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Helsinki, 15 November 2021

Addressee
Registrant of JS-trimethylamine-n-oxide-2018 as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
04/09/2019

Registered substance subject to this decision ("the Substance")
Substance name: Trimethylamine, N-oxide
EC number: 214-675-6
CAS number: 1184-78-7

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 ***22 November 2022***.

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

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

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

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. If negative results are obtained in tests performed for the information requirement of Annex VII, Section 8.4.1. and 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)

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

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

5. Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.; test method: OECD TG 203)

Reasons for the request(s) are explained in the following appendices:

- Appendix entitled "Reasons common to several requests";
- Appendices entitled "Reasons to request information required under Annexes VII to VIII 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 and VIII to REACH, for registration at 10-100 tpa.

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". For references used in this decision, please consult the Appendix entitled "List of references".

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

1. **Assessment of your read-across approach under Annex XI, Section 1.5.**

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

- In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.)
- In vitro cytogenicity study in mammalian cells or in vitro micronucleus study (Annex VIII, Section 8.4.2.)
- In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.)
- Short-term repeated dose toxicity (28 day), (Annex VIII, Section 8.6.1.)
- Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)
- Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.)
- Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.)
- Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.)
- Ready biodegradability (Annex VII, Section 9.2.1.1.)

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.

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, ecotoxicological and fate properties

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

You read-across between the structurally similar substances, Trimethylamine, EC No. 200-875-0 (CAS No. 1184-78-7) as source substance and the Substance as target substance.
You have provided the following information on structural similarity:

- *"Trimethylamin is a tertiary aliphatic amine. The trimethylamin N-oxide is its metabolite form after N-oxydation."*
- *"The two chemicals present common structure with three methyl groups and central nitrogen. The only difference is the presence of an oxygen atom linked to the nitrogen in TMAO form."*
- "*Both substances are monoconstituant with purity ≥ 98% w/w. The impurities are not classified for any hazard* […] *Hence, the influence of impurities on physico-chemical parameters and toxicity is considered as negligible*".

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

- *In physiologic condition, TMA is metabolized in TMAO in the liver. The toxicity of TMAO*

[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

is expected to be the same as TMA. As a consequence, the toxicity in human should be considered as equivalent."

- *"The assumption is done that TMAO is responsible for the common property or effect. It implies that the potential systemic toxicity of the TMA will be largely attributed to TMAO."*

In addition you have provided the following reasoning for the prediction of aquatic toxicity and fate properties:

- *"TMA and TMAO show common behavior in environmental water compartment due to their physicochemical similarities as water solubility, Kow and Henry's law constant values. The environmental and ecotoxicity behavior of the two substances in water should be similar".*

ECHA understands that you predict the properties of the Substance using a read-across hypothesis which is based on the formation of common (bio)transformation products for toxicological properties, or assumes that different compounds have the same type of effects for ecotoxicological and fate properties. The properties of your Substance are predicted to be quantitatively equal to those of the source substance.

ECHA notes the following shortcomings with regards to predictions of toxicological,ecotoxicological and fate properties.

A. Missing supporting information

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 data for reference substance(s)*". For this purpose "*it is important to provide supporting information to strengthen the rationale for the read-across*" (ECHA Guidance R.6.2.2.1.f). 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 toxicokinetic information on the formation of the common compound, information on the impact of exposure parent compounds on the prediction and bridging studies to compare properties of the Substance and source substances.

a) Toxicological properties

As indicated above, your read-across hypothesis is based on the (bio)transformation of the Substance and of the source substance to a common compound. In this context, exposure to the Substance and of the source substance may also lead to exposure to other compounds than the common compound of interest. The impact of exposure to these non-common compounds on the prediction of properties of the target needs to be assessed to ensure that a reliable prediction can be made.

In your read-across justification you state "*TMA is mainly metabolized in the liver by FMO enzyme into TMAO and widely distributed in the organism. The assumption is done that TMAO is responsible for the common property or effect*". However, you do not provide any toxicokinetics information regarding the rate of the metabolism and formation of TMAO (the Substance) from TMA (the source substance). Therefore, exposure to the parent source substance cannot be excluded and your assumption cannot be confirmed.

Furthermore, the source substance is corrosive (Skin Corr 1B, H314) in water solution whereas the Substance is not corrosive or irritating. Therefore, it could be assumed that higher doses of the Substance could be administered in toxicity testing compared to the source substance, without any local effects at the site of administration limiting the investigation of the potential systemic effects of the Substance. Therefore, the physico-chemical properties of the Substance may allow higher systemic exposure to be investigated in repeated dose toxicity studies compared to the source substance.

You have not provided information characterising the exposure to the non-common compounds resulting from exposure to the Substance and of the source substance. No adequate and reliable information addressing the impact of exposure to these non-common compounds and the differences in toxicological properties are included in the documentation of your read-across approach. In the absence of such information, you have not established that a reliable prediction of the property under consideration of the Substance can be derived on the basis of your read-across hypothesis. In addition, you have not provided any bridging studies of comparable design and duration for the Substance and the source substance to support you read-across prediction.

b) Ecotoxicological and fate properties

As indicated above, your read-across hypothesis is based on the assumption that the structurally similar substances cause the same type of effects. In this context, relevant, reliable and adequate information allowing to compare the properties of the Substance and of the source substance 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.

Your registration dossier does not contain any experimental data on the Substance or other adequate and reliable information to compare the properties of the target and source substance. In your justification, you did refer to some QSAR predictions, which according to you, provide support to the prediction. However, you have not provided any documentation (i.e. in the form of a (Q)SAR Model Reporting Format document (QMRF) and a (Q)SAR Prediction Reporting Format document (QPRF)) in order to assess the validity of this information. With regard to the prediction of ready biodegradability, ECHA notes that ECHA Guidance R.7.9.5.1. specifies that (Q)SARs for predicting ready biodegradation are not yet sufficiently accurate to predict rapid degradation.

Also, you state that the source substance is metabolised into the target substance in the liver of mammals. You have not provided any information to support that this hypothesis also applies to other organisms relevant to your read-across adaptations (namely, aquatic invertebrates, fish and algae) nor any information on the rate and extent of the conversion of TMA (the source substance) into TMAO (the Substance).

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

B. Adequacy and reliability of source study

In addition to issue A. above, we have identified deficiencies with the source study for *in vitro* gene mutation study in bacteria. These are addressed under Appendix A.1.

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.

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 adapted this information requirement under Annex XI, Section 1.5. ('Grouping of substances and read-across'). In support of your adaptation, you provided the following information:

i. A key study according to OECD TG 471 with an analogue substance Trimethylamine (EC 200-875-0) in *S. typhimurium* strains TA 98, TA 100, TA 1535 and TA 1537, and in *E. coli* strain WP2 uvrA, which all gave negative results ([redacted] 2001)

We have assessed this information and identified the following issues:

A. As explained in the Appendix on Reasons common to several requests your read-across adaptation under Annex XI, Section 1.5. is rejected.

B. Under Annex XI, Section 1.5, the results to be read across must provide adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3), in this case OECD TG 471. Therefore, the following specifications must be met:

   a) At least 5 doses must be evaluated, in each test condition.
   b) One positive control must be included in the study. The positive control substance must produce a statistically significant increase in the number of revertant colonies per plate compared with the concurrent negative control.
   c) The number of revertant colonies per plate for the concurrent negative control must be inside the historical control range of the laboratory.
   d) The mean number of revertant colonies per plate must be reported for the treated doses and the controls.

   However, the reported data for the study (i.) you have provided did not include:

   a) any information on how many doses were evaluated;
   b) positive control(s) and results for the positive controls;
   c) information whether the negative controls were inside the historical control range of the laboratory;
   d) the number of revertant colonies per plate for the treated doses and the controls.

   Therefore, the study (i.) does not provide an adequate and reliable coverage of the key parameters of the OECD TG 471.

On this basis, 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. Short-term toxicity testing on aquatic invertebrates

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

You have have adapted this information under Annex XI, Section 1.5. ('Grouping of substances and read-across'). In support of your adaptation, you provided the following information:

i. an non guideline study on *Daphnia magna*, performed according to EU Directive 79/831/EEC, Annex V, part C with N,N-dimethylmethanamine (EC 200-875-0), ([redacted], 1988).

We have assessed this information and identified the following issue:

For the reasons explained in the Appendix on Reasons common to several requests your read-across adaptation is rejected.

On this basis, the information requirement is not fulfilled.

3. 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 adapted this information under Annex XI, Section 1.5. ('Grouping of substances and read-across'). In support of your adaptation, you provided the following information, you have provided an OECD TG 201 on *Desmodesmus subspicatus*, performed with N,N-dimethylmethanamine (EC 200-875-0) ([redacted], 1988).

We have assessed this information and identified the following issue:

For the reasons explained in the Appendix on Reasons common to several requests your read-across adaptation is rejected.

On this basis, the information requirement is not fulfilled.

4. Ready biodegradability

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

You have adapted this information under Annex XI, Section 1.5. ('Grouping of substances and read-across'). In support of your adaptation, you provided the following information, you have provided an OECD TG 301C study performed with N,N-dimethylmethanamine (EC 200-875-0) ([redacted], 1992).

We have assessed this information and identified the following issue:

For the reasons explained in the Appendix on Reasons common to several requests your read-across adaptation is rejected.

On this basis, the information requirement is not fulfilled.

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 adapted this information requirement under Annex XI, Section 1.5. ('Grouping of substances and read-across'). In support of your adaptation, you provided the following information:

i. A key study according to OECD TG 473 with an analogue substance Trimethylamine (EC No. 200-875-0) ([redacted] 2010).

We have assessed this information and identified the following issue:

As explained in the Appendix on Reasons common to several requests your read-across adaptation under Annex XI, Section 1.5. is rejected.

On this basis, the information requirement is not fulfilled.

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. In vitro gene mutation study in mammalian cells

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.

Triggering of the study

Your dossier contains an adaptation for an *in vitro* gene mutation study in bacteria, and an adaptation for an in vitro cytogenicity study in mammalian cells or *in vitro* micronucleus study.

The information for the *in vitro* gene mutation study in bacteria and for the *in vitro* cytogenicity study in mammalian cells provided in the dossier are rejected for the reasons provided in Appendices A.1. and B.1.

The result of the requests for information in Appendices A.1. and B.1. 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.

Assessment of information provided

You have adapted this information requirement under Annex XI, Section 1.5. ('Grouping of substances and read-across'). In support of your adaptation, you provided the following information:

i. A key study according to OECD TG 476 with an analogue substance Trimethylamine (EC No. 200-875-0) ([redacted] 2010)

We have assessed this information and identified the following issue:

As explained in the Appendix on Reasons common to several requests your read-across adaptation under Annex XI, Section 1.5. is rejected.

On this basis, the information requirement is not fulfilled.

Consequently, you are required to provide information for this endpoint, if the *in vitro* gene mutation study in bacteria and the *in vitro* cytogenicity study in mammalian cells or an *in vitro* micronucleus study provide a negative result.

Study design

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.

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

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

You have adapted this information requirement under Annex XI, Section 1.5. ('Grouping of substances and read-across'). In support of your adaptation, you provided the following information:

i. A key study according to OECD TG 422 via oral route in rats with an analogue substance Trimethylamine (EC No. 200-875-0) ([redacted] 2003).

We have assessed this information and identified the following issue:

As explained in the Appendix on Reasons common to several requests your read-across adaptation under Annex XI, Section 1.5. is rejected.

On this basis, the information requirement is not fulfilled.

Study design

Referring to the criteria in Annex VIII, Section 8.6.1, Column 2, the oral route is the most appropriate route of administration to investigate repeated dose toxicity, because the Substance is reported to occur as a solid powder without a significant proportion (>1% on weight basis) of particles of inhalable size (MMAD < 50 µm).

Therefore the sub-acute toxicity study must be performed according to the OECD TG 407, in rats and with oral administration of the Substance.

When there is no information available neither for the 28-day repeated dose toxicity endpoint (OECD TG 407) nor for the screening study for reproductive/developmental toxicity (OECD TG 421) (see request B.4 below), 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.).

4. 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 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. There is no information available in your dossier indicating that your Substance may be a developmental toxicant.

You have adapted this information requirement under Annex XI, Section 1.5. ('Grouping of substances and read-across'). In support of your adaptation, you provided the following information:

i. A key study according to OECD TG 422 via oral route in rats with an analogue substance Trimethylamine (EC 200-875-0) ([redacted] 2003).

We have assessed this information and identified the following issue:

As explained in the Appendix on Reasons common to several requests your read-across adaptation under Annex XI, Section 1.5. is rejected.

On this basis, the information requirement is not fulfilled.

Study design

When there is no information available neither for the 28-day repeated dose toxicity endpoint (OECD TG 407) 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.).

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) of the Substance.

5. Short-term toxicity testing on fish

Short-term toxicity testing on fish is an information requirement under Annex VIII to REACH (Section 9.1.3.).

You have adapted this information under Annex XI, Section 1.5. ('Grouping of substances and read-across'). In support of your adaptation, you provided the following information, you have provided an OECD TG 203 study on *Oryzias latipes* performed with N,N-dimethylmethanamine (EC 200-875-0) ([redacted], 2010).

We have assessed this information and identified the following issue:

For the reasons explained in the Appendix on Reasons common to several requests your read-across adaptation is rejected.

On this basis, the information requirement is not fulfilled.

Appendix C: 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[4].

B. Test material

1. Selection of the Test material(s)

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

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

This information is needed to assess whether the Test Material is relevant for the Substance.

Technical instructions on how to report the above is available in the manual on How to prepare registration and PPORD dossiers[5].

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

Appendix D: 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 18 November 2020.

ECHA notified you of the draft decision and invited you to provide comments.

ECHA did not receive any comments within the commenting period.

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 E: List of references - ECHA Guidance[6] 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)[7]

RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017)[8]

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[9]

[6] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[7] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across
[8] https://echa.europa.eu/documents/10162/13630/raaf_uvcb_report_en.pdf/3f79684d-07a5-e439-16c3-d2c8da96a316
[9] http://www.oecd.org/chemicalsafety/testing/series-testing-assessment-publications-number.htm

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

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.

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Appendix F: 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.