EUROPEAN CHEMICALS AGENCY

~~Confidential~~

Helsinki, 1 June 2021

Addressees
Registrant(s) of JS_693-36-7 as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
14/07/2017

Registered substance subject to this decision ("the Substance")
Substance name: Dioctadecyl 3,3'-thiodipropionate
EC number: 211-750-5
CAS number: 693-36-7

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

DECISION ON A COMPLIANCE CHECK

Under Article 41 of Regulation (EC) No 1907/2006 (REACH), you must submit the information listed in C.1. below by ***6 September 2022*** and all other information listed below by ***6 September 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)

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

1. Only if a negative result in Annex VII, Section 8.4.1. is obtained, In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.; test method: OECD TG 476 or TG 490)

2. Justification for an adaptation of a Short-term repeated dose toxicity (28 days) based on the results of the Sub-chronic toxicity study (90 days) requested below (Annex VIII, Section 8.6.1.)

C. 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. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method: OECD TG 414) by oral route, in one species (rat or rabbit)

D. 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 (rat or rabbit)

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 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 and VIII to REACH, for registration at 10-100 tpa;
- the information specified in Annexes VII, VIII and IX to REACH, for registration at 100-1000 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 on Reasons common to several requests

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

You seek to adapt the following standard information requirements by applying (a) read-across approach(es) in accordance with Annex XI, Section 1.5:

- In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.)
- In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.)
- Sub-chronic toxicity study (90-day), (Annex IX, Section 8.6.2.)
- Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)
- Pre-natal developmental toxicity study in a second species (Annex IX, Section 8.7.2., column 2).

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

Grouping of substances and read-across approach

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

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

A. Predictions for toxicological properties

You have provided a read-across justification document in the CSR.

You read-across between the structurally similar substances, didodecyl 3,3'-sulfanediyldipropanoate, EC No. 204-614-1 (CAS No. 123-28-4) as source substance and the Substance as target substance.

You have provided the following reasoning for the prediction of toxicological properties: "*The proposed read-across substance didodecyl 3,3'-thiodipropionate is an analogue substance that differs in having two C12 alkyl chains instead of two C18 alkyl chains. The shorter alkyl chains are expected to result in slightly more favorable solubility and absorption after uptake. Considering the 1.3-fold difference in molecular weight, application of the C12 analogue results in a higher number of molecules so that overall, any hazard identified for didodecyl 3,3'-thiodipropionate is considered also relevant for dioctadecyl 3,3'-thiodipropionate. The higher number of molecules and the estimated better absorption of the read-across compound*

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

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

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

provide a [conservative] *approach and the proposed read across is considered adequate."* and *"In conclusion, the varying alkyl side chain lengths (C12 vs. C18) do not have a substantial impact on the toxicity profile of the two substances. The compounds are comparable regarding physical and chemical properties, structure and toxicological hazard."*

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(s) with regards to prediction(s) of toxicological properties.

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"*[5]. 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).

Supporting information must include bridging studies to compare properties of the Substance and source substance.

1. *Issue - Missing supporting information to compare properties of the substances*

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 substance cause the same type of effects. Such information can be obtained, for example, from bridging studies of comparable design and duration for the Substance and of the source substance.

In your read-across jutification, you claim that both the Substance and the source substance are comparable regarding toxicological hazard based on the available toxicity data summarised in the table named *"Data matrix for toxicological properties"*, which covers acute toxicity, irritation, sensitisation and *in vitro* chromosomal aberration. There is no reliable information available for other *in vitro* genotoxicity endpoints, for repeated dose toxicity and/or for toxicity to reproduction and development for the Substance.

In your comments to the draft decision, you indicate your intention to improve your read-across justification by generating further supporting data.

ECHA notes that the comments and proposed approaches to improve the read-across justification are different between the lead registrant and another registrant:

- The lead registrant proposes to strengthen the current analogue approach by conducting a tiered testing strategy for repeated dose toxicity and reproductive and pre-natal developmental toxicity endpoints on the Substance and the source substance, generating first OECD TG 422 bridging information and then considering the need for performing further OECD TG 408 and 414 studies.
- Another registrant proposes to use a Category approach for *"Mercaptocarboxylic acids, their esters and related compounds"* by performing further (higher tier) tests for some

[5] Guidance on information requirements and chemical safety assessment Chapter R.6: QSARs and grouping of Chemicals, Section R.6.2.2.1.f

key Category members to address the genotoxicity endpoints, and by conducting mechanistic assays *in vitro* to address the repeated dose toxicity and reproductive toxicity and pre-natal developmental toxicity endpoints.

With your comments, you have not provided new supporting (experimental) data to support a read-across adaptation.

From the lead registrant's comments, it is not clear how the proposed testing strategy will cover the request for an *in vitro* gene mutation study in mammalian cells. From the other registrant's comments, no details are provided on which genotoxicity tests are foreseen to be performed, and it is not specified whether the Substance will be tested.

Regarding the member registrant's comments on repeated dose toxicity and reproductive toxicity and pre-natal developmental toxicity, ECHA notes that mechanistic data may support the read-across hypothesis if they are relevant to the endpoints of interest, but they do not have the same value as bridging studies for the comparison of effects between substances since *in vitro* mechanistic studies may, for instance, not reflect similarities or differences in absorption or metabolism of the substances.

ECHA cannot conclude on the reliability of the read-across approach proposed in the comments because the acceptability will depend on the outcome of the proposed studies and the relevance of the supporting information. 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").

The data set reported in the technical dossier and through your comments does not include relevant, reliable and adequate information for the Substance and the source substance to support your read-across hypothesis. In particular, you did not provide any information on the properties of the Substance regarding the above-mentioned endpoints, which would allow a comparison with the properties of the source substance.

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

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.

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 a standard information requirement in Annex VII to REACH.

You have adapted the standard information requirement mentioned above according to Annex XI, Section 1.5 (grouping of substances and read-across) of REACH.

In support of your adaptation, you have provided:
- one *in vitro* gene mutation study in bacteria (OECD TG 471) with an analogue substance (1992)

In addition, you have submitted as supporting study an *in vitro* gene mutation study in bacteria (OECD TG 471) with the Substance (1989).

We have assessed this information and identified the following issues:

1. To fulfil the information requirement, the study has to meet the requirements of OECD TG 471 (1997). One of the key parameters of this test guideline is:
   a) 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)

The reported data for the study you have provided with the Substance did not include:
   a) results for the appropriate 5 strains, that is in TA98/TA100/TA1535/TA1537 or TA97a or TA97/the required fifth strain, S. typhimurium TA102 or E. coli WP2 uvrA or E. coli WP2 uvrA (pKM101).

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

2. As explained in the Appendix on Reasons common to several requests, your adaptation under Annex XI, Section 1.5 is rejected.

In his comments to the draft decision, the lead registrant indicates the intention to adapt the standard information requirement mentioned above according to Annex XI, Section 1.3 (Qualitative or Quantitative structure-activity relationship ((Q)SAR)) of REACH. ECHA notes that this approach is different from the other registrant's intention to improve the read-across justification for this endpoint (see ECHA's reply in the Appendix on *reasons common to several requests*). ECHA has nevertheless evaluated the QSAR information provided in the lead registrant's comments.

With his comments, the lead registrant has provided the following information:
- QSAR predictions from the Oasis Times and Derek Nexus models, both concluding that the Substance is not mutagenic in bacteria.

We have assessed this information and identified the following issues:

Annex XI, Section 1.3. specifies that the following conditions must be fulfilled whenever a (Q)SAR approach is used:
1. the prediction needs to be derived from a scientifically valid model,
2. the substance must fall within the applicability domain of the model,
3. results need to be adequate for the purpose of risk assessment or classification and

labelling, and
4. adequate and reliable documentation of the method must be provided.

With regard to these conditions, we have identified the following issue(s):

Modelled endpoint not well defined

Under ECHA Guidance R.6.1.3., a (Q)SAR model must fulfil the principles described in the OECD Guidance document on the validation of (Q)SAR models (ENV/JM/MONO(2007)2) to be considered scientifically valid. The first OECD principle requires the endpoint of a (Q)SAR model to be well defined. ECHA Guidance R.6.5.1.2 specifies that for a well-defined endpoint:
- the training set must be obtained from experimental data generated with homogeneous experimental protocols, and
- the effect modelled being predicted by the (Q)SAR must be the same as the effect measured by a defined test protocol relevant to the information requirement, which in this case includes an estimate for all five strains required to be tested in an OECD TG 471 study.

You specify that the effect that is modelled is mutagenicity in bacteria. You have provided (Q)SAR models (Oasis Times and Derek Nexus) which are based on data generated using the following methodology: experimental data from mutagenicity tests in bacteria.

The training set for Oasis Times was obtained based on heterogeneous protocols: the result data are from various compilations, without specifications of the test method used to obtain them. In addition, the training set for Derek Nexus was not provided and it is not clear and it cannot be excluded that it was obtained based on heterogeneous protocols.

Furthermore, the endpoint predicted by both (Q)SARs is not the same as the endpoint measured by the relevant test protocol since not all training set substances have results for the required five strains. The endpoint predictions do not provide an estimate for each strain. Since you did not specify close analogues of the Substance from the training sets, ECHA cannot verify if the five strains were accounted for when the predictions were made for the Substance.

Therefore the endpoint of the model is not well defined and you have not established that the use of this model is a scientifically valid approach to meet this information requirement.

Lack of or inadequate documentation of the prediction (QPRF)

ECHA Guidance R.6.1.6.3 states that the information specified in or equivalent to the (Q)SAR Prediction Reporting Format document (QPRF) must be provided to have adequate and reliable documentation of the applied method. For a QPRF this includes, among others:
- the model prediction(s), including the endpoint,
- a precise identification of the substance modelled,
- the relationship between the modelled substance and the defined applicability domain,
- the identities of close analogues, including considerations on how predicted and experimental data for analogues support the prediction.

You provided the following information about the prediction: Oasis Times QPRF and Derek Nexus report. The information you provided about the predictions lacks the following elements:
- the identities of close analogues, including considerations on how predicted and experimental data for analogues support the prediction.

In absence of such information, ECHA cannot establish that the prediction can be used to meet this information requirement.

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

To fulfil the information requirement, the study has to meet the requirements of OECD TG 471 (1997).

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

1. In vitro gene mutation study in mammalian cells

An *in vitro* gene mutation study in mammalian cells is a standard information requirement in Annex VIII to REACH in case of a negative result in the *in vitro* gene mutation test in bacteria and the *in vitro* cytogenicity test.

For Annex VIII, 8.4.3., you have adapted the standard information requirement mentioned above according to Annex XI, Section 1.5 (grouping of substances and read-across) of REACH.

In support of your adaptation, you have provided one *in vitro* gene mutation study in mammalian cells (OECD TG 476) with an analogue substance (1992).

As explained in the Appendix on Reasons common to several requests, your adaptation under Annex XI, Section 1.5 is rejected.

Your dossier contains (i) a negative result for *in vitro* cytogenicity study in mammalian cells, and (ii) inadequate data for the other study (*in vitro* gene mutation study in bacteria).

The *in vitro* gene mutation study in bacteria provided in the dossier and the information provided by the lead registrant in your comments to the draft decision for an adaptation according to Annex XI, Section 1.3 of REACH are rejected for the reasons provided in section A.1.

The result of the request for information in section A.1 will determine whether the present requirement for an *in vitro* mammalian cell gene mutation study in accordance with Annex VIII, Section 8.4.3 is triggered.

In your comments to this draft decision, you indicate your intention to improve the read-across justification for the genotoxicity endpoints. Please refer to ECHA's reply in the Appendix on *reasons common to several requests.*

Information on study design

To fulfil the information requirement for the Substance, either the *in vitro* mammalian cell gene mutation tests using the hprt and xprt genes (OECD TG 476) or the thymidine kinase gene (OECD TG 490) are considered suitable.

2. Justification for an adaptation of a Short-term repeated dose toxicity (28 days) based on the results of the Sub-chronic toxicity study (90 days)

A Short-term repeated dose toxicity study (28 days) is a standard information requirement in Annex VIII (Section 8.6.1) to REACH. This information may take the form of a study record or a valid adaptation in accordance with either a specific adaptation rule under Column 2 of Annex VIII or a general adaptation rule under Annex XI.

You have not provided any study for this information requirement in your dossier.

In your comments to the draft decision, you indicate your intention to submit a read-across justification for the repeated dose toxicity endpoints. Please refer to ECHA's reply in the Appendix on *reasons common to several requests.*

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

Column 2 of Annex VIII, Section 8.6.1. provides that an experimental study for this endpoint is not needed if a reliable sub-chronic (90 days) or chronic toxicity study is available.

The present decision requests the registrants concerned to generate and submit a reliable sub-chronic toxicity study (90 days) (see Section C.1). According to Column 2 of Annex VIII, Section 8.6.1., and to prevent unnecessary animal testing, a short term toxicity study (28 days) does not therefore need to be conducted.

Because you still must comply with the information requirement in Annex VIII, Section 8.6.1., you are requested to submit a justification for the adaptation provided in Column 2 of that provision.

Appendix C: 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 (Section 8.6.2) to REACH.

You have adapted the standard information requirement mentioned above according to Annex XI, Section 1.5 (grouping of substances and read-across) of REACH.

In support of your adaptation, you have provided one 90-day repeated dose toxicity study (OECD TG 408) with an analogue substance (1993).

As explained in the Appendix on Reasons common to several requests, your adaptation under Annex XI, Section 1.5 is rejected.

In your comments to the draft decision, you indicate your intention to improve the read-across justification for the repeated dose toxicity endpoints. Please refer to ECHA's reply in the Appendix on *reasons common to several requests.*

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

Information on study design

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 the substance is a solid, not present in particulate form.

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. Pre-natal developmental toxicity study in one species

A Pre-natal developmental toxicity (PNDT) study (OECD TG 414) in one species is a standard information requirement under Annex IX to REACH.

You have adapted the standard information requirement mentioned above according to Annex XI, Section 1.5 (grouping of substances and read-across) of REACH.

In support of your adaptation, you have provided one study in rat similar to Pre-natal developmental toxicity study (OECD TG 414 with deviations, no GLP) with an analogue substance (1972). In addition, you have provided three supporting studies (similar to OECD TG 414 with deviations, no GLP) in hamster, mice and rabbit with an analogue substance (1972-1973).

As explained in the Appendix on Reasons common to several requests your adaptation is rejected. In addition, the following endpoint-specific deficiency has been identified in your read-across adaptation:

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).

In order to be considered compliant and enable assessing if the Substance is a developmental toxicant, the study has to meet the requirements of OECD TG 414. The key parameter(s) of this test guideline include e.g.

- examination of the dams for weight and histopathology of the thyroid gland/thyroid hormone measurements/gravid uterus weight/uterine content/body weight of the dams/clinical signs of the dams.

In the pre-natal developmental toxicity study in rats (1972) you have provided, the following deviations were identified: no necropsy of dams, no uterine weight measured, no statistics and no historical control data. The weight and histopathology of the thyroid gland has not been examined in dams, thyroid hormone measurements have not been conducted in dams, and gravid uterus weight has not been measured.

In your comments to the draft decision, you indicate your intention to improve the read-across justification for the repeated dose toxicity endpoints. Please refer to ECHA's reply in the Appendix on *reasons common to several requests.*

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

Information on study design

A PNDT study according to the test method OECD TG 414 must be performed in rat or rabbit as preferred species with oral[6] administration of the Substance.

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

Appendix D: 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 adapted the standard information requirement mentioned above according to Annex XI, Section 1.5 (grouping of substances and read-across) of REACH.

In support of your adaptation, you have provided three supporting studies (similar to OECD TG 414 with deviations, no GLP) in hamster, mice and rabbit with an analogue substance (1972-1973).

As explained in OECD TG 414, paragraph 6, it is recommended that testing be performed in the most relevant species, and that laboratory species and strains which are commonly used in prenatal developmental toxicity testing be employed. The preferred rodent species is the rat and the preferred non-rodent species is the rabbit. Justification should be provided if another species is used.

As you have not provided justification for other species, ECHA has assessed the study performed in rabbit as the study submitted as second species for this endpoint.

As explained in the Appendix on Reasons common to several requests your adaptation is rejected. In addition, the following endpoint-specific deficiency has been identified in your read-across adaptation:

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).

You have provided a key study in a second, non-rodent, species (similar to OECD TG 414 in rabbit) in your dossier. Deviations from the test guideline OECD TG 414 are unacceptable and not justified, because based on your documentation, maternal mortality of 20% occured during the study independent of group or pregnancy status and therefore, insufficient number of animals were used. Moreover, you have assessed the reliability of the study as *"4; not assignable, documentation insufficient for assessment".*

In your comments to the draft decision, you indicate your intention to improve the read-across justification for the repeated dose toxicity endpoints. Please refer to ECHA's reply in the Appendix on *reasons common to several requests.*

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

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 second species, depending on the species tested in the first PNDT study (request C.2 in this decision).

The study must be performed with oral[7] administration of the Substance.

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

Appendix E: 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[8].

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[9].

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

Appendix F: 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 11 December 2019.

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 and the deadline.

The timeline indicated in the draft decision to provide the information requested was 12 months for request C.1 and 18 months for all other requets from the date of the decision.

In his comments to the draft decision, the lead registrant requested an extension of the timeline stating the following: *"In the draft decision, ECHA grants the registrants 12 months for the sub-chronic toxicity study and 18 months for all remaining studies. We would like to point out that 12 months are already very challenging for the subchronic study, let alone 18 months for the tiered testing strategy. Upon consultation with the lead registrant's experimental toxicology division, we would like to ask for the following time frame: Tier 1: Generation of bridging data (i.e. OECD 422) including substance characterization, dose range finding etc.): 18 months. Tier 2: Potential follow-up studies including OECD 408 and two OECD 414 studies: 24 months. We are asking for 24 months since we would like to perform the two OECD 414 studies in succession. Should in the first study the need for classification arise, the second study would be obsolete, therefore we are asking for sufficient time to avoid the parallel performance of these studies. In total, the time frame needed for the proposed tiered testing approach is 42 months. Please also see the attached letter from the lead registrant's laboratory confirming this timeline."*

Another registrant also requested an unspecified extension of the timeline, although proposing a different approach for improving the read-across justification, stating the following: *"Our intention is to constantly improve and optimize our strategy in the next years. We would like to further develop a strategy for a Category Approach: Mercaptocarboxylic acids, their esters and related compounds. This is a long and tedious process and we are glad to have the support from our former consultants working with us during the last registration periods. However, we see a risk not to comply with the timelines set in the draft decisions."*

ECHA observes that neither the additional OECD TG 422 study proposed as bridging study by the Lead registrant nor the mechanistic *in vitro* assays proposed by the Member registrant were requested in the draft decision on the Substance. It is at your discretion to agree on the approach to follow to improve your dossier and perform the above-mentioned study(ies), and they can be commenced at any point in time. The

present decision does not require you to perform such tests and thereby the imposed deadlines cannot be affected.

On this basis, ECHA has not modified the deadline to provide the information.

However, ECHA notes a clerical error in setting one of the deadlines and has corrected it from 18 to 24 months, to allow performing the two requested OECD 414 studies sequentially.

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 G: List of references - ECHA Guidance[10] 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)[11]

RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017)[11]

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[12]
Guidance Document on aqueous-phase aquatic toxicity testing of difficult test chemicals – No 23, referred to as OECD GD 23.

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