~~Confidential~~

Helsinki, 30 September 2021

Addressees
Registrant(s) of 2,6-xylenol as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
13/11/2015

Registered substance subject to this decision ("the Substance")
Substance name: 2,6-xylenol
EC number: 209-400-1
CAS number: 576-26-1

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 ***05 October 2023***.

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

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

1. In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.; test method: EU B.13/14. /OECD TG 471) using one of the following strains: E. coli WP2 uvrA, or E. coli WP2 uvrA (pKM101), or S. typhimurium TA102

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

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

B. 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

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

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

C. Information required from all the Registrants subject to Annex X of REACH

1. Pre-natal developmental toxicity study (Annex X, Section 8.7.2.; test method: OECD TG 414) by oral route, in a second species (rabbit)

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

- Appendices entitled "Reasons to request information required under Annexes VII to X 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 to X to REACH, for registration at more than 1000 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 VII of REACH

1. In vitro gene mutation study in bacteria

An *in vitro* gene mutation study in bacteria is an information requirement under Annex VII to REACH (Section 8.4.1.).

You have provided a key study in your dossier:

i. Bacterial reverse mutation assay (OECD TG 471) conducted with the Substance ([redacted] 1994).

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

To fulfil the information requirement, the study has to meet the requirements of OECD TG 471[2] (1997). One of the key parameters of this test guideline includes that the test must be performed with 5 strains: four strains of *S. typhimurium* (TA98; TA100; TA1535; TA1537 or TA97a or TA97) and one strain which is either *S. typhimurium* TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101).

You have provided bacterial reverse mutation assays (OECD TG 471) covering the following strains: *S. typhimurium* TA 1535, TA 1537, TA 98 and TA 100 with and without metabolic activation. The study did not include results for the appropriate 5 strains, in particular in *S. typhimurium* TA102 or E. coli WP2 uvrA or *E. coli* WP2 uvrA (pKM101).

The information provided does not cover the key parameters required by OECD TG 471.

Therefore, the information requirement is not fulfilled.

In your comments to the draft decision you agree to perform the test requested.

Study design

To fulfil the information requirement for the Substance, the *in vitro* gene mutation study in bacteria (OECD TG 471) should be performed using one of the following strains: *E. coli* WP2 uvrA, or *E. coli* WP2 uvrA (pKM101), or *S. typhimurium* TA102.

2. Short-term toxicity testing on aquatic invertebrates

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

You have 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:

i. Acute Immobilisation Test (*Daphnia sp.*), equivalent (or similar) to OECD TG 202 (Devillers, J, 1988), conducted with the Substance.

ii. Acute Immobilisation Test (*Daphnia sp.*), according to OECD TG 202 ([redacted], 2010), conducted with the Substance.

iii. Non-guideline study "*Aqueous Chlorination and Ozonation Studies I. Structure-Toxicity Correlations of Phenolic Compounds to Daphnia Magna.*" (Kopperman, H.L.; R. M. Carlson, and R. Caple, 1974), conducted with the Substance.

Annex XI, Section 1.2 states that there may be sufficient weight of evidence from several

[2] ECHA Guidance R.7a, Table R.7.7–2, p.557

independent sources of information leading to assumption/conclusion that a substance has or has not a particular dangerous (hazardous) property, while information from a single source alone is insufficient to support this notion.

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

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

However, you have not included a justification for your weight of evidence adaptations, which would include an adequate and reliable (concise) documentation as to why the sources of information provide sufficient weight to conclude that the Substance has or has not the dangerous property investigated by the required study.

In spite of this critical deficiency, which in itself could lead to rejection of the adaptation, ECHA has nevertheless assessed the provided sources of information and identified the following issue(s).

Relevant information that can be used to support weight of evidence adaptation for information requirement of Section 9.1.1. at Annex VII includes similar information that is produced by the OECD TG 202. OECD TG 202 requires the study to investigate the following key parameter:

- The concentration leading to 50% immobilisation of daphnids.

The sources of information (i), (ii) and (iii) provide relevant information on this key parameter. However, the reliability of these sources of information is significantly affected by the following deficiencies:

For a study conducted according to OECD TG 202, the following specifications must be met:

Reporting of the methodology and results

- the test design is reported (*e.g.* static or semi-static test, number of replicates, number of test concentrations and geometric progression used);
- the test procedure is reported (*e.g.* composition of the test medium, loading in number of *Daphnia* per test vessel);
- the number of immobilised daphnids is determined at 24 and 48 hours. Data are summarised in tabular form, showing for each treatment group and control, the number of daphnids used, and immobilisation at each observation;
- the dissolved oxygen and pH measured at least at the beginning and end of the test is reported;

Technical specifications impacting the sensitivity/reliability of the test

- the test duration is 48 hours or longer;
- test animals are not fed during the test;
- young daphnids, aged less than 24 hours at the start of the test, are used;

Characterisation of exposure

- chemical specific analysis of the test solutions is required to demonstrate stability of exposure concentrations during the test;
- the results can be based on nominal or measured initial concentration only if the concentration of the test material has been maintained within 20 % of the nominal or measured initial concentration throughout the test;

Validity criteria

- validity criteria specified in the test guideline must be met:
  - the percentage of immobilised daphnids is ≤ 10% at the end of the test in the controls (including the solvent control, if applicable);
  - the dissolved oxygen concentration is ≥ 3 mg/L in all test vessels at the end of the test;

In your dossier you have provided a study equivalent (or similar) to OECD TG 202 (study i.), a study according to OECD TG 202 (study ii.) and a non-guideline study (study iii.), showing the following:

Reporting of the methodology and results

- on the test design, for study (ii.) you have not specified test set-up (i.e static or semi-static test), number of replicates, number of test concentrations and geometric progression used; for study (iii.) you have not specified number of test concentrations and geometric progression used.
- on the test procedure, you have not specified composition of the test medium for any of the studies and loading in number of test organisms per test vessel for study (ii.);
- the number of immobilised daphnids at 24 and 48 hours in tabular form, as well as the dissolved oxygen are not reported in any of the studies.

Technical specifications impacting the sensitivity/reliability of the test

- the test duration was 24 hours for study (i.);
- for study (i.), the test was performed with animals aged more than 72 hours;
- for studies (i.) and (iii.), test organisms were fed during the test;

Validity criteria

- For study (i.), you have specified that the validity criteria were met. Regarding the studies (ii.) and (iii.) you have not specified whether the validity criteria of the test guideline are met.

On this basis there are major deficiencies impacting all sources of information provided in support of your weight-of-evidence adaptation, including the following:

- *Reporting of the methodology and results*: In the absence of information on the study design (i.e. study ii and iii) and on the procedure (for instance in term of test medium composition, this information was not provided in any of the studies), ECHA is not in a postion to make an independent assessment of the reliability of methodology and results.
- *Technical specifications impacting the sensitivity/reliability of the test:* the exposure duration was shorter than 48 hours (i.e. 24 hours) for study (i.). Shorter test duration generally leads to higher effect values and hence to an underestimation of the toxicity (ECHA Guidance R.7b). Furthermore, in studies (i.) and (iii.) the organisms were fed during the test and study (i.) was not conducted on neonate orgamisms (aged less than 24 hours). This may underestimate the toxicity, because the sensitivity of test

organisms may be lower if they are aged more than 24h at test start (ECHA Guidance R.7b) and/or if they are fed during the study.
- *Characterisation of exposure*: in the absence of analytical monitoring for study (i.) and in the absence of information on analytical monitoring for studies (ii.) and (iii.), you have not demonstrated the stability of the test substance.
- *Validity criteria*: as you have not provided information on dissolved oxygen and tabulated data on the number of immobilised daphnids for any of the studies, it is not possible to verify that the validity criteria are met.

As explained above, there are a number of major deficiencies impacting the reliability of the studies included in your weight-of-evidence. Considering these deficiencies, it cannot be concluded with sufficient confidence what is the concentration of the Substance leading to the immobilisation of 50% of daphnids.

On this basis, 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 dangerous properties foreseen to be investigated in an OECD TG 202 study.

Therefore, your adaptation is rejected and the information requirement is not fulfilled.

In your comments to the draft decision you agree to perform the test requested.

3. Growth inhibition study aquatic plants

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

You have provided the following information:

i. A key study (OECD TG 201) conducted with the Substance.
ii. A supporting study (non-guideline algal lawn pad assay) conducted with the Substance.

We have assessed this information and identified the following issue:

To fulfil the information requirement, a study must comply with OECD TG 201 (Article 13(3) of REACH). Therefore, the following specifications must be met:

Reporting of the methodology and results
- the test design is reported (*e.g.*, number of replicates, number of test concentrations and geometric progression used);
- the test conditions and procedure are reported (*e.g.*, composition of the test medium, test temperature, biomass density at the beginning of the test);
- the results of algal biomass determined in each flask at least daily during the test period are reported in a tabular form;
- the method for determination of biomass and evidence of correlation between the measured parameter and dry weight are reported;
- microscopic observation performed to verify a normal and healthy appearance of the inoculum culture are reported. Any abnormal appearance of the algae at the end of the test is reported;
- adequate information on the analytical method (including performance parameters of the method) and on the results of the analytical determination of exposure concentrations is provided;

Validity criteria

Validity criteria specified in the test guideline must be met:

- exponential growth in the control cultures is observed over the entire duration of the test;
- at least 16-fold increase in biomass is observed in the control cultures by the end of the test;
- the mean coefficient of variation for section-by-section specific growth rates (days 0-1, 1-2 and 2-3, for 72-hour tests) in the control cultures is ≤ 35%;
- the coefficient of variation of average specific growth rates during the whole test period in replicate control cultures is ≤ 7% in tests with *Pseudokirchneriella subcapitata* .

Your registration dossier provides an OECD TG 201 study (i.) showing the following:

Reporting of the methodology and results

- information on the test design is not reported;
- information on the test conditions and procedure is not reported;
- tabulated data on the algal biomass determined daily for each treatment group and control is not provided;
- the method used to determine algal biomass is not reported;
- microscopic observations are not reported;
- there is no information if analytical monitoring was performed;

Validity criteria

- You have indicated that the validity criteria were met.

You have also provided a non-guideline study (ii.) with Klimisch score of 3.

Based on the above:

With regard to study (i.):
The reporting of the study (i.) is not sufficient to conduct an independent assessment of its reliability. More specifically, information is lacking on test design and test procedure, methods to determine the algal biomass, microscopic observations, analytical monitoring, and finally on the tabulated data on the algal biomass determined daily which would allow to verify that the validity criteria are met. Therefore, the requirements of OECD TG 201 are not met.

With regard to study (ii.):
In the abence of the compliance of the key study with the REACH requirements, also the supporting study by itself cannot cover the endpoint because, in accordance with ECHA Guidance R.4.2., such a study with a Klimisch score of 3 is not considered as reliable.

On this basis, the information requirement is not fulfilled.

In your comments to the draft decision you agreed to perform the test requested.

Appendix B: 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 to REACH.

Adaptation according to Annex XI, Section 3

You have sought to adapt the standard information requirement according to Annex XI, Section 3.2(a) - Substance-tailored exposure-driven testing.

According to Annex XI, Section 3, you may adapt the information requirement, provided you fulfil any one of the criteria specified in section 3.2. (a), (b) or (c). In all cases, adequate justification and documentation must be provided, with a justification based on a thorough and rigorous exposure assessment in accordance with Section 5 of Annex I.

For an adaptation under the Annex XI, 3.2(a) the manufacturer or importer must demonstrate and document that all of the following conditions are fulfilled:

i. the results of the exposure assessment covering all relevant exposures throughout the life cycle of the substance demonstrate the absence of or no significant exposure in all scenarios of the manufacture and all identified uses as referred to in Annex VI section 3.5.;
ii. a suitable DNEL or a PNEC can be derived from results of available test data for the Substance taking full account of the increased uncertainty resulting from the omission of the information requirement, and that DNEL or PNEC is relevant and appropriate both to the information requirement to be omitted and for risk assessment purposes; and
iii. the comparison of the derived DNEL or PNEC with the results of the exposure assessment shows that exposures are always well below the derived DNEL or PNEC.

You provided the following justification for the adaptation "*It is considered to be scientifically unjustified to conduct the 90 day repeated dose toxicity study via the oral route […] it has been possible to set a precautionary DNEL based upon the results of the 28 day read across study. The calculated RCR values show a large margin of safety when derived using a Tier 1 model with minimal refinement. […] It is therefore considered that in accordance with section 3.2 of Annex XI, point a, the RCR values determined for the substance are always sufficiently low to mitigate the testing.*".

ECHA notes the following shortcoming(s) with regards to your adaptation according to Annex XI, Section 3.2 (a):

i) Exposure assessment

In the CSR, you have claimed that "*Exposure to the 2,6-Xylenol in the polymer is expected to be negligible throughout its life cycle based upon the physical state (i.e., monomer within a polymer) and low residual level in polymers*" and that "*The calculated RCR values show a large margin of safety when derived using a Tier 1 model with minimal refinement*."

You did not provide adequate and reliable documentation demonstrating that the "*Exposure to the 2,6-Xylenol in the polymer is expected to be negligible"* and that "*The calculated RCR values show a large margin of safety".* More specifically, you have not any information on the actual level of monomer in the polymer to support your expectation of "negligible" exposure. Similarly, you have neither reported the calculated RCR values on which you base your conclusions nor elaborated on what you consider to be a "*large margin of safety*".

In the comments to the draft decision, you propose to conduct a full and comprehensive exposure assessment and risk characterisation based on a conservative measure of the level of residual monomer in polymer, as means of demonstrating lack of risk to human health and environment. You indicate your intention to provide it in the future update of your registration dossier either jointly, on behalf of all co-registrants, or in the separate CSRs.

Based on the information provided in the comments, there is currently no information to address the shortcomings of your adaptation, as you have not provided a thorough and rigorous exposure assessment. Please note that this decision does not consider updates of the registration dossiers after the date on which you were notified of the draft decision according to Article 50(1) of REACH (see section 5.4. of ECHA's Practical Guide "How to act in Dossier Evaluation). You remain responsible for complying with this decision by the set deadline.

Therefore, based on the information provided in your dossier or in your comments, it is not possible to demonstrate the absence of or no significant exposure, and the conditions under Annex XI, Sections 3.2(a)(i) cannot be fulfilled.

ii) DNEL derivation

REACH Annex XI, section 3.2(a)(ii) contains a footnote which explicitly states "… *a DNEL derived from a 28-day repeated dose toxicity study shall not be considered appropriate to omit a 90-day repeated dose toxicity study.*"

In the registration dossier, you have provided the following key studies and used them to derive the worker, long-term systemic DNEL for inhalation effects and worker, long-term, systemic DNEL for dermal effects, respectively:

i. 10-Day repeated exposure inhalation toxicity study in rats (non-guideline, GLP; [redacted] 1991) conducted with the Substance (key study); and
ii. Combined repeated dose and reproduction / developmental screening study in rats via oral route (OECD TG 422, GLP; [redacted], 2005) conducted with analogue substance 2,4,6-trimethylphenol (key study; EC No. 208-419-2; CAS No. 527-60-6).

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

The duration of the inhalation study (i) is only 14 days (total of 10 days of exposure) and the combined repeated dose and reproduction / developmental screening study (ii, OECD TG 422) serve as an alternative for the short-term repeated dose toxicity (28-day) study.

Therefore, the duration of the provided studies is not appropriate to derive the relevant and appropriate DNEL for the 90-day repeated dose toxicity study (Section 8.6.2 at Annex IX), and the conditions under Annex XI, Section 3.2(a)(ii) cannot be fulfilled.

You have not provided in your comments any further information to address this.

iii) Comparison of the derived DNEL with the results of the exposure assessment

Annex XI, 3.2.(a)(iii) specifies that the manufacturer or importer shall demonstrate and document the comparison of the derived DNEL or PNEC with the results of the exposure assessment.

As specified above, you have not fulfilled the conditions specified in Annex XI, Section 3.2(a)(i) for exposure assessment, or 3.2(a)(ii) for DNEL derivation. Therefore, it is not possible to compare the exposure to the derived DNEL (3.2(a)(iii)), and the conditions under Annex XI, Sections 3.2(a)(i) and 3.2(a)(ii) cannot be fulfilled.

Conclusion on the assessment of the adaptation based on exposure-driven testing

In conclusion, based on above evaluation, your adaptation according to Annex XI, Section 3.2(a) is rejected, and does not fulfil the information requirement.

Read-across approach

Further, ECHA notes that you relied on information on the analogue substance 2,4,6-trimethylphenol (EC No. 208-419-2; CAS No. 527-60-6) in the above adaptation. However, for the following reasons ECHA considers that the information provided by you does not support your 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[3].

Predictions for toxicological properties

You have provided a read-across justification document in IUCLID Section 7.5.1.

You read-across between the structurally similar substances, 2,4,6-trimethylphenol (EC No. 208-419-2) as source substance and the Substance as target substance.

Under section 7.5 'Repeated dose toxicity' of IUCLID, you have provided the following reasoning for the prediction of toxicological properties: *"2,6-Xylenol and the structural analogue were determined to have sufficiently similar properties, such that available data on the structural analogue is considered to be suitable to address this endpoint".*

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 to compare properties of the substances

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*

[3] ECHA Guidance R.6

information to strengthen the rationale for the read-across"[4]. The set of supporting information should allow to verify the crucial aspects of the read-across hypothesis and establish that the properties of the Substance can be predicted from the data on the source substance(s).

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(s) is necessary to confirm that both substances 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(s).

In the read-across justification document you refer to the following repeat dose toxicity studies:

i. 10-Day repeated exposure inhalation toxicity study in rats (non-guideline, GLP; [redacted], 1991) conducted with the Substance; and
ii. Combined repeated dose and reproduction / developmental screening study in rats via oral route (OECD TG 422, GLP; [redacted], 2005) conducted with 2,4,6-trimethylphenol (EC No. 208-419-2; CAS No. 527-60-6); and
iii. Prenatal developmental toxicity study (OECD TG 414) GLP; [redacted] 1997) conducted with the Substance.

In addition, to support your claim that your Substance and source substance have similar properties for the endpoints under consideration in the read-across approach, you refer to their acute toxicity, irritation, and genotoxicity properties.

First, the studies (i and iii) conducted with the Substance involve exposure duration of maximum 10 days compared to the minimum of about 28 days in the combined repeated dose and reproductive toxicity screening study conducted with the source substance 2,4,6-xylenol (study ii). Furthermore, mature male animals are only exposed via inhalation (study i) compared to the oral exposure in the study conducted with the source substance. Therefore, these studies do not provide comparable design and duration to allow comparison of the properties of the substance.

Second, while the information on acute toxicity, irritation, and genotoxicity of the substances may provide support that the substances have similar properties for these toxicological properties, these studies do not inform on the systemic toxicity properties of the target and source substances following repeated exposure. Therefore, this information does not provide relevant information for the Substance and of the source substance to support your read-across hypothesis.

Finally, in your registration dossier, you have provided three supporting oral repeated toxicity studies conducted with the Substance. However, you specify that "*All were awarded a reliability score of 3 in accordance with the criteria for assessing data quality set forth by Klimisch et al. (1997) due to being non-guideline studies with limited information provided*.". ECHA agrees with your conclusion. Therefore, these studies do not provide reliable bridging information.

Based on above, the data set reported in the technical dossier does not include relevant, reliable and adequate information for the Substance and of the source substance(s) to support your read-across hypothesis.

[4] ECHA Guidance R.6: QSARs and grouping of Chemicals, Section R.6.2.2.1.f

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

Conclusions on the read-across approach

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

Based on all the above, the information requirement is not fulfilled.

Information on the design of the study to be performed

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 as specified in the dossier, the Substance is molten mass at room temperature.

Therefore, the sub-chronic toxicity study must be performed according to the OECD TG 408, in rats and with oral administration of the Substance.

2. Long-term toxicity testing on aquatic invertebrates

Long-term toxicity testing on aquatic invertebrates is an information requirement under Annex IX to REACH (Section 9.1.5.).

You have provided a key study conducted according to OECD 211 with the Substance.

We have assessed this information and identified the following issue

To fulfil the information requirement, a study must comply with the OECD TG 211 (Article 13(3) of REACH). Therefore, the following specifications must be met:

Reporting of the methodology and results

- the test design is reported (*e.g.* semi-static or flow-through, number of replicates, number of parents per replicate);
- the test conditions and procedure are reported (*e.g.* loading in number of *Daphnia* per litre, test medium composition);
- the nominal test concentrations and the results of all analyses to determine the concentration of the test substance in the test vessels are reported;
- water quality monitoring within the test vessels (*i.e.* pH, temperature and dissolved oxygen concentration, and TOC and/or COD and hardness where applicable) is reported;
- the full record of the daily production of living offspring during the test (i.e. by each parent animal/in each replicate) is provided;
- the number of deaths among the parent animals (if any) and the day on which they occurred is reported;

Validity criteria

- validity criteria specified in the test guideline must be met:
  - the percentage of mortality of the parent animals (female *Daphnia*) is ≤ 20% at the end of the test;
  - the mean number of living offspring produced per parent animal surviving is ≥ 60 at the end of the test;

Your registration dossier provides an OECD TG 211 study showing the following:

Reporting of the methodology and results

- information on the test design is not reported;
- information on the test conditions and procedure is not reported;
- the nominal test concentrations are not reported and you have not specified whether analytical measurement of test concentrations was conducted;
- water quality monitoring is not reported;
- tabulated data on the full record of the daily production of living offspring, as well as, the number of deaths among the parent animals, during the test are not reported.

Validity criteria

You have not specified if the validity criteria were met.

Based on the above, the reporting of the study is not sufficient to conduct an independent assessment of its reliability. More specifically, information is lacking on test design and test procedure, on analytical monitoring, and finally on the tabulated data with the full record of the daily production of living offspring during the test and the number of deaths among the parent animals which would allow to verify that the validity criteria are met.

Therefore, the requirements of OECD TG 211 are not met.

In your comments to the draft decision you indicate your intention to adapt this information requirement based on exposure considerations, according to Annex XI, Section 3 of REACH Regulation.

In particular, you propose to conduct a full and comprehensive exposure assessment and risk characterisation based on a conservative measure of the level of residual monomer in polymer, as a means of demonstrating lack of risk to human health and environment. You indicate your intention to provide it in the future update of your registration dossier either jointly, on behalf of all co-registrants, or in the separate CSRs.

Based on the information provided in the comments, there is currently no information to adapt the information requirement, as you have not provided a thorough and rigorous exposure assessment.

Please note that this decision does not take into account updates of the registration dossiers after the date on which you were notified of the draft decision according to Article 50(1) of REACH (see section 5.4. of ECHA's Practical Guide "How to act in Dossier Evaluation). You remain responsible for complying with this decision by the set deadline.

On this basis, the information requirement is not fulfilled.

3. Long-term toxicity testing on fish

Long-term toxicity testing on fish is an information requirement under Annex IX to REACH (Section 9.1.6.).

You have provided the following information:

- a justification to omit the study which you consider to be based on Annex IX, Section 9.1., Column 2. In support of your adaptation, you provided the following justification: "In *accordance with section 9.1 of Column 2 of Annex IX, long term toxicity testing shall be proposed by the registrant if the chemical safety assessment according to Annex I indicates the need to investigate further the effects on aquatic organisms. As the outcome*

of the chemical safety assessment indicated that there was no requirement for further testing, it is considered justified to omit this study".

We have assessed this information and identified the following issue:

Annex IX, Section 9.1., Column 2 does not allow omitting the need to submit information on long-term toxicity to fish under Column 1. It must be understood as a trigger for providing further information on long-term toxicity to fish if the chemical safety assessment according to Annex I indicates the need (Decision of the Board of Appeal in case A-011-2018).

Your adaptation is therefore rejected.

In your comments to the draft decision you indicate your intention to adapt this information requirement based on exposure considerations, according to Annex XI, Section 3 of REACH regulation.

In particular, you propose to conduct a full and comprehensive exposure assessment and risk characterisation based on a conservative measure of the level of residual monomer in polymer, as a means of demonstrating lack of risk to human health and environment. You indicate your intention to provide it in the future update of your registration dossier either jointly, on behalf of all co-registrants or in the separate CSRs.

Based on the information provided in the comments, there is currently no information to adapt the information requirement, as you have not provided a thorough and rigorous exposure assessment.

Please note that this decision does not take into account updates of the registration dossiers after the date on which you were notified of the draft decision according to Article 50(1) of REACH (see section 5.4. of ECHA's Practical Guide "How to act in Dossier Evaluation). You remain responsible for complying with this decision by the set deadline.

On this basis, the information requirement is not fulfilled

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

1. Pre-natal developmental toxicity study in a second species

Pre-natal developmental toxicity (PNDT) studies (OECD TG 414) in two species is a standard information requirement under Annex X to REACH.

You have not provided information on a second species. In order to be compliant and enable concluding if the Substance is a developmental toxicant, information provided has to meet the requirements of OECD TG 414 in two species.

In your comments to the draft decision you indicate your intention to adapt this information requirement based on exposure considerations, according to Annex XI, Section 3 of REACH regulation.

In particular, you propose to conduct a full and comprehensive exposure assessment and risk characterisation based on a conservative measure of the level of residual monomer in polymer, as means of demonstrating lack of risk to human health and environment. You indicate your intention to provide it in the future update of your registration dossier either jointly, on behalf of all co-registrants or in the separate CSRs.

Based on the information provided in the comments, there is currently no information to adapt the information requirement, as you have not provided a thorough and rigorous exposure assessment.

Please note that this decision does not take into account updates of the registration dossiers after the date on which you were notified of the draft decision according to Article 50(1) of REACH (see section 5.4. of ECHA's Practical Guide "How to act in Dossier Evaluation). You remain responsible for complying with this decision by the set deadline.

On this basis, the information requirement is not fulfilled.

Information on study design
A PNDT study according to the OECD TG 414 study should be performed in the rabbit or rat as the preferred species. The test in the first species was carried out by using a rodent species (rat). Therefore, a PNDT study in a second species must be performed in the rabbit as preferred non-rodent species.

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[5].

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[6].

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

Appendix E: Procedure

The information requirement for an Extended one-generation reproductive toxicity study (EOGRTS; Annexes IX or X, Section 8.7.3.) is not addressed in this decision. This may be addressed in a separate decision once the information from the Sub-chronic toxicity study (90-day) requested in the present decision is provided; due to the fact that the results from the 90-day study is needed for the design of the EOGRTS. Similarly the information requirement for a Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.) is not addressed in this decision; as the EOGRTS will cover the same parameters.

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 28 July 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 request(s).
ECHA notified the draft decision to the competent authorities of the Member States for proposals for amendment.

ECHA received proposal(s) for amendment and modified the draft decision.

ECHA invited you to comment on the proposed amendments and referred the modified draft decision to the Member State Committee.

In your comments on the proposed amendments, you expressed your disagreement with the proposal for amendment submitted by an MSCA to reduce the deadline to provide request B.1 from 21 to 12 months. You have claimed that a deadline of 12 months is not feasible for such a study due to lack of laboratory capacity and provided documentation from two CRO laboratories to support this claim.

Your comments on the proposed amendment(s) were taken into account by the Member State Committee and the deadline to submit request B.1 was kept to 21 months from the date of adoption of the decision.

The Member State Committee unanimously agreed on the draft decision in its MSC-75 written procedure. ECHA adopted the decision under Article 51(6) 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]
Guidance Document on aqueous–phase aquatic toxicity testing of difficult test chemicals – No 23, referred to as OECD GD 23.

[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 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 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]
[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.