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Helsinki, 20 June 2023

Addressee
Registrant of JS_214-122-9 as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
19/03/2020

Registered substance subject to this decision ("the Substance")
Substance name: Diallyl isophthalate
EC/List number: 214-122-9

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

DECISION ON A COMPLIANCE CHECK

Under Article 41 of Regulation (EC) No 1907/2006 (REACH), you must submit the information listed below by ***29 June 2026***.

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

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

1. In vivo mammalian alkaline comet assay combined with in vivo mammalian erythrocyte micronucleus test also requested below (triggered by Annex VII, Section 8.4., column 2).

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

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

4. Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: EU C.4. A/B/C/D/E/F/OECD TG 301A/B/C/D/E/F or EU C.29./OECD TG 310)

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

5. In vivo mammalian alkaline comet assay (triggered by Annex VIII, Section 8.4., column 2; test method: OECD TG 489) combined with in vivo mammalian erythrocyte micronucleus test (test method: OECD TG 474) in rats, or if justified, in mice, oral route. For the comet assay the following tissues shall be analysed: liver, glandular stomach and duodenum.

6. 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.)

7. Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.; test method: EU B.63/OECD TG 421 or EU B.64/OECD TG 422) by oral route, in rats

8. Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.; test method: EU C.1./OECD TG 203)

Information required from all the Registrants subject to Annex IX of REACH

9. Sub-chronic toxicity study (90-day) (Annex IX, Section 8.6.2.; test method: OECD TG 408) by oral route, in rats

10. 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)

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

The reasons for the decision(s) are explained in Appendix 1.

Information required depends on your tonnage band

You must provide the information listed above for all REACH Annexes applicable to you in accordance with Articles 10(a) and 12(1) of REACH. The addressee of the decision and its corresponding information requirements based on registered tonnage band are listed in Appendix 3.

In the requests above, the same study has been requested under different Annexes. This is because some information requirements may be triggered at lower tonnage band(s). In such cases, only the reasons why the information requirement is triggered are provided for the lower tonnage band(s). For the highest tonnage band, the reasons why the standard information requirement is not met and the specification of the study design are provided. Only one study is to be conducted; all registrants concerned must make every effort to reach an agreement as to who is to carry out the study on behalf of the others under Article 53 of REACH.

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 requirements for testing and reporting new tests under REACH, see Appendix 4.

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 Mike Rasenberg, Director of Hazard Assessment

[1] As this is an electronic document, it is not physically signed. This communication has been approved according to ECHA's internal decision-approval process.

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Appendix 1: Reasons for the request(s)

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0. Reasons common to several requests

0.1. Assessment of the read-across approach

1 You have adapted the following standard information requirements by using a grouping and read-across approach under Annex XI, Section 1.5:

- In vivo mammalian erythrocyte micronucleus test (Annex IX, Section 8.4., column 2)
- Transgenic rodent somatic and germ cell gene mutation assays (Annex IX, Section 8.4., column 2)
- Short-term repeated dose toxicity (28 day), (Annex VIII, Section 8.6.1.)
- Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)
- Sub-chronic toxicity study (90-day), (Annex IX, Section 8.6.2.)
- Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)
- Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.)
- Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.)
- Ready biodegradability (Annex VII, Section 9.2.1.1.)
- Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.)
- Long-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1., column 2)

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

3 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.

4 Additional information on what is necessary when justifying a read-across approach can be found in the Guidance on IRs and CSA, Chapter R.6. and related documents (RAAF, 2017; RAAF UVCB, 2017).

0.1.1. Predictions for (eco)toxicological and environmental fate properties

5 You provide a read-across justification document for toxicological and ecotoxicological properties attached under each corresponding endpoints listed above.

6 You predict the properties of the Substance from information obtained from the following source substance(s):

- [redacted], No EC No. or CAS RN provided
- Diallyl phthalate (DAP), EC No. 205-016-3.

7 You provide the following reasoning for the prediction of toxicological properties: "*This read-across strategy is based on the simple 1:1 analogue approach where read-across is performed from a single source substance (DAP) to a structurally similar single target substance (DAIP). It is proposed that any given toxicological property of one substance (the source substance) will predict the same property for another substance (the target substance) to fulfil a REACH information requirement. The read-across substance, DAP, has close structural similarity with the target substance (DAIP), the selected scenario proposes*

that different compounds have similar toxicological endpoint effects(s). It is therefore considered appropriate for use as read-across to predict the potential toxicity of the target substance, DAIP… The above substances are positional isomers, identical in chemical composition. DAP is the ortho form with the allyl sidechains at positions 1 and 2, DAIP is the meta form with the allyl sidechains at positions 1 and 3. Due to the close structural similarity between the two substances, read-across is considered appropriate and justifiable to avoid the further use of animals in toxicity testing in accordance with Regulation EC No 1907/2006 (REACH) (European Parliment, 18 December 2006)".

8 Additionally, you provide the following reasonings for the prediction of ecotoxicological and environmental fate properties:

- The target (DAIP) and source (DAP) substances can be considered to be analogues as they are structurally similar substances.
- the different positions of the ester groups on the aromatic hydrocarbon for DAIP and DAP are not likely to change the underlying mechanism of toxicity.
- Both DAP and DAIP have the same technical function and are used in similar industrial applications.
- The main variation between the target and source substance in terms of physico-chemical properties relates to vapour pressure which is not likely to have a major impact on environmental fate or effects to aquatic organisms.
- The difference in water solubility is not expected to impact the suitability of reading across from DAP to DAIP for environmental fate or aquatic toxicity effects.
- DAIP and DAP are different compounds but have qualitatively similar properties.

9 ECHA understands that your read-across hypothesis assumes that different compounds have the same type of effects. You predict the properties of your Substance to be quantitatively equal to those of the source substance.

10 We have identified the following issue(s) with the prediction(s) of (eco)toxicological and environmental fate properties:

0.1.1.1. Missing supporting information to compare the properties of the substances

11 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 supporting information to scientifically justify the read-across explanation for prediction of properties. The set of supporting information should strengthen the rationale for the read-across in allowing to verify the crucial aspects of the read-across hypothesis and establishing that the properties of the Substance can be predicted from the data on the source substance(s) (Guidance on IRs and CSA R.6, Section R.6.2.2.1.f.).

12 Supporting information must include bridging studies to compare properties of the source substance information to confirm your claim that the source and target substances have the quantatively equal properties.

13 As indicated above, your read-across hypothesis is based on the assumption that the structurally similar source substance(s) cause the same type of effect(s). In this context, relevant, reliable and adequate information allowing to compare the properties of the source substance(s) is necessary to confirm that the substances cause the same type of effects. Such information can be obtained, for example, from bridging studies of comparable design and duration for the Substance and of the source substance(s).

14 In the Appendix of the read-across justification for the ecotoxicological properties, you have provided the results and full output file from ECOSAR QSAR models for aquatic toxicity. However, the ECOSAR output does not include information on close analogues, including considerations on how predicted and experimental data for analogues support the prediction. In absence of this information, ECHA cannot assess the validity of these predictions to compare the property of source and target substance.

15 Furthermore, for the endpoints listed below, you have only provided studies on the source substance (DAP) in the registration dossier.

- repeated dose toxicity;
- reproductive toxicity;
- Short-term toxicity testing on aquatic invertebrate;
- Growth inhibition study aquatic plants;
- Ready biodegradability; and
- Long-term toxicity testing on aquatic invertebrates.

16 Apart from the QSAR predictions for aquatic endpoints and the studies on source stubstance, your read-across justification or the registration dossier does not include any robust study summaries or descriptions of data for the Substance that would confirm that both substances cause the same type of effects.

17 Thus the data reported in the read-across justification document does not include relevant, reliable and adequate information for the source substance to support your read-across hypothesis.

18 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 scientifically justify the read-across.

0.1.1.2. Inadequate or unreliable studies on the source substance

19 According to Annex XI, Section 1.5., if the grouping concept is applied then in all cases the results to be read across must have adequate and reliable coverage of the key parameters addressed in the corresponding study that shall normally be performed for a particular information requirement.

20 The studies submitted for the endpoints Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.), Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.), Ready biodegradability (Annex VII, Section 9.2.1.1.), Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.), Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.), and Long-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1., column 2) do not cover adequately and reliably key parameters from the corresponding test methods.

21 Specific reasons why the studies on the source substance do not meet these criteria are explained further below under the applicable information requirement sections 2, 3, 4, 8 and 11. Therefore, no reliable predictions can be made for these information requirements.

0.1.1.3. Read-across hypothesis contradicted by existing data

22 For the information on gene mutation, we have identified the following issue with the prediction:

23 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

supporting information to scientifically justify the read-across explanation for prediction of properties. The set of supporting information must strengthen the rationale for the read-across in allowing to verify the crucial aspects of the read-across hypothesis and establishing that the properties of the Substance can be predicted from the data on the source substance(s) (Guidance on IRs and CSA R.6, Section R.6.2.2.1.f.).

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

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

26 However, the results of the information on mutagenicity obtained with the source substance are indicating a different underlying mechanism of genotoxicity compared to the target substance. Specifically, positive results are observed in the in vitro gene mutation study in bacteria with strain TA 1535 in the absence of metabolic activation (indicating of GC basepair mutations) conducted with the source substance while positive results with strains TA1537 TA 98 in the absence of metabolic activation (indicating of frameshift mutations) and with E. coli WP2urvA/pKM 101 in the presence of metabolic activation (indicating of cross-linking mutagens) are reported for the equivalent study conducted for the Substance.

27 The available set of data on the Substance and on the source substance indicates differences in the toxicological properties of the substances. This contradicts your read-across hypothesis whereby the Substance and source substances cause the same type of effect(s) but a different underlying mechanism is identified. However, you have not supported and scientifically justified why such differences in the toxicological properties do not affect your read-across hypothesis.

0.1.2. Conclusion on the read-across approach

28 For the reasons above, you have not established that relevant properties of the Substance can be predicted from data on the source substance(s). Your read-across approach under Annex XI, Section 1.5. is rejected.

Reasons related to the information under Annex VII of REACH

1. *In vivo* mammalian alkaline comet assay combined with *in vivo* mammalian erythrocyte micronucleus test

29 Further mutagenicity studies must be considered under Annex VII, Section 8.4., column 2, in case of a positive result.

1.1. Triggering of the information requirement

30 Your dossier contains positive results for the in vitro gene mutation study in bacteria (Report number [redacted]) and in vitro cytogenicity tests (Report number [redacted]) and in vitro gene mutation study in mammalian cells (Report number [redacted]) which raise the concerns for gene mutations and chromosomal aberrations.

31 Therefore, the information requirement is triggered.

1.2. Information provided

32 You have adapted this information requirement by using Annex XI, Section 1.5. (Grouping of substances and read-across approach) based on experimental data from the following substances:

(i) in vivo gene mutation-micronucleus combination assay (OECD TG 488/474, oral route, 2016)

1.3. Assessment of the information provided

1.3.1. Read-across adaptation rejected

33 As explained in Section 0.1., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5 is rejected.

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

1.4. Test selection

35 The positive in vitro results available in the dossier indicate a concern for both chromosomal aberration and gene mutation.

36 The in vivo mammalian erythrocyte micronucleus test ("MN test", OECD TG 474) and the in vivo mammalian alkaline comet assay ("comet assay", OECD TG 489) can be combined in a single study (see OECD TG 474 paragraph 37c; OECD TG 489 paragraph 33; Guidance on IRs & CSA, Section R.7.7.6.3). While the MN test can detect both structural chromosomal aberrations (clastogenicity) and numerical chromosomal aberrations (aneuploidy), the comet assay can detect primary DNA damage that may lead to gene mutations and/or structural chromosomal aberrations. A combined study will thus address both the identified concerns for chromosomal aberration as well as gene mutation.

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

38 Therefore, the comet assay combined with the MN test is the most appropriate study for the Substance.

1.5. Specification of the study design

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

40 Having considered the anticipated routes of human exposure and adequate exposure of the target tissue(s) performance of the test by the oral route is appropriate.

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

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

1.5.1. Germ cells

43 You may consider collecting the male gonadal cells from the seminiferous tubules in addition to the other aforementioned tissues in the comet assay, as it would optimise the use of animals. You can prepare the slides for male gonadal cells and store them for up to 2 months, at room temperature, in dry conditions and protected from light. Following the generation and analysis of data on somatic cells in the comet assay, you should consider analysing the slides prepared with gonadal cells.

44 This type of evidence may be relevant for the overall assessment of possible germ cell mutagenicity including classification and labelling according to the CLP Regulation.

1.5.2. Cross-linking properties

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

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

2. Short-term toxicity testing on aquatic invertebrates

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

2.1. Information provided

47 You have adapted this information requirement by using Annex XI, Section 1.5. (Grouping of substances and read-across approach) based on experimental data from the analogue substance (EC 205-016-3):

(i) a study on short term toxicity on aquatic invertebrates according to OECD TG 202 (2003) with the analogue substance Diallyl phthalate (EC 205-016-3)

2.2. Assessment of the information provided

2.2.1. Read-across adaptation rejected

48 As explained in Section 0.1, your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5. is rejected. With regard to source study information, ECHA further identified the following endpoint specific issue:

2.2.1.1. The provided study does not meet the specifications of the test guideline

49 Under Annex XI, Section 1.5., the results to be read across must have an adequate and reliable coverage of the key parameters addressed in the test guideline for the corresponding study that shall normally be performed for a particular information requirement, in this case OECD TG 202. Therefore, the following specifications must be met:

50 Technical specifications impacting the sensitivity/reliability of the test

a) at least 20 animals are used at each test concentration and for the controls;

51 Reporting of the methodology and results

b) adequate information on the test material is provided (i.e. identifiers, purity and presence of impurities)

c) the number of immobilised daphnids is determined at 24 and 48 hours. Data are summarised in tabular form, showing for each treatment group and control, the number of daphnids used, and immobilisation at each observation.

52 In study (i) described as short-term toxiciy studies on aquatic invertebrates:

Technical specifications impacting the sensitivity/reliability of the test

a) you have reported that 10 animals were used per test concentration without replicates;

53 Reporting of the methodology and results

b) the purity of the test material and the presence of impurities are not reported;

c) key information on the test conditions are missing and, in particular, the suspended solid and TOC content of the test medium;

d) tabulated data on the number of immobilised daphnids after 24 and 48 hours for each treatment group and control are not reported;

54 Based on the above:

- there are critical methodological deficiencies resulting in the rejection of the study. More specifically,
  - the number of the animal used on the study is lower than required by the TG. Therefore, the statistical power of the submitted study is lower;
- the reporting of the study is not sufficient to conduct an independent assessment of its reliability. More specifically,
  - you have not provided adequate information to support that the test material used in these studies is representative of the Substance;
  - key information on the test conditions are missing and therefore it is not possible to conduct an independent assessment as to whether these studies where conducted under conditions that are consistent with the specifications of the OECD TG 202;
  - you have not provided adequate reporting of the study results and therefore it is not possible to verify that the validity criteria of the OECD TG 202 were met and to conduct an independent assessment of the interpretation of the results.

55 Therefore, the study submitted in your adaptation, as currently reported in your dossier, does not provide an adequate and reliable coverage of key parameter(s) of the OECD TG 202.

56 As explained above, you have not established that relevant properties of the Substance can be predicted from data on the source substance. Therefore, your read-across adaptation under Annex XI, Section 1.5. is rejected and this information requirement is not fulfilled.

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

3. Growth inhibition study aquatic plants

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

3.1. Information provided

59 You have adapted this information requirement by using Annex XI, Section 1.5. (Grouping of substances and read-across approach) based on experimental data from the following substances:

(i) a growth inhibition study on algae according to DIN 38412, Part 9 (1980) with the analogue substance "phthalic acid diallyl ester";

3.2. Assessment of the information provided

3.2.1. Read-across adaptation rejected

60 As explained in Section 0.1, your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5. is rejected. With regard to the source study information, ECHA identified the following additional endpoint specific issue:

3.2.1.1. The provided study does not meet the specifications of the test guideline

61 Under Annex XI, Section 1.5., the results to be read across must have an adequate and reliable coverage of the key parameters addressed in the test guideline for the corresponding study that shall normally be performed for a particular information requirement, in this case OECD TG 201. Therefore, the following specifications must be met:

62 Technical specifications impacting the sensitivity/reliability of the test

a) for *Desmodesmus subspicatus* cells/mL the initial cell density is 2-5 $x10^3$ cells/mL;

63 Characterization of exposure

b) analytical monitoring must be conducted. Alternatively, a justification why the analytical monitoring of exposure concentrations is not technically feasible must be provided;

64 Reporting of the methodology and results

c) adequate information on the test material is provided (i.e. identifiers, purity and presence of impurities)

d) the test design is reported (e.g., number of replicates, number of test concentrations);

e) the test conditions are reported (e.g., composition of the test medium, test temperature, biomass density at the beginning of the test);

f) the method for determination of biomass and evidence of correlation between the measured parameter and dry weight are reported. Algal biomass is normally determined based on dry weight per volume, or alternatively as cell counts or biovolume using microscopy or an electric particle counter. If an alternative method is used (e.g. flow cytometry, in vitro or in vivo fluorescence, or optical density), a satisfactory correlation with biomass must be demonstrated over the range of biomass occurring in the test;

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

65 In study (i) described as growth inhibition study on algae:

66 Technical specifications impacting the sensitivity/reliability of the test

a) the test was conducted on *Desmodesmus subspicatus* and the initial cell density was 10000 cells/mL;

67 Characterisation of exposure

b) no analytical monitoring of exposure was conducted and you provided no justification for omitting this information;

68 Reporting of the methodology and results

c) no identifiers are provided for the test material. In addition, the purity of the test material and the presence of impurities are not reported;

d) on the test design, you have not specified the number of replicates, the test concentrations;

e) on the test conditions, you have not specified the composition of the test medium and the test temperature.

f) you report that algal biomass was determined using optical density (turbidity). However, you have not reported evidence of correlation between the measured parameter and dry weight or cell numbers over the range of biomass occurring in the test. For study ii., you have not specified how cell density was determined;

g) tabulated data on the algal biomass determined daily for each treatment group and control are not reported.

69 Based on the above,

- there are critical methodological deficiencies resulting in the rejection of the studies results. More specifically,
  - the initial biomass was higher than the maximum value specified in the OECD TG 201 which may have impacted the sensitivity of the test;
  - in the absence of analytical monitoring, adequate exposure to the test material is not demonstrated.
- the reporting of the study is not sufficient to conduct an independent assessment of its reliability. More specifically,
  - you have not provided adequate information to support that the test material used in these studies is representative of the Substance;
  - key information on the test design and conditions are missing and therefore it is not possible to conduct an independent assessment as to whether these studies where conducted under conditions that are consistent with the specifications of the OECD TG 201;
  - you have not provided adequate information to support that the method used to determine algal biomass was adequate;
  - you have not provided adequate reporting of the study results and therefore it is not possible to verify that the validity criteria of the OECD TG 201 were met and to conduct an independent assessment of the interpretation of the results.

70 Therefore, the study submitted in your adaptation, as currently reported in your dossier, does not provide an adequate and reliable coverage of key parameter(s) of the OECD TG 201.

71 As explained above, you have not established that relevant properties of the Substance can be predicted from data on the source substance. Therefore, your read-across adaptation under Annex XI, Section 1.5. is rejected and this information requirement is not fulfilled.

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

4. Ready biodegradability

73 Ready biodegradability is an information requirement in Annex VII to REACH (Section 9.2.1.1.).

4.1. Information provided

74 You have adapted this information requirement by using Annex XI, Section 1.5. (Grouping of substances and read-across approach) based on experimental data from the following substance:

(i) an inherent biodegradability study according to OECD TG 302C (2001) with the analogue Diallyl phthalate (EC 205-016-3).

75 In addition, you have also adapted this standard information information requirement by applying weight of evidence (WoE) adaptation in accordance with Annex XI, section 1.2. In support of your adaptation, you provided the following information:

(ii) a ready biodegradability study according to OECD TG 301C (1992) with the analogue substance Diallyl phthalate (EC 205-016-3).

76 ECHA assumes that you intend to cover this information requirements through a weight of evidence that relies on information from the analogue substance Diallyl phthalate (EC 205-016-3). Therefore, ECHA has assessed the information provided on that basis.

4.2. Assessment of the information provided

4.2.1. Weight of Evidence adaptation rejected

77 Annex XI, Section 1.2 states that there may be sufficient weight of evidence from several independent sources of information enabling, through a reasoned justification, a conclusion on the information requirement, while the information from each single source alone is insufficient to fulfil the information requirement.

78 The justification must have regard to the information that would otherwise be obtained from the study that must normally be performed for this information requirement.

79 According to Guidance on IRs and CSA, Section 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 on the corresponding information requirement.

80 Annex XI, section 1.2 requires that adequate and reliable documentation is provided to describe your weight of evidence approach. This documentation must include robust study summaries of the studies used as sources of information and a justification explaining why the sources of information together provide a conclusion on the information requirement.

81 You have not included a justification for your weight of evidence, which would include an adequate and reliable (concise) documentation as to why the sources of information provide sufficient weight to conclude on the information requirements under consideration.

82 In spite of this critical deficiency, ECHA has nevertheless assessed the validity of your adaptation.

4.2.1.1. Relevance of the sources of information

4.2.1.1.1. The source of information (i) does not qualify for a ready biodegradability test

83 Relevant information that can be used for the information requirement of Annex VII, Section 9.2.1.1. includes similar information that is produced by the OECD TG 301 or 310. OECD TG 301 and 310 require the study to investigate the following key element:

- the ultimate aerobic biodegradation (as measured by parameters such as DOC removal, CO2 production and oxygen uptake) of the test material under low inoculum concentration is measured at sufficiently frequent intervals to allow the identification of the beginning and end of biodegradation

84 The study (i) was conducted according to the OECD TG 302C (Inherent Biodegradability: Modified MITI test (II)).

85 As set out in the ECHA Guidance on IRs and CSA, Section R.7.9.5.1, "the optimum conditions in inherent biodegradability tests stimulate adaptation of the microorganisms thus increasing the biodegradation potential, compared to natural environments. Therefore, positive results in these tests should not be interpreted as evidence for rapid degradation in the environment". Therefore, the study (i) cannot be used to conclude on the ready biodegradability and is therefore concluded to be irrelevant.

86 The source of information (ii) may provide relevant information on ready biodegradability. However, the reliability of this source of information is significantly affected as further explained below.

4.2.1.2. Reliability of the source of information (ii)

4.2.1.2.1. Read-across adaptation rejected

87 Information from source substance(s) can contribute to a weight of evidence adaptation only if the read-across is acceptable.

88 As explained in Section 0.1, and specifically Sections 0.1.1.1 and 0.1.1.2., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5. is rejected.

89 In addition, the reliability of the source of information (ii) is also affected by the following issue:

4.2.1.2.2. The reliability of the source of information (ii) cannot be assessed

90 To fulfil the information requirement, normally a study according to OECD TG 301/310 must be provided. In the case of the source of information (ii), OECD TG 301C applies. The specifications of OECD TG 301C include:

91 Reporting of the methodology and results

a) the source of the inoculum, its concentration in the test and any pre-conditioning treatment are reported.

b) the test design (e.g., number of replicates, description of test conditions, such as temperature) is reported.
c) the test procedure (e.g., test medium composition, analytical method) is reported.
d) the results of measurements at each sampling point in each replicate is reported in a tabular form.
e) any observed inhibition phenomena and/or abiotic degradation are reported.
f) for a study conducted according to the OECD TG 301C, the determination of the biodegradation using a specific chemical analytical method is reported.

92 For study (ii), you have not provided any of the information listed under points a) to f) above.

93 In the absence of the above information, it is not possible to conduct an independent assessment as to whether the study was conducted under conditions that are consistent with the specifications of the OECD TG 301C, whether the validity criteria of the test guideline were met and whether the interpretation of the results is adequate.

94 Therefore, study (ii) cannot be considered a reliable source of information that could contribute to the conclusion on this key parameter investigated by the required study.

4.2.1.3. Conclusion

95 As a result of the issues identified above, it is not possible to conclude, based on the information you provided, whether your Substance has or has not the particular dangerous property foreseen to be investigated in an OECD TG 301/310 study. Therefore, your adaptation is rejected.

96 On this basis, the information requirement is not fulfilled.

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

Reasons related to the information under Annex VIII of REACH

5. 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)

98 A short-term repeated dose toxicity study (28 days) is an information requirement under Annex VIII, Section 8.6.1. 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.

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

100 The present decision requests the registrants concerned to generate and submit a reliable sub-chronic toxicity study (90 days) (see request 8). According to Annex VIII, Section 8.6.1., Column 2 and to prevent unnecessary animal testing, a short-term toxicity study (28 days) does not therefore need to be conducted.

101 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.

102 In your comments to the draft decision, you agree with ECHA's assessment.

6. Screening for reproductive/developmental toxicity

103 A screening for reproductive/developmental toxicity study (OECD 421 or OECD 422) is an information requirement under Annex VIII, Section 8.7.1., if there is no evidence from analogue substances, QSAR or in vitro methods that the substance may be a developmental toxicant.

6.1. Information provided in your dossier

104 You have adapted this information requirement by using Annex XI, Section 1.5. (Grouping of substances and read-across approach) based on experimental data from the following substances:

(i) a Reproduction / Developmental Toxicity Screening Test (2002) with the analogue Diallyl phthalate (EC 205-016-3).

6.2. Assessment of the information provided

6.2.1. Read-across adaptation rejected

105 As explained in Section 0.1., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5 is rejected.

106 On this basis, the information requirement is not fulfilled.

6.3. Information provided in your comments to the draft decision

107 Under Annex VIII, Section 8.7., Column 2, the study does not need to be conducted if a pre-natal developmental toxicity study (OECD TG 414) referred to in Annex IX, Section 8.7.2. or an extended one-generation reproductive toxicity study (OECD TG 443) referred to in Annex IX, Section 8.7.3. is available or proposed by the registrant; or a two-generation reproductive toxicity study (OECD TG 416) is available.

108 In your comments to the draft decision, you claim that *A pre-natal developmental toxicity study (OECD 414) is proposed for DAIP. Hence this study can be waived based on the data obtained. This would negate the need to carry out a reproductive/developmental toxicity study (OECD 421/422) as requested by ECHA."*

109 However, a pre-natal developmental toxicity study is not available nor proposed by you, as it is requested by ECHA in the current decision.

110 Based on the above, your adaptation is rejected.

6.4. Specification of the study design

111 A study according to the test method EU B.63/OECD TG 421 or EU B.64/OECD TG 422 must be performed in rats.

112 The study must be conducted with oral administration of the Substance (Guidance on IRs and CSA, Section R.7.6.2.3.2.).

113 Therefore, the study must be conducted in rats with oral administration of the Substance.

7. Short-term toxicity testing on fish

114 Short-term toxicity testing on fish is an information requirement under Annex VIII to REACH (Section 9.1.3.).

7.1. Information provided

115 You have provided:

(i) a short-term toxicity study on fish (2015) with the Substance.

116 In addition, you have adapted this information requirement by using Annex XI, Section 1.5. (Grouping of substances and read-across approach) based on experimental data from the following substances:

(ii) a short-term toxicity study on fish (2003) with the analogue Diallyl phthalate (EC 205-016-3).

7.2. Assessment of information provided

7.2.1. The provided study (i) does not meet the specifications of the test guideline

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

118 Reporting of the methodology and results

h) adequate information on the results of the analytical determination of exposure concentrations are provided (i.e. individual measurements at each sampling time).

i) tabulated data on mortalities and sub-lethal effects (e.g. with regard to equilibrium, appearance, ventilator and swimming behaviour) obtained on at least 2 observations within the first 24 hours and at least two observations per day from day 2 to 4 for each treatment group and control are not reported.

119 In study (i) described as short-term toxicity study on fish, none of the information listed under points a) to c) above are provided.

120 Based on the above, the reporting of the study in your dossier is not sufficient to conduct an independent assessment of its reliability. In particular, it is not possible to verify that exposure was satisfactorily maintained thoughout the study and to assess the interpretation of the results.

121 In your comments to the draft decision, you submitted additional information on the study (i), supported by the study report ([redacted]). ECHA has assessed the information against the requirement in OECD TG 203. The information you have provided in your comments addresses the incompliances identified in this decision for this information requirement. However, as the information is currently not available in your registration dossier, the data gap remains. You should therefore submit this information in an updated registration dossier by the deadline set out in the decision.

7.2.2. Read-across adaptation rejected

122 For study (ii), as explained in Section 0.1, your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5. is rejected.

123 For the reasons explained under section 7.2.1 and 7.2.2., the information requirement is currently not fulfilled.

Reasons related to the information under Annex IX of REACH

8. Sub-chronic toxicity study (90-day)

124 A sub-chronic toxicity study (90 day) is an information requirement under Annex IX, Section 8.6.2.

8.1. Information provided

125 You have adapted this information requirement by using Annex XI, Section 1.5. (Grouping of substances and read-across approach) based on experimental data from the following substances:

(i) a chronic toxicity study (1985) with the analogue Diallyl phthalate (EC 205-016-3);

(ii) a combined repeated dose and carcinogenicity study (1983) with the analogue Diallyl phthalate (EC 205-016-3).

(i) Assessment of the information provided

8.1.2. Read-across adaptation rejected

126 As explained in Section 0.1., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5 is rejected.

127 On this basis, the information requirement is not fulfilled.

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

8.2. Specification of the study design

129 Following the criteria provided in Annex IX, Section 8.6.2, Column 2, and considering the guidance on IRs and CSA, Section R.7.5.6.3.2, the oral route is the most appropriate route of administration to investigate repeated dose toxicity of the Substance, because according to the Chemical Safety Report, risk management measures are in place to prevent exposure of humans via inhalation.

130 According to the OECD TG 408, the rat is the preferred species.

131 Therefore, the study must be performed in rats according to the OECD TG 408 with oral administration of the Substance.

9. Pre-natal developmental toxicity study in one species

132 A pre-natal developmental toxicity (PNDT) study (OECD TG 414) in one species is an information requirement under Annex IX, Section 8.7.2.

9.1. Information provided

133 You have adapted this information requirement by using Annex XI, Section 1.5. (Grouping of substances and read-across approach) based on experimental data from the following substances:

(i) a prenatal developmental toxicity study (2007) with the analogue Diallyl phthalate (EC 205-016-3).

9.2. Assessment of the information provided

9.2.1. Read-across approach rejected

134 As explained in Section 0.1., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5. is rejected. In addition, ECHA identified endpoint specific issue(s) addressed below.

135 On this basis, the information requirement is not fulfilled.

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

9.3. Specification of the study design

137 A PNDT study according to the test method OECD TG 414 should be performed in rat or rabbit as preferred species.

138 The study must be performed with oral administration of the Substance (Guidance on IRs and CSA, Section R.7.6.2.3.2.).

139 Therefore, the study must be conducted in rats or rabbits with oral administration of the Substance.

10. Long-term toxicity testing on aquatic invertebrates

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

10.1. Information provided

141 You have adapted this information requirement by using Annex XI, Section 1.5. (Grouping of substances and read-across approach) based on experimental data from the following substance:

(i) a long-term toxicity study on *daphnia magna* (1989) with the analogue substance "phthalic acid diallyl ester";

10.2. Assessment of the information provided

10.2.1. Read-across approach rejected

142 As explained in Section 0.1., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5. is rejected. In addition, ECHA identified endpoint specific issue addressed below.

10.2.2. Inadequate or unreliable study on the source substance

143 Under Annex XI, Section 1.5., the results to be read across must have an adequate and reliable coverage of the key parameters addressed in the test guideline for the corresponding study that shall normally be performed for a particular information requirement, in this case OECD TG 211. Therefore, the following specifications must be met:

144 Technical specifications impacting the sensitivity/reliability of the test

a) for semi-static tests, at least 10 animals individually held at each test concentration and in the control series;

b) the test temperature is within 18°C and 22°C and not varying by over ±1°C;

145 Characterisation of exposure

c) Analytical monitoring must be conducted. 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;

146 Reporting of the methodology and results

d) adequate information on the test material is provided (i.e. identifiers, purity and presence of impurities)

e) detailed information on feeding, including amount (in mgC/daphnia/day) and schedule is reported.

f) water quality monitoring within the test vessels (i.e., temperature and dissolved oxygen concentration, TOC and/or COD and hardness) is reported.

g) the full record of the daily production of living offspring during the test by each parent animal is provided.

h) the number of deaths among the parent animals (if any) and the day on which they occurred is reported.

147 In study (i) described as a long-term toxicity study on aquatic invertebrates:

148 Technical specifications impacting the sensitivity/reliability of the test

a) the test was conducted under semi-static but the organisms were not individually held (based on your record that number of the organism per vessel were 5);

b) the test temperature was 25°C hence above the maximum value set ou in the test guideline;

149 Characterisation of exposure

c) analytical monitoring of exposure was conducted was not conducted;

150 Reporting of the methodology and results

d) no identifiers are provided for the test material. In addition, the purity of the test material and the presence of impurities are not reported;

e)-h) you have not provided any of this information.

151 Based on the above,

- there are critical methodological deficiencies resulting in the rejection of the studies results. More specifically,
    - the test tempartaure was too high which may have impacted the reliability of the test in an unpredictable way. Further, in the absence of information on mortality of parental animal, it cannot be assessed whether the fact that parental animals were not held individually may have biased the results of the study;
    - in the absence of analytical monitoring, adequate exposure to the test material is not demonstrated.

- the reporting of the study is not sufficient to conduct an independent assessment of its reliability. More specifically,
    - you have not provided adequate information to support that the test material used in these studies is representative of the Substance;
    - key information on the test conditions are missing and therefore it is not possible to conduct an independent assessment as to whether these studies where conducted under conditions that are consistent with the specifications of the OECD TG 211;
    - you have not provided adequate reporting of the study results and therefore it is not possible to verify that the validity criteria of the OECD TG 211 were met and to conduct an independent assessment of the interpretation of the results.

152 Therefore, the study submitted in your adaptation, as currently reported in your dossier, does not provide an adequate and reliable coverage of key parameter(s) of the OECD TG 211.

153 As explained above, you have not established that relevant properties of the Substance can be predicted from data on the source substance. Therefore, your read-across adaptation under Annex XI, Section 1.5. is rejected and this information requirement is not fulfilled.

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

References

The following documents may have been cited in the decision.

Guidance on information requirements and chemical safety assessment (Guidance on IRs & CSA)

Chapter R.4 Evaluation of available information; ECHA (2011).
Chapter R.6 QSARs, read-across and grouping; ECHA (2008).
Appendix to Chapter R.6 for nanoforms; ECHA (2019).
Chapter R.7a Endpoint specific guidance, Sections R.7.1 – R.7.7; ECHA (2017).
Appendix to Chapter R.7a for nanomaterials; ECHA (2017).
Chapter R.7b Endpoint specific guidance, Sections R.7.8 – R.7.9; ECHA (2017).
Appendix to Chapter R.7b for nanomaterials; ECHA (2017).
Chapter R.7c Endpoint specific guidance, Sections R.7.10 – R.7.13; ECHA (2017).
Appendix to Chapter R.7a for nanomaterials; ECHA (2017).
Appendix R.7.13-2 Environmental risk assessment for metals and metal compounds; ECHA (2008).
Chapter R.11 PBT/vPvB assessment; ECHA (2017).
Chapter R.16 Environmental exposure assessment; ECHA (2016).

Guidance on data-sharing; ECHA (2017).
Guidance for monomers and polymers; ECHA (2012).
Guidance on intermediates; ECHA (2010).
All guidance documents are available online: https://echa.europa.eu/guidance-documents/guidance-on-reach

Read-across assessment framework (RAAF)

RAAF, 2017 Read-across assessment framework (RAAF); ECHA (2017).
RAAF UVCB, 2017 Read-across assessment framework (RAAF) – considerations on multi- constituent substances and UVCBs; ECHA (2017).

The RAAF and related documents are available online:
https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across

***OECD Guidance documents* (OECD GDs)**

OECD GD 23 Guidance document on aquatic toxicity testing of difficult substances and mixtures; No. 23 in the OECD series on testing and assessment, OECD (2019).
OECD GD 29 Guidance document on transformation/dissolution of metals and metal compounds in aqueous media; No. 29 in the OECD series on testing and assessment, OECD (2002).
OECD GD 150 Revised guidance document 150 on standardised test guidelines for evaluating chemicals for endocrine disruption; No. 150 in the OECD series on testing and assessment, OECD (2018).
OECD GD 151 Guidance document supporting OECD test guideline 443 on the extended one-generation reproductive toxicity test; No. 151 in the OECD series on testing and assessment, OECD (2013).

Appendix 2: Procedure

The information requirement for long-term toxicity testing on fish (Annex IX, Section 9.1.6.) is not addressed in this decision. This is because information that will be generated from the studies requested in the present decision is needed:

- to inform on the potential endocrine disrupting properties of the Substance; and
- to decide on the most appropriate test(s) to meet the information requirement.

This information requirement may be addressed in a separate decision at a later stage.

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 14 March 2022.

The deadline of the decision is set based on standard practice for carrying out OECD TG tests. It has been exceptionally extended by 12 months from the standard deadline granted by ECHA to take into account currently longer lead times in contract research organisations.

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.

In your comments on the draft decision, you requested an extension of the deadline to provide information from 36 to 48 months from the date of adoption of the decision. In support of your request, you provided documentation from a CRO which includes a schedule for the requests including in the decision. This information indicates that the requested studies could be performed within a period of 32 months. On this basis, ECHA has not amended the deadline.

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 3: Addressee of this decision and their corresponding information requirements

In accordance with Articles 10(a) and 12(1) of REACH, the information requirements for individual registrations are defined as follows:

- 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.

Registrant Name	Registration number	Highest REACH Annex applicable to you
[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.

Appendix 4: Conducting and reporting new tests for REACH purposes

1. Requirements when conducting and reporting new tests for REACH purposes

1.1. Test methods, GLP requirements and reporting

(1) Under Article 13(3) of REACH, all new data generated as a result of this decision must be conducted according to the test methods laid down in a European Commission Regulation or to international test methods recognised by the Commission or ECHA as being appropriate.

(2) Under Article 13(4) of REACH, ecotoxicological and toxicological tests and analyses must be carried out according to the GLP principles (Directive 2004/10/EC) or other international standards recognised by the Commission or ECHA.

(3) Under Article 10(a)(vi) and (vii) of REACH, all new data generated as a result of this decision must be reported as study summaries, or as robust study summaries, if required under Annex I of REACH. See ECHA Practical Guide on How to report robust study summaries[2].

(4) Under the introductory part of Annexes VII/VIII/IX/X to REACH, where a test method offers flexibility in the study design, for example in relation to the choice of dose levels or concentrations, the chosen study design must ensure that the data generated are adequate for hazard identification and risk assessment.

1.2. Test material

(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 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.

Technical instructions on how to report the above is available in the manual on How to prepare registration and PPORD dossiers[3].

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