~~Confidential~~

Helsinki, 28 November 2022

Addressees
Registrant(s) of JS_2,3-dichlorobutadiene-1,3 as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
16/05/2013

Registered substance subject to this decision ("the Substance")
Substance name: 2,3-dichlorobuta-1,3-diene
EC number: 216-721-0

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 information under request 8 and 11 below by ***05 March 2025*** and all other information listed below by ***05 March 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 vitro skin corrosion/irritation (Annex VII, Section 8.1.; test method: OECD TG 430, or OECD TG 431, or OECD TG 435 and OECD TG 439);

2. In vitro study for serious eye damage/irritation (Annex VII, Section 8.2.; following the testing strategy as outlined in the OECD GD on an Integrated Approach on Testing and Assessment for Serious Eye Damage and Eye irritation, Series on Testing and Assessment No.263.);

3. Skin sensitisation (Annex VII, Section 8.3.):

   i. in vitro/in chemico skin sensitisation information on molecular interactions with skin proteins (OECD TG 442C), inflammatory response in keratinocytes (OECD TG 442D) and activation of dendritic cells (EU B.71/OECD TG 442E)(Annex VII, Section 8.3.1.); and

   ii. Only if the in vitro/in chemico test methods specified under point .i. are not applicable for the Substance or the results obtained are not adequate for classification and risk assessment, in vivo skin sensitisation (Annex VII, Section 8.3.2.; test method: EU B.42./OECD TG 429);

4. Transgenic rodent somatic and germ cell gene mutation assays, or In vivo mammalian alkaline comet assay also requested below (triggered by Annex VII, Section 8.4., column 2)

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

5. Only if the results in Annex VII, Section 8.1. (request 1) are not adequate for classification and risk assessment, in vivo skin corrosion/irritation (Annex VIII, Section 8.1., column 2.; test method: OECD TG 404);

6. Only if the results in Annex VII, Section 8.2. (request A.2.) are not adequate for classification and risk assessment, in vivo serious eye damage/eye irritation (Annex VIII, Section 8.2., column 2.; test method: OECD TG 405);

7. Transgenic rodent somatic and germ cell gene mutation assays, or In vivo mammalian alkaline comet assay also requested below (triggered by Annex VIII, Section 8.4., column 2)

8. 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.)

9. 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

10. Transgenic rodent somatic and germ cell gene mutation assays (Annex IX, Section 8.4., column 2; test method: OECD TG 488) in transgenic mice or rats, inhalation route on the following tissues: liver and lungs; germ cells must be harvested and stored for up to 5 years.

    OR

    In vivo mammalian alkaline comet assay (Annex IX, Section 8.4., column 2; test method: OECD TG 489) in rats, or if justified, other rodent species, inhalation route, on the following tissues: liver and lungs.

11. Sub-chronic toxicity study (90-day) (Annex IX, Section 8.6.2.; test method: OECD TG 413) by inhalation route, in rats

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

13. Long-term toxicity testing on fish (Annex IX, Section 9.1.6.; test method: EU C.47./OECD TG 210)

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

14. Pre-natal developmental toxicity study (Annex X, Section 8.7.2.; test method: OECD TG 414) by inhalation route, in a second species (rabbit)

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 addressees of the decision and their corresponding information requirements based on registered tonnage band are listed in Appendix 3.

You are only required to share the costs of information that you must submit to fulfil your information requirements.

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

Appendix 1: Reasons for the decision
Appendix 2: Procedure
Appendix 3: Addressees of the decision and their individual information requirements
Appendix 4: Conducting and reporting new tests under REACH

[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 1: Reasons for the decision

Contents

0. Reasons common to several requests

0.1. Assessment of weight of evidence adaptations

1 You have adapted the following standard information requirements by applying weight of evidence (WoE) adaptation(s) under Annex XI, Section 1.2:

- Short-term repeated dose toxicity (28 day), (Annex VIII, Section 8.6.1.)
- Sub-chronic toxicity study (90-day), (Annex IX, Section 8.6.2.)

2 Your weight of evidence adaptation raises the same decifiencies irrespective of the information requirement for which it is invoked. Accordingly, ECHA addressed these deficiencies first, before assessing the specific standard information requirements in the following sections.

3 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.

4 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.

5 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.

6 Subsequently, relevance, reliability, coverage, consistency and results of these sources of information must be integrated in order to decide whether they together provide sufficient weight to conclude whether the Substance has or has not the (dangerous) property investigated by each of the key parameters foreseen by the study normally required for the information requirement. As part of the overall conclusion, an assessment of the residual uncertainty is also required.

7 You have not included a justification for your weight of evidence adaptation for each of the relevant information requirement, 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.

8 Additional issues related to weight of evidence are addressed under the corresponding information requirements.

Reasons related to the information under Annex VII of REACH

1. In vitro skin corrosion/irritation

9 In vitro Skin corrosion/irritation is an information requirement under Annex VII (Section 8.1.).

1.1. Information provided

10 You have provided the following information:

i. in vivo skin irritation study (1974) with the Substance.

ii. adaptation for not performing *in vitro* studies for irritation

1.2. Assessment of the information provided

1.2.1. Study not adequate for the information requirement

11 To fulfil the information requirement, and to enable concluding whether the Substance causes skin corrosion/irritation, a study must comply with the EU Method B.4/OECD TG 404 (Article 13(3) of REACH). The guideline requires that liquid substances are to be applied undiluted (paragraph 11, OECD TG 404).

12 Your dossier contains results from an in vivo skin irritation study that considers that the Substance is not corrosive to the skin. The study was performed with a mixture of Butadiene,2-3-dichloro-/methylene chloride (50/50) and not with the Substance itself. In addition, you refer in your dossier to public sources of information, such as the the OECD SIDS report from 2006 and studies discussed in that report indicating that the Substance is likely to be a skin irritant. You have self-classified the Substance as Skin irritant 2.

13 In your dossier, there is no skin irritation data, where the Substance would have been tested undilluted. As indicated above, according to the OECD TG 404 testing liquid as undiluted is a requirement in the in vivo skin corrosion/irritation studies. Other studies referred in the OECD SIDS report indicate severe irritation noted following exposure to the Substance. However, the purity of the Substance used in those studies is unknown. In addition, the OECD SIDS report, 2006, considers that there is no valid data available for the assessment of skin corrosion/irritation for the Substance (section 3.1.3.). Based on the information provided by you, it is not possible to conclude on the corrosion/irritation potential of the Substance.

1.2.2. Adaptation not adequate for the information requirement

14 According to column 2 of Annex VI, section 8.2, skin corrosion/irritation studies do not need to be conducted if the Substance is spontaneously flammable in air or in contact with water or moisture at room temperature.

15 You have reported in your dossier that the auto-flammability of the Substance is 415°C at 1014Pa, indicating that the Substance is not spontaneously flammable at room temperature.

16 As the conditions of the column 2 adaptation have not been met the adaptation is rejected.

17 On the basis of above, the information requirement is not fulfilled.

1.3. Specification of the study design

18 To fulfil the information requirement for the Substance, *in vitro* skin corrosion study (OECD TG 430/431/435) and *in vitro* skin irritation study (OECD TG 439) are considered suitable.

2. In vitro study for serious eye damage/irritation

19 In vitro serious eye damage/eye irritation is an information requirement under Annex VII (Section 8.2.).

2.1. Information provided

20 We understand that you seek to adapt this information requirement under Column 2 of Annex VII, Section 8.2. To support the adaptation, you have provided following justification:

i. "In vivo data have been presented in published literature reviews (OECD/ICCA - The BUA* Peer Review Process - OECD SIDS Initial Assessment Report draft 2006) indicating the test substance is a mild ocular irritant. Classification with R36 is appropriate and therefore is it not considered necessary to confirm the classification by conducting i. an *in vitro* assay, ii. further *in vivo* assessments which would contravene the requirement to avoid animal studies where possible."

2.2. Assessment of the information provided

2.2.1. Adaptation not adequate for the information requirement

21 According to column 2 of Annex VII, section 8.2, serious eye damage/eye irritation studies do not need to be conducted if the Substance is classified as skin irritation and the available information indicates that it should be classified as eye irritation (Category 2).

22 Your dossier contains a reference to the OECD SIDS report from 2006 on the Substance. You consider that based on the data included in the review, mild ocular effects have been noted. Based on this you have self-classified the Substance as Eye irritant 2.

23 You have not provided any information in your dossier supporting your claim the Substance is a mild ocular irritant. Therefore, based on the information provided by you, it is not possible to conclude on the serious eye damage/eye irritation potential of the Substance.

24 The publicly available OECD SIDS report on the Substance to which you refer to, indicates in section 3.1.3. that there is no valid data available for the assessment of serious eye damage/eye irritation for the Substance. According to the OECD SIDS report, some evidence is available showing some information on eye irritation potential (Marhold, 1986). However, the purity of the test material used in the study (Marhold, 1986) has not been reported. Therefore effects leading to serious eye damage (Category 1) cannot be excluded, because in the in vivo eye irritation assays liquid chemicals should be applied as such i.e. without dilution (paragraph 15, OECD TG 405).

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

2.1. Specification of the study design

26 To fulfil the information requirement for the Substance, to follow the testing strategy following the testing strategy as outlined in the OECD GD on an Integrated Approach on Testing and Assessment for Serious Eye Damage and Eye irritation, Series on Testing and Assessment No.263.)

3. Skin sensitisation

27 Skin sensitisation is an information requirement under Annex VII, Section 8.3. Under Section 8.3., Column 1, the registrants must submit information allowing (1) a conclusion whether the substance is a skin sensitiser and (2) whether it can be presumed to have the potential to produce significant sensitisation in humans (Cat. 1A).

3.1. Information provided

28 We understand that you seek to adapt this information requirement under Column 2 of Annex VII, Section 8.3. To support the adaptation, you have provided following justification:

(i) "Limited information relating to administration by repeated topical administration to ten guinea pigs concludes that no skin sensitisation was apparent. However the information is inadequate for a valid assessment of sensitising potential. The test material is flammable and so topical application may not be a feasible method for determining contact sensitisation according to Annex VII, REACH. The flammability of the material may also preclude intradermal injection of the material on animal welfare grounds."

3.2. Assessment of the information provided

3.2.1. Assessment whether the Substance causes skin sensitisation

3.2.1.1. Adaptation not adequate for the information requirement

29 According to column 2 of Annex VII, section 8.3, skin sensitisation studies do not need to be conducted if the Substance is spontaneously flammable in air or in contact with water or moisture at room temperature.

30 You have reported in your dossier that the auto-flammability of the Substance is 415°C at 1014Pa, indicating that the Substance is not spontaneously flammable at room temperature.

31 As the conditions of the column 2 adaptation have not been met the adaptation is rejected.

32 Furthermore, you claim that "Limited information relating to administration by repeated topical administration to ten guinea pigs concludes that no skin sensitisation was apparent", however you have not provided such data. Therefore ECHA cannot perform an independent evaluation of the information to consider whether it can be used to assess the skin sensitisation potential of the Substance.

33 Based on the information provided by you, it is not possible to conclude on the whether the Substance causes skin sensitisation.

3.2.2. No assessment of potency

34 To be considered compliant and enable a conclusion in cases whether the substance is considered to cause skin sensitisation, the information provided must also allow a conclusion whether it can be presumed to have the potential to produce significant sensitisation in humans (Cat. 1A).

35 As the currently available data does not allow to conclude whether the Substance causes skin sensitisation (see section 3.2.1.), this condition cannot be assessed.

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

3.3. Specification of the study design

37 To fulfil the information requirement for the Substance, information on molecular interaction with skin proteins and inflammatory response in keratinocytes and activation of dendritic cells (OECD TG 442C and OECD TG 442D and EU B.71/OECD TG 442E) must be provided. Furthermore an appropriate risk assessment is required if a classification of the Substance as a skin sensitiser (Cat 1A or 1B) is warranted.

38 In case no conclusion on the skin sensitisation potency can be made for the Substance based on the existing in vitro/in chemico data or newly generated in vitro/in chemico data, in vivo skin sensitisation study must be performed and the murine local lymph node assay (EU Method B.42/OECD TG 429) is considered as the appropriate study for the potency estimation.

4. Transgenic rodent somatic and germ cell gene mutation assay or In vivo mammalian alkaline comet assay

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

4.1. Triggering of the information requirement

40 Your dossier contains positive results for the in vitro gene mutation study in bacteria (Bacterial reverse mutation assay (1980)) which raise a concern for gene mutations.

41 Therefore, the information requirement is triggered.

4.2. Information requirement not fulfilled

42 The assessment of the information provided and the specifications of the study design are addressed under Request 10.

Reasons related to the information under Annex VIII of REACH

5. Only if the results in Annex VII, Section 8.1. (1.) are not adequate for classification and risk assessment, in vivo skin corrosion/irritation (Annex VIII, Section 8.1., column 2.; test method: OECD TG 404)

43 In vivo skin corrosion/irritation study is an information requirement in Annex VIII of the REACH Regulation. Column 2 of Annex VIII, Section 8.1. provides that in case the in vitro study(ies) under Annex VII, Section 8.1.1 and 8.1.2 are not applicable for the substance, or the results are not adequate for classification and risk assessment, an in vivo study shall be performed.

5.1. Information provided

44 The information that you have provided for the skin corrosion/ irritation is rejected for the reasons provided under request 1 above.

45 The result of the request for information under request 1 above will determine whether the present requirement for an in vivo skin corrosion/irritation study in accordance with Annex VIII, Section 8.1., column 2. is triggered. An in vivo skin corrosion/irritation is needed only if the results in Annex VII, Section 8.1. are not adequate for classification and risk assessment.

46 When considering the results obtained from the in vitro study/ies, it is important to consider whether a specific conclusion on classification according to CLP regulation can be made based on the results, i.e. interpretation of the results and prediction model of a particular test method[2].

5.2. Specification of the study design

47 In case no conclusion on the skin corrosion/irritation can be made for the Substance based on the newly generated in vitro data, an in vivo skin corrosion/irritation study must be performed and the acute dermal irritation/corrosion assay (EU Method B.4/OECD TG 404) is considered as the appropriate test method.

6. Only if the results in Annex VII, Section 8.2. (request 2.) are not adequate for classification and risk assessment, in vivo serious eye damage/eye irritation (Annex VIII, Section 8.2., column 2.; test method: OECD TG 405)

48 In vivo eye irritation is an information requirement in Annex VIII of the REACH Regulation. Column 2 of Annex VIII, Section 8.2. provides that in case the in vitro study(ies) under Annex VII, Section 8.2.1. are not applicable for the substance, or the results are not adequate for classification and risk assessment, an in vivo study shall be performed.

6.1. Information provided

49 The adaptation that you have provided for the eye damage/eye irritation is rejected for the reasons provided under request 2 above.

50 The result of the request for information under request 2 above will determine whether the present requirement for an in vivo serious eye damage/eye irritation study in accordance with Annex VIII, Section 8.2., column 2. is triggered. An in vivo serious eye damage/eye

[2] ECHA Guidance R.7a, Section R.7.2.4

irritation is needed only if the results in Annex VII, Section 8.2. are not adequate for classification and risk assessment.

51 When considering the results obtained from the in vitro study/ies, it is important to consider whether a specific conclusion on classification according to CLP regulation can be made based on the results i.e. interpretation of the results and prediction model of a particular test method.

6.1. Specification of the study design

52 In case no conclusion on the serious eye damage/eye irritation can be made for the Substance based on the newly generated in vitro data, as requested under request 2, in vivo eye irritation study must be performed and the acute eye irritation corrosion assay (EU Method B.5/OECD TG 405 is considered as the appropriate test method.

7. Transgenic rodent somatic and germ cell gene mutation assay or In vivo mammalian alkaline comet assay

53 Appropriate in vivo mutagenicity studies must be considered under Annex VIII, Section 8.4., column 2 in case of a positive result in any of the in vitro genotoxicity studies under Annex VII or VIII to REACH.

7.1. Triggering of the information requirement

54 Your dossier contains positive results for the in vitro gene mutation study in bacteria (Bacterial reverse mutation assay (1980)) which raise the concerns for gene mutations.

7.2. Information requirement not fulfilled

55 The information provided, its assessment and the specifications of the study design are addressed under request 10.

8. 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)

56 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.

8.1. Information provided

57 You have adapted this information requirement by using weight of evidence based on the following experimental data:

(i) Sub-acute toxicity study (14-days, 1979) with the Substance

(ii) Single generation reproductive toxicity study (2003)

(iii) Justification: "No data are presented for chronic exposure studies. The studies available provide adequate information to address the potential effects of repeated exposure and it is not considered warranted to conduct further animal tests to determine long term toxicity by non-primary exposure routes."

8.2. Assessment of the information provided

58 You have adapted this information requirement using weight of evidence under Annex XI, Section 1.2.

59 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.

60 Relevant information that can be used to support weight of evidence adaptation for information requirement of Section 8.6.1. at Annex VIII includes similar information that is produced by the OECD TG 412. The following aspects of systemic toxicity are covered: 1) in-life observations, 2) blood chemistry, 3) organ and tissue toxicity and assessment of.

61 We have assessed the individual sources of information with regard to relevance and identified the following issue(s):

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

63 As explained under section 0.1, 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.

64 Relevant information that can be used to support weight of evidence adaptation for the information requirement of Section 8.6.1 at Annex VIII includes similar information that is produced by the OECD TG 412. The following aspects of systemic toxicity are covered: 1) in-life observations, 2) blood chemistry, and 3) organ and tissue toxicity.

65 We have assessed the individual sources of information with regard to relevance and reliability and identified the following issue(s):

8.2.1. Aspect 1) In-life observations

66 In-life observations (aspect 1) must include information on survival, body weight development, clinical signs, functional observations, food/water consumption and other potential aspects of in life observations on the relevant physiological systems (circulatory, digestive/excretory, integumentary, musculoskeletal, nervous, renal/urinary, and respiratory).

67 The source of information (i) provides relevant information on some of the above-mentioned in life observations. However, functional observations and food/water consumption were not investigated in this study.

68 The source of information (ii) provides relevant information on some of the above-mentioned in life observations. However, functional observations was not investigated in this study.

69 The following deficiency affect the reliability of the contribution of study (i) to the weight of evidence adaptation.

70 Investigations/specifications in a sub-acute toxicity study (OECD TG 412) include dosing of the Substance daily for a minimum of 28 days.

71 The source of information (i) has an exposure duration of 14 days

72 This exposure duration is significantly shorter than the minimum exposure duration required from a study conducted according to the OECD TG 412. The exposure duration is essential

because the effects observed over the required period of exposure of 28-days might be considerably more pronounced than over a shorter study duration.

73 Therefore, the reliability of the contribution of the results obtained from this studiy to the weight of evidence with regard to aspect 1 is limited.

8.2.2. Aspect 2) blood chemistry

74 Information on blood chemistry (aspect 2) must include haematological (full-scale) and clinical chemistry analysis (full-scale), and other potential aspects related to blood chemistry to address relevant physiological systems (circulatory digestive/excretory, endocrine, immune, musculoskeletal, and renal/urinary).

75 None of the sources of information provide relevant information on this aspect.

8.2.3. Aspect 3) organ and tissue toxicity

76 Organ and tissue toxicity (aspect 3) must include information on terminal observations on organ weights, gross pathology and histopathology (full-scale) and other potential aspects related to organ and tissue toxicity to address relevant physiological systems (circulatory, digestive/excretory, endocrine, immune, integumentary, musculoskeletal, nervous, renal/urinary system, reproductive, and respiratory).

77 The source of information (i) provides relevant information on organ and tissue toxicity. However, histopathology was not conducted.

78 The source of information (ii) provides relevant information on organ and tissue toxicity. However, histopathology is limited to: "Reproductive organs and other selected organs, including potential target organs, were weighed and collected for all P1 rats. Potential target organs (liver, spleen, thymus, kidneys, urinary bladder, lungs, trachea, nose, larynx, pharynx, pituitary gland) and gross lesions" .

79 The reliability of the contribution of study (i) to the weight of evidence adaptation is hampered for the same reasons as explained for aspect 1).

80 Therefore, the reliability of the contribution of the results obtained from this studiy to the weight of evidence with regard to aspect 3) is limited.

8.3. Conclusion on the weight of evidence

81 Taken together, the sources of information provide some information on aspect 1 (in-life observations) and aspect 3 (organ and tissue toxicity). However, the sources do not cover the entire set of elements of histopathology and functional observations as expected to be obtained from the OECD TG 412. In addition, no information is provided for aspect 2 (blood chemistry).

82 Therefore, it is not possible to conclude, based on any source of information alone or together, whether your Substance has or has not the particular dangerous properties foreseen to be investigated in an OECD TG 412 study.

83 Based on the above, your adaptation is rejected and the information requirement is not fulfilled.

8.4. Specification of the study design

84 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.

85 The present decision requests the registrants concerned to generate and submit a reliable sub-chronic toxicity study (90 days) (see request 11). 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.

86 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.

9. Short-term toxicity testing on fish

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

9.1. Information provided

88 You have provided:

i. a key study with the Substance, that was performed according to EU Method C.1 (Acute toxicity for fish).

ii. A supporting study with the Substance, that did not follow the OECD test guidelines or equivalent.

9.2. Assessment of the information provided

89 We have assessed this information and identified the following issues:

9.2.1. The provided studies do not meet the information requirement

90 To fulfil the information requirement, a study must comply with the OECD TG 203 and the requirements of the OECD GD 23 if the substance is difficult to test (Article 13(3) of REACH). Therefore, the following specifications must be met:

91 Validity criteria

a) the analytical measurement of test concentrations is conducted;

92 Technical specifications impacting the sensitivity/reliability of the test

b) the test is conducted on juveniles of similar age (or size);

93 Your registration dossier provides studies showing the following:

94 Validity criteria

a) For study (ii) no analytical measurement of test concentrations was conducted;

95 Technical specifications impacting the sensitivity/reliability of the test

a) For both studies (i) and (ii) the mean size of fish was 3,41 cm and 2.5-3.5 cm, respectively, which does not correspond to juveniles for *Danio rerio*;

96 Based on the above

- Regarding the study (ii) the validity criteria of OECD TG 203 are not met, since the analytical monitoring was not conducted.
- There are critical methodological deficiencies resulting in the rejection of the study results. More, specifically the studies must be performed on juvenile organisms, as indicated above for both studies you have reported a length range above the range

indicated in the OECD TG 203 (i.e. *Danio rerio* 1-2 cm). You did not provide any justification to prove that the tested organisms were juveniles. Therefore, the sensitivity of the test and the reliability of the effect values indicated in your dossier might be impacted.

97 Therefore, the requirements of the OECD TG 203 are not met.

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

9.3. Study design and test specifications

99 The Substance is difficult to test due to the volatility (Henry's Law Constant of 5160 Pa m3/mol at 25°C and a Vapour pressure of 107.4 hPa).

100 The OECD TG 203 specifies that, for difficult to test substances, you must consider the approach described in the OECD GD 23 or other approaches, if more appropriate for your substance. In all cases, the approach selected must be justified and documented.

101 Due to the properties of Substance, it may be difficult to achieve and maintain the desired exposure concentrations.

102 Therefore, you must monitor the test concentration(s) of the Substance throughout the exposure duration and report the results. If it is not possible to demonstrate the stability of exposure concentrations (i.e. measured concentration(s) not within 80-120% of the nominal concentration(s)), you must express the effect concentration based on measured values as described in the OECD TG 203.

103 In case a dose-response relationship cannot be established (no observed effects), you must demonstrate that the approach used to prepare test solutions was adequate to maximise the concentration of the Substance in the test solutions.

Reasons related to the information under Annex IX of REACH

10. Transgenic rodent somatic and germ cell gene mutation assay or In vivo mammalian alkaline comet assay

104 Under Annex IX, Section 8.4., column 2, the information requirement for an appropriate in vivo somatic cell genotoxicity study is triggered if 1) there is a positive result in any of the in vitro genotoxicity studies in Annex VII or VIII and 2) there are no appropriate results already available from an in vivo somatic cell genotoxicity study.

10.1. Triggering of the information requirement

105 In relation to the first condition, your dossier contains positive results for the in vitro gene mutation study in bacteria (Bacterial reverse mutation assay (1980)) which raise the concern for gene mutation.

106 In relation to the second condition, your dossier contains the following in vivo study:

i. Mammalian Erythrocyte Micronucleus Test (2004) with the Substance.

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

108 The Guidance on IRs and CSA, Section R.7.7.6.3. clarifies that in order to justify that an in vivo somatic cell genotoxicity study does not need to be performed in accordance with Annex IX, Section 8.4., column 2, the results of the available in vivo study must address the specific concern raised by the in vitro positive result.

109 However, the in vivo study provided is not addressing the gene mutation concern raised by the in vitro data. Study i. addresses cytogenicity rather than gene mutations. Therefore, the provided in vivo test is not appropriate.

110 Therefore, the conditions set out in Annex IX, Section 8.4., column 2 are met and the information requirement for an appropriate in vivo somatic cell genotoxicity study is triggered.

10.2. Information provided and its assessment

111 You have provided an in vivo study. However, as explained above, this study is not appropriate to address the concern for gene mutation identified in the in vitro study.

112 Therefore, the information requirement is not fulfilled.

10.3. Test selection

113 According to the Guidance on IRs & CSA, Section R.7.7.6.3, either the in vivo mammalian alkaline comet assay ("comet assay", OECD TG 489) or the transgenic rodent somatic and germ cell gene mutation assay ("TGR assay", OECD TG 488) are suitable to follow up a positive in vitro result on gene mutation.

10.4. Specification of the study design

10.4.1. Comet assay

114 In case you decide to perform the comet assay, according to the test method OECD TG 489, rats are the preferred species. Other rodent species can be used if scientifically justified (OECD TG 489, paragraph 23).

115 Having considered the anticipated routes of human exposure and adequate exposure of the target tissue(s) performance of the test by the inhalation route is appropriate. The Substance is a liquid with a vapour pressure of 133 hPa at 25°C and is used at industrial sites in the production of rubber products with occasional controlled exposure of workers. ECHA therefore considers the inhalation route as the most appropriate route of administration.

116 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 and lung as site of contact.

10.4.1.1. Cross-linking properties

117 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 the OECD TG 489); the other set of slides submitted to modified experimental conditions that enable the detection of DNA. The modified experimental conditions may utilise one of the following options: (1) increase of electrophoresis time, e.g. as described in reference 23 [1] in the OECD TG 489; (2) treatment of isolated cells (either in suspension or embedded in the slides) with a chemical (e.g. MMS); or (3) treatment of isolated cells (either in suspension or embedded in the slides) with ionising radiation (options 2 and 3 are described e.g. in references 36-39 [2-5] in the OECD TG 489 or Pant et al. 2015 [6]). In order to ensure the robustness of the test result a specific positive control group of animals would be needed.

[1] Nesslany *et al.* (2007) *In vivo* comet assay on isolated kidney cells to distinguish genotoxic carcinogens from epigenetic carcinogens or cytotoxic compounds *Muta Res*;630(1-2):28-41.

[2] Merk and Speit (1999) Detection of crosslinks with the comet assay in relationship to genotoxicity and cytotoxicity. *Environ Mol Mutagen*;33(2):167-72.

[3] Pfuhler and Wolf (1996) Detection of DNA-crosslinking agents with the alkaline comet assay. *Environ Mol Mutagen*;27(3):196-201.

[4] Wu and Jones (2012) Assessment of DNA interstrand crosslinks using the modified alkaline comet assay. *Methods Mol Biol*;817:165-81.

[5] Spanswick *et al.* (2010) Measurement of DNA interstrand crosslinking in individual cells using the Single Cell Gel Electrophoresis (Comet) assay. *Methods Mol Biol*;613:267-282.

[6] Pant K *et al.* (2015) Modified *in vivo* comet assay detects the genotoxic potential of 14-hydroxycodeinone, an α,β -unsaturated ketone in oxycodone. *Environ Mol Mutagen*;56(9):777-87.

10.4.2. TGR assay

118 In case you decide to perform the TGR assay, according to the test method OECD TG 488, the test must be performed in transgenic mice or rats.

119 Also, according to the test method OECD TG 488, the test substance is usually administered orally. However, the Substance is a liquid with a vapour pressure of 133 hPa at 25°C and is used at industrial sites in the production of rubber products with occasional controlled exposure of workers. ECHA therefore considers the inhalation route as the most appropriate route of administration.

120 Based on OECD TG 488, you are requested to follow the 28+28d regimen, as it permits the testing of mutations in somatic tissues and as well as in tubule germ cells from the same animals.

121 According to the test method OECD TG 488, the test must be performed by analysing tissues from liver as slowly proliferating tissue and primary site of xenobiotic metabolism, and from lung as site of direct contact.

10.4.3. Germ cells

122 A subsequent germ cell genotoxicity study (TGR/OECD TG 488) may still be required under Annex IX, in case 1) an in vivo genotoxicity test on somatic cell is positive, and 2) no clear conclusion can be made on germ cell mutagenicity.

123 In case you choose to perform a comet assay, 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. 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.

In case you choose to perform a TGR assay, you must collect the male germ cells (from the seminiferous tubules) at the same time as the other tissues, to limit additional animal testing. According to the OECD 488, the tissues (or tissue homogenates) can be stored under specific conditions and used for DNA isolation for up to 5 years (at or below −70 ºC). This duration is sufficient to allow you or ECHA to decide on the need for assessment of mutation frequency in the collected germ cells. This type of evidence may be relevant for the overall assessment of possible germ cell mutagenicity including classification and labelling according to the CLP Regulation.

11. 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.

11.1. Information provided

125 You have adapted this information requirement by using weight of evidence based on the following experimental data:

(i) Sub-acute toxicity study (14-days, 1979) with the Substance

(ii) Single generation reproductive toxicity study (2003)

(iii) Justification: "No data are presented for chronic exposure studies. The studies available provide adequate information to address the potential effects of repeated exposure and it is not considered warranted to conduct further animal tests to determine long term toxicity by non-primary exposure routes."

11.2. Assessment of the information provided

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

127 As explained under section 0.1, 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.

128 Relevant information that can be used to support weight of evidence adaptation for the information requirement of Section 8.6.2 at Annex IX includes similar information that is produced by the OECD TG 413. The following aspects of systemic toxicity are covered: 1) in-life observations, 2) blood chemistry, and 3) organ and tissue toxicity.

129 We have assessed the individual sources of information with regard to relevance and reliability and identified the following issue(s):

11.2.1. Aspect 1) In-life observations

130 In-life observations (aspect 1) must include information on survival, body weight development, clinical signs, functional observations, food/water consumption and other potential aspects of in life observations on the relevant physiological systems (circulatory, digestive/excretory, integumentary, musculoskeletal, nervous, renal/urinary, and respiratory).

131 The source of information (i) provides relevant information on some of the above-mentioned in life observations. However, functional observations and food/water consumption were not investigated in this study.

132 The source of information (ii) provides relevant information on some of the above-mentioned in life observations. However, functional observations was not investigated in this study.

133 The following deficiencies affect the reliability of the contribution of these studies to the weight of evidence adaptation:

134 Investigations/specifications in a sub-chronic toxicity study (OECD TG 413) include dosing of the Substance daily for a minimum of 90 days.

135 The source of information (i) has an exposure duration of 14 days

136 This exposure duration is significantly shorter than the minimum exposure duration required from a study conducted according to the OECD TG 413. The exposure duration is essential because the effects observed over the required period of exposure of 90-days might be considerably more pronounced than over a shorter study duration.

137 Also for study (ii), the exposure duration is shorter than what is required by the OECD TG 413; the exposure is 77 days instead of the required 90 days. This deficiency affects the reliability of its contribution to the weight of evidence adaptation.

138 Therefore, the reliability of the contribution of the results obtained from these studies to the weight of evidence with regard to aspect 1 is limited.

11.2.2. Aspect 2) blood chemistry

139 Information on blood chemistry (aspect 2) must include haematological (full-scale) and clinical chemistry analysis (full-scale), and other potential aspects related to blood chemistry to address relevant physiological systems (circulatory digestive/excretory, endocrine, immune, musculoskeletal, and renal/urinary).

140 None of the sources of information provide relevant information on this aspect.

11.2.3. Aspect 3) organ and tissue toxicity

141 Organ and tissue toxicity (aspect 3) must include information on terminal observations on organ weights, gross pathology and histopathology (full-scale) and other potential aspects related to organ and tissue toxicity to address relevant physiological systems (circulatory, digestive/excretory, endocrine, immune, integumentary, musculoskeletal, nervous, renal/urinary system, reproductive, and respiratory).

142 The source of information (i) provides relevant information on some aspects of organ and tissue toxicity. However, histopathology was not perfomed.

143 The source of information (ii) provides relevant information on some aspects of organ and tissue toxicity. However, histopathology is limited to: "Reproductive organs and other selected organs, including potential target organs, were weighed and collected for all P1 rats. Potential target organs (liver, spleen, thymus, kidneys, urinary bladder, lungs, trachea, nose, larynx, pharynx, pituitary gland) and gross lesions" .

144 For both sources of information, the the reliability of their contribution to the weight of evidence adaptation is hampered for the same reasons as explained for aspect 1).

145 Therefore, the reliability of the contribution of the results obtained from these studies to the weight of evidence with regard to aspect 3 is limited.

11.3. Conclusion on the weight of evidence

146 Taken together, the sources of information provide some information on aspect 1 (in-life observations) and aspect 3 (organ and tissue toxicity). However, the sources do not cover the entire set of elements of histopathology and functional observations as expected to be obtained from the OECD TG 413. In addition, no information is provided for aspect 2 (blood chemistry).

147 Therefore, it is not possible to conclude, based on any source of information alone or together, whether your Substance has or has not the particular dangerous properties foreseen to be investigated in an OECD TG 413 study.

148 Based on the above, your adaptation is rejected and the information requirement is not fulfilled.

11.4. Specification of the study design

149 Following the criteria provided in Annex IX, Section 8.6.2, Column 2, the inhalation route is the most appropriate route of administration to investigate repeated dose toxicity of the Substance; Guidance on IRs and CSA, Section R.7.5.6.3.2.

150 According to the OECD TG 413, the rat is the preferred species.

151 Therefore, the study must be performed according to the OECD TG 413, in rats and with oral administration of the Substance.

12. Long-term toxicity testing on aquatic invertebrates

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

12.1. Information provided

153 You have adapted this information requirement by using Column 2 of Annex IX, Section 9.1. To support the adaptation, you have provided following information: "No environmental exposure is expected, therefore no long-term aquatic invertebrate are required".

12.2. Assessment of the information provided

154 We have assessed this information and identified the following issues:

12.2.1. Annex IX, Section 9.1., Column 2 is not a valid basis to omit the study and your exposure based adaptation is not valid

155 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).

156 For the sake of completeness, ECHA also evaluated your adaptation under Annex XI, Section 3.2(a)/(c) (Substance-tailored exposure-driven testing).

157 Under Annex XI, Section 3, this information may be omitted based on the exposure scenario(s) developed in the Chemical Safety Report. The justification must be based on a rigorous exposure assessment in accordance with Annex I, Section 5 and must meet any one of the following criteria:

(1) It can be demonstrated that all the following conditions are met:
   i. the absence or no significant exposure in all scenarios of the manufacture and all identified uses referred to in Annex VI, Section 3.5., and
   ii. a PNEC can be derived from available data, which:
      - must be relevant and appropriate both to the information requirement to be omitted and for risk assessment purposes and therefore must be based on reliable information on the hazardous properties of the substance on at least three trophic levels;
      - must take into account the increased uncertainty resulting from the omission of the information requirement, in this case by selecting an appropriate assessment factor (AF) as described in Guidance on IRs and CSA, Section R.10.3.
      - the ratio between the results of the exposure assessment (PECs) and the PNEC are always well below 1

(2) For substances that are not included in articles, it must be demonstrated for all relevant scenarios that strictly controlled conditions as set out in Article 18(4)(a) to (f) apply throughout the life cycle.

158 Your registration dossier provides the following: a Chemical Safety Report in which you have reported a Predicted Exposure Concentration i.e. PEC of 6.56 x 10^{-1}, 2.37 x 10^{-5} and 3.40 x 10^{-4} mg/L in sewage, aquatic and sediment compartments, respectively. Therefore, you did not demonstrate an absence of exposure to the environment.

159 Furthermore you have not demonstrated that for all relevant scenarios the strictly controlled conditions throughout the life cycle of the Substance are respected as set out in Article 18(4)(a) to (f)

160 Therefore, your adaptation is rejected.

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

12.3. Study design and test specifications

162 The OECD TG 211 specifies that, for difficult to test substances, the OECD GD 23 must be followed. As already explained above, the Substance is difficult to test. Therefore, you must fulfil the requirements described in 'Study design and test specifications' under Request 9.

13. Long-term toxicity testing on fish

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

13.1. Information provided

164 You have adapted this information requirement by using Column 2 of Annex IX, Section 9.1. To support the adaptation, you have provided following information: "No environmental exposure is expected, therefore no long-term aquatic invertebrate are required".

13.2. Assessment of the information provided

165 We have assessed this information and identified the following issue:

For the reasons explained under request 9, your dossier does not include information demonstrating an absence of exposure in the environment and therefore, your adaptation is rejected.

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

13.3. Study design and test specifications

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

168 The OECD TG 210 specifies that, for difficult to test substances, the OECD GD 23 must be followed. As already explained above, the Substance is difficult to test. Therefore, you must fulfil the requirements described in 'Study design and test specifications' under Request 9.

Reasons related to the information under Annex X of REACH

14. Pre-natal developmental toxicity study in a second species

169 Pre-natal developmental toxicity (PNDT) studies (OECD TG 414) in two species is an information requirement under Annex X, Section 8.7.2.

14.1. Information provided

170 You have provided:

i. Pre-natal developmental toxicity study with the Substance in a first species (rat)

ii. Publication *(Mylchreest et al.)* entitled *"Draft review paper evaluating various reproduction/developmental studies" which provide in formation on reproductive and developmental toxicity of inhaled 2,3-dichloro-1,3-butadiene in rats.*

14.2. Assessment of the information provided

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

172 You have not provided information on pre-natal developmenat toxicity in a second species.

173 In order to be compliant and enable concluding if the Substance is a developmental toxicant, information provided has to meet the requirements of OECD TG 414 in two species.

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

14.3. Specification of the study design

175 A PNDT study according to the test method OECD TG 414 should be performed in rat or rabbit as preferred species. The study in the first species was carried out by using a rodent species (rat).

176 Therefore, a PNDT study in a second species must be performed in the rabbit as preferred non-rodent species.

177 The study must be performed with inhalation exposure of the Substance because the substance is a volatile liquid (Guidance on IRs and CSA, Section R.7.6.2.3.2.).

178 Based on the above, the study must be conducted in rabbits with inhalation exposure of the Substance.

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).

All Guidance on REACH is 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 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 23 August 2021.

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

ECHA did not receive any comments within the commenting period.

ECHA notified the draft decision to the competent authorities of the Member States for proposals for amendment.

ECHA received proposal(s) for amendment and modified the draft decision.

The deadlines indicated in the draft decision have been exceptionally extended by 6 and 12 months, to take into account currently longer lead times in contract research organisations. ECHA has therefore extended the deadlines from 18 months and 24 months to 24 months and 36 months, respectively.

ECHA invited you to comment on the proposed amendment(s) and referred the modified draft decision to the Member State Committee.

You did not provide any comments on the proposed amendment(s).

The Member State Committee unanimously agreed on the draft decision in its MSC-79 written procedure. ECHA adopted the decision under Article 51(6) of REACH.

Appendix 3: Addressees 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 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]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

Where applicable, the name of a third party representative (TPR) may be displayed in the list of recipients whereas ECHA will send the decision to the actual registrant.

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[3].

(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

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[4].

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