~~Confidential~~

Helsinki, 04 October 2021

Addressees
Registrants of JS_DMP_203-412-0 as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
25/03/2020

Registered substance subject to this decision ("the Substance")
Substance name: 1,4-dimethylpiperazine
EC number: 203-412-0
CAS number: 106-58-1

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 ***11 January 2024***.

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

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

1. In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.; test method: EU B.13/14. / OECD TG 471)

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

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

1. 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)

2. and 3. Combined repeated dose toxicity study with the reproduction/developmental toxicity screening study (Annex VIII, Sections 8.6.1. and 8.7.1.; test method: OECD 422) in rats, oral route (gavage)

4. Adsorption/ desorption screening (Annex VIII, Section 9.3.1.; test method: OECD TG 106)

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

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

7. Bioaccumulation in aquatic species also requested below (triggered by Annex I, Sections 0.6.1. and 4; Annex XIII, Section 2.1.)

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

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

2. Long-term toxicity testing on fish (Annex IX, Section 9.1.6.; test method: OECD TG 210)

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

4. Identification of degradation products (Annex IX, 9.2.3.; test method: OECD TG 309)

5. Bioaccumulation in aquatic species (Annex IX, Section 9.3.2; test method: OECD TG 305, aqueous exposure)

Reasons for the requests are explained in the following appendices:

- Appendix entitled "Reasons common to several requests";
- Appendices entitled "Reasons to request information required under Annexes VII to IX of REACH", respectively.

Information required depends on your tonnage band

You must provide the information listed above for all REACH Annexes applicable to you, and in accordance with Articles 10(a) and 12(1) of REACH, the information specified in Annexes VII, VIII and IX to REACH, for registration at 100-1000 tpa.

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

For certain endpoints, ECHA requests the same study from registrants at different tonnages. In such cases, only the reasoning why the information is required at lower tonnages is provided in the corresponding Appendices. For the tonnage where the study is a standard information requirement, the full reasoning for the request including study design is given. Only one study is to be conducted; the registrants concerned must make every effort to reach an agreement as to who is to carry out the study on behalf of the other registrants under Article 53 of REACH.

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 testing and reporting requirements provided under the Appendix entitled "Requirements to fulfil when conducting and reporting new tests for REACH purposes". In addition, you should follow the general recommendations provided under the Appendix entitled "General recommendations when conducting and reporting new tests for REACH purposes". For references used in this decision, please consult the Appendix entitled "List of references".

The studies relating to biodegradation and bioaccumulation are necessary for the PBT assessment. However, to determine the testing needed to reach the conclusion on the persistency and bioaccumulation of the Substance you should consider the sequence in which these tests are performed and other conditions described in Appendix entitled "Requirements to fulfil when conducting and reporting new tests for REACH purposes".

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 Christel Schilliger-Musset, Director of Hazard Assessment

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

Appendix on Reasons common to several requests

You seek to adapt the following standard information requirements by applying (a) read-across approaches in accordance with Annex XI, Section 1.5:

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

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 appendices.

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 (addressed under 'Assessment of prediction(s)').

Additional information on what is necessary when justifying a read-across approach can be found in the ECHA Guidance R.6. and related documents[2,3].

A. Predictions for toxicological properties

You have provided a read-across justification document in IUCLID Section 13.

You read-across between the structurally similar substances, 1-methyl piperazine (N-methylpiperazine, NMP (CAS No. 109-01-3) as source substance and the Substance as target substance.

You have provided the following reasoning for the prediction of toxicological properties:

"the two chemicals are hypothesized to have the same type of effect(s) – Scenario 2 of the RAAF guidance." and

"*DMP is expected to have a similar toxicological profile as NMP based on chemical structure similarities, physico-chemical parameters and the available toxicological data*"

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.

ECHA notes the following shortcoming with regards to prediction of toxicological properties:

Annex XI, Section 1.5 of the REACH Regulation states that "*physicochemical properties, human health effects and environmental effects or environmental fate may be predicted from*

[2] Read-Across Assessment Framework (RAAF). 2017 (March) ECHA, Helsinki. 60 pp. Available online: Read-Across Assessment Framework (https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across)

[3] Read-across assessment framework (RAAF) - considerations on multi-constituent substances and UVCBs. 2017 (March) ECHA, Helsinki. 40 pp. Available online: https://doi.org/10.2823/794394

data for reference substance(s)". For this purpose "*it is important to provide supporting information to strengthen the rationale for the read-across*"[4]. The set of supporting information should allow to verify the crucial aspects of the read-across hypothesis and establish that the properties of the Substance can be predicted from the data on the source substance(s).

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

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 substance 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).

In the dossier you provided a key acute oral study with the target leading to a classification as Acute Tox 4. The acute study with the source did not lead to classification. You also provided a supporting study with the target showing a LD50 value in the same range as the source.

You have also provided studies with the target and the source for skin corrosion and eye irritation enpoints. Both substances are classified as Skin Corr 1 and Eye Damage.
For sensitisation you provided a study with the target but for the source, the study was performed with another analogue, and you considered that this endpoint is not relevant to support the proposed read-across.

You note in the read-across justification "*No long-term toxicological data are available for comparison between DMP and NMP to support the read-across approach*". On the high tier endpoints only an OECD 422 with the source is available.

Consequently, ECHA concludes that the data set reported in the technical dossier does not include relevant, reliable and adequate information for the Substance and of the source substance to support your read-across hypothesis for the endpoints concerned.

In the absence of such information, you have not established that the Substance and of the source substance are likely to have similar properties. Therefore you have not provided sufficient supporting information to strengthen the rationale for the read-across.

B. Conclusions on the read-across approach

As explained above, you have not established that relevant properties of the Substance can be predicted from data on the analogue substance. Therefore, your adaptation does not comply with the general rules of adaptation as set out in Annex XI, Section 1.5. and your grouping and read-across approach is rejected.

[4] Guidance on information requirements and chemical safety assessment Chapter R.6: QSARs and grouping of Chemicals, Section R.6.2.2.1.f

Appendix A: Reasons to request information required under Annex VII of REACH

1. In vitro gene mutation study in bacteria

An *in vitro* gene mutation study in bacteria is an information requirement under Annex VII to REACH (Section 8.4.1.).

You have provided a key study and a supporting study in your dossier:

i. [redacted], 1996 with the following *S. typhimurium* strains, TA 98, TA 100, TA 1535, TA 1537, and *E. coli* WP2 uvrA which all gave negative results.
ii. [redacted], 2006 with the following *S. typhimurium* strains, TA 98, TA 100, TA 1535, TA 1537, and *E. coli* WP2 uvrA which all gave negative results.

In your comments to draft decision you acknowledged that "*The studies presented to do not fulfill all requirements in the generally accepted guidelines*. " and you agreed to perform an in vitro gene mutation test in bacteria with the registered substance according to OECD TG 471.

We have assessed this information and identified the following issues:

A. Incompliance with the applicable test guideline

To fulfil the information requirement, the study has to meet the requirements of OECD TG 471[5] (1997). Some of the key parameters of this test guideline includes:

a) Triplicate plating must be used at each dose level. The use of duplicate plating is acceptable when scientifically justified.
b) The number of revertant colonies per plate for the concurrent negative control must be inside the historical control range of the laboratory.
c) The mean number of revertant colonies per plate must be reported for the treated doses and the controls.
d) Treatment procedures must be reported.

However, the reported data for the key study you have provided did not include:

a) triplicate plating at each dose level (duplicates plating was used and no scientific justification was provided)
b) a negative control with a number of revertant colonies per plate inside the historical control range of the laboratory.
c) data on the number of revertant colonies per plate for the treated doses and the controls.
d) Treatment procedure (preincubation or plate incorporation) used for the preliminary reverse mutation test

A dose related increase in the number of revertant colonies was observed in TA100 with and without metabolic activation but the finding is dismissed because "*all of the positive controls produced more than two-fold increases in the number of the revertant colonies in comparison with that of the solvent control with all bacterial strains with and without metabolic activation.*" However, the use of duplicates does notensure the reproducibility of the study and the number of revertant colonies observed in TA100 was not reported to allow to conclude on the biological significance of this finding. An increase in the number of revertant colonies in TA100 with and without metabolic activation can be seen also as a positive result for this strain redering the study at least ambiguous.

[5] ECHA Guidance R.7a, Table R.7.7–2, p.557

The information provided in the key study does not cover several of the key parameters required by OECD TG 471.

Therefore, the information requirement is not fulfilled.

B. *Absence of robust study summary*

Pursuant to Article 10(a)(vii) of the REACH Regulation, the information set out in Annex VII to XI must be provided in the form of a robust study summary. Article 3(28) defines a robust study summary as a detailed summary of the objectives, methods, results and conclusions of a full study report providing sufficient information to make an independent assessment of the study minimising the need to consult the full study report.

The supporting study provided in the dossier is not provided in the form of a robust study summary. The study was assigned a reliability 4 because "*it is difficult to judge the reliability based on a report in Japanese*.". Consequently, adequate and reliable documentation in the form of a robust study summary, as required by Article 10(a)(vii) and Article 3(28) is missing.

Therefore, the information requirement is not fulfilled.

Study design

To fulfil the information requirement for the Substance, the *in vitro* gene mutation study in bacteria (OECD TG 471) is considered suitable.

2. Growth inhibition study aquatic plants

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

You have provided the following information:

1. an OECD TG 201 study with the Substance ([redacted], 2014)

We have assessed this information and identified the following issue:

To fulfil the information requirement, a study must comply with OECD TG 201 and the requirements of OECD GD 23 (ENV/JM/MONO(2000)6/REV1) if the substance is difficult to test (Article 13(3) of REACH). Therefore, the following specifications must be met:

Validity criteria

a. exponential growth in the control cultures is observed over the entire duration of the test;
b. the mean coefficient of variation for section-by-section specific growth rates (days 0-1, 1-2 and 2-3, for 72-hour tests) in the control cultures is ≤ 35%;

However, in your dossier, the mean coefficient of variation section by section of the specific growth rates for control and in the control cultures are not reported either. Therefore it is not possible to verify points a. and b. above.

Characterisation of exposure

c. the test media prepared specifically for analysis of exposure concentrations during the test is treated identically to those used for testing (*i.e.* inoculated with algae and incubated under identical conditions);
d. for some substances (*e.g.* adsorbing substances), the results may only be expressed based on nominal concentrations if the decrease in measured concentrations of the

test substance during the test is not accompanied by a decrease in growth inhibition. If a reduction in growth inhibition is observed, a suitable model describing the decline of the concentration of the test material must be used;

However, in your dossier, you did not report clearly how the exposure concentrations were determined. For instance, you have not specified if the exposure concentrations were characterised with or without presence of algae.

Reporting of the methodology and results

e. the results of algal biomass determined in each flask at least daily during the test period are reported in a tabular form;
f. detailed information on the methodology and analytical verification of the exposure concentrations.

However, in your dossier, the tabulated data on the algal biomass determined daily for each treatment group and control are not reported.

In addition, you have not provided a comprehensive reporting of measured concentrations.

In your comments to the draft decision, you provide the missing information for study i. ECHA has assessed the information against the requirement in OECD TG 201. The information you have provided in your comments addresses the incompliances identified in this decision for this information requirement. However, as the information is currently not available in your registration dossier, the data gap remains. You should therefore submit this information in an updated registration dossier by the deadline set out in the decision.

On this basis, the information requirement is not fulfilled.

Study design

The Substance is difficult to test due to the potential adsorptive properties of the Substance as it is ionised at environmentally pH (pKb 1 = 9.78 and pKb 2 = 8.31 based on OECD TG 112). OECD TG 201 specifies that, for difficult to test substances, you must consider the approach described in OECD GD 23 or other approaches, if more appropriate for your substance. In all cases, the approach selected must be justified and documented. Due to the properties of Substance, it may be difficult to achieve and maintain the desired exposure concentrations. Therefore, you must monitor the test concentration(s) of the Substance throughout the exposure duration and report the results. If it is not possible to demonstrate the stability of exposure concentrations (i.e. measured concentration(s) not within 80-120% of the nominal concentration(s)), you must express the effect concentration based on measured values as described in OECD TG 201. 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.

Appendix B: Reasons to request information required under Annex VIII of REACH

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

An *in vitro* cytogenicity study in mammalian cells or an *in vitro* micronucleus study is an information requirement under Annex VIII to REACH (Section 8.4.2.).

You have provided a key study in your dossier: [redacted], 2011**,** according to OECD 473 (In Vitro Mammalian Chromosome Aberration Test) with source 1-methylpiperazine.

However, for the reasons explained in the *Appendix on reasons common to several requests*, your adaptation does not comply with the general rules of adaptation as set out in Annex XI, Section 1.5. and your grouping and read-across approach is rejected.

Therefore, the information requirement is not fulfilled. In your comments to draft decision you agreed to perform an in vitro cytogenicity study in mammalian cells or an in vitro micronucleus study with the registered substance, according to OECD TG 473 or OECD TG 487.

Study design

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.

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

A "short-term repeated dose toxicity study (28 days)" is a standard information requirement in Annex VIII of the REACH.

You have provided the following studies for a 28-day repeated dose toxicity study:

a. A key study (OECD 422), [redacted], 2013 with the source substance
b. A supporting study (short-term repeated dose toxicity), [redacted], 1964 with the target

In addition, in your comments on the draft decision, you stated that *"A 28-day repeated dose toxicity study in rats via oral gavage was performed according to OECD TG 407 and compliant to GLP requirements ([redacted], 2020). The robust study summary of this key study will be included in the dossier and is added to these replies as Appendix to this document (Appendix II)."*

We have assessed this information and identified the following issues:

A. *Rejected read-across*

The study (a) above is performed with the source substance. For the reasons explained in section 1 of the *Appendix on reasons common to several requests*, your adaptation does not comply with the general rules of adaptation as set out in Annex XI, Section 1.5. and your grouping and read-across approach is rejected.

B. *Documentation insufficient for assessment*

Pursuant to Article 10(a)(vii) of the REACH Regulation, the information set out in Annex VII to XI must be provided in the form of a robust study summary. Article 3(28) defines a robust

study summary as a detailed summary of the objectives, methods, results and conclusions of a full study report providing sufficient information to make an independent assessment of the study minimising the need to consult the full study report.

The supporting study (b) provided in the dossier doesn't have a robust study summary. The study was assigned a reliability 4 because of "significant methodological deficiencies. Not enough information on material and methods.". Consequently, adequate and reliable documentation in the form of a robust study summary, as required by Article 10(a)(vii) and Article 3(28) is missing.

C. The new study provided in your comments is not adequate

To be considered compliant and enable concluding whether the Substance has dangerous properties and supports the determination of the No-Observed Adverse Effect Level (NOAEL), a study has to meet the requirements of OECD TG 407. The following key parameter(s) of this test guideline include, among others:

- highest dose level should aim to induce some systemic toxicity, but not death or severe suffering.

In your comments you provided the robust study summary for an OECD 407 with the Substance ([redacted], 2020). The highest dose level in the study did not induce any systemic toxicity. Therefore, the dose level selection was too low, and the study does not fulfil the criterion set in OECD TG 407.

Therefore, the information requirement is not fulfilled.

When there is no information available neither for the 28-day repeated dose toxicity endpoint (EU B.7, OECD TG 407), nor for the screening study for reproductive/ developmental toxicity (OECD TG 421 or TG 422), the conduct of a combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (OECD TG 422) is preferred to ensure that unnecessary animal testing is avoided. Such an approach offers the possibility to avoid carrying out a 28-day study according to OECD TG 407, because the OECD TG 422 can at the same time fulfil the information requirement of REACH Annex VIII, 8.6.1 and that of REACH Annex VIII, 8.7.1.[6]

Information on study design

A study according to the test method EU B.64/OECD TG 422 must be performed in rats with oral[7] administration of the Substance.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test (test method: OECD TG 422) in rats by the oral route (gavage).

3. Screening for reproductive/developmental toxicity

A Screening for reproductive/developmental toxicity study (test method: EU B.63/OECD TG 421 or EU B.64/OECD TG 422) is a standard information requirement under Annex VIII to REACH, if there is no evidence from analogue substances, QSAR or *in vitro* methods that the Substance may be a developmental toxicant. There is no information available in your dossier indicating that your Substance may be a developmental toxicant.

[6] ECHA Guidance, Section R.7.6.2.3.2., pages 484 to 485 of version 6.0 – July 2017. (https://echa.europa.eu/documents/10162/13632/information_requirements_r7a_en.pdf)
[7] ECHA Guidance R.7a, Section R.7.6.2.3.2.

You have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation by providing a study record ([redacted], 2013) of one "screening for reproductive/developmental toxicity" studies with a source substance.

In addition, in your comments on the draft decision, you stated that *"A Reproduction/Developmental Toxicity screening test in Wistar rats via oral gavage was performed according to OECD TG 421 and compliant to GLP requirements ([redacted], 2020). The robust study summary of this key study will be included in the dossier and is added to these replies as Appendix to this document (Appendix III)".*

We have assessed this information and identified the following issues:

A. Rejected read-across

For the reasons explained in the *Appendix on reasons common to several requests*, your adaptation does not comply with the general rules of adaptation as set out in Annex XI, Section 1.5. and your grouping and read-across approach is rejected.

B. The new study provided in your comments is not adequate

To be considered compliant and enable concluding whether the Substance has dangerous properties and supports the determination of the No-Observed Adverse Effect Level (NOAEL), a study has to meet the requirements of OECD TG 421. The following key parameter(s) of this test guideline include, among others:

- highest dose level should aim to induce some systemic toxicity, but not death or severe suffering.

In your comments you provided the robust study summary for an OECD 421 with the Substance ([redacted], 2020). The highest dose level in the study did not induce any systemic toxicity. Therefore, the dose level selection was too low, and the study does not fulfil the criterion set in OECD TG 421.

Therefore, the information requirement is not fulfilled.

When there is no information available neither for the 28-day repeated dose toxicity endpoint (EU B.7, OECD TG 407) (as explained above under section 2), nor for the screening study for reproductive/developmental toxicity (OECD TG 421 or TG 422), the conduct of a combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (OECD TG 422) is preferred to ensure that unnecessary animal testing is avoided. Such an approach offers the possibility to avoid carrying out a 28-day study according to OECD TG 407, because the OECD TG 422 can at the same time fulfil the information requirement of REACH Annex VIII, 8.6.1 and that of REACH Annex VIII, 8.7.1.[8]

Information on study design

A study according to the test method EU B.64/OECD TG 422 must be performed in rats with oral[9] administration of the Substance.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present

[8] ECHA Guidance, Section R.7.6.2.3.2., pages 484 to 485 of version 6.0 – July 2017. (https://echa.europa.eu/documents/10162/13632/information_requirements_r7a_en.pdf)
[9] ECHA Guidance R.7a, Section R.7.6.2.3.2.

decision: Combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test (test method: OECD TG 422) in rats by the oral route (gavage).

4. Adsorption/desorption screening

Adsorption/Desorption screening is an information requirement under Annex VIII to REACH (Section 9.3.1.).

You have provided the following information:

1. an adaptation under Annex VIII, Section 9.3.1., column 2 ('low potential for adsorption') with the following justification: "the substance has a low octanol water partition coefficient (log Pow = -0.26)"
2. an adaptation under Annex XI, Section 1.3. ('QSAR') using a predictive model described in [redacted] (2008).

We have assessed this information and identified the following issues:

A. Incompliance with the adaptation under Annex VIII, Section 9.3.1, column 2

Annex VIII, Section 9.3.1., column 2 specifies that a study does not need to be conducted if the substance can be expected substance to have a low potential for adsorption (e.g. the log K_{ow} is low). To adapt this information requirement based on low Log K_{ow}, lipophilicity must be the sole characteristic driving the adsorption potential of a substance. However, for some groups of substances (e.g. ionisable substances, surfactants) other mechanisms than lipophilicity may drive adsorption.

You have justified the low potential for adsorption because the partition coefficient value (log K_{ow}) was determined to be -0.26 based on Eu Method A.8. You have provided dissociation constant data indicating that the Substance is ionized at environmentally relevant pH (pKb 1 = 9.78 and pKb 2 = 8.31 based on OECD TG 112).

However, cationic substances are expected to bind to negatively charged particles (e.g. clay mineral, organic matter). Therefore log Kow is not a valid descriptor for assessing the adsorption potential of the Substance and your adaptation is rejected.

B. Incompliance with the QSAR adadptation under Annex XI, Section 1.3

Annex XI, Section 1.3. states that results obtained from valid QSAR models may be used instead of testing when, among others cumulative conditions, adequate and reliable documentation of the applied method is provided.

According to Section 3.4 of ECHA's Practical guide "How to use and report (Q)SARs", a QSAR Model Reporting Format (QMRF) and a QSAR Prediction Reporting Format (QPRF) are required to establish the scientific validity of the model, to verify that the Substance falls within the applicability domain of the model, and to assess the adequacy of the prediction for the purposes of classification and labelling.

However, you have not included a QMRF and a QPRF in your technical dossier. Therefore, ECHA cannot establish whether the model is scientifically valid and whether the Substance falls within the applicability domain of the model. Therefore, your adaptation is rejected.

In your comments on the draft decision, you state that you consider that "*the model represents the substance's adsorption potential with sufficient reliability*" and you intend to provide appropriate QMRF and QPRF documentation.

However ECHA notes that you have not provided this information in your comments.

On this basis, the information requirement is not fulfilled.

Study design

As explained above, based on the pKa values of the Substance, it is expected to be ionised at environmentally relevant pH. For such substance OECD TG 121 may not be applicable. Therefore, you are requested to generate information on adsorption/desorption using the OECD TG 106 (ECHA Guidance R.7.1.15.3).

5. Simulation testing on ultimate degradation in surface water

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

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

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

  it meets the T criteria set in Annex XIII: NOEC or EC_{10} < 0.01 mg/L or classification as carc. 1A or 1B, muta. 1A or 1B, repro. 1A, 1B or 2, or STOT RE 1 or 2.

Your registration dossier provides the following:

- The Substance is not readily biodegradable (6% degradation after 28 days in OECD TG 301C);

Furthermore, the information in your dossier is currently incomplete and therefore:

- it is not possible to conclude on the bioaccumulation potential of the Substance (see Appendix B.6. of this decision), and
- it is not possible to conclude on the toxicity of the Substance see Appendices B1-2 above.

The information above indicates that the Substance is a potential PBT/vPvB substance.

In your comments on the draft decision, you disagree that the Substance is potentially PBT/vPvB as you consider the Substance as not B/vB. The information you have provided in your comments on the bioaccumulation would address the incompliances identified in this decision for this information requirement (C.5.). However, as the information is currently not available in your registration dossier, the data gap remains. You should therefore submit this information in an updated registration dossier by the deadline set out in the decision.

Furthermore you propose to predict potential degradation products of your Substance using EAWAG BBD pathway prediction system and to conduct a PBT/vPvB assessment of the estimated degradation products.

However as this information is currently not in your dossier the incompliance remains.

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

The examination of the available information or adaptations, as well as the selection of the requested test and the test design are addressed respectively in Appendix C.3.

6. Identification of degradation products

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

As already explained under Section B.4., the Substance is a potential PBT/vPvB substance. Therefore, the chemical safety assessment (CSA) indicates the need for further degradation investigation.

The examination of the available information or adaptations, as well as the selection of the requested test and the test design are addressed respectively in Appendix C.4.

7. Bioaccumulation in aquatic species

Bioaccumulation in aquatic species is required for the purpose of PBT/vPvB assessment (Annex I, Sections 0.6.1 and 4 to REACH).

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

As already explained under Section B.4., the Substance is a potential PBT/vPvB substance. Therefore, the chemical safety assessment (CSA) indicates the need for further investigation on bioaccumulation in aquatic species.

The examination of the available information or adaptations, as well as the selection of the requested test and the test design are addressed respectively in Appendix C.5.

In your comments on the draft decision, you disagree that the Substance may be B/vB. The justification from your comments is addressed under Appendix C.5 below.

Appendix C: Reasons to request information required under Annex IX of REACH

1. Long-term toxicity testing on aquatic invertebrates

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

You have provided the following information:

1. a justification to omit the study which you consider to be based on Annex IX, Section 9.1., Column 2. In support of your adaptation you provided the following justification: "*Based on the outcome of the CSA there is no need to further investigate the long-term toxicity to aquatic invertebrates*".

We have assessed this information and identified the following issue:

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).

Your adaptation is therefore rejected.

In your comments on the draft decision, you propose to cover this information requirement through a read-across from the structurally related substance 1-methylpiperazine (CAS 109-01-3).

As you have not provided supportive information on the structurally similar compound, or experimental data available as part of your comments, ECHA is not in a position to assess the corresponding information.

On this basis, the information requirement is not fulfilled.

Study design

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. As already explained above, the Substance is difficult to test. Therefore, you must fulfil the requirements described in 'Study design' under Appendix A.2.

2. Long-term toxicity testing on fish

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

You have provided the following information:

i. a justification to omit the study which you consider to be based on Annex IX, Section 9.1., Column 2. In support of your adaptation you provided the following justification: " "Based on the outcome of the CSA, there is no need to investigate further the long-term toxicity to fish".

We have assessed this information and identified the following issue:

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

Your adaptation is therefore rejected.

In your comments on the draft decision, while you recognize the rejection of the adaptation of the information requirement, you also specify that you intend to adapt this information requirement under Annex XI, Section 1.2. ('Weight of evidence'). You intend to provide the following justification:

i. The structure as well as the physico-chemical properties of the Substance are clearly identified. The Substance is found not to persist in a acclimated ready biodegradation test and, on that basis, you consider that persistence in water and soil is unlikely;
ii. The substance does not produce an alert for protein binding in the schemes by OECD and OASIS (OECD QSAR Toolbox v4.3; see Chapter 2.5 of the updated Read-Across Justification). According to the modified classification scheme of Verhaar, the mode of action of the Substance is narcosis of baseline toxicity. Therefore, it can be concluded that the Substance has no specific mode of action and critical long-term effects are not to be expected;
iii. You specify that no information on long-term toxicity to fish is available for the substance and that no reliable QSAR predictions or in-vitro results for long-term toxicity to fish are available;
iv. Fish are not the most sensitive aquatic trophic level;
v. The Substance is neither acutely nor chronically hazardous to the aquatic environment according to the CLP-Regulation (EC) No 1272/2008. You based your reasoning on aquatic chronic classification on the result of the data currently available on short-term toxicity to fish and the concept of acute-to-chronic ratio;
vi. You further consider that this information is not needed for the PBT assessment of the Substance as it is concluded no B/vB based on some QSARs estimations;
vii. You refer to Article 25 to REACH to specify that vertebrate animal testing should be undertaken as a last resort.

We take note of your intention to submit an adaptation. However, we emphasize that the justification above does not rely on any source of information that could be used to conclude on long-term fish toxicity.

Relevant information that can be used to support weight of evidence adaptation for long-term toxicity to fish includes similar information that is produced by the OECD TG 210. The following aspects need to be covered: Parameters related to the survival and development of fish in early life stages from the stage of fertilized egg until the juvenile life-stage following exposure to the test substance are measured, including:

1) the stage of embryonic development at the start of the test, and
2) hatching of fertilized eggs and survival of embryos, larvae and juvenile fish, and
3) the appearance and behaviour of larvae and juvenile fish, and
4) the weight and length of fish at the end of the test.

As you did not submit such information, ECHA concludes that there is, in your justification, no weight of evidence to be assessed. Finally, the use of the acute-to chronic ratio concept on its own is not regarded as providing sufficient weight of evidence to conclude on chronic toxicity (ECHA Guidance R.7.8.5.).

On this basis, the information requirement is not fulfilled.

Study design

To fulfil the information requirement for the Substance, the Fish, Early-life Stage Toxicity Test (test method OECD TG 210) is the most appropriate (ECHA Guidance R.7.8.2.).

OECD TG 210 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. As already explained above, the Substance is difficult to test. Therefore, you must fulfil the requirements described in 'Study design' under Appendix A.2.

3. Simulation testing on ultimate degradation in surface water

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

You have provided the following information:

1. an adaptation under Annex IX, Section 9.2., Column 2 with the following justification:
   i. "*From available biodegradation tests (OECD 301A and 301C)* […] *the substance is only readily biodegradable under acclimated test conditions (OECD 301A)*" and "*No further testing is deemed necessary as it is not expected to improve the current conclusion on biodegradation*";
   ii. "*Furthermore, the chemical safety assessment showed safe uses for all environmental compartments*".

We have assessed this information and identified the following issue:

Under Section 9.2., Column 2 of Annex IX to REACH, the study may be omitted if the chemical safety assessment (CSA) does not indicate the need for further biotic degradation testing. The CSA does indicate such need (Annex I, Section 4; Annex XIII, Section 2.1) if, for instance, the substance is a potential PBT/vPvB substance (ECHA Guidance R.11.4). This is the case if the Substance itself or any of its constituent, impurity or transformation/degradation product present in concentration ≥ 0.1% (w/w) meets the criteria already listed in Appendix B.4.

However, as already explained under Appendix B.4., you have not demonstrated that the CSA does not indicate the need for further biotic degradation testing and your adaption is rejected.

On this basis, the information requirement is not fulfilled.

Study design

Simulation degradation studies must include two types of investigations (ECHA Guidance R.7.9.4.1.):

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

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

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

As specified in ECHA Guidance R.7.9.4.1., the organic carbon (OC) concentration in surface water simulation tests is typically 2 to 3 orders of magnitude higher than the test substance concentration and the formation of non-extractable residues (NERs) may be significant in surface water tests. Therefore, non-extractable residues (NER) must be quantified. The

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

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

4. Identification of degradation products

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

You have provided the following information:

1. an adaptation under Annex IX, Section 9.2., Column 2 with the following justification: "*no degradation products resulting from aerobic biotransformations could be identified using the EAWAG-BBD Pathway Prediction System*". You have not provided any documentation on these predictions.

We have assessed this information and identified the following issue:

Annex XI, Section 1.3. states that results obtained from valid QSAR models may be used instead of testing when, among others cumulative conditions, adequate and reliable documentation of the applied method is provided.

According to Section 3.4 of ECHA's Practical guide "How to use and report (Q)SARs", a QSAR Model Reporting Format (QMRF) and a QSAR Prediction Reporting Format (QPRF) are required to establish the scientific validity of the model, to verify that the Substance falls within the applicability domain of the model, and to assess the adequacy of the prediction for the purposes of classification and labelling.

You have not provided sufficient documentation for the QSAR prediction 1. listed above. In particular, you have not included a QMRF and a QPRF in your technical dossier. Therefore, ECHA cannot establish whether the model is scientifically valid and whether the Substance falls within the applicability domain of the model. Therefore, your adaptation is rejected.

On this basis, the information requirement is not fulfilled.

This information is required for the purpose of the PBT/vPvB assessment (Annex I, Section 4) and the risk assessment (Annex I, Section 6) of the Substance (See Appendix B.5).

In your comments on the draft decision, you explain that you intend to meet the information requirement by providing results from a QSAR model (namely EAWAG BBD pathway prediction system). ECHA notes that you have not provided the results of the QSAR prediction in your comments, therefore ECHA is not in a position to assess the corresponding information.

Study design

Regarding the selection of appropriate and suitable test method(s), the method(s) will have to be substance-specific. Identity, stability, behaviour, and molar quantity of the degradation/transformation products relative to the Substance must be evaluated and reported, when analytically possible. In addition, degradation half-life, log K_{ow} and potential toxicity of the transformation/degradation may need to be investigated. You may obtain this information from the degradation study requested in Appendices B.4 and C.3 or by some other measure. If any other method is used for the identification of the transformation/degradation products, you must provide a scientifically valid justification for the chosen method.

To determine the degradation rate of the Substance, the requested study according to OECD TG 309 (Appendix B.4) must be conducted at 12°C and at a test concentration < 100 µg/L. However, to overcome potential analytical limitations with the identification and quantification of major transformation/degradation products, you may consider running a parallel test at higher temperature (but within the frame provided by the test guideline, *e.g.* 20°C) and at higher application rate (*i.e.* > 100 µg/L).

5. Bioaccumulation in aquatic species

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

You have provided the following information:

1. an adaptation under Annex IX, Section 9.3.2., Column 2 with the following justification: "*the substance has a low potential for bioaccumulation based on log Kow <=3*".

We have assessed this information and identified the following issue:

Under Section 9.3.2., Column 2, first indent of Annex IX to REACH, the study may be omitted if the substance has a low potential for bioaccumulation and/or a low potential to cross biological membranes. A low log Kow (*i.e.* log Kow < 3) may be used to support low potential for bioaccumulation if the partitioning of to lipids is the sole mechanism driving the bioaccumulation potential of a substance. For some groups of substances (e.g. organometals, ionisable substances, surfactants) other partitioning mechanisms may drive bioaccumulation (e.g. binding to protein/cell membranes). For this reason log Kow is not considered a valid descriptor of the bioaccumulation potential for such substances (ECHA Guidance R.7c, Appendix R.7.10-3).

Your registration dossier provides an adaptation stating that the log Kow is < 3. The Substance is ionisable at environmentally relevant pH (pKb 1 = 9.78 and pKb 2 = 8.31 based on OECD TG 112).

Therefore, log Kow is not a valid descriptor of the bioaccumulation potential of the Subtance and your adaptation is rejected.

In your comments on the draft decision, while you recognized the rejection of the adaptation of the information requirement, you also specified that you intend to adapt this information requirement under Annex XI, Section 1.2. ('Weight of evidence'). You intend to provide the following justification:

- i. some publications from [redacted] (2013) and [redacted] (2009) on ionisable substances and their hydrophobic potentials (Log Kow and Log Dow),
- ii. a read-across from the similar substance Piperazine (CAS No. 110-85-0) with a reference to an experimental bioaccumulation study on *C.carpio* showing low BCF,
- iii. some estimated BCF values using BCFBAF v3.01 for the Substance and some

analogue, including the QMRF and QPRF

We take note of your intention to submit an adaptation. The estimated BCF value from QSAR model you have provided in your comments would address the incompliance identified in this decision for this information requirement. However, as the information is currently not available in your registration dossier, the data gap remains.

On this basis, the information requirement is not fulfilled.

This information is required for the purpose of the PBT/vPvB assessment (Annex I, Section 4) and the risk assessment (Annex I, Section 6) of the Substance (See Appendix B.6).

Study design

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

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

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

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

Appendix D: Requirements to fulfil when conducting and reporting new tests for REACH purposes

A. 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[10].

B. 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[11].

[10] https://echa.europa.eu/practical-guides
[11] https://echa.europa.eu/manuals

Appendix E: General recommendations when conducting and reporting new tests for REACH purposes

A. Strategy for the PBT/vPvB assessment

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

You are advised to consult ECHA Guidance R.7b (Section R.7.9.), R.7c (Section R.7.10) and R.11 on PBT assessment to determine the sequence of the tests needed to reach the conclusion on PBT/vPvB. The guidance provides advice on 1) integrated testing strategies (ITS) for the P, B and T assessments and 2) the interpretation of results in concluding whether the Substance fulfils the PBT/vPvB criteria of Annex XIII.

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

Appendix F: 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 27 March 2020.

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.

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 G: List of references - ECHA Guidance[12] and other supporting documents

Evaluation of available information
Guidance on information requirements and chemical safety assessment, Chapter R.4 (version 1.1., December 2011), referred to as ECHA Guidance R.4 where relevant.

QSARs, read-across and grouping
Guidance on information requirements and chemical safety assessment, Chapter R.6 (version 1.0, May 2008), referred to as ECHA Guidance R.6 where relevant.

Read-across assessment framework (RAAF, March 2017)[13]

RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017)[13]

Physical-chemical properties
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Toxicology
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7c (version 3.0, June 2017), referred to as ECHA Guidance R.7c in this decision.

Environmental toxicology and fate
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7b (version 4.0, June 2017), referred to as ECHA Guidance R.7b in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7c (version 3.0, June 2017), referred to as ECHA Guidance R.7c in this decision.

PBT assessment
Guidance on information requirements and chemical safety assessment, Chapter R.11 (version 3.0, June 2017), referred to as ECHA Guidance R.11 in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.16 (version 3.0, February 2016), referred to as ECHA Guidance R.16 in this decision.

Data sharing
Guidance on data-sharing (version 3.1, January 2017), referred to as ECHA Guidance on data sharing in this decision.

OECD Guidance documents[14]
Guidance Document on aqueous–phase aquatic toxicity testing of difficult test chemicals – No 23, referred to as OECD GD 23.

[12] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[13] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across
[14] http://www.oecd.org/chemicalsafety/testing/series-testing-assessment-publications-number.htm

Guidance document on transformation/dissolution of metals and metal compounds in aqueous media – No 29, referred to as OECD GD 29.

Guidance Document on Standardised Test Guidelines for Evaluating Chemicals for Endocrine Disruption – No 150, referred to as OECD GD 150.

Guidance Document supporting OECD test guideline 443 on the extended one-generation reproductive toxicity test – No 151, referred to as OECD GD 151.

Appendix H: Addressees of this decision and their corresponding information requirements

You must provide the information requested in this decision for all REACH Annexes applicable to you.

Registrant Name	Registration number	Highest REACH Annex applicable to you
[redacted]	[redacted]	[redacted]

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