ECHA
EUROPEAN CHEMICALS AGENCY

Helsinki, 20 October 2020

Addressees
Registrants of JS_51772-35-1 as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
12 September 2017

Registered substance subject to this decision ("the Substance")
Substance name: N-[(1,1,3,3-tetramethylbutyl)phenyl]naphthalen-1-amine
EC number: 257-406-8
CAS number: 51772-35-1

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

DECISION ON A COMPLIANCE CHECK

Under Article 41 of Regulation (EC) No 1907/2006 (REACH), you must submit the information listed below, by the deadline of ***26 July 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. Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.; test method: EU C.3./OECD TG 201)

2. The same long-term toxicity testing on aquatic invertebrates as requested in C.3. (triggered by Annex VII, Section 9.1.1., column 2)

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

1. The same long-term toxicity testing on fish as requested in C.4. (triggered by Annex VIII, Section 9.1.3., column 2)

2. The same Soil simulation testing as requested in C5 (triggered by Annex VIII, Section 9.2.)

3. The same Sediment simulation testing as requested in C6 (triggered by Annex VIII, Section 9.2.)

4. The same Identification of degradation products as requested in C7 (triggered by Annex VIII, Section 9.2.)

5. The same Bioaccumulation in aquatic species as requested in C8 (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. Sub-chronic toxicity study (90-day) (Annex IX, Section 8.6.2.; test method: OECD TG 408) by oral route, in rats, with urinalysis to investigate kidney function, kidney

histopathology and immunohistochemical investigation of alpha-2u-globulin for all animals

2. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method: OECD TG 414) by oral route, in one species (rat or rabbit)

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

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

5. Soil simulation testing (Annex IX, Section 9.2.1.3.; test method: EU C.23./OECD TG 307) at a temperature of 12 °C

6. Sediment simulation testing (Annex IX, Section 9.2.1.4.; test method: EU C.24./OECD TG 308) at a temperature of 12 °C

7. Identification of degradation products (Annex IX, 9.2.3.; test method: using an appropriate test method

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

Reasons for the request(s) are explained in the 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 Annex VII to REACH, for registration at 1-10 tonnes per year (tpa), or as a transported isolated intermediate in quantity above 1000 tpa;
- the information specified in Annexes VII and VIII to REACH, for registration at 10-100 tpa;
- the information specified in Annexes VII, VIII and IX to REACH, for registration at 100-1000 tpa.

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

For certain endpoints, ECHA requests the same study from registrants at different tonnages. In such cases, only the reasoning why the information is required at lower tonnages is provided in the corresponding Appendices. For the tonnage where the study is a standard information requirement, the full reasoning for the request including study design is given.

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.

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

1. Growth inhibition study aquatic plants

Growth inhibition study aquatic plants is a standard information requirement in Annex VII Section 9.1.2. to REACH.

You have provided a key study according to OECD TG 201.

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

To fulfil the information requirement, a study must comply with the OECD TG 211 (Article 13(3) of REACH) and the requirements of OECD GD 23 (ENV/JM/MONO(2000)6/REV1) if the substance is difficult to test. Therefore, the following requirements must be met:

- provide evidence that the test solution preparation allowed achieving the maximum dissolved concentration under test conditions. In particular, justify the separation technique especially if filtration is used, as it can cause losses due to adsorption onto the filter matrix;
- provide analytical monitoring to verify the initial concentrations and maintenance of the exposure concentrations during the test. For this purpose, a sufficiently sensitive analytical method must be used for the analysis of the test chemical in the test solutions or a statement from an analytical chemist must be provided in the study report to justify why lower detection limits (LOD) were not feasible (any preliminary analytical efforts should also be described in the report);
- provide evidence that exposure concentrations have been maintained throughout the test (within [redacted] % of the nominal or initial measured concentration).

The Substance can be considered poorly/sparingly water-soluble (1.7 µg/L), hydrophobic and adsorptive (reported Log Kow of 8.2), and it is therefore a 'difficult to test' substance.

You report that the test solutions were prepared by addition of the test substance to dilution water (100 mg/L), followed by ultrasonic treatment and stirring for 96 h and removal of solid components by filtration through a membrane fiber (pore size 0.45 µm). You have not provided any justification for the methods used to prepare the test solutions.

You have carried out analytical monitoring of the test concentrations with HPLC-UV-VIS method (limit of quantification (LOQ) = 0.05 mg/L). You do not provide the results of the analysis.

You have not justified nor demonstrated that the method applied in the aquatic toxicity test, including the use of filter as a separation method and stirring time of 96 h, allowed achieving maximum dissolved concentrations.

You have not reported the analytical monitoring results. However, ECHA notes that the analytical method used is not sufficiently sensitive since its limit of quantification (LOQ = 0.05 mg/L) was above the water solubility of the Substance (1.7 µg/L). You have not provided a justification why a lower LOQ was not feasible.

You have not provided any evidence that the exposure concentrations have been maintained.

Therefore, the information requirement is not fulfilled.

In your comments on the draft decision, you agree to conduct the requested test as specified in the decision.

Study design

The Substance is difficult to test due to the low water solubility, hydrophobicity, and adsorptive properties as explained above. OECD TG 201 specifies that for difficult to test substances, the OECD GD 23 is to be followed. To get reliable results, the substance properties need to be considered when performing the test, in particular with regard to the test design; including exposure system, test solution preparation, and sampling. OECD GD 23 (Table 1) describes testing difficulties related to a specific property of the substance. You may use the approaches described in OECD GD 23 or other approaches if more appropriate for your substance. The approach selected must be justified and documented.

Due to the substance properties it may be difficult to achieve and maintain the exposure concentrations. Therefore, you have to demonstrate that the concentration of the substance is stable throughout the test (i.e. measured concentrations remains within 80-120% of the nominal concentration). If it is not possible to demonstrate the stability, you must express the effect concentration based on measured values as described in the applicable test guideline. In case a dose-response relationship cannot be established (no observed effects), you must demonstrate that the test solution preparation method applied was sufficient to maximise the concentration of the Substance in the test solution.

2. The same long-term toxicity testing on aquatic invertebrates as requested in C.3.

Short-term toxicity testing on aquatic invertebrates is a standard information requirement in Annex VII Section 9.1.1. to REACH. However, according to Annex VII, section 9.1.1, column 2, for poorly water soluble substances (i.e. water solubility below 1 mg/L) long-term toxicity study on aquatic invertebrates (Annex IX, Section 9.1.5) must be considered instead of an acute test. Poorly water soluble substances require longer time to reach steady-state conditions and the short-term tests may not give a true measure of toxicity for this type of substances.

The Substance is poorly water soluble (water solubility 1.7 µg/L).

Therefore, long-term toxicity testing is needed to accurately define the hazard of the Substance.

The examination of the available information or adaptations, as well as the selection of the requested test and the test design are addressed in Appendix C, section 3-4. Your comments on the draft decision are also addressed in that section.

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

1. The same long-term toxicity testing on fish as requested in C.4.

Short-term toxicity testing on fish is a standard information requirement in Annex VIII Section 9.1.3.to REACH. However, according to Annex VIII, section 9.1.3, column 2, long-term toxicity study on fish (Annex IX, Section 9.1.6) must be considered instead of an acute test. Poorly water soluble substances require longer time to reach steady-state conditions and the short-term tests may not give a true measure of toxicity for this type of substances.

The Substance is poorly water soluble (water solubility 1.7 µg/L).

Therefore, long-term toxicity testing is needed to accurately define the hazard of the Substance.

The examination of the available information or adaptations, as well as the selection of the requested test and the test design are addressed in Appendix C, section 3-4.

Your comments on the draft decision are also addressed in that section.

2. The same soil simulation testing as requested in C.5. and

3. The same sediment simulation testing as requested in C.6.

and

4. Identification of degradation products as requested in C.7.

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 indicates the need for further degradation investigation, e.g. if the result of the screening tests or other information indicates that the substance is a potential PBT or vPvB (Section 4, Annex I and Sections 2.1 and 3.2, Annex XIII to REACH; see also ECHA Guidance R.11, Section R.11.4). This is the case if the Substance, a constituent, an impurity or a transformation/degradation product meets the following criteria:

- the Substance is potentially persistent or very persistent (P/vP), i.e. it is not readily biodegradable, and
- the Substance is potentially bioaccumulative or very bioaccumulative (B/vB), i.e. log Kow > 4.5.

Screening information provided in your dossier indicates that the Substance may have PBT/vPvB properties:

- the Substance is potentially P/vP since it is not readily biodegradable (0% degradation after 28 days in OECD TG 301 B)
- the Substance is potentially B/vB since the Log Kow is above the threshold of 4.5 (Log Kow > 8.2)

The available screening information is not sufficient to conclude on the P/vP properties of the Substance, therefore further testing is required.

The examination of the available information or adaptations, as well as the selection of the requested tests and the tests design are addressed respectively in Appendix C, Sections 5-7.

Your comments on the draft decision are addressed in Appendix C, Sections C.5-7.

5. The same bioaccumulation in aquatic species as requested in C.8.

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

Annex I, Section 4 requires that the CSA includes the PBT (persistent, bioaccumulative and toxic) and vPvB (very persistent and very bioaccumulative) assessments.
In accordance with Annex XIII, Section 2.1., if the result of the screening tests or other information indicate that the substance may have PBT or vPvB properties, further testing on bioaccumulation as set out in Section 3.2 is required. (See also ECHA Guidance R.11, Section R.11.4). This is the case if the substance, a constituent, an impurity or a transformation/degradation product meets the following criteria:

- the Substance is potentially persistent or very persistent (P/vP), i.e. it is not readily biodegradable, and
- The Substance is potentially bioaccumulative or very bioaccumulative (B/vB), i.e. log Kow > 4.5 .

Screening information provided in your dossier indicates that the Substance may have PBT/vPvB properties:

- the Substance is potentially P/vP since it is not readily biodegradable (0 % degradation after 28 days in OECD TG 301 B); and
- the Substance is potentially B/vB since the Log Kow is above the threshold of 4.5 (Log Kow > 8.2).

The available screening information is not sufficient to conclude on the B/vB properties of the Substance, therefore further testing is required.

The examination of the available information or adaptations, as well as the selection of the requested tests and the tests design are addressed respectively in Appendix C, Section 8.

Your comments on the draft decision are addressed in Appendix C, section 8.

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

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

A Sub-chronic toxicity study (90 day) is a standard information requirement in Annex IX Section 8.6.2. to REACH.

In your dossier you have provided:
(i) a Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test (OECD TG 422) conducted with the Substance ([redacted], 2013);
(ii) a 14-day dose range finding study conducted with the Substance ([redacted] 2013); and
(iii) an adaptation according to Column 2 of Annex IX, Section 8.6.2 based on the Substance being not absorbed and not bioavailable.

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

A. To be considered compliant and enable concluding whether the Substance has dangerous properties and supports the determination of the No-Observed Adverse Effect Level (NOAEL), a study has to meet the requirements of OECD TG 408. The key parameter of this test guideline include dosing of the Substance daily for a period of 90 days until the scheduled termination of the study.

The two studies ([redacted] 2013) you have provided have exposure durations of 28 and 14 days.

The key parameter of OECD TG 408 regarding the exposure duration of 90 days is not met.

Therefore, the provided studies do not fulfil the information requirement.

B. As provided in Annex IX, Section 8.6.2, Column 2, you may adapt the information requirement, provided you fulfil the following cumulative criteria: the Substance is unreactive, insoluble and not inhalable and there is no evidence of absorption and of toxicity in a 28-day 'limit test', particularly if it is coupled with limited human exposure.

You claim that the Substance *"is expected to be absorbed poorly and to be not bioavailable as demonstrated by the lack of systemic toxicity in several acute and subchronic toxicity studies."*

However, evidence of systemic responses to the Substance, and therefore of absorption, was observed in the Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test (OECD TG 422) conducted with the Substance and included in your dossier ([redacted], 2013). In the study, following treatment related effects were reported:
- male rats showed significantly higher absolute and relative liver weights compared to controls at high dose (1000 mg/kg bw/d);
- serum bilirubin was significantly increased in females at mid (250 mg/kg bw/d) and high dose groups and in males at high dose; and
- male rats showed increase in severity of kidney hyaline droplets with mid- and high dose groups above the background levels.

These observations constitute evidence of absorption of the Substance after oral administration.

In addition, you have reported widespread professional and consumer uses of the Substance as a lubricating agent in functional fluids, lubricants and greases. Based on this, the human exposure cannot be considered as limited.

Therefore, as cumulative conditions are not met, your adaptation is rejected.

Information on study design

Referring to the criteria provided in Annex IX, Section 8.6.2, Column 2, the oral route is the most appropriate route of administration to investigate repeated dose toxicity, because although the Substance is reported to occur as a dust with a significant proportion (>1% on weight basis) of particles of inhalable size (MMAD < 50 µm), the available oral study (i) indicate(s) a concern for systemic toxicity that requires further information on repeated dose toxicity by the oral route.

If a substance leads to kidney effects in male but not in female rats, this may be indicative of an alpha 2u-globulin-mediated nephropathy. Since this mode of action is not considered relevant to humans, the involvement of alpha-2u-globulin in the kidney effects is a key parameter for establishing the relevance of the kidney effects for human risk assessment.[2]

The study (i) provided showed dose-dependent increase in the kidney hyaline droplets in the kidneys of male rats but not in male control rats or in any exposed/control female rats.

This indicates that the kidney may be a target organ for the Substance and the effects on the kidney mediated by alpha 2u-globulin. Therefore, further specific investigations are necessary to investigate the kidney function after administration of the Substance and histopathological examination of the kidneys of all animals.

Therefore the sub-chronic toxicity study must be performed according to the OECD TG 408, in rats and with oral administration of the Substance. In addition, a urinalysis is required to investigate further the kidney function after administration of the Substance, and histopathological examination of the kidneys must include all animals in all dose groups with an additional immunohistochemical staining for alpha-2u globulin.

In your comments on the draft decision, you agree to conduct the requested test as specified in the decision.

2. Pre-natal developmental toxicity study in one species

A Pre-natal developmental toxicity (PNDT) study (OECD TG 414) in one species is a standard information requirement under Annex IX Section 8.7.2. to REACH.

In your dossier you have provided:

(i) a Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test (OECD TG 422) conducted with the Substance ([redacted], 2013); and

(ii) an adaptation according to Column 2 of Annex IX, Section 8.7 based on the Substance not expected to be systemically available..

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

[2] ECHA Guidance R.7a, Section R.7.5.6.3.4

A. To comply with this information requirement, the study must be an OECD TG 414 study.

The provided OECD TG 422 study is not the study required under REACH. In addition, the provided OECD TG 422 study does not address the key parameters of OECD TG 414, such as structural malformations and variations.

Therefore the information provided is rejected.

B. According to Annex IX, Section 8.7., Column 2, first paragraph, third indent, the study does not need to be conducted if the substance is of low toxicological activity. This needs to be demonstrated with three concomitant criteria, one of them being:
   - it can be proven from toxicokinetic data that no systemic absorption occurs via relevant routes of exposure.

You claim that the Substance is expected to be absorbed poorly and to be not bioavailable as demonstrated by the lack of systemic toxicity in several acute and subchronic toxicity studies. Also, you have not provided any toxicokinetic data.

However, as already explained in detail above (Appendix C.1.B) evidence of systemic responses to the Substance, and therefore of absorption, was observed in the Combined repeated dose toxicity study with the reproduction/developmental Toxicity screening test (OECD TG 422) conducted with the Substance and included in your dossier ([redacted], 2013).

These observations constitute evidence of absorption of the Substance after oral administration, and consequently the criteria for the adaptation are not fulfilled.

Therefore, your adaptation is rejected.

Information on study design

A PNDT study according to the test method OECD TG 414 must be performed in rat or rabbit as preferred species with oral[3] administration of the Substance.

In your comments on the draft decision, you agree to conduct the requested test as specified in the decision.

3-4. Long-term toxicity testing on aquatic invertebrates and Long-term toxicity testing on fish

Long-term toxicity testing on aquatic invertebrates and fish are standard information requirement in Annex IX, Sections 9.1.5. and 9.1.6.1. to REACH.

You have sought to adapt these information requirements based on column 2 of Annex IX, Section 9.1, based on the consideration that chemical safety assessment does not indicate a need for further testing.

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

As specified in Annex IX, Section 9.1., Column 2, long-term toxicity on both invertebrates and fish must be performed unless the chemical safety assessment demonstrates that risks

[3] ECHA Guidance R.7a, Section R.7.6.2.3.2.

towards the aquatic compartment arising from the use of the Substance are controlled (as per Annex I, section 0.1). The justification must be documented in the chemical safety assessment.

In particular, the chemical safety assessment must take into account all relevant hazard information from your registration dossier to support that long-term aquatic toxicity testing is not required:

- all relevant hazard information from your registration dossier,
- the outcome of the risk assessment in relation to the uses of the Substance,
- the outcome of the PBT/vPvB assessment including information on relevant degradation products and constituents present in concentration at or above 0.1% (w/w).

The hazard information must at least cover species of three trophic levels: algae/aquatic plants, invertebrates (Daphnia preferred), and fish.[4]

For poorly water soluble and hydrophobic substances, risks cannot be reliably assessed based on short term toxicity tests (i.e. to derive a reliable PNEC for this substance).[5] Such substances require longer time to be significantly taken up by the test organisms and as a consequence steady state conditions are likely not reached within the duration of a short-term toxicity test. For this reason, short-term tests may not give a true measure of toxicity for this type of substances and long-term effects cannot be excluded.

In your adaptation you consider that long-term toxicity studies are not needed since:

a) the data provided for the Substance show lack of acute adverse effects in aquatic organisms from all trophic levels;
b) the risk assessment shows that risks are controlled (RCRs<1);
c) there is no PBT nor vPvB concern.

a-b) Hazard assessment and risk assessment

Based on the information you provided, the Substance is poorly water soluble (water solubility 1.7 μg/L) and hydrophobic (log Kow 8.2).

You have provided short-term toxicity on fish and *Daphnia* studies and algae growth inhibition. You have not provided a long-term toxicity on *Daphnia* study nor a long-term toxicity on fish study.

As indicated above, short-term studies are, due to the properties of the Substance, insufficient to assess the risks.

Furthermore, as specified in request A.1, the data on algae growth inhibition is not compliant with the REACH relevant requirements.

Therefore, your dossier currently does not include adequate information to characterise the hazardous property of the Substance to aquatic organisms covering the three trophic levels.

c) PBT/vPvB assessment

The screening information provided in your dossier indicates that the Substance may have PBT/vPvB properties (ECHA Guidance R.11, Section R.11.4 and Annex XIII of REACH) as

[4] ECHA Guidance R.7b, Section R.7.8.5.3
[5] ECHA Guidance R.7b, Section R.7.8.4.3

explained in Appendix B, Sections 2-5.

Further testing is requested on the B/vB and P/vP properties of the Substance and on the degradation products, as described in Appendix C, Sections 5-8. Therefore, no definitive conclusion can be yet reached for PBT/vPvB assessment.

In conclusion, in absence of all this information, your chemical safety assessment does not demonstrate that the risks of the Substance are adequately controlled. As a consequence, your adaptations are rejected as they do not meet the specific rules for adaptation of Annex IX, Section 9.1., Column 2.

In your comments on the draft decision, you agree to conduct a Long-term toxicity testing on aquatic invertebrates (request C.3) as specified in the decision, but you propose a tiered testing approach to decide whether to conduct Long-term toxicity testing on fish (request C.4).

You indicate that you will first conduct the studies requested in A.1 (algae growth inhibition) and C.3. If these studies will show no toxicity in the range of solubility, you do not agree to perform Long-term toxicity testing on fish (request C.4).

ECHA notes that absence of chronic effects in *Daphnia* and algae is not a valid adaptation for the standard information requirement Long-term toxicity testing on fish.

Furthermore, as explained above, the Substance is poorly water soluble and the long-term fish study (request C.4) must be conducted since, due to Substance properties, chronic data are needed for three trophic levels. Therefore, your tiered approach is not acceptable.

Based on the above, the information requirements are not fulfilled.

Study design

The Substance is difficult to test due to the low water solubility, hydrophobicity, and adsorptive properties as explained above. OECD TG 211 and OECD TG 210 specify that for difficult to test substances, the OECD GD 23 is to be followed as explained above under request A.1.

5. Soil simulation testing and
6. Sediment simulation testing

Soil and sediment simulation testing are standard information requirements in Annex IX to REACH for substances with a high potential for adsorption to soil and sediment. The Substance has low water solubility (1.7 µg/L, high partition coefficient (log Kow 8.2) and high adsorption coefficient (log Koc 6.1), indicating high adsorptive properties.

You have sought to adapt these information requirements based on column 2 of Annex IX, Section 9.2. You consider that the chemical safety assessment does not indicate a need to investigate further the degradation of the Substance and its degradation products since the Substance is poorly biodegradable and therefore no relevant new findings are expected from more investigations.

As specified in Annex IX, section 9.2., Column 2, testing on degradation must be performed unless the chemical safety assessment demonstrates that risks arising from the use of the Substance are controlled (as per Annex I, section 0.1).

In particular according to Annex I elements to be taken into account for that demonstration include:

- PBT/vPvB assessment including information on constituents present in concentration at or above 0.1% (w/w) and on relevant degradation products.

The information provided in your dossier indicate that:

- the Substance is potentially P/vP since it is not readily biodegradable (0% degradation after 28 days in OECD TG 301B);
- the Substance is potentially B/vB since the Log K_{ow} is above the threshold of 4.5 (Log K_{ow} > 8.2).

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, Section 8 of this decision), and
- it is not possible to conclude on the toxicity of the Substance see Appendix C, Section(s) 3-4 of this decision).

Based on the above the Substance may have PBT/vPvB properties and therefore your CSA does not rule out the need to investigate further the degradation of the substance and its degradation products for the purpose of the PBT/vPvB assessment.

Therefore, your adaptation is rejected.

In your comments on the draft decision, you propose a tiered testing approach to decide whether to conduct the soil simulation testing (request C.5) and the sediment simulation testing (request C.6) specified in the decision.

You provide the following information for your approach:

A. you propose to adapt soil simulation testing (request C.5) and the sediment simulation testing (request C.6) by providing in your comments a QSAR prediction for biodegradation.

B. if the information provided under point A. is not sufficient to conclude reliably on persistence and degradation, you agree to conduct the soil simulation testing (request C.5) as specified in the decision. You further propose to adapt the sediment simulation testing (request C.6) if the soil simulation testing (request C.5) is sufficient to conclude reliably on persistence and degradation.

ECHA has assessed the information provided and has identified the following issue(s):

A. In your comments on the draft decision, for soil simulation testing (request C.5) and sediment simulation testing (request C.6) you have provided an adaptation according to Annex XI, Section 1.3 (QSAR) by submitting a QSAR prediction for biodegradation to conclude on P/vP for the Substance.

ECHA assessed this information and identified the following issue(s):

Under Section 1.3., first paragraph, third indent of Annex XI to REACH, a study may be omitted if QSAR results are adequate for the purpose of classification and labelling and/or risk assessment, including PBT assessment. Results obtained from biodegradation (Q)SAR models are only regarded as screening information on P/vP properties (Annex XIII, Section 3.1.). As further explained in ECHA Guidance R.11.4.1.1.4., such information is not considered sufficient on its own to conclude on persistence and must be supported by additional information (*e.g.* test data information, read-across).

In your dossier, you have provided the following QSAR prediction:

- Catalogic 301C v11.15, to predict the biodegradability of the Substance. The prediction showed a biodegradability of 1% after 28d.

Based on these QSAR results, you conclude that the Substance fulfills the screening criteria for P/vP.

You have not provided additional information to support this conclusion.

As explained above, the provided QSAR results alone do not provide a robust approach to conclude that the Substance does not meet the P/vP criteria and therefore are not adequate for PBT assessment.

Therefore, your adaptation based on Annex XI, Section 1.3 (QSAR) is rejected.

B. In your comments to the draft decision, you indicate the possibility to adapt sediment simulation testing (request C.6) if the results of the soil simulation testing (request C.5) are sufficient to conclude on P/vP.

As described above, sediment simulation testing is a standard information requirement at Annex IX of REACH for your Substance. This standard information requirement is separate and independent from simulation testing study in soil.

As explained above, the Substance is potentially P or vP, and further testing is needed to conclude on this property.

Accordingly, your adaptation arguments cannot be accepted.

Study design

OECD TG 307 and 308 are the appropriate methods for studying degradation in soil and sediment. Under Annex XIII, the information must be based on data obtained under conditions relevant for the PBT/vPvB assessment. Therefore in accordance with the respective TG's:

- You must perform the OECD TG 308 test using two sediments samples. One sediment test material should have a high organic carbon content (2.5-7.5 %) and a fine texture, the other sediment test material should have a low organic carbon content (0.5-2.5%) and a coarse texture. In case where a chemical may also reach marine water, at least one of the water-sediment systems should be of marine origin.

- You must perform the OECD TG 307 test using at least four soil samples representing a range of relevant soils (*i.e.* varying in their organic content, pH, clay content and microbial biomass).

- You must perform the test at the temperature of 12 °C, the average environmental temperature for the EU (ECHA Guidance R.16, Table R.16-8). Performing the tests at this temperature is in line with the applicable test conditions of the OECD TG 307 and TG 308.

- Non-extractable residues (NER) must be quantified in all simulation studies. The reporting of results must include a scientific justification of the used extraction procedures and solvents. By default, total NER is regarded as non-degraded Substance. However, if reasonably justified and analytically demonstrated a certain part of NER may be differentiated and quantified as irreversibly bound or as degraded to biogenic NER. Such fractions could be regarded as removed when calculating the degradation half-life(s) (ECHA Guidance Chapter R.11).

Furthermore, you must perform the test at the temperature of 12 °C, the average environmental temperature for the EU (ECHA Guidance R.16, Table R.16-8). Performing the tests at this temperature is in line with the applicable test conditions of the OECD TG 307 and TG 308.

In your comments on the draft decision you have requested to perform the simulations tests at the temperature of 20 °C inststead 12 °C. In support of your request you have provided the following justification: "*If degradation products have to be identified experimentally, a simulation degradation test at 12°C will underestimate the potential degradation products which could be formed in the environment. Therefore, an experimental study for identifying the degradation products should be performed at least at 20°C*".

As specified above and according to ECHA Guidance R.16, Table R.16-8, in order to determine the half life of the Substance the test must be conducted in relevant environmental conditions and must be performed at temperature of 12 °C. Nevertheless, if needed you may consider to conduct a parallel test at 20 °C to identify the degradation products.

7. Identification of degradation products

Identification of the degradation products is a standard information requirement at Annex IX of REACH.

You have adapted this information requirement under Annex IX, Section 9.2., Column 2.

To comply with this information requirement, you must identify the relevant transformation/degradation products of the Substance (ECHA Guidance R.11). This information requirement may be adapted under column 2 if:
- the substance is readily biodegradable (Annex IX, Section 9.2.3, Column 2) and/or
- the chemical safety assessment demonstrates and documents that risks arising from the Substance are controlled (Annex I, Section 0.1; Annex IX, Section 9.2, Column 2).

You justified the adaptation by stating that "*In accordance with Annex VIII, IX and X of Regulation (EC) No. 1907/2006 further biotic degradation tests shall be proposed if the result of the Chemical Safety Assessment according to Annex I indicates the need to investigate further the degradation of the substance and its degradation products. The test substance was found to be poorly biodegradable in an OECD 301B study. No biodegradation was observed after 28 d of exposure. Simulation biodegradation tests in soil are not proposed, since no relevant new findings are expected from such investigations*".

However, the Substance is not readily biodegradable, you have not supported your general statement above by any (valid and reliable) scientific evidence and the information is needed for the PBT/vPvB assessment and risk assessment, as already discussed in sections C.5, 6 above. Therefore, your adaptation is rejected.

In your comment on the draft decision, you agree to provide information on the identity of degradation products using the following approach:

A. you propose to adapt this information requirement by providing in your comments a QSAR prediction.

B. if the information provided under point A. is not sufficient to conclude reliably on this endpoint, you agree to obtain information on identity of degradation products by performing the simulations tests (requested in sections C.5 and C.6 above) at the temperature of 20 °C instead 12 °C.

ECHA has assessed the information provided and has identified the following issue(s):

A. In your comments on the draft decision, you have provided an adaptation according to Annex XI, Section 1.3 (QSAR) by submitting QSAR prediction models to identify the relevant degradation products.

ECHA assessed this information and identified the following issue(s):

Under Section 1.3., first paragraph, third indent of Annex XI to REACH, a study may be omitted if QSAR results are adequate for the purpose of classification and labelling and/or risk assessment, including PBT assessment. ECHA Guidance R.7.9.3.1. explains that qualitative information on the identity of transformation/degradation products may be obtained from a number of models and databases (e.g. EAWAG Database, KEGG databases, CATALOGIC). However, the guidance specifies that this information may only contribute as part of a Weight of Evidence assessment if other data are available (e.g. information from biodegradation screening studies, information on analogue substances).

Your comments to the draft decision provide information on putative transformation/degradation products using the following QSAR model:

- Catalogic 301C v11.15. In total 57 metabolites were identified by the model. Only 11 metabolites have been identified as relevant (logKow >= 4 and quantity >= 0.001 mol/mol parent) and for which you have estimated the BCF value. Based on the estimated BCF values, you concluded that none of them has a potential of bioaccumulation.

However, you have not provided any other data to support the identification of the transformation/ degradation products of the Substance.

As explained above, the provided QSAR results alone do not provide a robust approach to conclude on the identity of transformation/degradation products and therefore are not adequate for the risk assessment including the PBT assessment. Therefore, your adaptation based on Annex XI, Section 1.3 (QSAR) is rejected.

B. In your comments on the draft decision, you indicate your intention to identify the degradation products performing the simulation studies at a temperature of 20 °C instead of 12 °C as requested (requests C.5-6). ECHA agrees that simulation studies may be used to obtain information for this endpoint, but draws your attention to the assessment of your comments regarding the simulation tests and the temperature to be used (sections C.5 and C.6 above).

Therefore, the information provided does not fulfil the information requirement.

Study design

Regarding appropriate and suitable test method, the methods will have to be substance-specific. Identity, stability, behaviour, and molar quantity of the degradation/transformation products relative to the Substance must be evaluated and reported, when analytically possible. In addition, degradation half-life, log Kow and potential toxicity of the transformation/degradation may be investigated. You may obtain this information from the degradation studies also requested in this decision or by some other measure, under the conditions discussed above. If the any other method than the requested tests under sections C.5 and C.6 above is used for identification of the transformation/degradation products, you must provide a scientifically valid justification for the chosen method.

8. Bioaccumulation in aquatic species

Bioaccumulation in aquatic species, preferably fish is a standard information requirement at Annex IX of REACH.

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

a. A non-guideline experimental study via aqueous exposure ([redacted], 1984) entitled "*Bioconcentration test for chemical substances in fishery product in accordance with Notification of Kanpogyo No. 5, Yakuhatsu No. 615, Kikyoku No. 49-392*", and
b. An adaptation according to Annex XI, Section 1.3 (QSAR). You have provided in your dossier four QSAR predictions (Catalogic v5.11.2, T.E.S.T. v4.01, EPISuite v4.10, VEGA CAESAR v1.0.8) indicating a range of Log BCF values.

   In addition, in your comment on the draft decision you have provided three additional QSAR predictions (Meylan (regression) model from EPISuite; Arnot-Gobas model from EPISuite and BCF baseline model from CATALOGIC).

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

Annex XI, Section 1.2 states that there may be sufficient 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.4.4, a weight of evidence adaptation involves an assessment of the relative values/weights of 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 of the information for the given regulatory information requirement. Subsequently, relevance, reliability, 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 approach.

However, 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, a study must provide information on at least one of the following key parameters, obtained from an aquatic species and measured in whole body of the test organisms:

1. the uptake rate constant (k_1) and loss rate constants including the depuration rate constant (k_2),
2. the steady-state bioconcentration factor (BCF_{SS}),
3. the kinetic bioconcentration factor (BCF_K),
4. the dietary biomagnification factor (BMF).

Neither of the sources of information (a) and (b) provide information on key parameters (1), (3) or (4) above.

Concerning key parameter (2) the steady-state bioconcentration factor (BCF_{SS}):

The sources of information (a) and (b) may provide relevant information on steady-state bioconcentration factor (BCF_{SS}) .

However, the reliability of these sources of information is significantly affected by the following deficiencies:

A. Regarding source of information (a):

A study must fulfil the requirements of the corresponding OECD test guideline (Article 13(3) of REACH), in this case OECD TG 305. Therefore, the following requirements must be met:

Validity criteria

- Mortality or other adverse effects/disease in both control and test group fish is ≤ 10% at the end of the test;
- the concentration of the test substance must be maintained within ±20% of the mean measured value during the uptake phase;
- the concentration of the test substance must be below the reported limit of solubility in water;

Reporting of the methodology and results

- The lipid content measured at least before the beginning and at the end of the uptake phase and the method used for its determination are reported;
- Tabulated test substance concentration data in individual fish and water (including mean values for test group and control, standard deviation and range, if appropriate) for all sampling times are reported;
- Curves showing the parameters indicated in OECD TG 305 and the steady-state bioconcentration factor (BCF_{SS}) if is achieved in the test.

The content of the dossier regards the validity criteria:

- you have not provided the analytical monitoring of exposure concentration,
- you have not provided information on the mortality in both control and treated fish,
- the test substance concentrations were 0.1 and 1 mg/L.

In consequence, the validity criteria are not met, as:
- you have not demonstrated that the variation of the test substance has been maintained within ±20% during the uptake phase,
- you have not demonstrated that the mortality or other adverse effects have not exceeded 10% at the end of the test.
- The test substance concentrations were above its water solubility limit (0.0017 mg/L);

Furthermore, you have not reported the mandatory information from the OECD TG 305 (as specified above) regarding the methodology and results. Therefore ECHA is not in position to assess the reliability of the study.

Therefore, as the validity of the study provided is affected, it cannot be considered a reliable source of information that could contribute to the conclusion on the steady-state bioconcentration factor (BCF_{SS}).

B. Regarding source of information (b):

Annex XI, Section 1.3. states that results obtained from valid QSAR models may be used instead of testing when the following cumulative conditions are met, in particular:

1. results are derived from a QSAR model whose scientific validity has been established;
2. the substance falls within the applicability domain of the QSAR model;
3. adequate and reliable documentation of the applied method is provided; and
4. the results are adequate for classification and labelling and/or risk assessment.

According to ECHA's Practical guide "How to use and report (Q)SARs", section 3.4, a QSAR Model Reporting Format (QMRF)[6] and a QSAR Prediction Reporting Format (QPRF)[7] are required to establish the scientific validity of the model, to verify that the Substance falls within the applicability domain of the model, and to assess the adequacy of the prediction for the purposes of classification and labelling.

In support of your adaptation you have provided in your dossier a range of BCF values which were calculated using four QSAR models:

i. BCF of 209 L/kg; predicted by Catalogic v5.11.2
ii. BCF of 1418 L/kg; predicted by T.E.S.T. v4.01
iii. BCF of 452-637-707-2576-3321 L/kg predicted by EPISuite-BCFBAF model (AG-upper-trophic; AG-mid-trophic; AG-lower trophic; AG-no biotransf and Meylan; respectively)
iv. BCF of 90 L/kg predicted by VEGA CAESAR v1.0.8

In your comments on the draft decision you have provided additional BCF predictions which were calculated using the following models:

v. Meylan (regression) model from EPISuite indicating a BCF value of 3320 L/kg;
vi. Arnot-Gobas model from EPISuite indicating a range of Log BCF 1187-1952 L/kg for different trophic levels
vii. BCF baseline model from CATALOGIC indicating a BCF value of 195 L/kg (taking into account mitigating factors).

[6] ECHA Guidance R.6, Section R.6.1.9
[7] ECHA Guidance R.6, Section R.6.1.10

For the models listed from "i" to "iv", you have not provided any documentation for the QSAR prediction. In particular, you have not included a QMRF and/or a QPRF in your technical dossier.

In the absence of any documentation, you have not established whether the model is scientifically valid and whether the Substance falls within the applicability domain of the model.

In addition, for the models listed from "i" to "iv", your predictions do not cover all the constituents of the Substance. In particular, based on the data provided in your dossier (IUCLID section 1.1 and 1.2) the Substance can have four different structures depending on the position of the alkyl chain:

- If the alkyl chain is on the phenyl ring, there are three different possible structures:
    1. <u>Para</u> position corresponding to the following SMILES CC(C)(C)CC(C)(C)c1ccc(Nc2cccc3ccccc23)cc1;
    2. <u>Meta</u> position corresponding to the following SMILEs CC(C)(C)CC(C)(C)c1cccc(Nc2cccc3ccccc23)c1;
    3. <u>Orto</u> position corresponding to the following SMILES CC(C)(C)CC(C)(C)c1ccccc1Nc1cccc2ccccc12
- If the alkyl chain is on the amine ring, the structure is corresponding to the following SMILES
    4. CC(CC(C)(C)C)(C)N(c1(ccccc1))c3(c2(c(cccc2)ccc3

For the models listed from "i" to "iv", you have provided the results of QSAR predictions covering a range of BCF values (from 90-3321 L/ kg). We were able to reproduce these results using as input the CAS number of the Substance (CAS no 51772-35-1). The results obtained are covering only the structure that has the alkyl chain on the amine ring (cf. SMILES CC(CC(C)(C)C)(C)N(c1(ccccc1))c3(c2(c(cccc2)ccc3). However you have not provided any information/justification regarding the others structures (para-, meta- and ortho-positions). Based on predictions using the three possible structures, the results showed that the predicted BCF values calculated from Meylan model and the Arnot-Gobas (without taking into account metabolism) are similar than those reported in your dossier.

Regarding the others models (i.e. AG-lower trophic; AG-mid trophic and AG-upper trophic), you have reported a range of BCF values (707, 637 and 452 L/kg respectively). Using the SMILES formula of the three possible stereoisomers, BCF values of 1952, 1739 and 1187 L/kg were obtained which are higher than those reported in your dossier. In addition taking into account the uncertainty of the prediction obtained from the model, these predicted values do not support that the Substance has low potential for bioaccumulation in aquatic species. In particular, regarding the results obtained from the Arnot-Gobas model for which the value is very close to the bioaccumulation threshold of 2000 L/kg.

As the predictions that you have provided from different models (listed from "i" to "iv") are not covering all the constituents of the registered Substance, consequently the results are not adequate for the purpose of risk assessment.

Regarding the additional predictions provided in your comments (models listed from "v" to "vii" above), you have reported the SMILES formula that was used to predict the BCF values. Based on that, ECHA was able to reproduce the prediction and found that the reported prediction provided from the model "vii" (CATALOGIC model) cannot be used for the following reasons:

- The Substance is out of the applicability domain, in particular one fragment is classified as incorrect by the model, therefore the criterion 2 is not met.

- Furthermore, regarding the metabolism predicted by the model, the Substance undergoes two transformations and none of them is considered as reliable by the model (one has a reliability of 0%, the other "not assessed"). In conclusion, the results are not adequate for the purpose of risk assessment.

In addition taking into account the outcomes provided from different models (listed from "*i*" to "*vii*"), the range of the BCF values is highly fluctuating (from 90 to 3320 L/kg) and therefore the results obtained are contradictory and inconclusive.

Therefore, as the criteria specified in Annex XI, Section 1.3. are not met, the predictions provided cannot be considered a reliable source of information that could contribute to the conclusion on the steady-state bioconcentration factor (BCF_{SS}).

Taken together, even if the sources of information (a) and (b) may provide information on one of the key parameters necessary to be investigated for this information requirement (the steady-state bioconcentration factor (BCF_{SS})), their reliability is affected significantly.

Accordingly, it is not possible to conclude, based on any source of information alone or considered together, whether your Substance has or has not the particular property foreseen to be under the corresponding endpoints. Therefore, your adaptation is rejected.
Study design

Bioaccumulation in fish: aqueous and dietary exposure (test method EU C.13. / OECD TG 305) is the preferred test to investigate bioaccumulation (ECHA *Guidance, Chapter R.7c, R.7.10.3.1)*. Whenever technically feasible, the aqueous route of exposure (OECD TG 305-I) must be used as the results obtained can be used directly for comparison with the B and vB criteria of Annex XIII of REACH. If testing through aquatic exposure is technically not possible, you must provide scientifically valid justification for the infeasibility. In case you conduct the study using the dietary exposure route (OECD 305-III), you must also attempt to 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. In any case you must report all data derived from the dietary test as listed in the OECD TG 305-III.

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[8].

B. Test material

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

1. Selection of the Test material(s)

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

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

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

Technical instructions on how to report the above is available in the manual on How to prepare registration and PPORD dossiers[9].

---

[8] https://echa.europa.eu/practical-guides
[9] 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

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 2 September 2019.

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

ECHA took into account your comments and did not amend the requests.

Deadline to submit the requested information in this decision

In the draft decision communicated to you, the time indicated to provide the requested information was 33 months from the date of adoption of the decision. In your comments on the draft decision you asked ECHA to extend the standard granted time to a total 45 months based on additional 9 months required for the ecotoxicity tests due to the anticipated delays with testing laboratories and based on extra time needed to ensure adequate time to conduct the aquatic toxicity, simulation and bioaccumulation studies. For these studies, you indicate that extra time is needed for technical difficulties for difficult to test items, for the synthesis of the radioactive test material (6 months), and for the update of the CSA and registration dossier.

Based on the documentary evidence from the laboratory provided in your comments to the draft decision and balancing all arguments brought forward, ECHA believes that a total of 9 additional months are sufficient to enable performing and submitting the studies.

Therefore, ECHA has only partially granted the request and set the deadline to 42 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[10] 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)[11]

RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017)[11]

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[12]

10 https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
11 https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across
12 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 the corresponding information requirements applicable to them

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]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]		
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

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