~~Confidential~~

Helsinki, 29 October 2021

Addressees
Registrant(s) of JS_111-20-6 as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
18/12/2019

Registered substance subject to this decision ("the Substance")
Substance name: Sebacic acid
EC number: 203-845-5
CAS number: 111-20-6

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. and B.3. below by ***4 August 2023*** and all other information listed below by ***5 August 2024***.

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

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

1. In vitro cytogenicity study in mammalian cells (Annex VIII, Section 8.4.2.; test method: OECD TG 473) or In vitro micronucleus study (Annex VIII, Section 8.4.2.; test method: OECD TG 487)

2. If negative results are obtained in test performed for the information requirement of Annex VIII, Section 8.4.2. then: In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.; test method: OECD TG 476 or TG 490)

3. 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)

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

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

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". 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 cytogenicity study in mammalian cells or in vitro micronucleus study (Annex VIII, Section 8.4.2.)
- 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 X, Section 8.7.2.)

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 R.6. and related documents[2,3].

A. Predictions for toxicological properties

You have provided a read-across justification document in IUCLID Section 13.

You read-across between the structurally similar substances, adipic acid (EC No. 204-673-3) and disodium sebacate (EC No. 241-300-3) as source substances and the Substance as target substance.

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

"In the following document, a justification for the read-across to sebacic acid (CAS 111-20-6, target substance) from the structural analogues disodium sebacate (CAS 17265-14-4, source substance 1) and adipic acid (CAS 124-04-9, source substance 2) is provided, addressing different aspects concerning a similar structure, similar physico-chemical properties and a comparable toxicity profile. According to ECHA's "Read-Across Assessment Framework (RAAF)" an analogue approach was chosen*".*

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

[2] 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)

[3] 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

properties of your Substance are predicted to be quantitatively equal to those of the source substances.

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

Adequacy and reliability of source studies for mutagenicity, repeated dose toxicity and reproductive toxicity

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 mutagenicity you have provided studies on adipic acid.
For repeated dose toxicity and pre-natal developmental toxicity you have provided studies on disodium sebacate.

Specific reasons why your source studies do not meet these criteria are explained further below under the relevant information requirement sections B.1., B.2., C.1., C.2. and D.1. In particular, none of the studies cover adequately and reliably the key parameters addressed in the corresponding test methods referred. Therefore, no reliable predictions can be made for these information requirements.

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 substances. 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 already for these general reasons.

As indicated above, there are issues that are common to all information requirements under consideration and also issues that are specific for these information requirements individually. Altogether they result in a failure to meet the requirement of Annex XI, Section 1.5. The common issues are set out in the above, while the specific issues are set out under the information requirement(s) concerned in the Appendices below.

2. Information provided in your comments on the draft decision

In the comments to the draft decision, you indicate your intention to adapt the following information requirements by means of a weight of evidence approach according to Annex XI, section 1.2 of the REACH Regulation:

- In vitro cytogenicity study in mammalian cells or in vitro micronucleus study (Annex VIII, Section 8.4.2.)
- 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 X, Section 8.7.2.)

As regards sources of information for each of the above endpoints, your refer not only to the information already included in your dossier but also to additional sources of information, which are not yet provided, on the following analogue substance(s):
- Dodecanedioic acid (CAS 693-23-2);
- Adipic acid (CAS 124-04-9);
- Sodium adipate.

You have provided the following reasoning for the use of information on analogue substances as part of your weight of evidence adaptations: you consider that the transformation of dicarboxylic acids such as sebacic acid leads to the formation of linear dicarboxylic acids of shorter chain length as intermediate metabolites and ultimately to acetyl CoA and glucose. On that basis you state that "*toxicological information on members of the homologues series of linear dicarboxylic acids are relevant to predict toxicological properties of sebacic acid for endpoints where no sufficiently reliable testing data are available with the substance itself. This is in line with existing assessments of sebacic acid by several chemical panels such as the OECD Cooperative Chemicals Assessment Programme (CoCAM) where sebacic acid as member of the 'Aliphatic Acids Category' has been assessed with outcome 'adequate screening-level data are available to characterize the hazard to human health' (OECD, 2014)*".

ECHA understands that your weight of evidence approach is under development and cannot be yet (fully) assessed. We have however taken the provided information into account and identified the following issues:

Annex XI, Section 1.2 states that there may be sufficient weight of evidence from several independent sources of information leading to assumption/conclusion that a substance has or has not a particular dangerous (hazardous) property, while information from a single source alone is insufficient to support this notion.

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

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

You have not included a justification with an assessment, integration and weighing of the individual sources of information for relevance, reliability, coverage, consistency and results, and subsequently decided whether they together provide sufficient weight to conclude that the Substance has or has not the dangerous property investigated by the required study. This observation applies for all the information requirements listed above other than *in vitro* cytogenicity study in mammalian cells or *in vitro* micronucleus study. Even for this information requirement, the justification provided is limited only to the sources of information already provided in the dossier.

Moreover, you have not provided individual endpoint study records for each additional sources of information referred to in your comments. Without such study records, it is not possible to carry out an independent assessment of the relevance and reliability of the information in a weight of evidence approach.

Furthermore, you have indicated that with the additional sources of information you intend to identify the relevant toxicological properties of the Substance using the data obtained with analogue substances in a read-across approach as part of your weight of evidence adaptation.

However, using information obtained with analogue substances requires that conditions specified in Annex XI, Section 1.5. are met. 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 endpoint-specific hypothesis, explanation of the rationale for the prediction of properties and robust study summary(ies) of the study(ies) on the source substance(s) (Guidance on IRs and CSA, Section R.6.2.6.1.).

In your comments, you have provided a generic statement only and there is no specific justification per each of the relevant information requirements, establishing why the additional information on the analogue substances that you listed in your comments can reliably contribute to weight of evidence approaches intended to identify the toxicological properties of the Substance.

Appendix A: Reasons to request information required under Annex VII of REACH

1. Growth inhibition study aquatic plants

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

You have provided the following information:

i. key study [redacted], 2009, according to ISO 10253 [*Water quality - Marine Algal Growth Inhibition Test with Skeletonema costatum and Phaeodactylum tricornutum*]

We have assessed this information and identified the following issue:

To fulfil the information requirement, a study must comply with OECD TG 201 (Article 13(3) of REACH) or with acceptable alternatives to OECD TG 201 (as listed in ECHA Guidance R.7b, Appendix R.7.8-2). Therefore, the following specifications must be met:

Characterisation of exposure

- a reliable analytical method for the quantification of the test material in the test solutions with reported specificity, recovery efficiency, precision, limits of determination (*i.e.* detection and quantification) and working range must be available. Alternatively, a justification why the analytical monitoring of exposure concentrations is not technically feasible must be provided;
- the results can be based on nominal or measured initial concentration only if the concentration of the test material has been maintained within 20 % of the nominal or measured initial concentration throughout the test;

Technical specifications impacting the sensitivity/reliability of the test

- the test concentrations are below the limit of solubility of the test material in the dilution water;

Reporting of the results

- the results of algal biomass determined in each flask at least daily during the test period are reported in a tabular form;

Validity criteria

- 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* or *Desmodesmus subspicatus*. For other less frequently tested species, the value is ≤ 10%.

Your registration dossier provides one algae growth inhibition study with *Skeletonema costatum* according to an alternative to OECD TG 201 showing the following:

Characterisation of exposure

- no analytical monitoring of exposure was conducted and no justification is provided in your dossier or in your comments to the draft decision whether analytical monitoring was not technically feasible;

- effect values are based on nominal concentrations and you claim that the '*substance was insoluble*';

Technical specifications impacting the sensitivity/reliability of the test

- the nominal test concentrations were from 3 to 320 mg/L. You do not report in your dossier a limit of solubility of the test material in the test medium (natural seawater), but you claim that the '*substance was insoluble*'. In your comments to the draft decision you refer to reported water solubility in demineralized water (224 mg/L) and you claim that achievement of saturation concentration can be confirmed from observed effects;

Reporting of the results

- tabulated data on the algal biomass determined daily for each treatment group and control are not reported in your dossier. In the comments to the draft decision you have provided tabulated data of fluorescence however, you have not reported effective biomass nor how to extrapolate it. Furthermore, you have not specified if cell fluorescese measurements were impacted by other sources, e.g. you have not reported background fluorescence levels.

Validity criteria

- you have not specified in your dossier if the validity criteria were met. In the comments to the draft decision you claim that validity criteria were met.

Based on the above, there are major deficiencies impacting the study, conducted according to an acceptable alternative to the OECD TG 201, including the following:

a) *Characterization of exposure:* in the absence of analytical monitoring of effective exposure concentration or justification as to why analytical monitoring was not technically feasible, you have not demonstrated the stability of the test substance.
b) *Technical specifications impacting the sensitivity/reliability of the test:* in the absence of information on solubility in pelagic test media, you have not demonstrated that the test concentrations were below the water solubility. Your comments to the draft decision do not address the issue as the test media was seawater and you still report solubility in demineralized water. Increasing salitnity is often linked to decreased solubility of chemicals in aqueous systems. Thus, the solubility of the Substance in seawater is expected to be highly impacted, and this is further confirmed by your comments on the long term toxicity study in aquatic invertebrates request were you state that 'the actual solubility in aqueous media is apparently fairly low'.
c) *Reporting of results and validity criteria*: the tabulated data provided in your comments to the draft decision refer to fluorescence measurements only. In the absence of correlation between fluorescence and biomass it is not possible to assess the actual growth performance of the culture replicates. Although the reported fluorescence measurements are indicative of exponential cell growth in the control cultures, it does not allow extrapolation of biomass therefore, it is not possible to verify that the validity criteria are met, in particular with regards to the coefficient variations refered above.

On this basis, the information requirement is not fulfilled.

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

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

An *in vitro* cytogenicity study in mammalian cells or an *in vitro* micronucleus study is an information requirement under Annex VIII to REACH (Section 8.4.2.).

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

i. *In vitro* chromosome aberration study in mammalian cells (1974) with adipic acid
ii. *In vivo* mammalian bone marrow chromosome aberration test (1974) with adipic acid

As explained in the Appendix on Reasons common to several requests, 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.

We have assessed this information and identified the following issues:

Study i.

To fulfil the information requirement, the study has to be an *in vitro* chromosomal aberration test or an *in vitro* micronucleus test, conducted in mammalian cells in accordance with OECD TG 473 or OECD TG 487, respectively[4]. The key parameter of these test guidelines include that two separate test conditions must be assessed: in absence of metabolic activation and in presence of metabolic activation.

The reported data for the study you have provided did not include two separate test conditions. Testing was conducted only in absence of metabolic activation.

The information provided does not cover key parameter required by OECD TG 473.

Therefore, the study submitted in your adaptation does not provide a reliable coverage of the key parameters of the corresponding OECD TG and your adaptation is rejected.

Study ii.

For the data from an *in vivo* cytogenicity test to be considered adequate, the *in vivo* study you submitted has to meet the requirements of OECD TG 475, and the specifications/conditions of this test guideline include:

a) The study must include a positive control group.
b) Each group must have a minimum of 5 analysable animals (the test can be performed in either sex).
c) The mitotic index must be determined as a measure of cytotoxicity in at least 1000 cells per animal for all treated animals (including positive controls), untreated or vehicle/solvent negative control animals. At least 200 metaphases must be analysed for each animal for structural chromosomal aberrations including and excluding gaps.

The reported data for the *in vivo* study you submitted did not include:

a) a positive control group (or scoring control);
b) a minimum of 5 animals per group;

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

the analysis of the adequate number of cells.

Therefore, the study submitted in your adaptation does not provide a reliable coverage of the key parameters of the corresponding OECD TG and your adaptation is rejected.

Based on the information provided in your comments, ECHA agrees that several deficiencies of the study as pointed out in the initial draft decision do not remain and ECHA has accordingly removed them from the discussion on study ii. deficiencies above. However, you continue to argue in your comments that the low animal number in the negative control group and the lower number of analysed cells per animal are acceptable limitations. Those limitations were already considered in the initial draft decision, and found to jeopardize the statistical power of the study. The study cannot be used as key study, and unique source of information, due to those limitations. The information provided in your comments does not change this conclusion.

However, in the comments to the draft decision, while you acknowledge that neither study i. nor study ii. provide on their own the information to fulfil this information requirement you consider that the information from these studies can contribute to a weight of evidence adaptation according to Annex XI, Section 1.2, of the REACH Regulation.

More specifically you consider that study i. "*provides evidence that sebacic acid does not induce structural chromosomal aberrations in cultured mammalian cells*". You point out that study ii. makes up for the absence of metabolic activation in the design of study i. and "*provides sufficient evidence that metabolic activation has no effect regarding the induction of structural chromosomal aberrations*".

You also express your intention to include additional sources of information in your weight of evidence adaptation:

i. *in vivo* mammalian erythrocyte micronucleus test conducted with the analogue substance dodecanedioic acid (CAS 693-23-2);
ii. QSAR analysis using TIssue MEtabolism Simulator (TIMES) on the Substance. You specify that this QSAR model can be used to predict the potential of chemicals to induce chromosomal aberrations while accounting for metabolic activation.

ECHA understands that your weight of evidence approach is under development and as such cannot be yet (fully) assessed. We have however taken the provided information into account and identified the following issues:
As explained under Appendix on Reasons common to several requests, the weight of evidence adaptation must fulfil the information requirement based on relevant and reliable sources of information. These sources of information must provide sufficient weight to conclude that the Substance has or has not the (dangerous) property investigated by the required study.

Relevant information that can be used to support weight of evidence adaptation for information requirement of Section 8.4.2 at Annex VIII includes similar information that is produced by the OECD TG 473 or OECD TG 487. The key parameter(s) of these test guidelines include the detection and quantification of structural or numerical chromosomal aberrations in cultured mammalian cells, including data on the cytotoxicity and the frequency of cells with chromosomal aberrations or micronuclei.

Based on the information provided in your dossier and in your comments, the key parameters listed above may be covered by the information from studies i. and ii.

As the adaptation you refer to in your comment is yet to be fully described and justified, no assessment of the relevance of the information from the additional sources of information

only indicated in your comments and of the reliability of its contribution to a weight of evidence approach for this information requirement is completed. You remain responsible for complying with this decision by the set deadline.

To fulfil the information requirement for the Substance, either in vitro cytogenicity study in mammalian cells (Annex VIII, Section 8.4.2., test method OECD TG 473) or in vitro micronucleus study (Annex VIII, Section 8.4.2., test method OECD TG 487) are considered suitable.

2. In vitro gene mutation study in mammalian cells

An *in vitro* gene mutation study in mammalian cells is an information requirement under Annex VIII to REACH (Section 8.4.3.) in case of a negative result in the *in vitro* gene mutation test in bacteria and the *in vitro* cytogenicity test.

Your dossier contains (i) a negative result for *in vitro* gene mutation study in bacteria with the Substance and (ii) data for the other study with adipic acid (*in vitro* cytogenicity test).

The data to cover the *in vitro* cytogenicity study (ii) in mammalian cells provided in the dossier is rejected for the reasons provided in section B.1

The result of the request for information in section B.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.

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

i. *In Vitro* Mammalian Cell Gene Mutation Test (2009) with adipic acid

As explained in the Appendix on Reasons common to several requests, 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.

We have assessed this information and identified the following issues:

To fulfil the information requirement, the *in vitro* gene mutation study on mammalian cells has to meet the requirements of OECD TG 476 or OECD TG 490[5]. The key parameter(s) of these test guidelines include:

a) The maximum concentration tested must induce 80-90% of cytotoxicity compared to the negative control, or the precipitation of the tested substance. If no precipitate or limiting cytotoxicity is observed, the highest test concentration must correspond to 10 mM, 2 mg/mL or 2 µl/mL, whichever is the lowest.
b) The response for the concurrent negative control must be inside the historical control range of the laboratory.
c) Data on the cytotoxicity and the mutation frequency for the treated and control cultures must be reported.

The reported data for the study you have provided do not include:

a) a maximum tested concentration of 10 mM, 2 mg/mL or 2 µl/mL, or that induced 80-90% of cytotoxicity compared to the negative control, or the precipitation of the tested substance.

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

b) a negative control with a response inside the historical control range of the laboratory.
c) data on the cytotoxicity and the mutation frequency for the treated and control cultures.

The information provided does not cover key parameters required by OECD TG 476.

Therefore, the study submitted in your adaptation does not provide a reliable coverage of the key parameters of the corresponding OECD TG and your adaptation is rejected.

In the comments to the draft decision, you have provided information addressing the deficiencies identified (a-c) in the robust study summary included in your dossier. You should submit this information in an updated registration dossier by the deadline set in the decision.

As the information is currently not available in your registration dossier, the data gap remains.

Consequently, you are required to provide information for this endpoint, if an *in vitro* cytogenicity study in mammalian cells or an *in vitro* micronucleus study provides a negative result.

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.

3. 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 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 provided a study for a 28-day repeated dose toxicity study:

i. short-term repeated dose toxicity (1941, Vertraeglichke und Ausscheidungsverhaeltn isse von Dicarbonsaeuren) with the Substance

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

To be considered compliant and enable concluding whether the Substance has dangerous properties and supports the determination of the No-Observed Adverse Effect Level (NOAEL), a study has to meet the requirements of OECD TG 407. The following key parameter(s) of this test guideline include
a) 5 female and 5 male animals should be used at each dose level (including control group)
b) examination of the animals for histopathology (including thyroid gland/ thyroid hormone measurements), organ weights, clinical biochemistry

The study was conducted with less than 10 animals per test dose group. The statistical power of the information provided is not sufficient because it does not fulfil the criterion of 10 animals for each test group set in OECD TG 407.
The study you have provided was not performed according to the criteria of the OECD TG 407, since the following key parameters are missing: histopathology investigations, organ weight, clinical biochemistry investigations (with the exception of BUN (blood urea nitrogen) measurements).

Based on the above, the information you provided do 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) in rodents is a standard information requirement in Annex IX to REACH.

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

i. Chronic toxicity: oral feed study in rat (1990) with disodium sebacate (key study);
ii. Chronic toxicity: oral feed study in rabit (1990) with disodium sebacate (supporting study).

We consider that the proposed read-across approach for Sub-chronic toxicity study information request is plausible and could fulfil the information gaps as long as reliable studies with the analogue substance disodium sebacate will be reported in the registration dossier.

We have assessed the information included in your dossier and identified the following issues:

Reliability of source studies

As explained in the Appendix on Reasons common to several requests, under Annex XI, Section 1.5., the results to be read across must have a reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3).

The corresponding test method to fulfil this information requirement is the OECD TG 408.
The following key parameter(s) of this test guideline include, among others:

a) Testing is to be conducted in a rodent species,
b) Clinical observations, ophthalmological examination, sensory reactivity to various stimuli and functional observations of the animals, Recording of body weight, hematology, clinical biochemistry, and pathology of sexual (male and female) organs, full detailed gross necropsy and subsequent histopathology of both types tissues.

Study i.:
You provided a chronic toxicity study in rat on the source substance disodium sebacate.

The following issues are identified with the design of this study:

a) The following key parameters required to be investigated in a study conducted according to the OECD TG 408 are missing from your study: specific organ weight data, ophthalmological examination, urinalysis findings, behaviour examination, immunological findings, neuropathological findings and most of standard clinical chemistry and hematology findings.

Study ii.
You provided a Chronic toxicity study in rabbit on the source substance disodium sebacate.

The following issues are identified with the design of this study:

a) The study you have provided was performed in rabbits, which is not a rodent species, and you have not justified how a study in rabbits could be used to cover, or to support, an information requirement for a study in rodents as set in Annex IX, Section 8.6.2 column 1

Therefore, the studies i. and ii. submitted in your adaptation do not provide a reliable coverage of the key parameters of the corresponding OECD TG and your adaptation is rejected.

In the comments to the draft decision, you acknowledge that neither study i. nor study ii. provide on their own the information to fulfil this information requirement. Despite the recognised limitations from the studies included in the dossier, you consider that the information from these studies can contribute to an upcoming weight of evidence adaptation according to Annex XI, Section 1.2, of the REACH Regulation.

You also express your intention to include additional sources of information currently not provided in the dossier in your weight of evidence adaptation:

iii. Subchronic oral toxicity study in rats with dodecanedioic acid (CAS 693-23-2);
iv. Subchronic oral toxicity study in rats with sodium adipate;
v. Chronic oral toxicity study in rats with adipic acid (CAS 124-04-9).

ECHA understands that your weight of evidence approach is under development and cannot be yet (fully) assessed. We have however taken the provided information into account and identified the following issues:
As indicated under Appendix on Reasons common to several requests, the weight of evidence adaptation must fulfil the information requirement based on relevant and reliable sources of information. These sources of information must provide sufficient weight to conclude that the Substance has or has not the dangerous property investigated by the required study.
Relevant information that can be used to support weight of evidence adaptation for information requirement of Section 8.6.2 at Annex IX includes similar information that is produced by the OECD TG 408. The following aspects of systemic toxicity are covered: 1) in-life observations, 2) blood chemistry, 3) organ and tissue toxicity.

As explained under section 2 of the Appendix on Reasons common to several requests, essential elements of your weight of evidence adaptation are currently not provided neither in your dossier nor in your comments.

Since this adaptation is yet to be fully described and justified and sources of information (iii-v) still to be provided, no assessment of the relevance of the information already included in the dossier and currently not provided in the dossier but only mentioned in your comments to a weight of evidence approach for this information requirement is completed. Similarly, no evaluation of the reliability of the contribution of all these sources of information to a weight of evidence approach for this information requirement is completed

Therefore the information provided in your dossier and in your comments do not fulfil the information requirement nor allow to adapt it.

Information on the design of the study to be performed (route)

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. This is because although the Substance is reported to occur as a dust with a significant proportion (>1% on weight basis) of particles of inhalable size (MMAD < 50 µm),there is no concern for effects in the respiratory tract (e.g. substance is water soluble and not irritating/ corrosive to skin/eyes) and no oral repeated dose toxicity study is available to evaluate systemic toxicity following oral administration

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

i. Prenatal developmental toxicity study in rat (1990) with disodium sebacate (key study)
ii. Prenatal developmental toxicity study in rabbit (1990) with disodium sebacate (key study)

We consider that the proposed read-across approach for pre-natal developmental toxicity study information request is plausible and could fulfil the information gaps as long as reliable studies with the analogue substance disodium sebacate will be reported in the registration dossier.

We have assessed this information and identified the following issues:

Reliability of source studies

As explained in the Appendix on Reasons common to several requests, under Annex XI, Section 1.5., the results to be read across must have a reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3).

The corresponding test method to fulfil this information requirement is the OECD TG 414.
The following key parameter(s) of this test guideline include, among others:

1. testing of at least three dose levels and a concurrent control,
2. highest dose level should aim to induce some developmental and/or maternal toxicity,
3. 20 female animals with implantation sites for each test and control group,
4. examination of the foetuses for sex and body weight, external, skeletal and soft tissue alterations (variations and malformations) and number of resorptions and or live foetuses.

Study i.:
You provided a pre-natal developmental toxicity study in rat on the source substance disodium sebacate.

The following issues are identified with the design of this study:

The study was conducted with one dose level, lower than the limit dose of 1000 mg/kg/d specified in the OECD TG 414. Therefore it does not fulfil the criterion of at least three dose levels and concurrent control set in OECD TG 414. The highest dose level in the study did not induce any developmental and/or maternal toxicity and you have not shown that the aim was to induce toxicity. Therefore, the dose level selection was too low, and the study does not fulfil the criterion set in OECD TG 414.

In your comments you recognise that the dose level investigated in the study was half of the limit dose specified in the OECD TG 414. However you still consider that "*the results of this study provide evidence that an effect on development in rats would not be expected if sebacic acid was tested up to a level of 1000 mg/kg bw/day in a new study according to OECD TG 414*". You have not provided evidence or arguments to substantiate your assumption on the absence of developmental toxicity of the Substance if it were tested up to the limit dose.

The study was conducted with 10 pregnant females for each test group. The statistical power of the information provided is not sufficient because it does not fulfil the criterion of 20 pregnant females for each test group set in OECD TG 414.

In the comments to the draft decision you indicate that 20 pregnant females were dosed with the test substance at the start of the study. These females were distributed over 2 groups of 10 animals each: dams from the group 1 were sacrificed on gestation day 19 whereas feamles from the group 2 were allowed to deliver their pups and were dosed for 3 months after delivery. Only the pups from the 10 dams from group 1 were subjected to the investigations required to be conducted on all the pups according to the OECD TG 414. Therefore, since only the pups of half of the dams used in this study have been investigated, ECHA considers, as indicated above, that the study does not fulfil the criterion of 20 pregnant females for each test group set in the OECD TG 414.

In this study the sex and body weight of the foetuses has not been examined, external, skeletal and soft tissue alterations (variations and malformations) have not been examined and number of resorptions and or dead foetuses have not been recorded as required in OECD TG 414.

Study ii.:
You provided a pre-natal developmental toxicity study in rabbit on the source substance disodium sebacate.

The following issues are identified with the design of this study:

The study you have provided was conducted with 10 pregnant females for each test group. The statistical power of the information provided is not sufficient because it does not fulfil the criterion of 20 pregnant females for each test group set in OECD TG 414.

In the comments to the draft decision you indicate that 20 pregnant females were dosed with the test substance. These female were distributed over 2 groups of 10 animals: dams from the group 1 were sacrificed on gestation day 25 whereas females from the group 2 were allowed to deliver their pups and were dosed for 3 months after delivery. For the reasons presented above under the response to your comments on the deficiencies of study i., ECHA considers that the study ii. also does not fulfil the criterion of 20 pregnant females for each test group set in the OECD TG 414.

In the study you have provided the sex and body weight of the foetuses has not been examined, external, skeletal and soft tissue alterations (variations and malformations) have not been examined and number of resorptions and or dead foetuses have not been recorded as required in OECD TG 414

Therefore, the studies i. and ii. submitted in your adaptation do not provide a reliable coverage of the key parameters of the corresponding OECD TG and your adaptation is rejected.

In the comments to the draft decision, you acknowledge that neither study i. nor study ii. provide on their own the information to fulfil this information requirement. Despite the recognised limitations from the studies included in the dossier, you consider that the information from these studies can contribute to an upcoming weight of evidence adaptation according to Annex XI, Section 1.2, of the REACH Regulation.

You also express your intention to include additional sources of information currently not provided in the dossier in your weight of evidence adaptation:

iii. combined repeated dose Toxicity study with the reproduction/developmental toxicity

screening Test with dodecanedioic acid,
iv. prenatal developmental toxicity study in rats with adipic acid,
v. prenatal developmental toxicity study in mice with adipic acid,
vi. prenatal developmental toxicity study in hamsters with adipic acid,
vii. prenatal developmental toxicity study in rabbits with adipic acid.

ECHA understands that your weight of evidence approach is under development and cannot be yet (fully) assessed. We have however taken the provided information into account and identified the following issues:

As indicated under Appendix on Reasons common to several requests, the weight of evidence adaptation must fulfil the information requirement based on relevant and reliable sources of information. These sources of information must provide sufficient weight to conclude that the Substance has or has not the dangerous property investigated by the required study.

Relevant information that can be used to support weight of evidence adaptation for information requirement of Section 8.7.2 at Annex IX includes similar information that is produced by the OECD TG 414. The following aspects are covered:

1) Prenatal developmental toxicity: Prenatal developmental toxicity includes information after prenatal exposure on embryonic/foetal survivial (number of live foetuses; number of resorptions and dead foetuses, postimplantation loss), growth (body weights and size) and structural malformations and variations (external, visceral and skeletal) and other potential aspects of developmental toxicity due to in utero exposure. This information in two species should be covered to address the potential species differences.
2) Maternal toxicity: Maternal toxicity inlcudes information after gestational exposure on maternal survival, body weight and clinical signs and other potential aspects of maternal toxicity in the pregnant dam. This information in two species should be covered to address the potential species differences.
3) Maintenance of pregnancy: Maintenance of pregnancy includes information on abortions and/or early delivery as a consequence of gestational exposure.

As explained under section 2 of the Appendix on Reasons common to several requests, essential elements of your weight of evidence adaptation are currently not provided in your dossier and in your comments.

Since this adaptation is yet to be fully described and justified and sources of information (iii-vii) still to be provided, no assessment of the relevance of the information already included in the dossier and currently not provided in the dossier but only mentioned in your comments to a weight of evidence approach for this information requirement is completed. Similarly, no evaluation of the reliability of the contribution of all these sources of information to a weight of evidence approach for this information requirement is completed.

Therefore the information provided in your dossier and in your comments do not fulfil the information requirement nor allow to adapt it.

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.

3. Long-term toxicity testing on aquatic invertebrates

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

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

You have provided a justification to omit the study which you consider to be based on Annex IX, Section 9.1., Column 2. In support of your adaptation, you provided the following justification: *"In Annex IX of Regulation (EC) No 1907/2006, it is laid down that long-term toxicity testing shall be proposed by the registrant if the chemical safety assessment indicates the need to investigate further the effects on aquatic organisms. According to Annex I of this regulation, the chemical safety assessment triggers further action when the substance or the preparation meets the criteria for classification as dangerous according to Directive 67/548/EEC or Directive 1999/45/EC or is assessed to be a PBT or vPvB. The hazard assessment of sebacic acid reveals neither a need to classify the substance as dangerous for the environment, nor is it a PBT or vPvB substance, nor are there any further indications that the substance may be hazardous to the environment. Therefore a long-term toxicity study in aquatic invertebrates is not provided.".*

We have assessed this information and identified the following issue:

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

Your adaptation is therefore rejected.

In the comments to the draft decision, you agree to perform the requested study.

4. Long-term toxicity testing on fish

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

You have provided a similar adaptation as provided under C.3 above. In addition, you have referred to "reasons of animal welfare".

We have assessed this information and identified the following issue:

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

In addition, the minimisation of vertebrate animal testing is not on its own a legal ground for adaptation under the general rules of Annex XI.

Your adaptation is therefore rejected.

In the comments to the draft decision, you do not agree to perform the requested study. Instead, you further elaborate on your Annex IX, Section 9.1., Column 2 adaptation to conclude that the need for the requested study should be reevaluated after performing the long-term toxicity study on aquatic invertebrates, requested under Section C.3 of this decision.
Furthermore, you indicate your intention to adapt this information requirement according to Annex XI, Section 3.1 of REACH regulation. You claim that the Substance has only industrial uses and you provide an environmental exposure assessment and risk characterization to support your claim of safe use of the Substance without risk for the environment.

ECHA has assessed the information provided in the comments on the draft decision and identified the following issues:

Firstly ECHA reiterate that the Column 1 information requirement of Annex IX, Section 9.1 cannot be waived based on Column 2 referring to the Chemical Safety Assessment.

Secondly, regarding your intention to provide a new adaptation under Annex XI, Section 3.1, ECHA notes the following.

As stated in Annex XI, Section 3, testing in accordance with Sections 8.6 and 8.7 of Annex VIII and in accordance with Annexes IX and X may be omitted based on the exposure scenario(s) developed in the CSR, by providing an adequate and scientifically-supported justification based on a thorough and rigorous exposure assessment in accordance with Section 5 of Annex I Any one of the following criteria 3.2.(a),(b) or (c) shall be met. In particular :

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

- 3.2 (b) where the substance is not incorporated in an article the manufacturer or the importer demonstrates and documents for all relevant scenarios that throughout the life cycle strictly controlled conditions as set out in Art 18(4)(a) to (f) apply; and/or

- 3.2 (c) where the substance is incorporated in an article in which it is permanently embedded in a matrix or otherwise rigorously contained by technical means, it is demonstrated and documented that all of the following conditions i) to (iii) are fulfilled, where the first condition is
  - i. the substance is not released during its life cycle.
  - ii. the likelihood that workers or the general public or the environment are exposed to the substance under normal or reasonably foreseeable conditions of use is negligible; and
  - iii. the substance is handled according to the conditions set out in Article 18(4)(a) to (f) during all manufacturing and production stages including the waste management of the substance during these stages.

We have assessed this information and identified the following issues:

The first criterion 3.2(a) requires "*absence of or no significant exposure in all scenarios of the manufacture and all identified uses*". Moreover, relevant PNECs or DNELs are to be derived and exposure results are to be well below the derived PNECs or DNELs.

The PNEC in your dossier is not considered reliable since your dossier does not contain reliable information for all trophic levels to support its derivation. In particular, as per Section A.1 and C.3 of this draft decision, data on aquatic plants and aquatic invertebrates are yet to be generated, so criterion 3.2(a) cannot be fulfilled.

As regards criteria for 3.2.(b) and /or (c), you have not provided any information that the Substance is held in strictly controlled conditions set out in Article 18(4)(a) to (f). Furthermore, ECHA remarks that other members of the joint submission report widespread uses, including professional and consumer uses, which must be considered for an acurate and conservative risk asessment.

In conclusion, the arguments provided in your comments do not fulfil the conditions of the adaptation in accordance with Annex XI, section 3.

Additionally, ECHA reminds 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).

On this basis, the information requirement is not fulfilled.

Study design

To fulfil the information requirement for the Substance, the Fish, Early-life Stage Toxicity Test (test method OECD TG 210) is the most appropriate (ECHA Guidance R.7.8.2.).

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

i. Prenatal developmental toxicity study in rat (1990) with disodium sebacate (key study)
ii. Prenatal developmental toxicity study in rabbit (1990) with disodium sebacate (key study)

We consider that the read-across approach for a pre-natal developmental toxicity study in a second species information request is plausible and could fulfil the information gaps as long as reliable studies with the analogue substance disodium sebacate are reported in the registration dossier.

As explained in the Appendix on Reasons common to several requests, under Annex XI, Section 1.5., the results to be read across must have a reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3).

We have assessed the information included in your dossier and identified issues, as detailed in request C.2. above.

The studies i. and ii. submitted in your adaptation do not provide a reliable coverage of the key parameters of the corresponding OECD TG and your adaptation is rejected.

Your comments on the draft decision for this information requirement are the same as those provided for the information of Annex IX, 8.7.2 for a pre-natal developmental toxicity study in a first species. The comments are addressed under Appendix C, Section 2 above.

In your comments, you acknowledge that neither study i. nor study ii. provide on their own the information to fulfil this information requirement. Despite the recognised limitations from the studies included in the dossier, you consider that the information from these studies can contribute to an upcoming weight of evidence adaptation according to Annex XI, Section 1.2, of the REACH Regulation.

You also express your intention to include additional sources of information currently not provided in the dossier in your weight of evidence adaptation:

iii. combined repeated dose Toxicity study with the reproduction/developmental toxicity screening Test with dodecanedioic acid,
iv. prenatal developmental toxicity study in rats with adipic acid,
v. prenatal developmental toxicity study in mice with adipic acid,
vi. prenatal developmental toxicity study in hamsters with adipic acid,
vii. prenatal developmental toxicity study in rabbits with adipic acid.

ECHA understands that your weight of evidence approach is under development and cannot be yet (fully) assessed. We have however taken the provided information into account and identified the following issues:

As indicated under Appendix on Reasons common to several requests, the weight of evidence adaptation must fulfil the information requirement based on relevant and reliable

sources of information. These sources of information must provide sufficient weight to conclude that the Substance has or has not the dangerous property investigated by the required study.

Relevant information that can be used to support weight of evidence adaptation for information requirement of Section 8.7.2 at Annex X includes similar information that is produced by the OECD TG 414 on a second species (two species taking the first species into account to address the potential species differences). The following aspects are covered:

1) Prenatal developmental toxicity: Prenatal developmental toxicity includes information after prenatal exposure on embryonic/foetal survivial (number of live foetuses; number of resorptions and dead foetuses, postimplantation loss), growth (body weights and size) and structural malformations and variations (external, visceral and skeletal) and other potential aspects of developmental toxicity due to in utero exposure. This information in two species should be covered to address the potential species differences.

2) Maternal toxicity: Maternal toxicity inlcudes information after gestational exposure on maternal survival, body weight and clinical signs and other potential aspects of maternal toxicity in the pregnant dam. This information in two species should be covered to address the potential species differences.

3) Maintenance of pregnancy: Maintenance of pregnancy includes information on abortions and/or early delivery as a consequence of gestational exposure.

As explained under section 2 of the Appendix on Reasons common to several requests, essential elements of your weight of evidence adaptation are currently not provided neither in your dossier nor in your comments.

Since this adaptation is yet to be fully described and justified and sources of information (iii-vii) still to be provided, no assessment of the relevance of the information already included in the dossier and currently not provided in the dossier but only mentioned in your comments to a weight of evidence approach for this information requirement is completed. Similarly, no evaluation of the reliability of the contribution of all these sources of information to a weight of evidence approach for this information requirement is completed.

Therefore the information provided in your dossier and in your comments do not fulfil the information requirement not allow to adapt it.

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 shall 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 07 December 2020.

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

ECHA took into account your comments and did not amend the requests, however, amended the deadline.

Deadline to provide the information

In your comments on the draft decision, you requested an extension of the deadline for Sub-chronic toxicity study (90-day) from 12 to 18 months and of the deadline for both pre-natal developmental toxicity studies from 24 to 30 months. You justified the request based on limited laboratory capacity, development of analytical methods, performing range finding studies and the need to avoid parallel performance of the OECD 414 studies.

Based on the documentary evidence provided regarding laboratory capacity and the development of a suitable analytical method, ECHA has granted the request and extended the deadlines to 18 and 30 months.

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)[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]

[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] https://echa.europa.eu/documents/10162/13630/raaf_uvcb_report_en.pdf/3f79684d-07a5-e439-16c3-d2c8da96a316
[13] http://www.oecd.org/chemicalsafety/testing/series-testing-assessment-publications-number.htm

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.

Appendix H: 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]
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[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
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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.