quantitative assessment.

113 In addition to your claim of strictly controlled conditions and rigorously contained conditions provided in your registrant's comments, we note the supporting documentation (RMM Report for transported intermediate) in section 13.2 of IUCLID which was already included in your submission under compliance check. In this report you include similar argumentation regarding rigorous containment measures to those provided in your comments. You also provide various exposure scenarios in your CSR (3 July 2013).

6.2. Assessment of information provided

6.2.1. Read-across adaptation is rejected

114 In relation to all the studies provided, as explained in Section 0.1., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5 is rejected.

6.2.2. Studies (i) and (ii) do not comply with the applicable test guideline

115 As explained in Section 0.1., the study to be read across must have an adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3), in this case EU B.63/OECD TG 421 or EU B.64/OECD TG 422. Therefore, the following specifications must be met:

a) at least weekly food consumption measurements;
b) terminal organ weights (paragraph 46 of OECD TG 421); gross pathology, including incidence and severity, as specified in paragraphs 45-48 of OECD TG 421; full histopathology, including incidence and severity, as specified in paragraph 49 of OECD TG 421;
c) thyroid hormone measurements as specified in paragraph 42 of OECD TG 421);
d) monitoring of oestrus cycles;
e) examination of offspring parameters such as number and sex of pups, stillbirths and live births, gross abnormalities, pup body weight, litter weight, anogenital distance, number of nipples/areolae in male pups.

116 The study (i) is described as Combined repeated dose toxicity study with reproduction/developmental toxicity screening test. However, the following specifications are not according to the requirements of EU B.63/OECD TG 421 or EU B.64/OECD TG 422:

c) information on thyroid hormones;
d) monitoring of oestrus cycles;
e) full examination of offspring parameters was not performed as only mean number of pups/litter and clinical signs for F1 pups were reported.

117 The study (ii) is described as One-generation reproduction toxicity study. However, the following specifications are not according to the requirements of EU B.63/OECD TG 421 or EU B.64/OECD TG 422:

a) food consumption was not measured;
b) terminal organ weights, gross pathology and full histopathology as the reporting does not allow an independent assessment whether these parameters were examined as required in the test guideline;
c) information on thyroid hormones;
d) monitoring of oestrus cycles;
e) full examination of offspring parameters was not performed as only mean litter size, sex ratio, body weights and gross abnormalities for F1 pups were reported.

118 Based on the above, the studies (i) and (ii) do not provide an adequate and reliable coverage of the key parameter(s) addressed by the EU B.63/OECD TG 421 or EU B.64/OECD TG 422 and these studies are not an adequate basis for your read-across predictions.

6.2.3. Exposure-based adaptation under Annex XI, Section 3(2)(b) is rejected

119 Under Annex XI, Section 3(2)(b), it must be demonstrated and documented for all relevant scenarios that throughout the life cycle strictly controlled conditions as set out in Article 18(4)(a) to (f) apply (see further Guidance on Intermediates and Practical Guide 16).

120 In your RMM Report for transported intermediate you describe rigorous containment and minimisation technologies that could potentially rigorously contain the substance. You also describe management, training and special procedures regarding cleaning and maintenance.

121 However, in your CSR you estimate exposures (with ECETOC TRA version 2) that are not indicative of strictly controlled conditions as set out in Article 18(4)(a) to (f). For instance, in exposure scenarios 2 and 3 you estimate long-term inhalation exposure of [redacted]

[redacted]. This information contradicts your claim that the Substance is used under strictly controlled conditions or rigorous containment.

122 On this basis your proposed substance-tailored exposure-driven testing in accordance with Annex XI 3.2.(b) is rejected.

123 Therefore, the information you provided do not fulfil the information requirement.

6.2.4. Specification of the study design

124 When there is no information available neither for the 28-day repeated dose toxicity endpoint (OECD TG 407/412) nor for the screening study for reproductive/developmental toxicity (OECD TG 421/422), the conduct of a combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (OECD TG 422) is preferred to avoid unnecessary animal testing and because it fulfils the information requirement in both Annex VIII, Section 8.6.1. and 8.7.1. of REACH (ECHA Guidance R.7.6.2.3.2.).

125 The Substance is a corrosive liquid and you apply a self-classification as Skin Corr. 1B (H314). ECHA Guidance R.7.6.2.3.2. specifies that corrosive or highly irritating substances must be tested preferably via the oral route. However, testing at concentration/dose levels causing corrosivity must be avoided. Testing of neutral salts of alkaline or acidic substances is therefore more appropriate as it allows the investigation of intrinsic properties at adequate dose levels.

126 In your comments on the draft decision, you do not agree that an OECD 422 study with oral administration must be performed due to the following reasons:

- *"[…] inhalation is the most relevant human exposure route for the registered substance."*
- "*[…] the registered substance propylamine is a liquid with a very high vapor pressure (330 hPa at 20 ºC*) […]"
- "*Therefore, hazard characterization for propylamine from studies with oral administration is not appropriate and any testing should be conducted by inhalation."*

127 ECHA agrees that based on the vapor pressure of the Substance, the inhalation route is relevant. According to ECHA guidance R.7.6.2.3.2. *"[…] the test methods for reproductive toxicity which focus on the detection of reproductive hazards, the oral route (gavage, in diet, or in drinking water) is the "default" route, except for gases*". Therefore, and despite your arguments, ECHA considers that, in this case and also taking into account the corrosivity of the Substance as explained above, the oral route is the most appropriate administration route for a screening study according to OECD TG 422.

128 According to ECHA guidance R.7.6.2.3.2. "[…] *in vivo testing with corrosive substances at concentration/dose levels causing corrosivity must be avoided (see REACH Annex VII-X preamble). The vehicle should be chosen to minimise gastrointestinal irritation.* […] *In certain cases, testing of neutral salts of alkaline or acidic substances may be appropriate and allows investigation of intrinsic properties at adequate dose levels*". Therefore, ECHA considers that testing of a neutralised form of the Substance via oral route will enable to investigate intrinsic properties related to reproductive toxicity in a screening study (OECD TG 422) by allowing to use adequate dose levels. Otherwise, the already known corrosivity of the Substance may not allow investigation of reproductive toxicity in relation to systemic toxicity. Also, the corrosivity/irritation of the Substance may affect the behaviour of the animals confounding the interpretation of reproducitve toxicity-related parameters. In addition, local effects might induce unnecessary stress to the animals with consequences to the outcome of the study.

129 ECHA notes that similar absorption and systemic effects are expected for the Substance and its neutralised form under physiological conditions. The dissociation constant (pKa) of the Substance is 10.68. Therefore, the Substance will exist as a protonated form under physiological conditions as will the neutralised form of the Substance.

130 Therefore, a study according to the test method EU B.64/OECD TG 422 must be performed in rats with oral administration (ECHA Guidance R.7.6.2.3.2). The test sample must be chosen to minimise gastrointestinal irritation and to allow investigation of intrinsic properties at adequate dose levels. This could be achieved by testing a neutralised salt of the Substance.

131 If the Screening for reproductive/developmental toxicity study submitted in response of this decision does not deliver reliable results because of gastrointestinal irritation, further testing may be considered necessary in order to investigate the intrinsic properties at adequate dose levels. Therefore, if the Member State competent authorities consider that a concern must be clarified in that respect, they may decide to require further testing under Substance Evaluation.

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 6 July 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 requests.

In your comments to the draft decision, you requested also an extension of the deadline from 12 to 30 months from the date of adoption of the decision to perform the requested screening study (OECD TG 422). You consider that the extension of the deadline is needed "*to conduct further range finding studies prior to the requested main studies*". Furthermore, you also refer to testing capacities of laboratories "*the laboratories/CROs currently have limited capacities due to an increased request of these types of studies. For example, the capacity of the* [redacted] *laboratory is currently booked for at least 9 months in advance, which means that an initial planning phase of 9 months is needed as soon as the test order is definitive. This time schedule is based on the laboratories experience with other substances. This is especially true in the current situation due to the COVID-19 pandemic. Additionally, specific safety measures in the lab facilities are needed for specific safety measures which reduce the capacity to a certain extent. The registrants consider facing a comparable situation in external labs (CROs). The registrants have seen lead-times of 3-9 months to get the work at CROs initiated for other studies in the past few months.*".

ECHA took into accound your comments. However, you did not provide sufficient supporting information, including the scheduling timeline for the requested study (OECD TG 422).

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.

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

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].

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,
- as explained in Section 6., the test sample must be chosen to minimise gastrointestinal irritation andto allow the investigation of intrinsic properties at adequate dose levels. This could be achieved by testing a neutralised salt of the Substance. When selecting a neutral salt, the potential impact of the counterion must be considered. The counterion must have no known systemic toxicity.

(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