ECHA
EUROPEAN CHEMICALS AGENCY

~~Confidential~~

Helsinki, 23 February 2021

Addressees
Registrant(s) of Joint Submission [redacted]_new as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
20/03/2020

Registered substance subject to this decision ("the Substance")
Substance name: [redacted]
EC number: [redacted]
CAS number: NS

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 in A.3 below by ***29 November 2021*** and all other information listed below by ***31 May 2022.***

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

A. 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.) to be combined with the Screening for reproductive/developmental toxicity below

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

3. Hydrolysis as a function of pH (Annex VIII, Section 9.2.2.1.; test method: EU C.7./OECD TG 111)

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

Appendix entitled "Reasons to request information required under Annex VIII of REACH".

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;

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

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 A: Reasons to request information required under Annex VIII of REACH

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

A Short-term repeated dose toxicity study (28 days) is a standard information requirement in Annex VIII to REACH.

In your technical dossier, under this endpoint, you have claimed that "*Toxicological data other than the mentioned in vitro genotoxicity results required for the tonnage band of 10 - 100 t/a are therefore not yet available but will be generated and provided as soon as possible*".

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

To be considered compliant with the endpoint, you need to submit a study performed according to the OECD TG 407, or a valid adaptation according to either the specific rules of Column 2, Annex VIII, Section 8.6.1. or the general rules of Annex XI.

You have provided neither a study performed according to the OECD TG 407 nor a valid adaptation according to either the specific rules of Column 2, Annex VIII, Section 8.6.1. or the general rules of Annex XI.

Based on the above, the information you provided do not fulfil the information requirement.

Study design

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

Referring to the criteria in Annex VIII, Section 8.6.1, Column 2, the oral route is the most appropriate route of administration to investigate repeated dose toxicity, because the Substance is a liquid of very low vapour pressure (≤ 0.18 Pa at 20°C) and no uses with spray application are reported that could potentially lead to aerosols of inhalable size.

Therefore the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test must be performed according to the OECD TG 422, in rats and with oral administration of the Substance.

In your comments to the draft decision you inform ECHA that you have already finalized a short-term repeated dose toxicity (28-day, oral, rat) study according to OECD TG 407 and a screening for reproductive/developmental toxicity study (oral, rat) according to OECD TG 421. You justified the conduction of two separate studies instead of OECD TG 422 study because "[...] *the substance will be also registered in other parts of the world where this combined test is not accepted".*

However, since you did not provide any further information on the OECD TG 407 study you refer to in your comments, ECHA cannot assess its compliance. Any registration update will

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

be considered by ECHA in the follow-up to dossier evaluation after the expiry of the deadline set in this decision.

2. Screening for reproductive/developmental toxicity

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

In your technical dossier, under this endpoint, you have claimed that "*Toxicological data other than the mentioned in vitro genotoxicity results required for the tonnage band of 10 - 100 t/a are therefore not yet available but will be generated and provided as soon as possible*".

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

To be considered compliant and to generate information concerning the effects of the Substance on male and female reproductive performance as well as specific target organ toxicity, the study has to meet the requirements of EU B.63/OECD TG 421 or EU B.64/OECD TG 422.

You have provided neither a study performed according to the OECD TG 421 or OECD TG 422, nor a valid adaptation according to either the specific rules of Column 2, Annex VIII, Section 8.7.1. or the general rules of Annex XI.

Based on the above, the information you provided do not fulfil the information requirement.

Study design

For the reasons explained in this Appendix under section 1, the conduct of a combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (OECD TG 422) is preferred to ensure that unnecessary animal testing is avoided.

Therefore, a study according to the test method EU B.64/OECD TG 422 must be performed in rats with oral administration of the Substance.

In your comments to the draft decision you inform ECHA that you have already finalized a short-term repeated dose toxicity (28-day, oral, rat) study according to OECD TG 407 and a screening for reproductive/developmental toxicity study (oral, rat) according to OECD TG 421. You justified the conduction of two separate studies instead of OECD TG 422 study because "[...] *the substance will be also registered in other parts of the world where this combined test is not accepted".*

However, since you did not provide any further information on the OECD TG 421 study you refer to in your comments, ECHA cannot assess its compliance. Any registration update will be considered by ECHA in the follow-up to dossier evaluation after the expiry of the deadline set in this decision.

3. Hydrolysis as a function of pH

Hydrolysis as a function of pH is a standard information requirement in Annex VIII Section 9.2.2.1. to REACH.

You have provided a key study ([redacted], 2013), OECD TG 111 with the Substance, in your dossier.

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

Hydrolysis as a function of pH must be determined according to OECD TG 111. Therefore the following requirements must be met:

- a main hydrolysis testing (tier 2) is performed if more than 10 % hydrolysis occurs after 5 days in the preliminary test (tier 1). The tier 2 test must be conducted at three temperatures in the range of 10-70°C (preferably with at least one temperature below 25°C utilised) and at pH values of 4, 7 and 9.
- identification of hydrolysis products (tier 3) using appropriate analytical method must be performed for major hydrolysis products (present at least ≥ 10 % of the applied dose)

Your have provided a study report indicating the following:

- main hydrolysis testing (tier 2) indicating hydrolysis rates of the Substance at temperatures 20, 50 and 70 °C and at pHs 7 and 9, but no measurements at pH 4;
- you have not provided analytical identification of the hydrolysis products (tier 3 test).

Therefore, based on the information in your registration dossier the provided study does not fulfil the information requirement.

In your comments to the draft decision you do not agree to perform the requested study. You consider that the study available in the dossier covers the requirements listed above, but you acknowledge that the details about these requirements were not reported. Therefore, in your comments you have provided the study report (final report on [redacted] performed by [redacted]), as well as a statement of your analytical department (Statement regarding ECHA comments on Study Report [redacted] (OECD 111 for [redacted])) with the following details:

- explanation why measurements at pH 4 were carried out but not reported ('due to immediate hydrolysis, the test item could not be detected in the pH 4 test solutions');
- information on the identification of hydrolysis products, including:
  - the reaction scheme for the hydrolysis;
  - a claim that only one hydrolysis product ('[redacted]') was identified, while due to high polarity the other reaction product ([redacted]) was not extracted from the aqueous phase in enough amonts to be identified;
  - the identified hydrolysis product 'is one of the starting materials used in the synthesis of [redacted].

ECHA has assessed the information provided in the comments against the requirements in OECD TG 111:

- The information related to tier 2 test of OECD TG 111 (measurements at pH 4) is considered acceptable.

Regarding the information on the identification of hydrolysis products, the proposed reaction scheme is considered plausible.

However, while you report that the recovered hydrolysis product ('[redacted]') corresponds to the starting material, in your comments you do not provide any identifiers for the recovered hydrolysis product (i.e. EC No., CAS No. or IUPAC name). Furthermore, in your registration dossier, the starting material is identified as [redacted] This substance is reported as being composed of two constituents ([redacted]): 1) [redacted]

[redacted]

However, the reaction scheme provided in your comments only reports as hydrolysis product one of the constituents of this starting material.

Due to the above, we consider that you have not provided identification (including identifiers) of all hydrolysis products as per tier 3 test of OECD TG 111.

ECHA understands that the information provided with your comments is relevant for this data requirement. However, the information is considered incomplete. Furthermore, the information is currently not available in your registration dossier. You are required to submit comprehensive information in an updated registration dossier by the applicable deadline set out in this decision. Your registration update will be considered by ECHA in the follow-up to dossier evaluation.

Appendix B: 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[3].

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:

   a) the variation in compositions reported by all members of the joint submission,
   b) the boundary composition(s) of the Substance,
   c) 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*

   a) 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.
   b) The reported composition must include all constituents of each Test Material and their concentration values.

With that detailed information, ECHA can confirm 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[4].

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

Appendix C: 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.

As regards your comments to the draft decision providing a revised PBT assessment, which is, however, not related to the scope of this decision, ECHA notes that, as explained in ECHA Guidance R.11 (Explanatory notes to Figure R.11-3), concern for P/vP screening cannot be removed by significant and substantial loss of the parent substance by hydrolysis alone and additional evidence should be provided to examine whether the fate properties of the substance would cause attenuation of the hydrolysis rate in sediment or soil, or whether DOC would similarly affect the rate in aquatic media such as river or sea water. Furthermore, careful consideration should be given to the potential formation of stable degradation products with PBT/vPvB properties.

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 synthesize its relevant constituents and/or fractions.

Appendix D: Procedure

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

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

The compliance check was initiated on 24 April 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 E: List of references - ECHA Guidance[5] 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)[6].

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

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

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

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

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

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

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

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

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

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

OECD Guidance documents[7]
Guidance Document on aqueous-phase aquatic toxicity testing of difficult test chemicals – No 23, referred to as OECD GD 23.

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

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

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

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

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

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

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