~~Confidential~~

Helsinki, 11 March 2022

Addressees
Registrants of Rh_cpd_EC234-014-5_PMC2016 listed in the last Appendix of this decision

Date of submission of the dossier subject of a decision
22/12/2020

Registered substance subject to this decision, hereafter 'the Substance'
Substance name: Dirhodium trisulphate
EC number: 234-014-5
CAS number: 10489-46-0

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

DECISION ON TESTING PROPOSAL(S)

Based on Article 40 of Regulation (EC) No 1907/2006 (REACH), you must submit the information listed below by ***17 June 2024***.

The requested information must be generated using the Substance unless otherwise specified.

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

1. *In vitro* cytogenicity study in mammalian cells (test method: OECD TG 473) or *In vitro* micronucleus study (test method: OECD TG 487);

2. *In vivo* genetic toxicity study to be selected according to the following specifications:

    a. If the results of the *in vitro* test requested under A.1 are **negative**:

    In vivo mammalian alkaline comet assay (test method: OECD TG 489) in rats, or if justified, other rodent species, oral route, on the following tissues: liver, glandular stomach and duodenum. It is at your discretion to perform the toxicokinetic assessment in combination to this study.

    b. If the results of the *in vitro* test requested under A.1 are **positive**:

    In vivo mammalian alkaline comet assay (test method: OECD TG 489) combined with *in vivo* mammalian erythrocyte micronucleus test (test method: OECD TG 474) in rats, or if justified, in mice, oral route. For the comet assay the following tissues shall be analysed: liver, glandular stomach and duodenum. It is at your discretion to perform the toxicokinetic assessment in combination to this study.

Reasons for the request(s) are explained in the following appendix entitled "Reasons to request information required under Annexes VII 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 Annex VII to REACH, for registration at 1-10 tonnes per year (tpa), or as a transported isolated intermediate in quantity above 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". For references used in this decision, please consult the Appendix entitled "List of references".

Appeal

This decision can be appealed to the Board of Appeal of ECHA within three months of its notification. An appeal, together with the grounds thereof, has to be submitted to ECHA in writing. An appeal has suspensive effect and is subject to a fee. Further details are described under: http://echa.europa.eu/regulations/appeals.

Approved[1] under the authority of Mike Rasenberg, 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

This decision is based on the examination of the testing proposals you submitted.

1. In vitro cytogenicity study in mammalian cells or In vitro micronucleus study

Under Annex VII, Section 8.4, column 2 of REACH, further mutagenicity studies must be considered in case of a positive result in an *in vitro* gene mutation study in bacteria. The ECHA guidance R.7a, section R.7.7.6.3 (p.570), further specifies that "*REACH Annex VII substances for which only a bacterial gene mutation test has been conducted and for which the result is positive should be studied further, according to the requirements of Annex VIII*." Therefore, it is necessary to request an *in vitro* cytogenicity or micronucleus study as an additional test to further investigate the mutagenicity of the Substance in accordance with the REACH integrated testing strategy. The obtained *in vitro* data will inform on the genotoxic concern(s) associated with the substance and help identify the most adequate follow-up *in vivo* study.

Your dossier contains positive results for the *in vitro* gene mutation study in bacteria, which raise the concern for gene mutation.

1.1. Information provided to fulfil the information requirement

You have submitted a testing proposal for an *In vivo* mammalian alkaline comet assay to be performed with the Substance with a concomitant micronucleus assay to further investigate the mutagenicity of the substance.

However, no information from an *in vitro* cytogenicity study or an *in vitro* micronucleus study in mammalian cells on the Substance is available in the dossier.

ECHA therefore considers that an appropriate *in vitro* cytogenicity or micronucleus study is necessary to further investigate the mutagenicity of the Substance and to help identify the most adequate follow-up *in vivo* study.

You have provided data with other substance(s). However, as set out in the following section 1.1.2, the information available in your dossier currently does not allow ECHA to accept an adaptation of the information on an *in vitro* cytogenicity or micronucleus study by read-across.

1.1.2 Grouping of substances and read-across approach

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

Additional information on what is necessary when justifying a read-across approach can be found in the ECHA Guidance R.6 and related documents.

You have provided a read-across justification document in IUCLID Section 13 ('*Justification of a read-across approach for in vivo genotoxicity*').

In your read-across justification document you refer to a category approach, however for the *in vitro* cytogenicity or micronucleus endpoint you provide data with only one substance.

Therefore, for this particular endpoint, ECHA understands that you predict the properties of the Substance from the following structurally similar substance:

- rhodium(III) trichloride hydrate, EC No. 606-630-8 (CAS No. 20765-98-4), i.e. the source substance.

The source study that you have used in your read-across approach, '*In vitro mammalian micronucleus assay in Chinese Hamster V79 cells with rhodium (III) chloride hydrate, solution*' ([redacted], 2007), corresponds to the *in vitro* mammalian cell micronucleus test performed according to the OECD TG 487.

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

- the '*rhodium is in the 3+ oxidation state, coordinated to inorganic or organic counterions*';
- they '*are readily water-soluble, and will dissociate rapidly when taken up orally and on reaching the gastric environment (low pH, high chloride-concentration)*'; and
- there is '*chemical similarity, as well as their similar profiles of biological activity – particularly related to mutagenicity outcomes.'*

ECHA understands that you predict the properties of the Substance using a read-across hypothesis which is based on the formation of common (bio)transformation products. The properties of your Substance are predicted to be quantitatively equal to those of the source substance.

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

a) Missing supporting information

Annex XI, Section 1.5 of the REACH Regulation states that "*physicochemical properties, human health effects and environmental effects or environmental fate may be predicted from data for reference substance(s)*". For this purpose "*it is important to provide supporting information to strengthen the rationale for the read-across*" (ECHA Guidance R.7a, Section R.6.2.2.1.f.). The set of supporting information, such as toxicokinetics, 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).

i.) Missing information on the formation of common compound

As indicated above, your read-across hypothesis is based on the (bio)transformation of the Substance and of the source substance(s) to a common compound(s). In this context, information characterising the rate and extent of the (bio)transformation of the Substance and of the source substance(s) is necessary to confirm the formation of the proposed common (bio)transformation product and to assess the impact of the exposure to the parent compounds.

However, you have not provided any comparative experimental information about the (bio)transformation of the substances to support your claims regarding formation of a common compound. In particular, there are no comparative toxicokinetic or other data to support the claim that the same ionic species is formed for the different substance(s). In addition, the impact of exposure to the parent compound cannot be assessed as the information provided does not allow comparison of the rate and extent of ion release from the substances.

In the absence of this information, you have not provided supporting evidence establishing that the proposed common (bio)transformation product is formed to a comparable extent as assumed in your read-across hypothesis.

ii.) Missing information on the impact of non-common compounds

As indicated above, your read-across hypothesis is based on the (bio)transformation of the Substance and of the source substance(s) to a common compound(s). In this context, exposure to the Substance and of the source substance(s) may also lead to exposure to other compounds than the common compound of interest. The impact of exposure to these non-common compounds on the prediction of properties of the target needs to be assessed to ensure that a reliable prediction can be made.

You have not provided information characterising the exposure to the non-common compounds resulting from exposure to the Substance and to the source substance(s). No experimental data or other adequate and reliable information addressing the impact of exposure to these non-common compounds is included in the documentation of your read-across approach.

In the absence of such information, you have not established that a reliable prediction of the property under consideration of the Substance can be derived on the basis of your read-across hypothesis.

Therefore, based on the above, you have not provided sufficient supporting information to strengthen the rationale for the read-across.

b) Relevance of the supporting information

According to the ECHA Guidance R.7a, Section R.6.2.2.1.f., "*it is important to provide supporting information to strengthen the rationale for the read-across approach. Thus, in addition to the property/endpoint being read across, it is also useful to show that additional properties, relevant to the endpoint, are also (qualitatively or quantitatively) similar between the source and target chemicals*".

(i) Water solubility

You currently consider that to compare bioavailability *in vitro,* you rely on "[…] *comparative water-solubility data and related inferences on bioavailability* […]". However, the substances have more than a 2-fold difference in water solubility. There is currently no information to support the claim that water solubility is indicative of *in vitro* bioavailability. Therefore, it cannot be confirmed that the substances may have similar properties due to similar bioavailability.

(ii) Genotoxicity & other toxicological properties

In order to support your claim that the Substance and the source substance have similar properties for the genetic toxicity endpoint under consideration, you refer to studies relating to the acute toxicity, skin irritation, eye irritation, skin sensitisation properties.

However, these studies do not inform on the mutagenicity properties of the Substance and the source substance. Accordingly, this information is not considered as relevant to support your hypothesis.

Additionally, for the genotoxicity endpoint you provide information on *in vitro* bacterial gene mutations for the Substance and the source substance. However, as mentioned above, for the *in vitro* cytogenicity endpoint you only provide an *in vitro* study with the source substance.

The data provided for chromosomal aberration is not enough to be able to determine whether the properties of the source substance can be extrapolated to the Substance.

Accordingly, the information provided is not sufficient to support your hypothesis and you have not established a reliable basis for predicting the properties of the endpoint under consideration.

c) Conclusions on the read-across approach

As explained above, you have not established that relevant properties of the Substance can be predicted from data on the source substance(s). 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.

1.2 Test design

Either the *in vitro* cytogenicity study in mammalian cells (test method OECD TG 473) or the *in vitro* micronucleus study (test method OECD TG 487) are considered suitable.

1.3 Outcome

Under Article 40(3)(c) of REACH, you are requested to carry out the additional test, as indicated above.

In the testing proposal examination, ECHA has only assessed the read-across adaptation provided to address the *in vitro* cytogenicity endpoint (section 1.1.2 above) and the need to perform an *in vivo* follow up test (section 2 below) with the Substance.

In your comments on the draft decision, you agree to take the Substance out of the read-across group and to compile and/or generate a substance-specific dataset for the endpoint under consideration. In addition, you question whether the *in vitro* study is really needed since you proposed to perform the comet assay in combination with the micronucleus test, as mentioned in section 2 below.

As already explained above, according to the ECHA Guidance R.7a, section R.7.7.6.3 and Figure R.7.7-1 (*Flow chart of the mutagenicity testing strategy*), if there is a positive result in the gene mutation test in bacteria, the Substance should be studied further according to the requirements of Annex VIII. Therefore the *in vitro* cytogenicity or micronucleus study must be performed first to determine which appropriate *in vivo* follow-up study is required for the Substance, as specified in section 2.2. below.

2. In vivo genetic toxicity study

Under Annex VII Section 8.4., column 2 of REACH, further mutagenicity studies must be considered in case of a positive result in an *in vitro* gene mutation study in bacteria.

Your dossier contains positive results with the Substance for the *in vitro* gene mutation study in bacteria which raise the concern for gene mutations.

2.1 Information provided to fulfil the information requirement

You have submitted a testing proposal for an *In vivo* mammalian alkaline comet assay to be performed with the Substance with a concomitant micronucleus assay coupled to an ancillary toxicokinetic assessment.

ECHA requested your considerations for alternative methods to fulfil the information requirement for Genetic toxicity *in vivo*. You provided your considerations concluding that there were no alternative methods which could be used to adapt the information requirement(s) for which testing is proposed. ECHA has taken these considerations into account.

ECHA agrees that an appropriate *in vivo* follow up genotoxicity study is necessary to address the concern identified *in vitro.*

2.2 Test selection

The proposed *in vivo* mammalian alkaline comet assay ("comet assay", OECD TG 489) is appropriate to investigate effects on gene mutations *in vivo* (ECHA Guidance R.7a, Section R.7.7.6.3. and Figure R.7.7-1*)*.

However, by this decision ECHA also requests an *in vitro* cytogenicity or micronucleus test, which may raise a concern for chromosomal aberration, in case of positive results. The obtained *in vitro* data will inform on the genotoxic concern(s) associated with the substance and help identify the most adequate follow-up *in vivo* study. For the detailed reasons see section A.1 above.

In case there is also a concern for chromosomal aberration, you must combine the comet assay and the *in vivo* mammalian erythrocyte micronucleus test ("MN test", OECD TG 474) into a single study (see OECD TG 489 para. 33; OECD TG 474 para. 37c; ECHA Guidance R.7a, Section R.7.7.6.3). While the comet assay can detect primary DNA damage that may lead to gene mutations and/or structural chromosomal aberrations, the MN test can detect both structural chromosomal aberrations (clastogenicity) and numerical chromosomal aberrations (aneuploidy). A combined study will thus address both the identified concerns for chromosomal aberration as well as gene mutation.

The combined study, together with the results of the *in vitro* mutagenicity studies, can be used to make definitive conclusions about the mechanism(s) inducing *in vivo* mutagenicity and lack thereof. Furthermore, the combined study can help reduce the number of tests performed and the number of animals used while addressing (structural and numerical) chromosomal aberrations as well as gene mutations.

Therefore, you must wait for the results of the *in vitro* test requested under A.1. and, depending on these results, to conduct either a) Comet assay if the test results of request A.1 are negative; or b) Comet assay combined with MN test if the test results of request A.1 are positive. The deadline set in this decision allows for sequential testing.

2.3 Specification of the study design

*a) Comet assay (if the test results of request A.1 are **negative**)*

You proposed testing in the rat. According to the test method OECD TG 489, rats are the preferred species. Other rodent species can be used if scientifically justified (OECD TG 489, para. 23).

You proposed testing by the oral route. Having considered the anticipated routes of human exposure and adequate exposure of the target tissue(s) performance of the test by the oral route is appropriate. Since the Substance is corrosive (self-classified for Skin Corr. 1B, H314), you propose to perform a preliminary dose range-finding study with the aim of identifying the maximum tolerated dose (MTD). ECHA reminds you that *in vivo* testing with corrosive substances at concentration/dose levels causing corrosivity must be avoided (see REACH Annex VII-X preamble).

You proposed testing on the following tissues: liver, glandular stomach, and duodenum. 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.

ECHA notes that it is at your discretion to perform the toxicokinetic study in combination to the study requested.

Germ cells
You may consider to collect the male gonadal cells 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.

Potential cross-linking properties
You are reminded that you may decide to take into account the potential cross-linking properties of the Substance in the experimental setup of the comet assay and perform a modified comet assay in order to detect cross links. Therefore, you may consider preparing and analysing two sets of slides: one set of slides submitted to the standard experimental conditions (as described in OECD TG 489); the other set of slides submitted to modified experimental conditions that enable the detection of DNA. The modified experimental conditions may utilise one of the following options: (1) increase of electrophoresis time, e.g. as described in reference 23 *[1]* in the OECD TG 489; (2) treatment of isolated cells (either in suspension or embedded in the slides) with a chemical (e.g. MMS); or (3) treatment of isolated cells (either in suspension or embedded in the slides) with ionising radiation (options 2 and 3 are described e.g. in references 36-39 *[2-5]* in the OECD TG 489 or Pant et al. 2015 *[6]*). In order to ensure the robustness of the test result a specific positive control group of animals would be needed.

References:
[1] Nesslany *et al.* (2007) In vivo comet assay on isolated kidney cells to distinguish genotoxic carcinogens from epigenetic carcinogens or cytotoxic compounds *Muta Res*;630(1-2):28-41.
[2] Merk and Speit (1999) Detection of crosslinks with the comet assay in relationship to genotoxicity and cytotoxicity. *Environ Mol Mutagen*;33(2):167-72.

[3] Pfuhler and Wolf (1996) Detection of DNA-crosslinking agents with the alkaline comet assay. *Environ Mol Mutagen*;27(3):196-201.
[4] Wu and Jones (2012) Assessment of DNA interstrand crosslinks using the modified alkaline comet assay. *Methods Mol Biol*;817:165-81.
[5] Spanswick *et al.* (2010) Measurement of DNA interstrand crosslinking in individual cells using the Single Cell Gel Electrophoresis (Comet) assay. *Methods Mol Biol*;613:267-282.
[6] Pant K *et al.* (2015) Modified *in vivo* comet assay detects the genotoxic potential of 14-hydroxycodeinone, an α,β -unsaturated ketone in oxycodone. *Environ Mol Mutagen*;56(9):777-87.

*b) Comet assay combined with MN test (if the test results of request A.1 are **positive**)*

You proposed testing in the rat. According to the test method OECD TG 489, rats are the preferred species. Other rodent species can be used if scientifically justified. According to the test method OECD TG 474, the test may be performed in mice or rats. Therefore, the combined study must be performed in rats, or if justified, in mice.

You proposed testing by the oral route. 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. Since the Substance is corrosive (self-classified for Skin Corr. 1B, H314), you propose to perform a preliminary dose range-finding study with the aim of identifying the maximum tolerated dose (MTD). ECHA reminds you that *in vivo* testing with corrosive substances at concentration/dose levels causing corrosivity must be avoided (see REACH Annex VII-X preamble).

For the comet assay you proposed testing on the following tissues: liver, glandular stomach, and duodenum. 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.

For the MN test you proposed testing the bone marrow. According to OECD TG 474, the study can either be performed using the bone marrow or peripheral blood cells.

The combination of OECD TGs 489 and 474 should not impair the validity of and the results from each individual study. Careful consideration should be given to the dosing, and tissue sampling for the comet analysis alongside the requirements of tissue sampling for the mammalian erythrocyte micronucleus test (see OECD TG 489, e.g. Bowen *et al*. 2011 [1]).

ECHA notes that it is at your discretion to perform the toxicokinetic study in combination to the study requested.

Germ cells
You may consider to collect the male gonadal cells 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.

Potential cross-linking properties
You are reminded that you may decide to take into account the potential cross-linking properties of the Substance in the experimental setup of the comet assay and perform a modified comet assay in order to detect cross links. Therefore, you may consider preparing and analysing two sets of slides: one set of slides submitted to the standard experimental conditions (as described in OECD TG 489); the other set of slides submitted to modified experimental conditions that enable the detection of DNA. The modified experimental conditions may utilise one of the following options: (1) increase of electrophoresis time, e.g. as described in reference 23 *[2]* in the OECD TG 489; (2) treatment of isolated cells (either in suspension or embedded in the slides) with a chemical (e.g. MMS); or (3) treatment of isolated cells (either in suspension or embedded in the slides) with ionising radiation (options 2 and 3 are described e.g. in references 36-39 *[3-6]* in the OECD TG 489 or Pant et al. 2015 *[7]*). In order to ensure the robustness of the test result a specific positive control group of animals would be needed.

References:
[1] Bowen DE et al. (2011) Evaluation of a multi-endpoint assay in rats, combining the bone-marrow micronucleus test, the comet assay and the flow-cytometric peripheral blood micronucleus test. *Muta Res*;722:7–19.
[2] Nesslany *et al.* (2007) In vivo comet assay on isolated kidney cells to distinguish genotoxic carcinogens from epigenetic carcinogens or cytotoxic compounds *Muta Res*;630(1-2):28-41.
[3] Merk and Speit (1999) Detection of crosslinks with the comet assay in relationship to genotoxicity and cytotoxicity. *Environ Mol Mutagen*;33(2):167-72.
[4] Pfuhler and Wolf (1996) Detection of DNA-crosslinking agents with the alkaline comet assay. *Environ Mol Mutagen*;27(3):196-201.
[5] Wu and Jones (2012) Assessment of DNA interstrand crosslinks using the modified alkaline comet assay. *Methods Mol Biol*;817:165-81.
[6] Spanswick *et al.* (2010) Measurement of DNA interstrand crosslinking in individual cells using the Single Cell Gel Electrophoresis (Comet) assay. *Methods Mol Biol*;613:267-282.
[7] Pant K *et al.* (2015) Modified *in vivo* comet assay detects the genotoxic potential of 14-hydroxycodeinone, an α,β -unsaturated ketone in oxycodone. *Environ Mol Mutagen*;56(9):777-87.

2.4 Outcome

Under Article 40(3)(b) your testing proposal is accepted under modified conditions and you are requested to conduct the test with the Substance, as specified above.

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[2].

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[3].

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

Appendix C: Procedure

ECHA started the testing proposal evaluation in accordance with Article 40(1) on 21 August 2020.

ECHA held a third party consultation for the testing proposal(s) from 19 October 2020 until 3 December 2020. ECHA did not receive information from third parties.

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

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 took the decision according to Article 51(3) of the REACH Regulation.

Appendix D: List of references - ECHA Guidance[4] 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)[5]

RAAF - considerations on multi-constituent 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.

[4] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[5] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across
[6] https://echa.europa.eu/documents/10162/13630/raaf_uvcb_report_en.pdf/3f79684d-07a5-e439-16c3-d2c8da96a316

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

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

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

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

[7] http://www.oecd.org/chemicalsafety/testing/series-testing-assessment-publications-number.htm

Appendix E: Addressees of this decision and the corresponding information requirements applicable to them

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

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

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.