~~Confidential~~

Helsinki, 11 June 2021

Addressees
Registrant(s) of JS 4-ethylphenol as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
07/02/2018

Registered substance subject to this decision ("the Substance")
Substance name: 4-ethylphenol
EC number: 204-598-6
CAS number: 123-07-9

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

DECISION ON A COMPLIANCE CHECK

Under Article 41 of Regulation (EC) No 1907/2006 (REACH), you must submit the information listed below, by the deadline of ***16 September 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)

3. Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: OECD TG 301A/B/C/D/E/F or OECD TG 310)

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

1. In vivo mammalian erythrocyte micronucleus test, oral route; or In vivo mammalian bone marrow chromosomal aberration test, oral route; or In vivo mammalian alkaline comet assay, oral route, on the following tissues: liver, glandular stomach and duodenum (triggered by Annex VIII, Section 8.4., column 2).

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

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

- Appendix entitled "Reasons common to several requests";
- 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 Annex VII to REACH, for registration at 1-10 tonnes per year (tpa), or as a transported isolated intermediate in quantity above 1000 tpa;
- the information specified in Annexes VII and VIII to REACH, for registration at 10-100 tpa.

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 on Reasons common to several requests

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

ECHA has considered that you seek to adapt the following standard information by applying read-across approach in accordance with Annex XI, Section 1.5:

- Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.)
- Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.)
- Ready biodegradability (Annex VII, Section 9.2.1.1.)

For the information requirements listed above you have provided studies performed with a test material named "[redacted]", which includes [redacted] with a concentration of [redacted]%), [redacted], with a concentration of [redacted]%), and [redacted] (the Substance, with a concentration of [redacted]%). While you have not identified this information as a read-across approach, the test material used and reported in the technical dossier corresponds to a multiconstituent Substance in the context of the REACH Regulation, and the Substance is one of the constituent of the test material. Therefore, the provided studies conducted with this multiconstituent Substance (hereafter referred to as the "source substance") are considered as performed on a different substance than the Substance and are evaluated as a read-across adaptation under Annex XI, Section 1.5 of REACH.

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 'Predictions for ecotoxicological properties'). 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].

ECHA notes that with regards to prediction(s) of ecotoxicological properties there are issues that are common to all information requirements under consideration and also shortcoming(s) that are specific for these information requirements individually. Altogether they result in a failure to meet the requirement of Annex XI, 1.5. The common issues are set out here, while the specific issues are set out under the information requirement concerned in the Appendices below.

Absence of read-across documentation

Annex XI, Section 1.5 requires that whenever read-across is used adequate and reliable documentation of the applied method must be provided. Such documentation must provide a justification for the read-across including a hypothesis, explanation of the rationale for the prediction of properties and robust study summary(ies) of the source study(ies).[5]

You have provided studies conducted with other substance(s) than your Substance in order to comply with the REACH information requirements. You have not provided documentation as to why this information is relevant for your Substance.

Therefore, your adaptation does not comply with the general rules of adaptation as set out in

[2] ECHA Guidance R.6.
[3] Read-Across Assessment Framework (RAAF).
[4] Read-across assessment framework (RAAF) - considerations on multi-constituent substances and UVCBs.
[5] ECHA Guidance R.6, Section R.6.2.6.1

Annex XI, Section 1.5. and your grouping and read-across approach is rejected already for this general reason.

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.).

As explained in the Appendix on Reasons common to several requests ECHA has considered that you have adapted this information requirement by using a Grouping of substances and read-across approach under Annex XI, Section 1.5. Your dossier contains the following study conducted with the source substance "[redacted]":

- Daphnia sp. Acute Immobilisation Test (OECD TG 202; [redacted] 2005).

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

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

In addition, according to Annex XI, Section 1.5., if the grouping concept is applied then in all cases the results to be read across must:

- be adequate for the purpose of classification and labelling and/or risk assessment;
- have adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3);
- cover an exposure duration comparable to or longer than the corresponding test method referred to in Article 13(3) if exposure duration is a relevant parameter.

For short-term toxicity testing on aquatic invertebrates the source study used in the read across approach must have a reliable coverage of the key parameters addressed in the OECD TG 202. Therefore, the following specifications of the test guideline 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, age of daphnids);
- 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 are reported;
- adequate information on the analytical method (including performance parameters of the method) and on the results of the analytical determination of exposure concentrations are provided;

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;

Your registration dossier provides an OECD TG 202 study showing the following:

Reporting of the methodology and results

- information on the test design is not reported;

- information on the test procedure is not reported;
- tabulated data on the number of immobilised daphnids after 24 and 48 hours for each treatment group and control is not provided;
- the dissolved oxygen and pH measured at least at the beginning and end of the test are not reported;
- you have stated that the analytical monitoring was performed, however information on sampling and analysis, analytical method and the results of the analyses to determine the concentration of the test substance in the test vessels are not reported.

Validity criteria
- you indicate that 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, details on analytical monitoring, as well as on number of immobilised daphnids and dissolved oxygen which would allow to verify that the validity criteria are met.

Therefore, ECHA cannot assess if the study provided would deliver adequate and reliable information on the key parameters addressed in the OECD TG 202.

For all these reasons the read-across approach does not meet the criteria set out in Annex XI, Section 1.5.

On this basis, the information requirement is not fulfilled.

2. Growth inhibition study aquatic plants

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

As explained in the Appendix on Reasons common to several requests ECHA has considered that you have adapted this information requirement by using a Grouping of substances and read-across approach under Annex XI, Section 1.5. Your dossier contains the following study conducted with the source substance "[redacted]":

- Alga, Growth Inhibition Test (OECD TG 201; [redacted] 2005)

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

As explained in the Appendix on Reasons common to several requests, your adaptation in accordance with Annex XI, Section 1.5. is rejected already for general reasons.

In addition, according to Annex XI, Section 1.5., if the grouping concept is applied then in all cases the results to be read across must:
- be adequate for the purpose of classification and labelling and/or risk assessment;
- have adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3);
- cover an exposure duration comparable to or longer than the corresponding test method referred to in Article 13(3) if exposure duration is a relevant parameter.

For a Growth inhibition study on aquatic plants the source study used in the read across approach must have a reliable coverage of the key parameters addressed in the OECD TG 201. Therefore, the following specifications of the test guideline 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 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;
- you have stated that the analytical monitoring was performed, however information on sampling and analysis, analytical method and the results of the analyses to determine the concentration of the test substance in the test vessels are not reported.

Validity criteria

- you indicate that 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, methods to determine the algal biomass, microscopic observations, details on 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, ECHA cannot assess if the study provided would deliver adequate and reliable information on the key parameters addressed in the OECD TG 201.

For all these reasons, the read-across approach does not meet the criteria set out in Annex XI, Section 1.5.

On this basis, the information requirement is not fulfilled.

3. Ready biodegradability

Ready biodegradability is an information requirement under Annex VII to REACH (Section 9.2.1.).

As explained in the Appendix on Reasons common to several requests ECHA has considered that you have adapted this information requirement by using a Grouping of substances and read-across approach under Annex XI, Section 1.5. Your dossier contains the following study conducted with the source substance "[redacted]":

- Ready Biodegradability - CO2 in Sealed Vessels (Headspace Test) (similar or equivalent to OECD TG 310; [redacted] 2004)

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

As explained in the Appendix on Reasons common to several requests, your adaptation in accordance with Annex XI, Section 1.5. is rejected already for general reasons.

In addition, according to Annex XI, Section 1.5., if the grouping concept is applied then in all cases the results to be read across must:

- be adequate for the purpose of classification and labelling and/or risk assessment;
- have adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3);
- cover an exposure duration comparable to or longer than the corresponding test method referred to in Article 13(3) if exposure duration is a relevant parameter.

For ready biodegradability the source study used in the read across approach must have a reliable coverage of the key parameters addressed in the OECD TG 301 or 310. For a study according to OECD TG 310, as in this case, the following specifications of the test guideline must be met:

Reporting of the methodology and results

- description of the test system (*e.g.* volume of the vessel, head space to liquid ratio, method of stirring etc.) is reported;
- the test design is reported (*e.g.*, number of replicates, controls included in the test design);
- the test conditions and procedure are reported (*e.g.*, temperature, bacteria density of the inoculum cells/L; suspended solid concentration, contribution of the inoculum to the intitial organic carbon concentration, test substance concentration in the test vessels);
- the method used for inorganic carbon (IC) analysis is described and the method validation is reported;
- the results of measurements at each sampling point in each replicate is reported in a tabular form;
- any observed inhibition phenomena and/or abiotic degradation is reported;

Validity criteria

Validity criteria specified in the test guideline must be met:

- A reference substance (e.g. aniline, sodium benzoate, ethylene glycol or 1-octanol) of known biodegradability is tested in parallel. Biodegradation of these substances is ≥ 60% ThIC within 14 days;
- The mean amount of TIC present in the blank controls at the end of the test is ≤

3mg C/L;

Your registration dossier provides a study similar (or equivalent) to OECD TG 310, showing the following :

Reporting of the methodology and results

- description of test system is not reported;
- information on the test design is not reported;
- information on the test conditions and procedure is not reported;
- the method used for inorganic carbon (IC) analysis and validation is not reported;
- tabulated data on the measurements at each sampling point in each replicate are not provided;
- observations on inhibition phenomena and/or abiotic degradation are not provided.

Validity criteria

- you indicate that 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 system, test design and conditions, method used for inorganic carbon (IC) analysis, tabulated data on measurements, observations on inhibition phenomena and/or abiotic degradation, and finally on the degradation of the reference substance and TIC measurements in blank controls which would allow to verify that the validity criteria are met.

Therefore, ECHA cannot assess if the study provided would deliver an adequate and reliable information on the key parameters addressed in the OECD TG 310.

For all these reasons the read-across approach does not meet the criteria set out in Annex XI, Section 1.5.

On this basis, the information requirement is not fulfilled.

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

1. In vivo mammalian erythrocyte micronucleus test; or In vivo mammalian bone marrow chromosomal aberration test or In vivo mammalian alkaline comet assay

Under Annex VIII, Section 8.4, column 2 of REACH, the performance of an appropriate *in vivo* somatic cell genotoxicity study must be considered if there is a positive result in any of the *in vitro* genotoxicity studies in Annex VII or VIII.

Your dossier contains positive results for the *in vitro* cytogenicity test conducted with the Substance which raise the concern for chromosomal aberration.

You have adapted this information requirement by using a Grouping of substances and read-across approach under Annex XI, Section 1.5.

Your dossier contains the following *in vivo* study conducted with 4-vinylphenol (EC no 220-103-6):

i. Mammalian Erythrocyte Micronucleus Test (OECD TG 474; [redacted], 2016)

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

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 R.6. and related documents[6,7].

A. Predictions for toxicological properties

You have provided a read-across justification document in IUCLID Section 7.6.2 '[redacted]

You read-across between the structurally similar substances, 4-vinylphenol, EC No. 220-103-6 (CAS No. 2628-17-3) as source substance and the Substance as target substance.

You have provided the following reasoning for the prediction of toxicological properties: *"The read-across is based on the hypothesis that 4-Ethylphenol (target substance) and 4-Vinylphenol (source substance) have similar toxicological properties. This prediction is based on structural similarities, physicochemical properties, metabolism and toxicological data of both substances."*.

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

[6] Read-Across Assessment Framework (RAAF). 2017. 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)

[7] Read-across assessment framework (RAAF) - considerations on multi-constituent substances and UVCBs. 2017. Available online: https://doi.org/10.2823/794394

substance.

ECHA notes the following shortcomings with regards to prediction of toxicological properties.

Read-across hypothesis contradicted by existing data

Annex XI, Section 1.5. provides that "*substances whose physicochemical, toxicological and eco-toxicological properties are likely to be similar or follow a regular pattern as result of structural similarity may be considered as a group or 'category' of substances*". The ECHA Guidance[8] indicates that "*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(s).

The observation of differences in the toxicological properties between the source substance(s) and the Substance would contradict the hypothesis that the properties of the Substance can be predicted from the data on the source substances. An explanation why such differences do not affect the read-across hypothesis needs to be provided and supported by scientific evidence.

As indicated above, your read-across hypothesis is based on the assumption that the structurally similar target and source substances cause the same type of effect(s).

You have provided positive *in vitro* chromosome aberration tests (OECD TG 473) conducted with the source substance and with the Substance. You indicate that "*The results for both substances were equal depending on the genotoxicity assay.*"

The results of the *in vitro* chromosome aberration tests obtained with the Substance and the source substance vary. Specifically, the Substance induces an 11-fold increase in the % of aberrant cells excluding gaps from 1 (for solvent control) to 11 (for top concentration of 0.075 mg/mL). On the other hand, the source substance induces a 3.5-fold increase in the % of aberrant cells excluding gaps from 1.7 (for solvent control) to 6 (for top concentration of 2 mM = 240 mg/L = 0.24 mg/mL). Therefore, rather than equal, the Substance seems to be quantitatively more genotoxic than the source substance.

Furthermore, based on the provided tabular data, the Substance was positive in the experiment with and without metabolic activation (S9) while the source substance was negative in the test without S9, but positive in tests with S9. This indicates that the Substance may be more readily converted into electrophilic intermediate(s) leading to the clastogenicity than the source substance.

Therefore, the available set of data on the Substance and source substances indicates differences in the toxicological properties of the substances. This contradicts your read-across hypothesis whereby the structurally similar substances cause the same type of effect(s) predicted to be quantitatively equal. Therefore you have not demonstrated and justified that the properties of the source substance(s) and of the Substance are likely to be similar despite the observation of these differences.

Adequacy and reliability of source study

According to Annex XI, Section 1.5., if the grouping concept is applied then in all cases the results to be read across should have adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3).

[8] ECHA Guidance R.6, Section R.6.2.2.1.f

To be considered adequate, the study has to meet the requirements of OECD TG 474, and the key parameters of this test guideline include that the highest dose studied must be the maximum tolerated dose (MTD), i.e. the highest dose that is tolerated without evidence of toxicity (e.g. body weight depression or hematopoietic system cytotoxicity, but not death or evidence of pain, suffering or distress necessitating humane euthanasia). The highest dose can also be a dose that produces toxicity in the bone marrow (e.g. a reduction in the proportion of immature erythrocytes among total erythrocytes in the bone marrow or peripheral blood).

The *in vivo* study ([redacted] 2016) you have used as source study in your read-across approach was performed via intraperitoneal administration of the test substance using a 9.7 % (w/w) solution of source substance 4-vinylphenol in propylene glycol. The highest dose used in the study was limited to 97 mg/kg of the source substance. You indicated that "*The maximum dose chosen was based on the highest non-toxic dose level of propylene glycol.*" Therefore, ECHA understands that the highest dose studied was based on the toxicity of [redacted] (which is 90% of the test material) rather than the MTD of the source substance 4-vinylphenol. Based on this, it is considered that the study did not include a maximum studied dose of the test substance 4-vinylphenol that is a MTD or induces toxicity.

Therefore the information provided does not cover the key parameters required by the OECD TG 474.

B. 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.

Therefore, the information requirement is not fulfilled.

Information on the study design

i. Test selection

According to the ECHA Guidance Chapter R.7a, Section R.7.7.6.3, the mammalian erythrocyte micronucleus test ("MN test", OECD TG 474) or the mammalian bone marrow chromosomal aberration test ("CA test", OECD TG 475) are suitable to follow up a positive *in vitro* result on chromosomal aberration if the Substance or its metabolite(s) will reach the target tissue. Alternatively, the *in vivo* mammalian alkaline comet assay ("comet assay", OECD TG 489) is a suitable test to be performed. Therefore, the MN test, the CA test and the comet assay are suitable tests to follow up the chromosomal aberration concern identified for the Substance.

ii. Test design

In case you decide to perform a MN or CA assay, according to the test method OECD TG 474 / OECD TG 475, the test must be performed in mice or rats. Having considered the anticipated routes of human exposure and the need for adequate exposure of the target tissue(s) performance of the test by the oral route is appropriate.

Regarding the exposure of the target tissue, the applicable test guideline (OECD TG 474 / OECD TG 475) states "If there is evidence that the test substance(s), or its metabolite(s), will not reach the target tissue, it may not be appropriate to use this test". Additionally, a negative

test result can be considered reliable if "Bone marrow exposure to the test substance(s) occurred". Accordingly, if the Substance is negative in this test, but it is not possible to demonstrate that bone marrow exposure to the Substance occurred, then ECHA will consider any remaining uncertainty concerning the mutagenic potential of the Substance and whether to request any further information.

In case you decide to perform the comet assay according to the test method OECD TG 489, the test must be performed in rats. Having considered the anticipated routes of human exposure and the need for adequate exposure of the target tissue(s) performance of the test by the oral route is appropriate.

In line with the test method OECD TG 489, the test must be performed by analysing tissues from liver as primary site of xenobiotic metabolism, glandular stomach and duodenum as sites of contact. There are several expected or possible variables between the glandular stomach and the duodenum (different tissue structure and function, different pH conditions, variable physico-chemical properties and fate of the Substance, and probable different local absorption rates of the Substance and its possible breakdown product(s)). In light of these expected or possible variables, it is necessary to analyse both tissues to ensure a sufficient evaluation of the potential for genotoxicity at the site of contact in the gastro-intestinal tract.

iii. Germ cells

Comet
You may consider to collect the male gonadal cells collected from the seminiferous tubules in addition to the other aforementioned tissues in the comet assay, as it would optimise the use of animals. You can prepare the slides for male gonadal cells and store them for up to 2 months, at room temperature, in dry conditions and protected from light. Following the generation and analysis of data on somatic cells in the comet assay, you should consider analysing the slides prepared with gonadal cells. This type of evidence may be relevant for the overall assessment of possible germ cell mutagenicity including classification and labelling according to the CLP Regulation.

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.).

Your dossier contains the following study conducted with the Substance:

- Fish, Acute Toxicity Test (equivalent or similar to OECD TG 203; Geiger et al., 1986)

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

To fulfil the information requirement, a study must comply with OECD TG 203 (Article 13(3) of REACH). Therefore, the following specifications must be met:

<u>*Reporting of the methodology and results*</u>
- details on the test organisms are reported (e.g. size of test fish);
- the test conditions and procedure are reported (e.g. number of test animals, composition of the test medium, fish loading);
- adequate information on the analytical method (including performance parameters of the method) is provided;
- mortalities and sub-lethal effects (*e.g.* with regard to equilibrium, appearance, ventilator and swimming behaviour) are reported. The frequency of observations

includes at least 2 observations within the first 24 hours and at least two observations per day from day 2 to 4;

Validity criteria
Validity criteria specified in the test guideline must be met, among others:

- mortality in the control(s) is ≤ 10% (or one fish, if fewer than 10 control fish are tested) at the end of the test;

Your registration dossier provides a study similar (or equivalent) to an OECD TG 203 study for which you have not reported any of the following:

- whether the study meets the validity criteria;
- size of the test organisms;
- information on the test conditions and procedure;
- performance parameters of the analytical method (e.g. LOD/LOQ/recovery);
- tabulated data on mortalities and sub-lethal effects and frequency of observations.

Based on the above, the reporting of the study is not sufficient to conduct an independent assessment of its reliability and if it would meet the validity criteria of OECD TG 203. More specifically, information is lacking on fish size, test conditions and procedure, performance parameters of the analytical method, tabulated data with observations, as well as on mortality data in the controls which would allow to verify if the validity criteria were met.

On this basis, the information requirement is not fulfilled.

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[9].

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[10].

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

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 28 July 2020.

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

ECHA did not receive any comments within the notification period.

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[11] 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)[12]

RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017)[12]

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[13]
Guidance Document on aqueous–phase aquatic toxicity testing of difficult test chemicals – No 23, referred to as OECD GD 23.

[11] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[12] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across
[13] 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.