~~Confidential~~

Helsinki, 21 October 2020

Addressees
Registrant of JS_[redacted] as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
09/04/2018

Registered substance subject to this decision ("the Substance")
Substance name: Dimethylcyclohex-3-ene-1-carbaldehyde
EC number: 248-742-6
CAS number: 27939-60-2

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 ***28 April 2022***.

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

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

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

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

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

1. Short-term repeated dose toxicity (28 days) (Annex VIII, Section 8.6.1.; test method: EU B.7./OECD 407) by oral route, in rats, modified to include urinalysis and immuno-histochemical investigation of renal pathology allowing the determination of whether the pathology is mediated by alpha-2u globulin nephropathy.

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

3. Simulation testing on ultimate degradation in surface water (triggered by Annex VIII, Section 9.2.; test method: EU C.25./OECD TG 309) at a temperature of 12 °C

4. Identification of degradation products (triggered by Annex VIII, Section 9.2; test method: using the simulation test method requested under Section B.3

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

- Appendix entitled "Reasons common to several requests";
- Appendix/Appendices entitled "Reasons to request information required under

Annexes VII to VIII of REACH", respectively.

Information required depends on your tonnage band

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

How to comply with your information requirements

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

You must follow the general testing and reporting requirements provided under the Appendix entitled "Requirements to fulfil when conducting and reporting new tests for REACH purposes". 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".

Appeal

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

Failure to comply

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

Authorised[1] under the authority of Christel Schilliger-Musset, Director of Hazard Assessment

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

Appendix on Reasons common to several requests

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

You have adapted the following standard information requirements by applying a read-across approach in accordance with Annex XI, Section 1.5:

- Short-term repeated dose toxicity (28 day), (Annex VIII, Section 8.6.1.)
- Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.)
- Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.)
- Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.)

ECHA has considered the scientific and regulatory validity of your read-across approach in general before assessing the specific standard information requirements in the following appendices.

Grouping of substances and read-across approach

Annex XI, Section 1.5. specifies two conditions which must be fulfilled whenever a read-across approach is used. Firstly, there needs to be structural similarity between substances which results in a likelihood that the substances have similar physicochemical, toxicological and ecotoxicological properties so that the substances may be considered as a group or category. Secondly, it is required that the relevant properties of a substance within the group may be predicted from data for reference substance(s) within the group (addressed under 'Assessment of prediction(s)').

Additional information on what is necessary when justifying a read-across approach can be found in the ECHA Guidance[2] and related documents[3, 4].

A. Predictions for toxicological properties

You have provided a read-across justification in the endpoint summary record of Section 7.5 in IUCLID.

You read-across between the structurally similar substance Reaction mass of 3,5-dimethylcyclohex-3-ene-1-carbaldehyde and 2,4-dimethylcyclohex-3-ene-1-carbaldehyde, EC No. 943-728-2 as source substance and the Substance as target substance.

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

- The Substance and the selected analogue have similar structure: "[They] *both have di-methyl-cyclohexene backbone with an aldehyde function which is not alpha-beta conjugated with the double bond in the ring*". "[For the Substance], *the methyl groups are attached at the 3,6 or the 4,6 position*". "[For the source substance], *the methyl groups* [are] *at the 2,4 or the 3,5 positions*";
- The Substance and the selected analogue have similar physico-chemical properties (*e.g.* Log Kow);

[2] Guidance on information requirements and chemical safety assessment Chapter R.6: QSARs and grouping of Chemicals. 2008 (May) ECHA, Helsinki. 134. pp. Available online: https://echa.europa.eu/documents/10162/13632/information_requirements_r6_en.pdf/77f49f81-b76d-40ab-8513-4f3a533b6ac9

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

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

- You assume that the Substance and the source substance have similar ADME properties as they have "*almost the same molecular structure, weight and similar physico-chemical properties*";
- You assume similar toxicological properties as:
  - "[The] *position of the methyl group is predicted to have no effect on reactivity and therefore the toxicological profile (OECD toolbox)*";
  - you consider that the similar skin sensitization potential of both substances supports similar reactivity;
  - *"An oral reproductive/developmental toxicity screening test (OECD TG 421) is available for* [the Substance]*, in which similar effects are observed as* [the source substance] *in the OECD TG 407 study"*.

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

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

Missing supporting information

Annex XI, Section 1.5 of the REACH Regulation states that "*physicochemical properties, human health effects and environmental effects or environmental fate may be predicted from data for reference substance(s)*". For this purpose "*it is important to provide supporting information to strengthen the rationale for the read-across*". The set of supporting information should allow to verify the crucial aspects of the read-across hypothesis and establish that the properties of the Substance can be predicted from the data on the source substance.

As indicated above, your read-across hypothesis is based on the assumption that the structurally similar substances cause the same type of effect(s). In this context, relevant, reliable and adequate information allowing to compare the properties of the Substance and of the source substance is necessary to confirm that both substance cause the same type of effects. Such information can be obtained, for example, from bridging studies of comparable design and duration for the Substance and of the source substance.

You have provided a screening study for reproductive/developmental toxicity on the Substance with the following observations:

- liver and kidney weights increased in the high-dose group (*i.e.* 500 mg/kg/day) in males and at the mid- and high-dose groups in females;
- in 6/12 males from the high-dose group, a treatment-related increase of accumulation of hyaline droplets in tubular epithelial cells in the outer cortex of the kidneys was observed, accompanied by degenerative changes. Immunohistochemical staining did not allow identifying the hyaline droplets as α2μ-globulin.

You have also provided a short-term (28 days) repeated-dose toxicity study on the source substance with the following observation:

- minimal hypertrophy of the centrilobular hepatocytes were observed in the high-dose group (*i.e.* 750 mg/kg bw/day) of both sexes;
- in males, minimal to mild hyaline droplet in proximal tubular epithelium was observed from the mid- and high-dose groups. Accumulation of α2μ-globulin was confirmed by immunohistochemical staining;
- liver and kidney effects were reversible by the end of the recovery period.

You consider these observations as sufficient bridging information to demonstrate that

the Substance and the source substance cause the same type of effects.

In your comments to the draft decision you also provided two tables to show more explicitly 1) the profiling results of the OECD Toolbox to support the same mode of action between the two substances; and 2) the quantitative similar increases in relative liver and kidney weights noted in the studies with the source and target substances. Moreover, you indicated that the requirement of bridging information "*for the read across of sub-acute repeated dose toxicity is not transparently presented in the Regulation or ECHA guidance.*"

Firstly we note that, based on the Read-across assessment framework (RAAF - considerations on multiconstituent substances and UVCBs), bridging studies allow side-by-side comparison of the substances for a particular property that may enable the demonstration that two multi-constituent substances or UVCBs have similar properties for a particular endpoint, and thus play a key role in a read-across justification. In the absence of such an empirical demonstration, read across cannot be demonstrated with sufficient reliability for complex compositions.

You only provided a screening study for reproductive/developmental toxicity according to OECD TG 421 with the source substance. This OECD TG 421 study cannot be regarded as adequate information allowing to compare the properties of the Substance and of the source substance for short-term repeated dose toxicity because it provides no information on haematology or clinical chemistry, urinalysis or behavioural effects. Furthermore, it does not provide a sufficient coverage of key organs and tissues as only kidneys, liver, gastro-intestinal tract and the thyroid gland were subject to gross pathology.

In addition, while "*quantitative similar increases in relative [...] kidney weights*" and similar gross lesions were observed on kidneys in both studies, it remains unclear if the effects noted result from the same mode of action. In the study on the Substance the hyaline droplets were not identified as α2μ-globulin, contrary to the study on the source substance. The information provided in your comments (i.e., 1) OECD toolbox profiling and 2) effects on liver and kidneys) do not clarify if the source and target substances have the same mode of action. Furthermore, the reversibility of the effects was not evaluated in the screening study for reproductive/developmental toxicity on the Substance.

Based on the above, there are no relevant, reliable and adequate information that allow the comparison of the properties of the Substance and of the source substance for short-term repeated dose toxicity. Therefore, you have not provided sufficient supporting information, neither in the dossier nor in your comments, to strengthen the rationale for the read-across.

B. Predictions for ecotoxicological properties

You have provided a read-across justification in the endpoint summary record of Section 6.1 in IUCLID.

You read-across between the structurally similar substance Reaction mass of 3,5-dimethylcyclohex-3-ene-1-carbaldehyde and 2,4-dimethylcyclohex-3-ene-1-carbaldehyde, EC No. 943-728-2 as source substance and the Substance as target substance.

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

- as already explained under Section A. above, you state that the Substance and the selected analogue have similar structure and physico-chemical properties (*e.g.* Log Kow);
- you assume that the Substance and the selected analogue have similar "*bioavailability*

because they have a similar chemical structure, the same molecular weight and similar physico-chemical properties";

- you assume that the Substance and the selected analogue have similar reactivity because the only difference in their structure is the position of methyl groups.

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

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

Missing supporting information

Annex XI, Section 1.5 of the REACH Regulation states that "*physicochemical properties, human health effects and environmental effects or environmental fate may be predicted from data for reference substance(s)*". For this purpose "*it is important to provide supporting information to strengthen the rationale for the read-across*". The set of supporting information should allow to verify the crucial aspects of the read-across hypothesis and establish that the properties of the Substance can be predicted from the data on the source substance.

As indicated above, your read-across hypothesis is based on the assumption that the structurally similar substances cause the same type of effect(s). In this context, relevant, reliable and adequate information allowing to compare the properties of the Substance and of the source substance is necessary to confirm that both substance cause the same type of effects. Such information can be obtained, for example, from bridging studies of comparable design and duration for the Substance and of the source substance.

You have not provided any information on the toxicity of the Substance to aquatic organisms. Therefore, data set reported your dossier does not include such relevant, reliable and adequate information on the Substance and on the source substance to support your read-across hypothesis.

In your comments on the draft decision, you provide further justification for the read-across including 1) a summary table of ECOSAR predictions for fish, Daphnia and algae for the Substance and the selected analogue substance, 2) the profiling results of the OECD Toolbox to support the same mode of action between the two substances, and a statement that both substances belong to the same Verhaar class (class 3), are assigned to the group "aldehydes" using MOA in Oasis and to the class "mono aldehydes" by ECOSAR. You also consider that the differences in reported log Kow values between the Substance and the source substance is due to experimental variability and that, as the difference in only "*0.4 log Kow units this will have minor effect on the aquatic toxicity*". You conclude that "*further testing on acute aquatic toxicity would not lead to different results as those derived from* [the selected analogue]"

As already explained under A. above, bridging studies allowing side-by-side comparison of multi-constituent substances or UVCBs are key to enable the demonstration that they have similar properties for a particular endpoint.

In the absence of such information, you have not established that the properties of the Substance can be expected to be quantitatively equal to those of the selected source substance for the prediction of the properties under consideration. Therefore, you have not provided sufficient supporting information to strengthen the rationale for the read-

across.

C. Conclusions on the read-across approach

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

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

1. Short-term toxicity testing on aquatic invertebrates

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

You have adapted this information requirement under Section 1.5, Annex XI to REACH using an OECD TG 202 study with the analogue substance Reaction mass of 3,5-dimethylcyclohex-3-ene-1-carbaldehyde and 2,4-dimethylcyclohex-3-ene-1-carbaldehyde, EC No. 943-728-2.

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

Therefore, the information requirement is not fulfilled.

Study design
The substance is difficult to test due to its Henry's Law constant of 20.8 Pa.m^3/mole (predicted by HENRYWIN v3.20 in EPI SUITE). OECD TG 202 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 202. 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 solutions.

2. Growth inhibition study aquatic plants

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

You have adapted this information requirement under Section 1.5, Annex XI to REACH using an OECD TG 201 study with the analogue substance Reaction mass of 3,5-dimethylcyclohex-3-ene-1-carbaldehyde and 2,4-dimethylcyclohex-3-ene-1-carbaldehyde, EC No. 943-728-2.

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

Therefore, the information requirement is not fulfilled.

Study design
As already explained in Section A.1, the substance is difficult to test. 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, as already described under Section A.1.

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

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

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

You have provided the following information:

i. OECD TG 421 study with the Substance;
ii. an adaptation under Section 1.5, Annex XI to REACH using an OECD TG 407 study with the analogue substance Reaction mass of 3,5-dimethylcyclohex-3-ene-1-carbaldehyde and 2,4-dimethylcyclohex-3-ene-1-carbaldehyde, EC No. 943-728-2.

We have assessed this information and identified the following issues:

A. To fulfil the information requirement, a study must comply with the requirements of OECD TG 407 (Article 13(3) of REACH), which include:
   - haematological examination made at the end of the test period (including at least haematocrit, haemoglobin concentrations, erythrocyte count, reticulocytes, total and differential leucocyte count, platelet count and a measure of blood clotting time/potential);
   - clinical biochemistry determinations on blood samples obtained of all animals at the time of euthanasia (including at least include sodium, potassium, glucose, total cholesterol, urea, creatinine, total protein and albumin, at least two enzymes indicative of hepatocellular effects (such as alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, γ-glutamyl trans-peptidase and glutamate dehydrogenase), and bile acids);
   - full histopathology of all preserved tissues (*i.e.* all gross lesions, brain, spinal cord, eye, stomach, small and large intestines, liver, kidneys, adrenals, spleen, heart, thymus, thyroid, trachea and lungs, gonads, accessory sex organs (uterus and cervix, epididymides, prostate and seminal vesicles with coagulating glands), vagina, urinary bladder, lymph nodes, peripheral nerve, skeletal muscle and bone with bone marrow) of all animals in the control and high dose groups. These examinations must be extended to animals of all other dosage groups, if treatment-related changes are observed in the high dose group.

   The study i. on the Substance you have provided cannot be considered equivalent to an OECD TG 407, since it provides no haematological examinations, clinical biochemistry determinations and an incomplete coverage of histopathological observations (only the liver, kidneys and reproductive organs were investigated.

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

Therefore, the information requirement is not fulfilled.

Study design

Referring to the criteria in Annex VIII, Section 8.6.1, Column 2, the oral route is the most appropriate route of administration to investigate repeated dose toxicity. The Substance is a water soluble liquid of very low vapour pressure (0.0661 kPa). Therefore the sub-acute toxicity study must be performed according to the OECD TG 407, in rats and with oral administration of the Substance.

Additional parameters

The OECD TG 421 study on the Substance you submitted in your dossier showed that adverse effects such as hyaline droplets in tubular epithelial cells in the outer cortex of the kidneys accompanied by degenerative changes (at 500 mg/kg bw/day) were observed in the kidneys of male rats but not in female rats.

This indicates that the kidney is a target organ of the Substance which may induce alpha-2u-globulin-mediated nephropathy. Since this mode of action is considered not 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 risk assessment.

Therefore, although optional (as per paragraph 35 of OECD TG 407), a urinalysis is required to investigate further the kidney function after administration of the Substance. Additionally, a full histopathological examination (paragraphs 43 and 47 of OECD TG 407), including immune-histochemical investigation of renal pathology is required to determine if the pathology is mediated by alpha-2u globulin.

2. Short-term toxicity testing on fish

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

You have adapted this information requirement under Section 1.5, Annex XI to REACH using an OECD TG 203 study with the analogue substance Reaction mass of 3,5-dimethylcyclohex-3-ene-1-carbaldehyde and 2,4-dimethylcyclohex-3-ene-1-carbaldehyde, EC No. 943-728-2.

However, for the reasons explained in the Appendix on Reasons common to several requests, your adaptation is rejected.

Therefore, the information requirement is not fulfilled.

Study design

As already explained in Section A.1, the substance is difficult to test. OECD TG 203 specifies that, for difficult to test substances, you must consider the approach described in OECD GD 23 or other approaches, if more appropriate for your substance, as already described under Section A.1.

3. Simulation testing on ultimate degradation in surface water

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

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

- the Substance is potentially persistent or very persistent (P/vP) if, for instance:
  - it is not readily biodegradable (*i.e.* <60/70% degradation in an OECD 301D);

- the Substance is potentially bioaccumulative or very bioaccumulative (B/vB) if, for instance:
  - it has a high potential for bioaccumulation in air-breathing organisms (log K_{ow} >2 and log K_{oa} >5);
- the Substance is potentially toxic (T) if, for instance:
  - its lowest effect value in short-term aquatic toxicity test (*i.e.* E(L)C_{50}) is < 0.1 mg/L.

The information provided in your dossier indicates that:

- the Substance is potentially P/vP since it is not readily biodegradable (4 % degradation after 28 days in OECD TG 301D);
- the Substance is potentially B/vB in air-breathing organisms since the Log K_{ow} is above the threshold of 2 (Log K_{ow} = 3.1 based on OECD TG 117) and K_{oa} is above the threshold of 5 (Log K_{oa} = 5.134 ± 0.526 as predicted by KOAWIN v1.10 using the water solubility and vapour pressure estimates reported in your dossier);
- it cannot be excluded that the Substance is potentially T as, for the reasons explained under Sections A.1-2 and B.2, the information requirements for short-term toxicity to aquatic organisms are not fulfilled.

In your comments on the draft decision, you have attached a robust study summary for an OECD TG 301C study on the Substance. The study showed now mineralisation of the test material. However, you consider that this study indicates that the Substance is subject to rapid primary degradation and that therefore it does not meet the P/vP criteria. You further claim that bioaccumulation in air-breathing organisms is not relevant for metabolizing substances and you provided a statement that "*BCFBAF predicts a half-life of 1.1 day and* [redacted] *of 1.6 days* [for the Substance]". You further explain that "[the Substance] *is a small oxygen containing hexylcyclic alkene- aldehyde (non-conjugated). The aldehyde functionality is somewhat reactive. The degradation or metabolisation of* [redacted] [...] *will be due to oxidation or reduction of the aldehyde into an acid or an alcohol* [...]. *This transformation is expected to occur in all (air-breathing) organisms.* [redacted]*-acid and –alcohol fulfil the same criteria as* [redacted] *as presented in* [redacted] *(2020) for non bioaccumulation in air-breathing organisms because these are oxygen containing substances and are excreted via the kidneys*". Finally, you consider that based on available evidence from your registration dossier, the Substance does not meet the T criterion.

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

A. Information provided to support that the Substance is not P/vP

Information from a reliable ready biodegradability studies may be used to provide information on primary biodegradation and, if the primary half-life of the substance is determined to be < 40 days, to conclude that the parent substance is not P/vP (ECHA Guidance R.11.4.1.1.3. and R.11.4.2.1.1.). When the mineralisation half-life for the whole system is not below the P criterion, a full mass balance of the substance and any degradation/transformation must be determined.

In your comments on the draft decision, you have provided a robust study summary for an OECD TG 301C study on the Substance showing the following:

- The initial test material concentration in the test vessels was 100 mg/L. However, you report that the theoretical amount of the test material at the end of the test is 30.2 mg/L;
- The measured concentration of the test material in the control vessel containing only water and the test item was 26.3 mg/L after 28 days (as determined by a

specific analytical method);
- The measured concentration of the test material in the test vessels containing the inoculum and the test item was c.a. 4 mg/L in average after 28 days (as determined by a specific analytical method);
- You report that "*the amount of each degradants could not be quantified*".

Based on the above, the provided robust summary includes inconsistencies that affect significantly the interpretation of the study results. In particular, you report that the theoretical test material concentration at the end of the test is 30.2 mg/L while the initial test concentration was 100 mg/L. Furthermore, as i) the amounts of degradation/transformation products were not quantified and ii) no information is provided on potential abiotic losses (e.g. by volatilisation or absorption), it is not possible to determine full mass balance of the substance and any degradation/ transformation. Therefore, this study does not provide reliable evidence that the primary half-life of the Substance is < 40 days and this information is rejected.

B. Information provided to support that the Substance is not B/vB

As explained in ECHA Guidance R.11.4.1.2.10, in case a substance screens to be potentially bioaccumulative in air-breathing organisms, further information and potentially further assessment on bioaccumulation in air-breathing organisms may be necessary. This may include monitoring data, mammalian toxicokinetics data and other information for air-breathing organisms.

In your comments on the draft decision, you have provided a statement that the BCFBAF model predicts rapid biotransformation in fish with no further documentation. You state that the Substance and its potential degradation/transformation products are "*oxygen-containing substances and are excreted via the kidneys*". You have not provided any monitoring data or mammalian toxicokinetics data to support that bioaccumulation in air-breathing organisms is unlikely.

Firstly, we note that you have not provided any documentation for the prediction of the biotransformation half-life in fish from the BCFBAF model and therefore an independent assessment of this information is not possible. Secondly, this prediction does not inform on the biotransformation rate in air-breathing organisms. It should also be noted that there is no universal threshold for elimination processes in the context of the B-assessment which would cover all (aquatic/terrestrial -water breathing/air breathing) organisms because the elimination rate depends on several factors (e.g. species). Finally, you have not provided any experimental evidence that rapid excretion through kidneys does occur. Therefore, the information from your comments on the draft decision does not provide reliable evidence that bioaccumulation in air-breathing organisms is unlikely.

C. Information provided to support that the Substance is not T

For the reasons explained in Appendices A1-2 and B1-2, your registration dossier does not include reliable information on aquatic toxicity and repeated-dose toxicity. Therefore, it cannot be excluded that the Substance might meet the screening criteria for T.

Based on the above the Substance may have PBT or vPvB properties and therefore further information on biodegradation must be provided.

Therefore, the information requirement is not fulfilled.

Study design

Under Annex XIII, the information must be based on data obtained under conditions relevant for the PBT/vPvB assessment. Therefore:

- You must perform the OECD TG 309 test, by following the pelagic test option with natural surface water containing approximately 15 mg dw/L of suspended solids (acceptable concentration between 10 and 20 mg dw/L) (ECHA Guidance R.11).

- The required temperature of 12 °C is 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 309.

- As specified in ECHA Guidance R.7.9.4.1, the organic carbon (OC) concentration in surface water simulation tests is typically 2 to 3 orders of magnitude higher than the test substance concentration and the formation of NERs may be significant in surface water tests also. Therefore, as for soil and sediments simulation tests, the NERs should be quantified and the extraction procedure and solvent used should be explained and scientifically justified. 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).

4. Identification of degradation products

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

As already explained under Section B.3, the Substance is a potential PBT/vPvB substance. Therefore, the chemical safety assessment (CSA) indicates the need for further degradation investigation.

You have not provided information on the identity of transformation/degradation products for the Substance.

As explained in Appendix B.3 above, you have attached a robust study summary for an OECD TG 301C study on the Substance in your comments to the draft decision. In this study, the identity of some metabolites formed in the course of the experiment is provided. You consider that this information is adequate to meet the information requirement.

However, for the reasons explained in Appendix B.3 this information is unreliable and cannot therefore change the finding that the information requirement is not fulfilled.

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 simulation study also requested in this decision or by some other measure. If any other method than the test requested under Section B.3 is used for identification of the transformation/degradation products, you must provide a scientifically valid justification for the chosen method.

To determine the degradation rate of the Substance, the requested study according to OECD TG 309 (Section B.3) must be conducted at 12°C and at a test concentration < 100 µg/L. However, to overcome potential analytical limitations with the identification and quantification of major transformation/degradation products, you may consider running a parallel test at higher temperature (but within the frame provided by the test guideline, *e.g.* 20°C) and at higher application rate (*i.e.* > 100 µg/L).

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

A. Test methods, GLP requirements and reporting

1. Under Article 13(3) of REACH, all new data generated as a result of this decision must be conducted according to the test methods laid down in a European Commission Regulation or to international test methods recognised by the Commission or ECHA as being appropriate.

2. Under Article 13(4) of REACH, ecotoxicological and toxicological tests and analyses must be carried out according to the GLP principles (Directive 2004/10/EC) or other international standards recognised by the Commission or ECHA.

3. Under Article 10(a)(vi) and (vii) of REACH, all new data generated as a result of this decision must be reported as study summaries, or as robust study summaries, if required under Annex I of REACH. See ECHA Practical Guide on How to report robust study summaries[5].

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[6].

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

Appendix D: 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.

B. Environmental testing for substances containing multiple constituents

Your Substance contains multiple constituents and, as indicated in ECHA Guidance R.11 (Section R.11.4.2.2), you are advised to consider the following approaches for persistency, bioaccumulation and aquatic toxicity testing:

- the "known constituents approach" (by assessing specific constituents), or
- the "fraction/block approach, (performed on the basis of fractions/blocks of constituents), or
- the "whole substance approach", or
- various combinations of the approaches described above

Selection of the appropriate approach must take into account the possibility to characterise the Substance (i.e. knowledge of its constituents and/or fractions and any differences in their properties) and the possibility to isolate or synthetize its relevant constituents and/or fractions.

Appendix E: Procedure

This decision does not prevent ECHA from initiating further compliance checks at a later stage on the registrations present.

ECHA followed the procedure detailed in Articles 50 and 51 of REACH.

The compliance check was initiated on 27 January 2020.

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

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

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

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

Appendix F: List of references - ECHA Guidance[7] 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)[8]

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

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

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

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

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

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

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

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

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

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

OECD Guidance documents[9]

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

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

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

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

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

Appendix G: 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]

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.