~~Confidential~~

Helsinki, 04 May 2023

**Addressee(s)**
Registrant(s) of Hexan-6-olide as listed in Appendix 3 of this decision

**Date of submission of the dossier subject to this decision**
14/08/2020

**Registered substance subject to this decision ("the Substance")**
Substance name: Hexan-6-olide
EC/List number: 207-938-1

**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 ***9 February 2027***.

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* gene mutation study in bacteria (Annex VII, Section 8.4.1.; test method: Bacterial reverse mutation test OECD TG 471 (2020)) using one of the following strains: *E. coli* WP2 uvrA, or *E. coli* WP2 uvrA (pKM101), or *S. typhimurium* TA102

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

2. In vitro micronucleus study (Annex VIII, Section 8.4.2.; test method: OECD TG 487). The aneugenic potential of the Substance must be assessed with an additional control group for aneugenicity on top of the control group for clastogenicity, if the Substance induces an increase in the frequency of micronuclei.

3. 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

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

4. 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)

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

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

The reasons for the requests 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.

**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 request(s)
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 request(s)

**Contents**

**Reasons common to several requests**

*0.1. Read-across adaptation rejected*

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

- In vitro micronucleus study (Annex VIII, Section 8.4.2.)
- Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)

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

5 You provide a read-across justification document in IUCLID Section 13.

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

- Adipic acid, EC 204-673-3

7 You provide the following reasoning for the prediction of toxicological properties: "The toxicological data requirements for ε-caprolactone can be adequately addressed through the provision of data for the substance and, by read-across to the hydrolysis product 6-hydroxthexanoic acid, through data for adipic acid."

8 ECHA understands that your read-across hypothesis is based on the formation of common (bio)transformation products. You predict the properties of your Substance to be quantitatively equal to those of the source substance.

9 We have identified the following issue(s) with the prediction(s) of toxicological properties:

*0.1.1.1. Read-across hypothesis contradicted by existing data*

10 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.).

11 As indicated above, your read-across hypothesis is based on the (bio)transformation of the Substance and the source substance to a common compound.

12 In your read-across justification you state that: "A theoretical assessment of the toxicokinetics of ε-caprolactone indicates that this lactone substance will be rapidly

chemically or enzymatically hydrolysed under physiological conditions (i.e. in the stomach or following absorption into the bloodstream) with the subsequent production of the hydrolysis product 6-hydroxyhexanoic acid. The half-life of ε-caprolactone in the stomach is approximately 0.4 hours (pH 1.2, temperature 37°C).”

13 We understand that, as a consequence, you assume that exposure to the parent compound does not take place.

14 You have not demonstrated that a half-life of 0.4 hours excludes exposure to the parent compound. This contradicts your claim whereby the Substance is rapidly converted into 6-hydroxyhexanoic acid which is common to the metabolite of the source substance.

15 Therefore your read-across is rejected.

#### *0.1.2. Comments to the draft decision*

16 In your comment to the draft decision you explain that, to substantiate your read-across approach, you will in addition to your current hypothesis that is based on the formation of common (bio)transformation products (RAAF Scenario 2) add information supporting the hypothesis that structurally similar substances have the same effect (RAAF Scenario 1). For that purpose, you intend to perform a screening study on the Substance. Provided that the screening study supports read-across you will use data both on adipic acid and δ-valerolactone for read-across. The new data will be assessed against the read-across hypothesis to inform further actions (i.e., if additional data generation is warranted). Provided that the screening study supports read-across, you will use data both on adipic acid and δ-valerolactone for read-across, as you still find that data on adipic acid contributes to the evaluation.

17 As the outlined strategy relies on an approach that has not yet been fully described and justified, as well as on data which are yet to be generated, no assessment or conclusion on the compliance of the proposed adaptation can presently be made.

#### *0.1.3. Conclusion on the read-across approach*

18 Based on the above and the issue identified specifically for the pre-natal developmental toxicity under Section 3 below, 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 vitro* gene mutation study in bacteria

19 An *in vitro* gene mutation study in bacteria is an information requirement under Annex VII, Section 8.4.1.

### *1.1. Information provided*

20 You have provided:

(i) an *in vitro* gene mutation study in bacteria (1975) with the Substance;

(ii) an *in vitro* gene mutation study in bacteria (1979a) with the Substance;

(iii) an *in vitro* gene mutation study in bacteria (1979b) with the Substance.

### *1.2. Assessment of the information provided*

#### *1.2.1. The provided studies do not meet the specifications of the test guideline(s)*

21 To fulfil the information requirement, a study must comply with OECD TG 471 (Article 13(3) of REACH). Therefore, the following specifications must be met:

- the test is performed with 5 strains: four strains of *S. typhimurium* (TA98; TA100; TA1535; TA1537 or TA97a or TA97) and one strain which is either *S. typhimurium* TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101).

22 In study (i):

- the test was performed with the strains TA 98, TA 100, TA 1535, and TA 1537.

23 In study (ii):

- the test was performed with the strains TA 98, TA 100, TA 1530, TA 1535, TA 1536, TA 1537, TA 1538.

24 In study (iii):

- the test was performed with the strains TA 1530, TA 1535, TA 1538, and "*E. coli, other: The strains were either normal (pol A+) or DNA polymerase I-deficient (pol A-)*".

25 The strain(s) *S. typhimurium* TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101) is missing from studies (i), (ii) and (iii).

26 The information provided does not cover the specification(s) required by the OECD TG 471.

27 Therefore, the information requirement is not fulfilled.

### *1.3. Comments on the draft decision*

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

### *1.4. Specification of the study design*

29 To fulfil the information requirement for the Substance, the *in vitro* gene mutation study in bacteria (OECD TG 471, 2020) should be performed using one of the following strains: *E. coli* WP2 uvrA, or *E. coli* WP2 uvrA (pKM101), or *S. typhimurium* TA102.

**Reasons related to the information under Annex VIII of REACH**

## 2. In vitro cytogenicity study in mammalian cells or In vitro micronucleus study

30 An in vitro cytogenicity study in mammalian cells or an in vitro micronucleus study is an information requirement under Annex VIII, Section 8.4.2.

### *2.1. Information provided*

31 You have adapted this information requirement by using Annex XI, Section 1.2. (weight of evidence) based on the following:

(i) In vitro cytogenicity/chromosome aberration study in mammalian cells (1977) with the Substance;

(ii) In vitro cytogenicity/chromosome aberration study in mammalian cells (1977) with the analogue substance adipic acid, EC no 204-673-3;

(iii) in vivo mammalian germ cell study: cytogenicity / chromosome aberration (rat bone marrow cytogenetics, 1971) with the analogue substance adipic acid, EC no 204-673-3;

(iv) in vivo mammalian germ cell study: cytogenicity / chromosome aberration (rat dominant lethal assay, 1971) with the analogue substance adipic acid, EC no 204-673-3.

### *2.2. Assessment of the information provided*

32 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.

33 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.

34 According to ECHA Guidance R.4, a weight of evidence adaptation involves an assessment of the relative values/weights of the different sources of information submitted. The weight given is based on the reliability of the data, consistency of results/data, nature and severity of effects, and relevance and coverage of the information for the given regulatory information requirement. Subsequently, relevance, reliability, coverage, consistency and results of these sources of information must be balanced in order to decide whether they together provide sufficient weight to conclude on the corresponding information requirement.

35 You have not provided a justification for your adaptation according to Annex XI, Section 1.2.

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

37 Relevant information that can be used to support weight of evidence adaptation for information requirement of Section 8.4.2. at Annex VIII includes:

- Detection and quantification of structural or numerical chromosomal aberrations in cultured mammalian cells, including data on the cytotoxicity and the frequency of cells with chromosomal aberrations or micronuclei.

38 This information is covered by studies (i) to (iv).

*2.2.1.1. Reliability of the provided information*

39 *Issue 1:*

40 To fulfil the information requirement of OECD TG 473 or OECD TG 487, respectively[2], the following conditions have to be met:

- Two separate test conditions must be assessed: in absence of metabolic activation and in presence of metabolic activation.

41 Study (i) and (ii) have only been performed without metabolic activation.

42 Therefore, they have a significant reliability issue and cannot contribute to the conclusion on the potential of the Substance to cause cytotoxicity and cannot provide information on the frequency of cells with structural chromosomal aberration(s) or the frequency of micronuclei in cultured mammalian cells.

43 *Issue 2:*

44 The Guidance on IRs and CSA, Section R.7.7.6.3 and Table R.7.7–3 clarifies that the in vivo somatic cell cytogenicity test must be either a micronucleus test or a chromosomal aberration test, performed according to the OECD TG 474 or 475, respectively.

45 The study (iv) is described as a dominant lethal assay.

46 This study is neither a micronucleus test nor a chromosomal aberration test.

47 Therefore, study (iv) has a significant reliability issue and cannot contribute to the conclusion on the potential of the Substance to cause cytotoxicity and cannot provide information on the frequency of cells with structural chromosomal aberration(s) or the frequency of micronuclei in cultured mammalian cells.

48 *Issue 3:*

49 For the data from an in vivo somatic cell cytogenicity test to be considered adequate, the in vivo study you submitted has to meet the requirements of the OECD TG 474 or 475. Therefore, the following specifications must be met:

- a clear negative outcome is concluded when the data available shows that bone marrow exposure to the Substance or its metabolites occurred.

50 The study (iii) is described as a non-guideline chromosome aberration (rat bone marrow cytogenetics study.

51 For study (iii) you did not demonstrate that bone marrow exposure to the Substance, or its metabolite(s), occurred.

52 Therefore, study (iii) has a significant reliability issue and cannot contribute to the conclusion on the potential of the Substance to cause cytotoxicity and cannot provide information on the frequency of cells with structural chromosomal aberration(s) or the frequency of micronuclei in cultured mammalian cells.

53 *Issue 4:*

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

54 The information from (ii to iv) with a read across source substance is already rejected as unreliable under "Appendix on Reasons common to several requests". Therefore the studies cannot be used as part of the weight of evidence adaptation.

*2.2.1.2. Conclusion*

55 In summary, the sources of information (i) to (iv) provide relevant information on cytogenicity. However, these sources of information have significant reliability issues as described above and cannot contribute to the conclusion on the information requirement for in vitro cytotoxicity study in mammalian cells.

56 It is not possible to conclude, based on any source of information alone or considered together, on the information requirement for in vitro cytotoxicity study in mammalian cells.

57 Based on the above, your adaptation is rejected.

58 Therefore, the information requirement is not fulfilled.

*2.3. Comments on the draft decision*

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

*2.4. Specification of the study design*

60 According to the Guidance on IR & CSA, Section R.7.7.6.3., either the in vitro mammalian chromosomal aberration ("CA") test (test method OECD TG 473) or the in vitro mammalian cell micronucleus ("MN") test (test method OECD TG 487) can be used to investigate chromosomal aberrations in vitro. However, while the MN test detects both structural chromosomal aberrations (clastogenicity) and numerical chromosomal aberrations (aneuploidy), the CA test detects only clastogenicity, as OECD TG 473 is not designed to measure aneuploidy (see OECD TG 473, paragraph 2). Therefore, you must perform the MN test (test method OECD TG 487), as it enables a more comprehensive investigation of the chromosome damaging potential in vitro. Moreover, in order to demonstrate the ability of the study to identify clastogens and aneugens, you must include two concurrent positive controls, one known clastogen and one known aneugen [1] (OECD TG 487, paragraphs 33 to 35).

*2.4.1. Assessment of aneugenicity potential*

61 If the result of the MN test is positive, i.e. your Substance induces an increase in the frequency of micronuclei, you must assess the aneugenic potential of the Substance.

62 In line with the OECD TG 487 (paragraph 4), you should use one of the centromere labelling or hybridisation procedures to determine whether the increase in the number of micronuclei is the result of clastogenic events (i.e. micronuclei contain chromosome fragment(s)) and/or aneugenic events (i.e. micronuclei contain whole chromosome(s)).

[1] According to the TG 487 (2016) "At the present time, no aneugens are known that require metabolic activation for their genotoxic activity" (paragraph 34).

## 3. Screening for reproductive/developmental toxicity

63 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.

### *3.1. Information provided*

64 You have adapted this information requirement by referring to Annex VIII, Section 8.7.1., Column 2 and by using the results of a 90-day study with additional considerations.

### *3.2. Assessment of the information provided*

#### *3.2.1. Your justification to omit the study has no legal basis*

65 A registrant may only adapt this information requirement based on the general rules set out in Annex XI or the specific rules set out in Annex VIII, Section 8.7.1., Column 2.

66 Your justification to omit this information refers to Annex VIII, Section 8.7.1., Column 2. However, your justification does not address any of the provisions of Annex VIII, Section 8.7.1., Column 2.

67 Therefore, you have not demonstrated that this information can be omitted.

### *3.3. Comments on the draft decision*

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

### *3.4. Specification of the study design*

69 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.

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

71 As the Substance is a liquid, the study must be conducted with oral administration of the Substance (Annex VIII, Section 8.7.1, Column 1).

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

**Reasons related to the information under Annex IX of REACH**

## 4. Pre-natal developmental toxicity study in one species

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

### *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) a pre-natal developmental toxicity study in rabbits (1974) with the source substance adipic acid EC 204-673-3.

### *4.2. Assessment of the information provided*

#### *4.2.1. Read-across adaptation rejected*

75 As explained under Reasons common to several requests your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5. is rejected.

76 In addition, ECHA identified endpoint specific issue(s) addressed below.

##### *4.2.1.1. Inadequate or unreliable study on the source substance(s)*

77 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 be normally performed for a particular information requirement, in this case OECD TG 414. Therefore, the following specifications must be met:

- the highest dose level aims to induce toxicity or aims to reach the limit dose.

78 In study (i) the highest dose level tested was 250 mg/kg bw/day, which is below the limit dose of the test guideline, and no adverse effect were observed, and no justification for the dose setting was provided.

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

80 Therefore, the information requirement is not fulfilled.

### *4.3. Comments on the draft decision*

81 In your comments to the draft decision you propose to wait for the outcome of the OECD 421/422 study on ε-caprolactone to assess whether read-across from δ-valerolactone is supported. If the outcome of the screening study with ε-caprolactone would not allow to justify a read-across to δ-valerolactone, you would perform an OECD 414 study with ε-caprolactone in rats. ECHA has addressed the comment related to read-across under Reasons common to several requests above. Regarding your proposal to delay the initiation of the OECD TG 414 study in a first species, ECHA notes that for the reasons explained

above, your dossier is currently not compliant with the information requirement and therefore, you remain responsible for complying with this decision by the set deadline.

*4.4. Specification of the study design*

82 A PNDT study according to the test method OECD TG 414 should be performed in rats or rabbits as preferred species.

83 As the Substance is a liquid, the study must be conducted with oral administration of the Substance (Annex IX, Section 8.7.2, Column 1).

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

## 5. Long-term toxicity testing on aquatic invertebrates

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

*5.1. Information provided*

86 You have adapted this information requirement and provided the following justification:

(i) *"Long-term toxicity studies to invertebrates are not required as the substance is readily biodegradable indicating that long-term exposure and toxicity is not expected in the aquatic environment. Furthermore, according to Annex IX column 2 of REGULATION (EC) No 1907/2006, long-term study are not required as the CSA shows low/no risk to the environment."*

*5.2. Assessment of the information provided*

*5.2.1. Annex IX, Section 9.1., Column 2 is not a valid basis to omit the study*

87 Under Annex IX, Section 9.1., Column 2 is not a basis for omitting information on long-term toxicity to aquatic invertebrates referred to under Column 1, Section 9.1.5.

88 We further note that your argumentation about ready biodegradability of the Substance does not refer to any legal ground for adaptation under Annex IX, Section 9.1, Column 2.

89 Your adaptation is therefore rejected.

90 Therefore, the information requirement is not fulfilled.

*5.3. Comments on the draft decision*

91 In your comments to the initial draft decision you agree with the request.

## 6. Long-term toxicity testing on fish

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

*6.1. Information provided*

93 You have adapted this information requirement and provided the following justification:

(i) *"Long-term toxicity studies to fish are not required as the substance is readily biodegradable indicating that long-term exposure and toxicity is not expected in the aquatic environment. Furthermore, according to Annex IX column 2 of REGULATION (EC) No 1907/2006, long-term studies are not required as the CSA shows low/no risk to the environment."*

*6.2. Assessment of information provided*

*6.2.1. Annex IX, Section 9.1., Column 2 is not a valid basis to omit the study*

94 Under Annex IX, Section 9.1., Column 2 is not a basis for omitting information on long-term toxicity to fish referred to under Column 1, Section 9.1.6.

95 We further note that your argumentation about ready biodegradability of the Substance does not refer to any legal ground for adaptation under Annex IX, Section 9.1, Column 2.

96 Your adaptation is therefore rejected.

97 Therefore, the information requirement is not fulfilled.

*6.3. Comments on the draft decision*

98 In your comments to the initial draft decision you agree with the request.

*6.4. Study design and test specifications*

99 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.).

**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**

This decision does not prevent ECHA from initiating further compliance checks at a later stage on the registrations present. This decision does not address your testing proposals for an Extended one-generation reproductive toxicity study or a pre-natal developmental toxicity study in a second species. These will be addressed in a separate decision.

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

The compliance check was initiated on 17 November 2021.

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 but amended the deadline.

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

In your comments you requested an additional extension of the deadline with reference to the remaining work on your read-across approach. This affects both the information to be submitted in consequence of this decision as well as the parallel decision on your testing proposals concerning two further reproductive toxicity studies. In this specific case ECHA sees the need to evaluate read-across when the full data base is available, and has therefore considered this for the deadline set in alignment in both decisions.

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

## 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.

With that detailed information, ECHA can confirm 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 (https://echa.europa.eu/manuals).

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