~~Confidential~~

Helsinki, 09 February 2022

Addressee
Registrant of JS_1860-26-0_Tris-2-EH as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
05/05/2020

Registered substance subject to this decision ("the Substance")
Substance name: 2-ethyl-N,N-bis(2-ethylhexyl)hexylamine
EC number: 217-461-0
CAS number: 1860-26-0

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 ***16 May 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) using one of the following strains: E. coli WP2 uvrA, or E. coli WP2 uvrA (pKM101), or S. typhimurium TA102

2. Long-term toxicity testing on aquatic invertebrates also requested below (triggered by Annex VII, Section 9.1.1., column 2)

3. 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. Long-term toxicity testing on fish also requested below (triggered by Annex VIII, Section 9.1.3., column 2)

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

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

4. 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. Extended one-generation reproductive toxicity study (triggered by Annex IX, Section 8.7.3., column 1; test method: OECD TG 443) by oral route, in rats, specified as

follows:

- Ten weeks premating exposure duration for the parental (P0) generation;
- Dose level setting shall aim to induce systemic toxicity at the highest dose level;
- Cohort 1A (Reproductive toxicity);
- Cohort 1B (Reproductive toxicity) without extension to mate the Cohort 1B animals to produce the F2 generation.

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

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

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

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

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

Reasons for the requests are explained in the following appendices:

- 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.

For certain endpoints, ECHA lists in the above the same study under the information required at different registered tonnages. This is because the reasoning for the requirement differs at different tonnages (see the below Appendices for the detailed reasons). It does not mean that the same type of information is needed multiple times. Only one study is to be conducted.

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 Mike Rasenberg, 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 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 in your dossier:

i. a study according to OECD TG 471 on the Substance and with the following strains, TA 98, TA 100, TA 1535 and TA 1537, which
ii. h all gave negative results ([redacted] 1985).

We have assessed this information and identified the following issue:

To fulfil the information requirement, the study has to meet the requirements of OECD TG 471 (1997) (ECHA Guidance R.7a, Table R.7.7–2). Therefore, the following specifications must be met:

- The test must be performed with 5 strains: four strains of *S. typhimurium* (TA98; TA100; TA1535; TA1537 or TA97a or TA97) and one strain which is either *S. typhimurium* TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101)

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

- the required fifth strain, *S. typhimurium* TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101).

The information provided does not cover one of the key investigations required by 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) should be performed using one of the following strains: *E. coli* WP2 uvrA, or *E. coli* WP2 uvrA (pKM101), or *S. typhimurium* TA102.

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

2. Long-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.). Long-term toxicity testing on aquatic invertebrates must be considered (Section 9.1.1., Column 2) if the substance is poorly water soluble.

You have provided an OECD TG 202 study on *Daphnia magna* ([redacted], 2010) and an OECD TG 211 on *Daphnia magna* ([redacted], 2014), both performed with the substance.

We have assessed this information and identified the following issue:

Water soluble substances require longer time to reach steady-state conditions. As a result, the short-term tests does not give a true measure of toxicity for this type Poorly of substances and the long-term test is required. A substance is regarded as poorly

water soluble if, for instance, it has a water solubility below 1 mg/L or below the detection limit of the analytical method of the test material (ECHA Guidance R.7.8.5).

In the provided OECD TG 105 ([redacted], 2010), the saturation concentration of the Substance in water was < 0.002 mg/L at 20 °C and pH 5.9 ([redacted], 2010).

Therefore, the Substance is poorly water soluble and information on long-term toxicity on aquatic invertebrates must be provided.

The examination of the information provided, as well as the selection of the requested test and the test design are addressed under Appendix C.2.

In your comments on the draft decision, you state that the available OECD TG 211 study on Daphnia magna ([redacted], 2014) fulfils the information requirement. We have assessed the information and we address your comment in Appendix C.2.

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 provided an OECD TG 201 with the Substance and in accordance with OECD GD 23 ([redacted], 2010).

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) (Article 13(3) of REACH). Therefore, the following specifications must be met:

Requirements applicable to difficult to test substances

- if the test material is poorly water soluble, the maximum dissolved concentration that can be achieved in the specific test solution under the test conditions is determined and reported;
- if losses of the test material are expected within the timeframe of the test, a preliminary stability study is conducted and reported, which meets the following requirements:
- if the test material is tested at the saturation concentration, evidence must be provided that all reasonable efforts have been taken to achieve a saturation concentration, which include:
    1) information on the saturation concentrations of the test material in water and in the test solution, and
    2) the results of a preliminary experiment demonstrating that the test solution preparation method is adequate to maximize the concentration of the test material in solution.

In your comments on the draft decision, you provided information on the test solution preparation "test solutions were prepared by directly adding 100.87 mg of test substance to 1 L test medium" and you also state "that test solutions were prepared following the general guidance provided in OECD GD 23 (OECD,2000)".

You have not reported the results of a preliminary solubility experiment demonstrating that the test solution preparation method is adequate to maximize the concentration of the test material in solution. Therefore, the requirements of OECD TG 201 and the OECD GD 23 are not met.

Characterisation of exposure

- a reliable analytical method for the quantification of the test material in the test solutions with reported specificity, recovery efficiency, precision, limits of determination (*i.e.* detection and quantification) and working range must be available. Alternatively, a justification why the analytical monitoring of exposure concentrations is not technically feasible must be provided;

  In the comments to the draft decision, you stated that "*no reliable method for analyses in the required concentration range could be developed*". You further aknowldedge that while "*a decline in the concentration could be possible by adsorption based on the high log Kow*" you consider this as not an issue as the "*undissolved test material was not removed from the test solution*" and "*thus it could have served as a reservoir to compensate for any losses*".

  You have not provided documentary evidence that support your claim that development of analytical method was not feasible. As you acknowledge in your comments, losses of the substance could occur. You specifically sate that "*a decline in the concentration could be possible by adsorption based on the high log Kow*". Whether the leftover undissolved test material could act as a reservoir to the aqueous phase concentration of the test material is speculative. Therefore, the requirements of OECD TG 201 and the OECD GD 23 are not met.

Exposure concentration to the tested organism cannot be confirmed and therefore ECHA maintains that an appropriate study is needed. This decision does not take into account updates of the registration dossiers after the date on which you were notified of the draft decision according to Article 50(1) of REACH.

On this basis, the information requirement is not fulfilled.

Study design

The Substance is difficult to test due to the low water solubility (< 0.002 mg/L, OECD TG 105, [redacted], 2010) and its adsorptive properties (log kow = 10.38, QSAR prediction, [redacted], 2014). 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. Long-term toxicity testing on fish

Short-term toxicity testing on fish is an information requirement under Annex VIII to REACH (Section 9.1.3.). Long-term toxicity testing on fish must be considered (Section 9.1.3., Column 2) if the substance is poorly water soluble.

You have provided an OECD TG 203 study on *Oncorhynchus mykiss* with the Substance ([redacted], 1985) and a supporting short term study *Leuciscus idus* with the Substance performed according to the German Industrial Standard DIN 38412, part L15 ([redacted], 1988). However, you have provided no information on long-term toxicity on aquatic invertebrates for the Substance.

We have assessed this information and identified the following issue:

> Poorly water soluble substances require longer time to reach steady-state conditions. As a result, the short-term tests does not give a true measure of toxicity for this type of substances and the long-term test is required. A substance is regarded as poorly water soluble if, for instance, it has a water solubility below 1 mg/L or below the detection limit of the analytical method of the test material (ECHA Guidance R.7.8.5).
>
> As already explained under Section A.2, the Substance is poorly water soluble and information on long-term toxicity on fish must be provided.

The examination of the information provided, as well as the selection of the requested test, the test design and your comments on the draft decision are addressed under section C.3.

2. Soil simulation testing

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 301F)
- it is potentially bioaccumulative or very bioaccumulative (B/vB) as:
  - it has a high potential to partition to lipid storage (*e.g.* log K_{ow} > 4.5);

Your registration dossier provides the following:

- The Substance is not readily biodegradable based on a weight of evidence (WoE) approach (0% degradation after 28 days in OECD TG 301F and is predicted not readily biodegradable based on BIOWIN v4.10 and CATALOGIC v5.13.1 (OECD 301C) v11.15) results;
- The Substance has a high potential to partition to lipid storage (Log K_{ow} 10.38 based on non guideline method);

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 C.6. of this decision), and
- it is not possible to conclude on the toxicity of the Substance (see Appendices A.3. and C.1-3 of this decision).

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.

In your comments on the draft decision, you specified that you do not agree to perform the study. You consider that " *the Substance is potentially persistent or very persistent, it is not potentially bioaccumulative or very bioaccumulative*" and that the "*Substance is classified as potentially P/vP from a precautionary point of view*". Furthermore you argue that the substance is not potentially bioaccumulative or very bioaccumulative since "*the log Kow alone is not considered a valid descriptor for ionizable substances*" and the estimated BCF "*do not indicate BCF values above the critical limit for B/vB substances (BCF > 2000) when considering relevant mitigating factors*".

The information above indicates that the Substance is a potential PBT/vPvB substance. The Substance has low water solubility (< 0.002 mg/L), high partition coefficient (log Kow = 10.38) and is ionisable under environmentally relevant pH, indicating high potential to adsorb to soil. Additionally, as explained under section C.6. no definitive conclusion on bioaccumulation potential of the substance can be reached based on the available data.

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

The examination of your comments to the draft decision are also addressed respectively in Appendix C.4.

3. Sediment simulation testing

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 in Appendix B.2., the Substance is a potential PBT/vPvB substance. The Substance has low water solubility (<0.002 mg/L), high partition coefficient (log Kow = 10.38) and is ionisable under environmentally relevant pH, indicating high potential to adsorb to sediment.

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

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.

Your comments as described under B.2 also apply here. Therefore the examination of your comments to the draft decision are also addressed in Appendix C.4.

4. 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).

As already explained in Appendix B.2., 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, the test design and your related comments are addressed in Appendix C.6.

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

1. Extended one-generation reproductive toxicity study

The basic test design of an Extended one-generation reproductive toxicity (EOGRT) study (OECD TG 443) is an information requirement under Annex IX to REACH (Section 8.7.3.), if the available repeated dose toxicity studies indicate adverse effects on reproductive organs or tissues or reveal other concerns in relation with reproductive toxicity. Furthermore Column 2 of Section 8.7.3. defines when the study design needs to be expanded.

You have provided the following statement:

"*According to Annex IX of the REACH regulation 1907/2006, an extended one-generation reproductive toxicity study (EOGRTS) must be fulfilled if toxicity studies indicate adverse effects on reproductive organs or tissues for a substance in quantities of 100 tpa or more. The test substance was tested in a 90d repeated dose oral toxicity study (OECD 408), in a screening study for reproductive and developmental toxicity (OECD 422, oral route), and a prenatal developmental toxicity study (OECD 414, oral route). In the OECD 408 and OECD 422 studies predominantly dose-related histiocytic/mixed cell infiltrates in multiple organs (ovaries, intestines and their draining lymph nodes) were observed resulting in systemic, secondary local inflammatory reactions. In the screening study OECD 422, the test substance did not cause adverse effects on fertility of the F0 parental animals of both sexes at all dose levels tested (1500, 4000 and 12000 ppm). Mating behaviour, conception and parturition were not influenced.*"

In addition, we understand that you have submitted a justification for an adaptation under Annex IX, Section 8.7., column 2 according to which

"A slightly lower number of implants in all treated groups was suggested to be a potential adverse effect on reproductive performance. This effect is presumed to be caused by the dose-related inflammations observed in maternal animals. Thus, the substance is classified as a potential toxicant to reproduction, Cat. 2 (H361f "Suspected of damaging fertility"). The available data are adequate for hazard assessment of the test substance, for its classification, and to support a robust risk assessment. The classification as a suspected toxicant to fertility is implemented. And a prenatal developmental toxicity study (OECD 414) did not reveal any test-substance induced adverse fetal findings. Thus, further testing for reproduction/fertility and developmental toxicity will not provide further knowledge and is not proposed by the registrant"

We have assessed this information and identified the following issues:

A. As already mentioned above, an EOGRT study is required if the available repeated-dose studies indicate adverse effects or concerns related to reproductive toxicity.

   Adverse effects on reproductive organs or tissues or other concerns in relation with reproductive toxicity are observed in studies available from your registration dossier. More specifically, effects in the ovaries were observed in the sub-chronic toxicity study (OECD TG 408) and screening study (OECD TG 422). In addition, the Substance caused "*A slightly lower number of implants in all treated groups*" in the screening study and you consider it "*to be a potential adverse effect on reproductive performance.*".

   In your comments on the draft decision, you stated that accumulation of substance-lipid complexes is the leading health effect. You also stated that the "*slightly, but dose-dependently reduced number of implantations and consequently pubs is not due to a*

specific interaction of the registered substance with normal pregnancy, but is secondary to accumulation of the test substance in the ovaries (among other organs) and subsequent inflammation a response to a foreign substance." You consider that this inflammation affected the corpora lutea and likely interfered with their function to ensure successful implantation. Finally, you question the need for an EOGRT study as you do not expect any changes in classification, NOAEC or DNEL.

ECHA notes that accumulation of the Substance in ovaries is an intrinsic property of the Substance. This intrinsic property may lead to perturbation of normal ovary/corpora lutea functions, and to further downstream effects such as lower number of implantations and pups born, and it is therefore relevant for hazard identification, for sexual function and fertility.

ECHA notes that in the registration dossier you consider that a *"slightly lower number of implants in all treated groups was suggested to be a potential adverse effect on reproductive performance."* Consequently, you have self-classified the Substance as Repr. 2 (H361f).

As stated in Annex I, Section 1.0.1. of REACH, *"the objectives of the human health hazard assessment shall be to determine the classification of a substance in accordance with Regulation (EC) No 1272/2008"* (the CLP Regulation). The aim of the requested test must be to demonstrate whether the classification criteria of the most severe hazard category for sexual function and fertility (Repr. 1B; H360F) and developmental toxicity (Repr. 1B; H360D) under the CLP Regulation apply for the Substance (OECD TG 443, para. 22; OECD GD 151, para. 28; Annex I Section 1.0.1. of REACH and Recital 7, Regulation 2015/282), and whether the Substance meets the criteria for a Substance of very high concern regarding endocrine disruption according to Art.57(f) of REACH as well as supporting the identification of appropriate risk management measures in the chemical safety assessment.

The current self-classification for the Substance is Repr. 2 (H361f) based on effects on sexual function and fertility observed in a screening study according to OECD TG 422. To demonstrate whether the classification criteria of the most severe hazard category for sexual function and fertility (Repr.1B; H360F) apply, an EOGRT study will provide conclusive information on this hazard. The requested study design with ten weeks exposure duration before mating ensures that development of follicles is fully covered and any potential adverse effect on corporal lutea function and embryo implantation can be identified, also with the higher statistical power than based on OECD TG 422. Therefore, results from an EOGRT study can change the hazard classification.

In addition, the EOGRT study can provide a defined NOAEL and/or DNEL.

In your comments, you also state that the accumulation of substance-lipid complexes is addressed in the STOT RE classification. You have self-classified the Substance as STOT RE 2, with ovaries as one of the target organs. ECHA notes that according to CLP Annex I, 3.9.1.1, specific toxic effects covered by other hazard classes are not included in STOT RE. STOT RE should only be assigned where the observed toxicity is not covered more appropriately by another hazard class. For example, specific effects on the reproductive organs (such as ovaries) should be used for classification for reproductive toxicity but not for STOT RE.

As explained above, the available repeated dose toxicity studies indicate adverse effects on reproductive organs and reveal other concerns in relation with reproductive toxicity. You have identified a potential adverse effect on reproductive performance,

however there is no information, which allows to conclude whether the classification criteria of the most severe hazard category for sexual function and fertility (Repr. 1B; H360F) and developmental toxicity (Repr. 1B; H360D) under the CLP Regulation apply for the Substance.

Therefore, an EOGRT study according to OECD TG 443 is an information requirement for your registration.

B. According to Annex IX, Section 8.7., Column 2, second paragraph, the study does not need to be conducted if the substance meets the criteria for classification as toxic for reproduction category 1A or 1B: May damage the unborn child (H360D), and the available data are adequate to support a robust risk assessment […] However, testing for effects on fertility must be considered.

You have justified the adaptation by stating that the Substance meets the classification criteria to Repr 2. (H361f). Classification as Repr. 2 is not a valid adaptation possibility according to Annex IX, 8.7., column 2.

Therefore, adaptation according to Annex IX, Section 8.7., Column 2 is not possible.

On this basis, the information you provided do not fulfil the information requirement.

Study design

Premating exposure duration and dose-level setting

The length of premating exposure period must be ten weeks to cover the full spermatogenesis and folliculogenesis before the mating, allowing meaningful assessment of the effects on fertility.

Ten weeks premating exposure duration is required to obtain results adequate for classification and labelling and /or risk assessment. There is no substance specific information in the dossier supporting shorter premating exposure duration.

Therefore, the requested premating exposure duration is ten weeks.

In order to be compliant and not to be rejected due to too low dose levels, the highest dose level shall aim to induce systemic toxicity, but not death or severe suffering of the animals, to allow comparison of reproductive toxicity and systemic toxicity. The dose level selection should be based upon the fertility effects. A descending sequence of dose levels should be selected in order to demonstrate any dose-related effect and to establish NOAELs.

If there is no relevant data to be used for dose level setting, it is recommended that range-finding results are reported with the main study.

You have to provide a justification with your study results that demonstrates that the dose level selection meets the conditions described above.

Cohorts 1A and 1B

Cohorts 1A and 1B belong to the basic study design and must be included.

Species and route selection

The study must be performed in rats with oral administration (ECHA Guidance R.7.6.2.3.2.).

Further expansion of the study design

The conditions to include the extension of Cohort 1B are currently not met. Furthermore, no triggers for the inclusion of Cohorts 2A and 2B (developmental neurotoxicity) and/or Cohort 3 (developmental immunotoxicity) were identified. However, you may expand the study by including the extension of Cohort 1B, Cohorts 2A and 2B and/or Cohort 3 if relevant information becomes available from other studies or during the conduct of this study. Inclusion is justified if the available information meets the criteria and conditions which are described in Annex IX, Section 8.7.3., Column 2. You may also expand the study due to other scientific reasons in order to avoid a conduct of a new study. The study design, including any added expansions, must be fully justified and documented. Further detailed guidance on study design and triggers is provided in ECHA Guidance R.7.6.

2. 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:

i. A study according to OECD TG 211 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 the OECD TG 211 and the requirements of OECD GD 23 (ENV/JM/MONO(2000)6/REV1) (Article 13(3) of REACH). Therefore, the following specifications must be met:

Requirements applicable to difficult to test substances

- if the test material is poorly water soluble, the maximum dissolved concentration that can be achieved in the specific test solution under the test conditions is determined and reported;
- if losses of the test material are expected within the timeframe of the test, a preliminary stability study is conducted and reported, which meets the following requirements:
- if the test material is tested at the saturation concentration, evidence must be provided that all reasonable efforts have been taken to achieve a saturation concentration, which include:
  1) information on the saturation concentrations of the test material in water and in the test solution, and
  2) the results of a preliminary experiment demonstrating that the test solution preparation method is adequate to maximize the concentration of the test material in solution.

In your comments on the draft decision, you provided information on the test solution preparation "test solutions were prepared by directly adding y adding 24.5 µL of test substance to 2000 mL test medium to achieve a nominal loading of 10 mg/L" and you also state "that test solutions were prepared following the general guidance provided in OECD GD 23 (OECD, 2000)".

You have not reported the results of a preliminary solubility experiment demonstrating that the test solution preparation method is adequate to maximize the concentration

of the test material in solution. Therefore, the requirements of OECD TG 211 and the OECD GD 23 are not met.

Characterisation of exposure

- a reliable analytical method for the quantification of the test material in the test solutions with reported specificity, recovery efficiency, precision, limits of determination (i.e. detection and quantification) and working range must be available

In the comments to the draft decision, you stated that "*no reliable method for analyses in the required concentration range could be developed*". You further acknowledge that while "*a decline in the concentration could be possible by adsorption based on the high log Kow*" you consider this as not an issue as the "*undissolved test material was not removed from the test solution*" and "*thus it could have served as a reservoir to compensate for any losses*".

You have not provided documentary evidence that support your claim that development of analytical method was not feasible. As you acknowledge in your comments, losses of the substance could occur. You specifically sate that "*a decline in the concentration could be possible by adsorption based on the high log Kow*". Therefore, the requirements of OECD TG 201 and the OECD GD 23 are not met.

Exposure concentration to the tested organism cannot be confirmed and therefore, ECHA maintains that an appropriate study is needed. This decision does not take into account updates of the registration dossiers after the date on which you were notified of the draft decision according to Article 50(1) of REACH.

On this basis, the information requirement is not fulfilled.

Study design

OECD TG 211 specifies that for difficult to test substances OECD GD 23 must be followed. As already explained above, the Substance is difficult to test. Therefore, you must fulfil the requirements described in 'Study design' under Appendix A.3..

3. 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 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:

i. *"the chemical safety assessment does not indicate the need to investigate further the effects on fish"* and

ii. *"in accordance with Annex XI Section 3, it can be demonstrated in the risk assessment that the manufacture and the use of the substance do not pose an unacceptable risk for all environmental compartments as the risk characterization ratios (RCRs) of the chemical safety assessment are below 1 for all compartments (see Chemical Safety Report Ch. 10). In addition, the substance is not classified as a PBT or vPvB substance (see IUCLID Ch. 2.3). Therefore, and for reasons of animal welfare, a long-term toxicity test on fish is not provided."*

We have assessed information and identified the following issues:

A. 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).

Furthermore, ECHA considers that an adaptation under Annex XI, Section 3.2(a) (Substance-tailored exposure-driven testing) is not justified because:

B. The general rule of adaptation from Annex XI, Section 3 (a) is not applicable to potential PBT/vPvB substances

Under Section 2.1 of Annex XIII to REACH, if the result from the screening tests or other information indicate that the substance may have PBT or vPvB properties, the registrant must generate relevant additional information as set out in Section 3.2 of Annex XIII. This additional information may only be omitted if the substance meets the conditions as specified in Section 3.2(b) or (c) of Annex XI , in which case the Substance is considered as if it were a PBT or vPvB.

As already explained in Appendix B.2., the Substance is a potential PBT/vPvB substance and has high potential for adsorption to soil. But you have not provided justification to omit the information based on Section 3.2(b) or (c) of Annex XI of REACH.

C. The proposed adaptation under Annex XI, Section 3.2(a) is not valid due to missing aquatic toxicity data

Under Annex XI, Section 3.2(a), the information could in any case only be omitted based on the exposure scenario(s) developed in the Chemical Safety Report. The justification must be based on a rigorous exposure assessment in accordance with Annex I, Section 5 and the following condition, amongs others, must be met:

A PNEC can be derived from available data, which among others, must be relevant and appropriate both to the information requirement to be omitted and for risk assessment purposes and therefore must be based on reliable information on the hazardous properties of the substance on at least three trophic levels.

For the reasons explained under request A.2., A.3. and C.2., your dossier does not include reliable information on the hazardous properties of the substance on at least three trophic levels.

Therefore, you have not demonstrated that an appropriate PNEC can be derived and therefore the requirements of Annex XI, Section 3.2(a) are not met.

On this basis, ECHA concludes that 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 OECD GD 23 must be followed. As already explained above, the Substance is difficult to test. Therefore, you must fulfil the requirements described in 'Study design' under Appendix A.3.

4. Soil simulation testing

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

As already explained in Appendix B.3., the Substance is a potential PBT/vPvB substance and has high potential for adsorption to soil.

You have provided the following information:

i. an adaptation under Annex IX, Section 9.2.1.3., Column 2 with the following justification: "*test substance is not supposed to be directly applied to sediments. Indirect exposure to sediments is unlikely to occur in significant dimensions since due to the extremely low water solubility, the substance will reach sewage treatment plants (STPs) in only very small amounts. In the STP, due to the high Koc the substance will distribute to a high extent to the sewage sludge. If any, only negligible amounts will reach surface water and sediment by the STP effluent. Therefore, exposure to sediment can be neglected. Additionally, the analogous compound Di-(2-ethylhexyl)amine (CAS 106-20-7) turned out to be moderately biodegradable (not readily biodegradable) in a ready test according to OECD TG 301B. The same result may be applied to biodegradation simulation testing in water and sediment*". Considering the last sentence, ECHA has considered that in the before you intended to refer to "soil" instead of "sediment".

ii. You also state "*Moreover, the risk characterisation ratio (RCR) does not indicate the need for further investigation of risks for the sediment compartment (RCR < 1)*". While you have not explicitly claimed such adaptation, we understand that this statement is provided as an adaptation under Annex XI, Section 3.2(a) ('Exposure-driven testing').

We have assessed this information and identified the following issue:

A. The lack of exposure of the soil compartment is not demonstrated

Under Annex IX, Section 9.2.1.3., Column 2, the study may be omitted if direct and indirect exposure of the soil compartment is unlikely. Soil exposure will occur unless it can be shown that there is no sludge application to land from exposed STPs and that aerial deposition are negligible and the relevance of other exposure pathways such as irrigation and/or contact with contaminated waste is unlikely (ECHA Guidance R.7.11.2.1.).

Based on the uses reported for the Substance, exposure of the soil compartment cannot be excluded as you reported the following Environmental Release Categories that correspond to the uses of the substance: ERC 1, ERC 2, ERC 3, ERC 6B and ERC [redacted]. These ERCs indicate some degree of realease to the soil compartment and furthermore you have not demonstrated that indirect exposure through sludge application to land can be excluded.

Therefore, you have not demonstrated that exposure to the soil is unlikely.

In your comments on the draft decision, you agree that indirect exposure via sewage sludge cannot be excluded.

B. The general rule of adaptation from Annex XI, Section 3 2. (a) is not applicable to potential PBT/vPvB substances

The reasons explained under issue A. of Appendix C.3. equally apply to this endpoint. Therefore your adaptation under Annex XI, Section 3.2.(a) is rejected.

In your comments on the draft decision, you disagree on the PBT/vPvB potential of the substance. The reply to your comment under Appendix B.2 also applies to this issue.

C. *The proposed adaptation under Annex XI, Section 3.2(a) is not valid due to missing aquatic toxicity data*

The reasons explained under issue B. of Appendix C.3. equally apply to this endpoint. Therefore your adaptation under Annex XI, Section 3.2.(a), is rejected.

In your comments on the draft decision, while you disagree that aquatic toxicity data are missing, you have not provided an appropriate adaptation to omit the study as specified under Annex XI to REACH. As explained under Appendix B.2 the substance is potentially PBT/vPvB substance.

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.

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

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 307.

In accordance with the specifications of OECD TG 307, non-extractable residues (NER) must be quantified. The reporting of results must include a scientific justification of the used extraction procedures and solvents (ECHA Guidance R.7.9.4.1.). By default, total NER is regarded as non-degraded Substance. However, if reasonably justified and analytically demonstrated a certain part of NER may be differentiated and quantified as irreversibly bound or as degraded to biogenic NER, such fractions could be regarded as removed when calculating the degradation half-life(s) (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 307; ECHA Guidance R.11.4.1.).

5. Sediment simulation testing

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

As already explained in Appendix B.4., the Substance is a potential PBT/vPvB substance and has high potential for adsorption to sediment.

You have provided the following information:

i. an adaptation under Annex IX, Section 9.2.1.4., Column 2 with the following justification: "*The test substance is not supposed to be directly applied to sediments. Indirect exposure to sediments is unlikely to occur in significant dimensions since due to the extremely low water solubility, the substance will reach sewage treatment plants (STPs) in only very small amounts. In the STP, due to the high Koc the substance will distribute to a high extent to the sewage sludge. If any, only negligible amounts will reach surface water and sediment by the STP effluent. Therefore, exposure to sediment can be neglected. Additionally, the analogous compound Di-(2-ethylhexyl)amine (CAS 106-20-7) turned out to be moderately biodegradable (not readily biodegradable) in a ready test according to OECD TG 301B.*

ii. You also state: *Moreover, the risk characterisation ratio (RCR) does not indicate the need for further investigation of risks for the sediment compartment (RCR <* [redacted]*).*" While you have not explicitly claimed such adaptation, we understand that this statement is provided as an adaptation under Annex XI, Section 3.2(a) ('Exposure-driven testing').

We have assessed this information and identified the following issue:

A. The lack of exposure of the sediment compartment is not demonstrated

Under Annex IX, Section 9.2.1.3., Column 2, the study may be omitted if direct and indirect exposure of the sediment compartment is unlikely. ECHA Guidance specifies that If the substance is considered a PBT/vPvB candidate, then it may be necessary to consider this test if soil is the environmental compartment of concern

Based on the uses reported for the Substance, exposure of the sediment compartment cannot be excluded. In particular, Table R.16-7 of ECHA Guidance R.16. specifies that the default worst-case release factors to the water resulting from the conditions of use of ERC 1, ERC 2, ERC 3, ERC 6B, ERC 6D and ERC 8A are 6%, 2%, 0.2, 5%, 0.025% and 100% respectively.

In your comments on the draft decision you refer to the release factors being "*far lower than the default values (ERC 1 to ERC6d: max.* [redacted]*%; ERC 8a: max.* [redacted]*%)*" based on "*information from the industry*".

ECHA is not in a position to assess and confirm the information on the release factors as provided in your comment without further documentary evidences. In any case, the information provided supports that sediment is an environmental compartment of concern as release to the water is occurring.

Therefore, the sediment is an environmental compartment of concern for the substance and your adaptation is rejected.

B. The general rule of adaptation from Annex XI, Section 3.2(a) is not applicable to potential PBT/vPvB substances

The reasons explained under issue A. of Appendix C.3. equally apply to this endpoint. Therefore your adaptation under Annex XI, Section 3.2(a) is rejected.

In your comments on the draft decision, you disagree on the PBT/vPvB potential of the substance. The reply to your comment under Appendix B.2 also applies to this issue.

C. *The proposed adaptation under Annex XI, Section 3.2(a) is not valid due to missing aquatic toxicity data*

Also the reasons explained under issue B. of Appendix C.3. equally apply to this endpoint.

In your comments on the draft decision, while you disagree that aquatic toxicity data are missing you have not provided an appropriate adaptation to omit the study. As explained under Appendix B.2 the substance is potentially PBT/vPvB substance.

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.

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

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 308.

In accordance with the specifications of OECD TG 308, non-extractable residues (NER) must be quantified. The reporting of results must include a scientific justification of the used extraction procedures and solvents (ECHA Guidance R.7.9.4.1.). By default, total NER is regarded as non-degraded Substance. However, if reasonably justified and analytically demonstrated a certain part of NER may be differentiated and quantified as irreversibly bound or as degraded to biogenic NER, such fractions could be regarded as removed when calculating the degradation half-life(s) (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 308; ECHA Guidance R.11.4.1.).

6. Bioaccumulation in aquatic species

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

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

i. QSAR predictions of BCF with OASIS Catalogic v5.13.1.-BCF baseline model v.03.10 (a) with and (b) without mitigating factors ([redacted], 2019) based on Log Kow =10.83.
ii. QSAR predictions of BCF with OASIS Catalogic v5.13.1.-BCF baseline model v.03.10 (a) with and (b) without mitigating factors ([redacted], 2019) based on Log Kow =8.7.
iii. QSAR predictions of BCFwith EPI Suite v4.11.BCFBAF v3.01 according to (a) [redacted], 1999 and (b) [redacted], 2003 ([redacted], 2019) based on Log Kow =10.83.
iv. QSAR predictions of BCFwith EPI Suite v4.11.BCFBAF v3.01 according to (a) [redacted], 1999 and (b) [redacted], 2003 ([redacted], 2019) based on Log Kow =8.7
v. a QSAR prediction of BCF with US EPA T.E.S.T. v4.2.1 ([redacted], 2019)

Based on the presented sources of information, you argue that the available data gives sufficient information to conclude on Bioaccumulation in aquatic species because predicted BCF values showed limited potential for bioaccumulation.

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

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

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

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

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

To fulfil the information requirement, normally a study performed according to OECD TG 305 must be provided (ECHA Guidance R.7.10.3.1.). Information normally expected for this endpoint include:

1) the uptake rate constant (k1) and loss rate constants including the depuration rate constant (k2), and/or
2) the steady-state bioconcentration factor (BCF_{SS}), and/or
3) the kinetic bioconcentration factor (BCF_K), and/or
4) the biomagnification factor (BMF).

1. *Concerning key parameters (1) uptake rate constant (k1) and loss rate constants including the depuration rate constant (k2), (3) kinetic bioconcentration factor (BCFK), and (4) biomagnification factor (BMF).*

None of the sources of information provided investigate these key parameters. Therefore, they do not provide information that would contribute to the conclusion on these key parameters.

2. *Concerning key parameter (3) steady-state bioconcentration factor (BCF_{SS}),*

The sources of information (i) to (v) provide relevant information on bioaccumulation in aquatic species. However, the reliability of these sources of information is significantly affected by the following deficiencies:

A. The prediction is not adequate due to low reliability

Under ECHA Guidance R.6.1.3.4 a prediction is adequate for the purpose of classification and labelling and/or risk assessment when the model is applicable to the chemical of interest with the necessary level of reliability. ECHA Guidance R.6.1.5.3. specifies that, among others, the following condition must be met:

- reliable input parameters are used. 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).
- the selected structures falls within descriptor, structural, mechanistic and metabolic domain;
- the model predicts well chemicals that are similar to the chemical of interest.

Your registration dossier provides the following information:

- The substance is ionisable with calculated a pKa= 10.38 at 25 °C ([redacted], 2019)
- Log Kow=10.83, calculated with KOWWIN v1.68 ([redacted], 2014) (used as input for the predictions)
- Log Kow > 8.7, unbounded value, calculated ([redacted], 2010) (used as input for the predictions)
- a BCF prediction based on the consensus method and an assessment of the prediction as a prediction with low confidence based on the mean absolute values of the model.
- the mean absolute error of the entire set is slightly lower than the mean absolute error for the similar substances (SC ≥ 0.5).

For sources (i), (ii), (iii) and (iv) the log Kow values of 10.83 and 8.7 were used as input values. These LogKow values represent the neutral or unionized form of the substance and thus take no account of the ionisation state of the substance.

For source (v) we agree with your assessment that there is low confidence in the predicition and this is illustrated by the reported small difference between the mean absolute error of the entire set in comparison with the mean absolute error for the similar substances (SC ≥ 0.5).

Therefore, you have not demonstrated that the prediction for the Substance is adequate for the purpose of classification and labelling and/or risk assessment.

B. The provided documentation of the prediction (QPRF) for source (v) is inadequate.

Under ECHA Guidance R.6.1.6.3 states that the information specified in or equivalent to the (Q)SAR Prediction Reporting Format document (QPRF) must be provided to have adequate and reliable documentation of the applied method. For a QPRF this includes, among others:

- a precise identification of the substance modelled,
- the relationship between the modelled substance and the defined applicability domain,
- the identities of close analogues, including considerations on how predicted and experimental data for analogues support the prediction.

Your registration dossier provides the following information in relation to source v:

- QMRF and QPRF reports for you model
- Additional information on the results in the section 5.3.1 of the registration dossier. The information you provided about the prediction lacks the following elements:
  - Details on the input for prediction
  - The descriptors used to describe the substance
  - Similarity with analogues in the training set and similarity coefficients

In absence of such information, ECHA cannot establish that the prediction can be used to meet this information requirement.

In your comments on the draft decision, you state that you do not agree to perform the study and you intent to adapt the information requirement according to Annex XI, section 1.3 ((Q)SAR). For this purpose you have provided QSAR predictions of BCF with Catalogic BCF base-line model v4.11 of OASIS Catalogic v5.14.1.5. You also state your intention "withdrawn all of the BCF estimations" on which your adaptation was based on under Annex XI, Section 1.2. of REACH (weight of evidence). You further questioned the feasibility of the OECD 305 for ionisable substances and particular on the testing of the neutral form of the substance that you consider to be more bioaccumulative. You also provide further supporting information on the mechanisms driving bioaccumulation other than lipophilicity.

We have assessed the information from your comments on the draft decision and identified the following issues:

C. Under ECHA Guidance R.6.1.3.4 a prediction is adequate for the purpose of classification and labelling and/or risk assessment when the model is applicable to the chemical of interest with the necessary level of reliability. ECHA Guidance R.6.1.5.3. specifies that, among others, the following cumulative conditions must be met:
   - the model predicts well substances that are similar to the substance of interest, and
   - reliable input parameters are used, and
   - the prediction is consistent with information available for other related endpoint(s).

   In your comments you provide the following QSAR BCF predictions with Catalogic BCF base-line model v4.11 of OASIS Catalogic v5.14.1.5:
   - BCF = 2673 with log Kow > 8.7 as an input value. No mitigation effects considered.
   - BCF = 8.5 with log Kow > 8.7 as an input value. Mitigation effects considered.
   - BCF = 210 with log Kow = 10.1 as an input value. No mitigation effects considered.
   - BCF = 6.5 with log Kow = 10.1 as an input value. Mitigation effects considered.

The log Kow values of 10.1 and 8.7 were used as input values. You acknowledge that "the lower log Kow is the unbound value based on the measured single solubilities (log Kow > 8.7, pH 5.9, 20 °C), while the other log Kow value (log Kow = 10.1, 25 °C) is the estimated value for the uncharged molecule based on the QSAR model KOWWIN v1.68" . These LogKow values represent the neutral or unionized form of the substance and thus take no account of the ionisation state of the substance. Hence, some degree of uncertainty lies with the logKow input values.

The predictions for the Substance used as input are not reliable because predictions are not consistent with other experimental data for tertiary amines. The model's training set includes tertiary amines of smaller size. Trioctylamine (EC 214-242-1) is the closest analogue to the substannce identified in the training set of the model. Trioctylamine (EC 214-242-1) is a linear tertiary amine with the same number of carbon atoms as the substance. The experimental BCF for the analogue trioctylamine (EC 214-242-1) is log BCF 1.92, whereas the predicted log BCF is 0.86. This indicates that a possible underestimation of the BCF and a possible overestimation of metabolism for this type of substances.

You therefore have not demonstrated that the prediction for the Substance is adequate for the purpose of risk assessment.

D. Annex IX, Section 9.1., Column 2 does not allow omitting the need to submit information on Bioaccumulation in aquatic species based on animal welfare grounds.

In the comments to the draft decision, you state that: "*testing of the unionized form of the Substance is not feasible with regard to the OECD criteria and animal welfare*"

Minimisation of vertebrate animal testing is not on its own an adaptation authorised under the general rules of Annex XI. Also as stated in the Study design section below you may 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.

Therefore, you have not demonstrated that this information can be omitted and ECHA maintains that an appropriate study is needed. This decision does not take into account updates of the registration dossiers after the date on which you were notified of the draft decision according to Article 50(1) of REACH.

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[2].

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[3].

[2] https://echa.europa.eu/practical-guides
[3] 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 18 November 2020.

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

ECHA took into account your comments and removed the request on Identification of degradation products (triggered by Annex VIII, Section 9.2; Annex IX, Section 9.2.3), but did not amend the other requests. Due to the removed request, ECHA has shortened the deadline from 33 to 27 months.

ECHA notified the draft decision to the competent authorities of the Member States for proposals for amendment.

As no amendments were proposed, ECHA adopted the decision under Article 51(3) of REACH.

Appendix G: List of references - ECHA Guidance[4] 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)[5]

RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017)[6]

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[7]

[4] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[5] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across
[6] https://echa.europa.eu/documents/10162/13630/raaf_uvcb_report_en.pdf/3f79684d-07a5-e439-16c3-d2c8da96a316
[7] 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.

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.