

Helsinki, 14 May 2024

**Addressees**

Registrants of JS\_471-920-1 as listed in Appendix 3 of this decision

**Date of submission of the dossier subject to this decision**

30 March 2020

**Registered substance subject to this decision ("the Substance")**

Substance name: Reaction products of amines, dicoco alkyl and glycollic acid

EC/List number: 471-920-1

**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 **19 August 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. Long-term toxicity testing on aquatic invertebrates, also requested below (triggered by Annex VII, Section 9.1.1., Column 2).
2. Growth inhibition study on aquatic plants (Annex VII, Section 9.1.2.; test method: EU C.3/OECD TG 201).
3. Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: EU C.4. C/D/E/F/OECD TG 301B/C/D/F or EU C.29./OECD TG 310) on relevant constituent(s)/fraction(s) of the Substance, as described under the corresponding appendix on reasons for the request.

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

4. Long-term toxicity testing on fish, also requested below (triggered by Annex VIII, Section 9.1.3., Column 2).

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

5. Sub-chronic toxicity study (90 days), oral route (Annex IX, Section 8.6.2.; test method: OECD TG 408) in rats.
6. 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).

7. Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.; test method: EU C.20./OECD TG 211).
8. Long-term toxicity testing on fish (Annex IX, Section 9.1.6.; test method: EU C.47./OECD TG 210).
9. Long-term toxicity testing on terrestrial invertebrates (triggered by Annex IX, Section 9.4.1., Column 2; test method: OECD TG 222 or OECD TG 220 or OECD TG 232)
10. Effects on soil micro-organisms (Annex IX, Section 9.4.2.; test method: EU C.21./OECD TG 216)
11. Long-term toxicity on terrestrial plants (triggered by Annex IX, Section 9.4.3., Column 2; test method: EU C.31./OECD TG 208 with at least six species or ISO 22030)

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.

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.

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<sup>1</sup> under the authority of Mike Rasenberg, Director of Hazard Assessment

Appendix 1: Reasons for the requests

Appendix 2: Procedure

Appendix 3: Addressees of the decision and their individual information requirements

Appendix 4: Conducting and reporting new tests under REACH

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<sup>1</sup> 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 requests**

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## Reasons related to the information under Annex VII of REACH

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

1 Short-term toxicity testing on aquatic invertebrates is an information requirement under Annex VII, Column 1, Section 9.1.1. However, under Column 2, long-term toxicity testing on aquatic invertebrates may be required by the Agency if the substance is poorly water soluble, i.e. solubility below 1 mg/L.

#### 1.1. Triggering of the information requirement

2 In the provided OECD TG 105 (2006), the saturation concentration of the Substance in water was determined to be < 1.6 mg/L. In addition, you have provided information which indicate that the Substance includes constituents that are poorly water soluble. In particular, you report a predicted value of 1.21E-05 mg/L (at 25°C) for the primary component of the Substance (i.e., 2 -hydroxy,N,N-dicoco alkyl acetamide).

3 Therefore, the Substance is poorly water soluble and information on long-term toxicity on aquatic invertebrates must be provided.

#### 1.2. Information requirement not fulfilled

4 The information provided, its assessment and the specifications of the study design are addressed under request 7.

### 2. Growth inhibition study aquatic plants

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

#### 2.1. Information provided

6 In your registration dossier, you have provided

(i) a Growth inhibition study on algae (2006) performed according to OECD TG 201 with the Substance.

7 In your comment to the draft decision and in your updated registration dossier (28/02/2024), you provided the following additional study:

(ii) a Growth inhibition study on algae (2019) performed according to OECD TG 201 with the Substance.

#### 2.1.2. The provided studies (i) and (ii) do not meet the specifications of the test guideline

8 To fulfil the information requirement, a study must comply with OECD TG 201 and the specifications of OECD GD 23 if the substance is difficult to test (Article 13(3) of REACH). The Substance is a UVCB substance which contains poorly water soluble and highly adsorptive constituents (e.g., the main constituent has a reported water solubility of 1.21E-05 mg/L, a log K<sub>ow</sub> >6 and Log K<sub>oc</sub> >5) and constituents that are ionisable. Therefore, the following specifications must be met:

*Additional requirements applicable to difficult to test substances*

- a) if the test material is tested at the saturation concentration, evidence must be provided that all reasonable efforts have been taken to achieve a saturation concentration, which include:
  - (1) an analytical method validation report demonstrating that the analytical method is appropriate;
  - (2) information on the saturation concentrations of the test material in water and in the test solution; and
  - (3) the results of a preliminary experiment demonstrating that the test solution preparation method is adequate to maximize the concentration of the test material in solution;
- b) when the Water Accommodated Fraction (WAF) approach is used, loading rates must be sufficiently low to be in the solubility range of most constituents (or that are consistent with the PEC value). This condition is mandatory to provide relevant information for the hazard and risk assessment (Guidance on IRs and CSA, Appendix R.7.8.1-1, Table R.7.8-3).

*Reporting of the methodology and results*

- c) water quality monitoring within the test vessels (i.e., TOC and/or COD) is reported. For adsorbing test chemicals, the OECD GD 23 specifies that total dissolved organic carbon concentrations (other than that due to the test chemical) in all test solutions must be maintained  $\leq 2$  mg/L.

*Characterisation of exposure*

- d) for volatile, unstable or strongly adsorbing test substances, additional samplings for analysis at 24-hour intervals is required;
- e) where a measured concentration at the end of the exposure period indicates that the substance is not detected, the concentration may be taken as the limit of detection for the method (Guidance on IRs & CSA Chapter R.7b, Appendix R.7.8—1). In particular, where the water solubility is below the detection limit of the analytical method for a substance, and toxicity is recorded, the effect concentration for classification purposes may be considered to be less than the analytical detection limit (Guidance on the Application of the CLP Criteria, ANNEX I: AQUATIC TOXICITY, I.4.2 Poorly soluble substances).

9 In the provided studies (i) and (ii):

*Additional requirements applicable to difficult to test substances*

- a) For both studies (i) and (ii), you do not provide the information listed under (1) to (3);
- b) the loading rates used in the studies (i) and (ii) (i.e., 10-160 mg/L) are orders of magnitude higher than the expected solubility range of most constituents. As already explained above, you report a water solubility estimate of <1.6 mg/L for the Substance as a whole and of 1.21E-05 mg/L at 25°C for the main constituent 2-hydroxy,N,N-dicoco alkyl acetamide (C12).

*Reporting of the methodology and results*

- c) For both studies (i) and (ii), you do not report TOC and/or COD concentrations in the test vessels;
- d) for the study (ii) provided in your comments to the draft decision, you state that "[m]easured concentrations of less than the LOQ were obtained for all

*test preparations at 72 hours indicating possible losses of the test item due to instability and/or adsorption under the conditions of the test*", highlighting the potential importance of the adsorption. Additionally based on this statement, it is not clear whether and to what extent the test organism has been exposed to the Substance during the whole duration of the test;

- e) In addition to the statement above, you also state that "*Analysis of the test preparations at 0 hours showed measured test concentrations of less than the limit of quantification (LOQ) of the analytical method employed (determined to be 0.0020 mg/L) for all test preparations with the exception of the 100 mg/L loading rate WAF where a measured test concentration of 0.011 mg/L was obtained*" and *[i]t was not possible to calculate a NOEL based on yield as a statistically significant difference was observed in all test loading rates employed*". Based on your statements above, the NOEC could be much lower than the concentration reported based on loading rate. In theory, if the measured concentration of the loading rate at 100 mg/L was 0.011 mg/L at the start of the test, the actual dissolved concentrations of EC50/NOEC at loading rates of 19 mg/L and 10 mg/L (based on biomass, as reported in the study (ii)) must have been significantly lower than 0.011 mg/L. ECHA points out that, EC50 and NOEC based on yield are reported to be even lower (7.7 mg/L and 1.0 mg/L respectively based on loading rate) than those based on biomass. The Substance could thus meet the classification criteria for aquatic toxicity.

10 Based on the above,

- The Substance is difficult to test and there are critical methodological deficiencies resulting in the rejection of the study results. More specifically, the loading rates used to prepare the test solutions were too high and therefore cannot be considered a reliable estimate of the exposure to the dissolved substance. Therefore, the reported effect concentrations based on loading rates does not reflect the intrinsic toxicity of the Substance. Furthermore, you have provided no experimental evidence to support that the methodology you used allowed to maximize the exposure to the test material;
- The reporting of the studies (i) and (ii) is not sufficient to conduct an independent assessment of its reliability. More specifically, considering the adsorptive properties of the Substance, in the absence of information on total dissolved organic carbon concentrations in the test solution, it is not possible to verify that the specifications of the OECD TG 201 in combination with the OECD GD 23 were met.

11 In your comments to the draft decision, you state that:

- you are confident that the provided study (i) is "*reliable, reproducible and meets the specification of OECD TG 201 test and the criteria of difficult to test substance as per OECD TG 23*";
- the additional study (ii) provided in your comments is deemed "*more robust*";
- the Substance "*does not meet classification criteria based on growth rate*".

12 As explained above, ECHA disagrees with all three statements in your comments to the draft decision, and the information provided in your comments does not change the assessment outcome.

13 On this basis, the specifications of OECD TG 201 are not met and the information requirement is not fulfilled.

## 2.2. Study design

- 14 As already explained above, the Substance is difficult to test. The OECD TG 201 specifies that, for difficult to test substances, you must consider the approach described in OECD GD 23 or other approaches, if more appropriate for your substance. In all cases, the approach selected must be justified and documented. Due to the properties of Substance, it may be difficult to achieve and maintain the desired exposure concentrations. 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 OECD TG 201. 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 solution.
- 15 For multi-constituents/UVCBs, the analytical method must be adequate to monitor qualitative and quantitative changes in exposure to the dissolved fraction of the test material during the test (e.g. by comparing mass spectral full-scan GC or HPLC chromatogram peak areas or by using targeted measures of key constituents or groups of constituents).
- 16 If you decide to use the Water Accommodated Fraction (WAF) approach, in addition to the above, you must:
- use loading rates that are sufficiently low to be in the solubility range of most constituents (or that are consistent with the PEC value). This condition is mandatory to provide relevant information for the hazard and risk assessment (Guidance on IRs and CSA, Appendix R.7.8.1-1, Table R.7.8-3);
  - provide a full description of the method used to prepare the WAF (including, among others, loading rates, details on the mixing procedure, method to separate any remaining non-dissolved test material including a justification for the separation technique);
  - prepare WAFs separately for each dose level (i.e. loading rate) and in a consistent manner.

## 3. Ready biodegradability

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

### 3.1. Information provided

- 18 In your registration dossier, you have provided:
- (i) a ready biodegradability study (2006), performed according to OECD TG 301B with the Substance.
- 19 In your comments to the draft decision and in your updated registration dossier (28/02/2024), you provide the following two additional studies:
- (ii) A ready biodegradability study (2006), performed according to MITI with the Substance, concluding that the Substance is not readily biodegradable;
  - (iii) A ready biodegradation study (2013), performed according to OECD TG 301 B with the substance.



### 3.2. Assessment of the information provided

#### 3.2.1. The provided studies (i), and (iii) do not meet the specifications of the test guideline(s)

20 To fulfil the information requirement, a study must comply with the OECD TG 301 or 310 (Article 13(3) of REACH). Therefore, for a study according to OECD TG 301, the following specifications must be met:

##### *Reporting of the methodology and results*

- a) the source of the inoculum, its concentration in the test and any pre-conditioning treatment are reported;
- b) the methods of preparation of test solutions/suspensions are reported (only for poorly water soluble substances);
- c) the results of measurements at each sampling point in each replicate is reported in a tabular form;
- d) the calculation of the ThCO<sub>2</sub> is described and justified;
- e) the inorganic carbon content (IC) and total carbon content (TC) of the test material suspension in the mineral medium at the beginning of the test is reported;
- f) the total CO<sub>2</sub> evolution in the inoculum blank at the end of the test is reported.

21 In the provided study (i):

##### *Reporting of the methodology and results*

- a) You do not specify the bacterial cell density of the inoculum and whether the inoculum was pre-adapted to the Substance. In the comments to the draft decision, you provide information on the study (i) that the inoculum was not pre-adapted but you did not provide information on the bacterial cell density.
- b) the methods of preparation of test solutions/suspensions are not reported. In your comments to the draft decision, you provide the information on the study (i);
- c) you report average percentages of degradation but you have not provided the results of measurements at each sampling point in each replicate. In your comments to the draft decision you provide this information for the study (i);
- d) the calculation of the ThCO<sub>2</sub> is not described. In your comments to the draft decision, you state that "% ThCO<sub>2</sub> (aka. biodegradation) = (mg IC in test flask - mg IC in control) ÷ (mg TOC as test material)\*100%". However, you do not provide information on how you calculate the ThCO<sub>2</sub> to reflect the composition of the test material (i.e. UVCB);
- e) the inorganic carbon content (IC) and total carbon content (TC) of the test material suspension in the mineral medium at the beginning of the test is not reported. In your comments to the draft decision, you report the inorganic carbon content (IC) and total carbon content (TC). However, the technical dossier is not updated with the information;
- f) the total CO<sub>2</sub> evolution in the inoculum blank at the end of the test is not reported. In your comments to the draft decision you provide this information.

22 In the provided study (iii):

- a) You do not specify the bacterial cell density of the inoculum (i.e. in cells/L) nor that the activated sludge was taken from a treatment plant or laboratory-scale unit receiving predominantly domestic sewage;

23 In addition, you do not provide information on d-f) above.

24 Based on the above, the reporting of the studies (i) and (iii) is not sufficient to conduct an independent assessment of its reliability. In the absence of the above information, it is not possible to conduct an independent assessment as to whether (i) the study was conducted under conditions that are consistent with the specifications of the OECD TG 301B, (ii) the validity criteria of the test guideline were met and (iii) the interpretation of the results is adequate.

25 In your comments to the draft decision, you provided some of the missing information of the study (i). However, you do not provide information on the bacterial cell density (issue a)) and calculation of ThCO<sub>2</sub> (issue d) above).

26 In addition, on study (iii) provided in your comments to the draft decision and in your updated registration dossier (28/02/2024), critical information to verify validity criteria (e.g. degradation of the reference compound) and technical specifications (e.g. domestic sewage is used or not, pH adjustment) are missing.

27 In the provided study (ii), which is also provided in the technical dossier, you indicate that you consider the study reliability is not assignable (Klimisch score 4). Furthermore, the study (ii) shows that the Substance is not readily biodegradable (average 36% based on BOD) and hence does not support your claim.

28 On this basis, the specifications of OECD TG 301B are not met.

### 3.2.2. Ready biodegradation tests are normally intended for pure substances

29 The revised introduction to the OECD Guidelines for testing of chemicals, Section 3 Part I states that ready biodegradability tests are intended for pure substances but may also be relevant, on a case-by-case basis, to mixtures of structurally similar chemicals (i.e. which are composed of constituents expected to show similar degradation kinetics). However, such tests are not generally applicable for complex mixtures or substances (i.e. UVCB or multi-constituent substances) containing different types of constituents. For complex substances, a single ready biodegradability test does not allow to conclude on the ready biodegradability of all constituents and therefore, does not fulfil the information requirement. In this case, the ready biodegradability test must be performed on relevant constituent(s)/fraction(s) of the Substance.

30 You have provided a study conducted on the Substance as a whole. In Section 1.1. of your dossier you describe the Substance as UVCB. In Section 1.2, you describe the substance as [REDACTED]

[REDACTED]. Considering the large range of carbon chain length within this fraction, it is unlikely that all constituents have similar degradation kinetics. In addition, the Substance contains [REDACTED]

[REDACTED]. These constituents are structurally different from the mixture of [REDACTED] and thus they may also show different degradation kinetics. Finally, based on the reported sum of the typical concentrations, there is c.a. 10% of the remaining composition which is not characterised.

31 The Substance is a complex substance and contains constituents with significant structural differences described above. Therefore, the provided study does not provide

unequivocal conclusion that all constituents can safely be regarded as readily biodegradable.

32 In your comments to the draft decision, you argue that “*ECHA’s draft decision incorrectly assumes that individual constituent of the UVCB is readily available, on the contrary, such a test item is NOT routinely isolated or produced, and QSAR predictions are unfeasible because SMILES cannot be generated for all structural variations*”. You conclude that new biodegradation studies are not needed. However, your comments neither provide justification as to why you believe that all the different constituents of the Substance are readily biodegradable nor provide remaining ca. 10 % unknown constituents. The information provided in your comments does not change the assessment outcome.

33 Therefore, the information requirement is not fulfilled.

### 3.3. Study design

34 To fulfil the information requirement, the test method(s) according to OECD TG 301B/C/D/F or OECD TG 310 are in general appropriate. You can choose any of these methods, but you must ensure that the Substance is within the applicability domain of the test method chosen.

35 For the reasons provided above, testing on the Substance as a whole does not fulfil the information requirement. For the generation of information on ready biodegradability, you must consider the level of information required for the purposes of classification and labelling and, if applicable to your registration, the PBT/vPvB assessment and the exposure assessment/risk characterisation. In order to conclude on which of constituents of the Substance are and which are not readily biodegradable, you may have to consider conducting more than one study using selected individual constituents and/or fractions. If you choose to test one (or more) fraction(s) of the Substance, you must provide a justification that their constituents within chosen fraction(s) are similar enough so that similar degradation kinetics can be assumed. If you decide to conduct a single study in order to prove that all constituents of the Substance are readily biodegradable, you must provide a justification that the selected constituent/fraction can be considered a reasonable worst-case for the Substance as a whole in terms of degradation kinetics.

36 Justification for selection of relevant constituent and/or fractions for the testing, must consider degradation kinetics of constituents of the Substance based, as minimum, on the similarity/differences of the chemical structures and the physico-chemical properties of constituents of the Substance. For that purpose, tools and approaches mentioned in Guidance on IRs and CSA, Sections R.7b and R.11 should be considered.

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

### **4. Long-term toxicity testing on fish**

37 Short-term toxicity testing on fish is an information requirement under Annex VIII, Column 1, Section 9.1.3. However, long-term toxicity testing on fish may be required by the Agency (Section 9.1.3., Column 2) if the substance is poorly water soluble, i.e. solubility below 1 mg/L.

#### *4.1. Triggering of the information requirement*

38 As explained in request 1, the Substance is poorly water soluble and information on long-term toxicity on fish must therefore be provided.

#### *4.2. Information requirement not fulfilled*

39 The information provided, its assessment and the specifications of the study design are addressed under request 8.

**Reasons related to the information under Annex IX of REACH****5. Sub-chronic toxicity study (90-day)**

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

*5.1. Information provided*

41 In your registration dossier, you have provided:

(i) a sub-acute toxicity study (2006) according to the OECD TG 407 with the Substance;

(ii) a waiver which ECHA understands uses Annex IX, Section 8.6.2., Column 2, Indent 4 as the legal basis: "[...] *the substance is unreactive, insoluble and not inhalable and there is no evidence of absorption and no evidence of toxicity in a 28-day 'limit test' and human exposure is limited*".

42 In your comments to the draft decision, you refer to the following additional studies:

(iii) an OECD TG 422 (2019) study (included in your updated dossier; 28/02/2024)

(iv) An oral reproductive/developmental toxicity screening study (2011) currently in your dossier.

*5.2. Assessment of the information provided**5.2.1. Study not adequate for the information requirement (studies i, iii and iv)*

43 To fulfil the information requirement, a study must comply with the OECD TG 408 (Article 13(3) of REACH). Therefore, the following specifications must be met:

a) the exposure duration is at least 90 days;

44 However, the exposure duration was insufficient in studies (i and iii): 28 days. Exposure duration was also insufficient for study (iv), as you state: "*Male rats were treated for 43 days, females were dosed for 14 days prior to mating and continuing through Lactation Day 4.*"

45 In addition, the study (i) is described as a Repeated Dose 28-Day Oral Toxicity Study in Rodents. This study has been conducted using OECD TG 407 which investigates sub-acute rather than sub-chronic toxicity.

46 For these reasons, these studies do not cover the specifications required by the OECD TG 408.

*5.2.2. Column 2 criteria not met (waiver ii)*

47 Under Annex IX, Section 8.6.2., Column 2, Indent 4, the study may be omitted if the following cumulative conditions are met:

(1) the substance is unreactive, insoluble and not inhalable;

(2) there is no evidence of absorption; and

(3) no evidence of toxicity in a 28-day 'limit test', particularly if such a pattern is coupled with limited human exposure.

- 48 You claim that the Substance is unreactive, insoluble and not inhalable (1) as well as that there is no evidence of absorption (2). Furthermore, you state that there is (3) no evidence of toxicity in a 28-day 'limit test'.
- 49 To support these claims, you provide the following:
- (1) The physicochemical characteristics of the Substance: "[...] *an average molecular weight of 448 gm/mol [...] poorly water soluble ( $<1.6 \times 10^{-3}$ gm/L) [...] relative high octanol/water partition coefficient ( $\log K_{o/w} > 6$ ) [...] very low vapour pressure ( $2.3 \times 10^{-8}$ Pa @ 25oC)*". Furthermore, you state that "*the substance vapor pressure indicates a very low propensity to enter atmospheric air in a respirable form. Thus, respiratory absorption under normal use and handling of this material is expected to be inconsequential*". You state that the Substance "[...] *is a material of limited and restricted use within the automotive engineering industry, for lifetime enclosure, as a dilute fluid, within an automobile component [...] The substance will not be used to produce products which would be made available to the general public*".
  - (2) No experimental toxicokinetic data was provided to show that there is no systemic absorption. Moreover, you speculate based on physicochemical characteristics that "*the substance is of adequate molecular size to participate in endogenous absorption mechanisms within the mammalian gastrointestinal tract should that material be ingested*";
  - (3) An OECD TG 407 study (Repeated Dose 28-Day Oral Toxicity Study in Rodents) is provided with a NOEL of 1000 mg/kg bw/day.
- 50 Your assumption on the Substance being unreactive is unsubstantiated and therefore cannot be accepted. Your claim that there is no evidence of absorption (2) is not supported by any toxicokinetic data on the Substance, nor by the evidence you provide in your registration dossier. In particular, in the summary of an OECD TG 474 Mammalian Erythrocyte Micronucleus Test (2013), you state that "*The maximum dose level caused clinical signs that were considered to be evidence of absorption and of exposure to the target tissue. The maximum dose level was considered to be the maximum tolerated dose level*". This information is indicative that the Substance can be absorbed.
- 51 In your comments to the draft decision, you refer specifically to studies (i), (iii) and (iv). You continue by stating that "*From the three studies covering a range of endpoints, male animals were dosed for 28 or 43 days, non-pregnant females were dosed for 28 days, or pregnant females received treatment up to lactation day 13 did not show any adverse effects at the highest dosage level*". ECHA understands that the highest tested dose for all studies was 1000 mg/kg bw/day. Although these studies may further support your data under point (3), they do not address the concerns raised under points (1) and (2). More specifically, an absence of adverse effects in these studies does not demonstrate that the Substance is unreactive, insoluble and not inhalable, nor does it demonstrate a lack of absorption.
- 52 You continue by stating: "*Due to the similar nature of the repeated dose tests, it is feasible to avoid duplication to conduct a 90-day study and reduce animal testing in this situation.*" A "*similar nature of the repeated dose tests*" does not constitute a legal basis for adaptation. In addition to the above, you state that "*This approach agrees with the research published by Taylor K. et al (Taylor K, Andrew D.J., Rego L. The added value of the 90-day repeated dose oral toxicity test for industrial chemicals with a low (sub)acute toxicity profile in a high quality dataset, Regulatory Toxicology and Pharmacology, 69 (2014): 320-332.)*." ECHA understands that by referring to this publication, you suggest that in your case a 90-day study would not provide any added value over a 28-day study. However, a lack of toxic effects in a short-term study is not a legal basis for adaptation of

the sub-chronic toxicity study (90 days) information requirement under Annex IX, Section 8.6.2.

53 Based on the above, your adaptation is rejected.

54 Therefore, the information requirement is not fulfilled.

### 5.3. Study design

55 Following the criteria provided in Annex IX, Section 8.6.2., Column 2, and considering the Guidance on IRs and CSA, Section R.7.5.6.3.2., the oral route is the most appropriate route of administration to investigate repeated dose toxicity of the Substance, because the Substance is a viscous liquid with low vapour pressure, and there is no indication that dermal or inhalation exposure would lead to more severe adverse effects (or lead to lower effect levels) than oral exposure.

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

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

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

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

### 6.1. Information provided

59 In your registration dossier, you have provided:

(i) a Reproduction / Developmental Toxicity Screening Test (2011) with the Substance;

(ii) a waiver which ECHA understands uses Annex IX, Section 8.7., Column 2 as the legal basis: “[...] *the substance is of low toxicological activity (no evidence of toxicity seen in any of the tests available), it can be proven from toxicokinetic data that no systemic absorption occurs via relevant routes of exposure (e.g. plasma/blood concentrations below detection limit using a sensitive method and absence of the substance and of metabolites of the substance in urine, bile or exhaled air) and there is no or no significant human exposure*”;

60 In your comments to the draft decision, you refer to the following additional study:

(iii) an OECD TG 422 (2019) study (included in your updated dossier; 28/02/2024)

### 6.2. Assessment of the information provided

#### 6.2.1. Studies not adequate for the information requirement (studies i and iii).

61 To fulfil the information requirement, a study must comply with OECD TG 414 (Article 13(3) of REACH). Therefore, the following specifications must be met:

- a) at least 20 female animals with implantation sites are included for each test and control group to ensure a statistical power equivalent to OECD TG 414;
- b) the foetuses are examined for external, skeletal and soft tissue alterations (variations and malformations) and anogenital distance.

62 The study (i) has been conducted using the OECD TG 421 and study (iii) using OECD TG 422, which are screening tests rather than conclusive developmental toxicity studies.

63 In addition, we identified the following issues with studies (i) and (iii):

- a) In study (i), only 12 female animals, and in study (iii), only 10-15 female animals (i.e., less than 20 female animals) with implementation sites are included in each group, and therefore the statistical power is not equivalent to OECD TG 414.
- b) In studies (i) and (iii), the foetuses are not examined for external, skeletal and soft tissue alterations (variations and malformations), and in study (i) anogenital distance is not measured in live rodent foetuses. In your comments to the draft decision, you state that in study (iii): "*Skeletal system was not examined, but they would have led to gross abnormalities or abnormal physical conditions if there were skeletal malformations.*" However, skeletal defects do not always lead to gross abnormalities or abnormal physical conditions, and thus this concern has not been fully addressed.

64 The information provided does not cover the specifications required by the OECD TG 414.

65 On this basis, the studies are not adequate for the information requirement.

6.2.2. *Criteria for the application of the adaptation for Annex IX, Section 8.7., Column 2 not met*

66 Under Annex IX, Section 8.7., Column 2, the study does not need to be conducted if the following cumulative conditions are met:

- (1) the substance is of low toxicological activity, demonstrated by a comprehensive and informative dataset showing no toxicity in any of the tests available; and
- (2) that it can be proven from toxicokinetic data that no systemic absorption occurs via relevant routes of exposure; and
- (3) that there is no or no significant human exposure.

67 You claim that "*the substance is of low toxicological activity (no evidence of toxicity seen in any of the tests available), it can be proven from toxicokinetic data that no systemic absorption occurs via relevant routes of exposure (e.g. plasma/blood concentrations below detection limit using a sensitive method and absence of the substance and of metabolites of the substance in urine, bile or exhaled air) and there is no or no significant human exposure*".

68 To support these claims, you provide the same justification as already described under section 5.2.2.

69 Your assumption that no systemic absorption occurs via relevant routes of exposure (2) is not supported by any toxicokinetic data on the Substance, nor by the evidence you provide in your registration dossier. In particular, in the summary of an OECD TG 474 Mammalian Erythrocyte Micronucleus Test (2013), you state that "*The maximum dose level caused clinical signs that were considered to be evidence of absorption and of exposure to the target tissue. The maximum dose level was considered to be the maximum tolerated dose level*". This information is indicative that the Substance can be absorbed. Moreover, you speculate that "*the substance is of adequate molecular size to participate in endogenous absorption mechanisms within the mammalian gastrointestinal tract should that material be ingested*".



70 Your claim that there is no or no significant human exposure (3) appears to be contradicted by the professional uses you report in your dossier. In particular, you indicate that:

- *“general exposure [may occur] during maintenance work including draining, refilling.*

71 In your comments to the draft decision, you refer to study (iii). You state that *“The two studies are complementary and illustrate this substance is not toxic for reproduction. They are effective in providing sufficient data to interpret the substance safety.”* ECHA understands that you raise this statement to support your waiver submitted as part of an Annex IX, Section 8.7., Column 2 adaptation, specifically to meet condition (2) *“the substance is of low toxicological activity, demonstrated by a comprehensive and informative dataset showing no toxicity in any of the tests available”*. A claimed lack of reproductive toxicity alone is only one element contributing to *“low toxicological activity”*, and as such ECHA cannot conclude that you have met this condition. In addition, for the reasons explained under 6.2.1., studies (i) and (iii) cannot individually or taken together fulfil the information requirement. On this basis, you have not demonstrated that the criteria for this adaptation are fulfilled and your adaptation is rejected.

72 Therefore, the information requirement is not fulfilled.

### *6.3. Study design*

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

74 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).

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

## **7. Long-term toxicity testing on aquatic invertebrates**

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

### *7.1. Information provided*

77 You have provided a long-term toxicity study on *Daphnia magna* (2006), performed according to OECD TG 211 with the Substance.

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

#### *7.2.1. The provided study does not meet the specifications of the test guideline(s)*

78 To fulfil the information requirement, a study must comply with the OECD TG 211 and the specifications of OECD GD 23 if the substance is difficult to test (Article 13(3) of REACH). As explained in Request 2, the Substance is difficult to test. Therefore, the following specifications must be met:

*Additional requirements applicable to difficult to test substances*

- a) if the test material is tested at the saturation concentration, evidence must be provided that all reasonable efforts have been taken to achieve a saturation concentration, which include:
- (1) an analytical method validation report demonstrating that the analytical method is appropriate;
  - (2) information on the saturation concentrations of the test material in water and in the test solution; and
  - (3) the results of a preliminary experiment demonstrating that the test solution preparation method is adequate to maximize the concentration of the test material in solution;
- b) when the Water Accommodated Fraction (WAF) approach is used loading rates must be sufficiently low to be in the solubility range of most constituents (or that are consistent with the PEC value). This condition is mandatory to provide relevant information for the hazard and risk assessment (Guidance on IRs and CSA, Appendix R.7.8.1-1, Table R.7.8-3).

79 Reporting of the methodology and results

- c) water quality monitoring within the test vessels (i.e., TOC and/or COD) is reported. For adsorbing test chemicals, the OECD GD 23 specifies that total dissolved organic carbon concentrations (other than that due to the test chemical) in all test solutions must be maintained  $\leq 2$  mg/L.

80 In the provided study :

*Additional requirements applicable to difficult to test substances*

- a) you do not provide the information listed under (1) to (3) and you report that:
- *"The results from the analysis were highly variable and did not show an increase in measured concentrations with increasing nominal loading rates";* and
  - *"soluble components of the WAF present at the loading rate were toxic to Daphnia magna but were not detected by chemical analysis".*
  - In your comments to the draft decision, you provide the information that *"In the daphnia reproduction test, the test material concentrations were determined by GC, recovery was low at 1.0 mg/L, thus it is not possible to analyze WAF preparation at solubility of the main constituents (i.e. 1.21E05 mg/L)"* that it *"[...] probably cannot go lower than 1.0 mg/L"*. These comments also indicate that the analytical method used was not appropriate for the Substance.
- b) the loading rates used in this study (i.e., 1.8-180 mg/L) are orders of magnitude higher than the expected solubility range of most constituents. As already explained above, you report a water solubility estimate of  $<1.6$  mg/L for the Substance as a whole and of  $1.21E-05$  mg/L at 25°C for the main constituent [REDACTED] (C12). Furthermore, you report that *"Chemical analysis of the test loading rates throughout the test showed measured concentrations of soluble test material to range from less than the LOQ of the analytical method (i.e. 0.0018 mg/L) to 0.674 mg/L"*. In your comments to the draft decision, you provide statement that *"In this complex substance [the Substance], the constituents in a WAF will not be present in the same concentration as in the original test substance since each constituent will reach saturation limit in the WAF proportional to its water solubility and its concentration in the test substance. That is why the high loading rate were employed over a range of nominal loading rate. Moreover,*

*the water accommodating fraction was siphoned from the soluble fraction of the WAF preparation and then be used as the exposure medium. The insoluble particles or droplet were removed from the solution. It can ensure the saturation of UVCB has been attained".* However, your comments do not address the issues pointed out by ECHA, as explained below, the reported effect concentrations based on loading rates does not reflect the intrinsic toxicity of the Substance.

#### *Reporting of the methodology and results*

- c) you do not report TOC and/or COD concentrations in the test vessels. In your comments to the draft decision, you state that the test solution commonly contains 0.5 mg/L to 2 mg/L TOC. However, you do not provide any evidence of the total dissolved organic carbon of the test solution used in the study, nor whether the concentration had been maintained to 2.0 mg/L throughout the study. You also state that as measured concentration of the Substance did not decrease linearly along the loading rate, you believe that the Substance was not adsorbed in the study. However, this statement cannot be substantiated with the information provided in the dossier nor in your comments to the draft decision.

81 Based on the above,

- the Substance is difficult to test and there are critical methodological deficiencies resulting in the rejection of the study results. More specifically, the loading rates used to prepare the test solutions were too high and therefore cannot be considered a reliable estimate of the exposure to the dissolved substance. Therefore, the reported effect concentrations based on loading rates does not reflect the intrinsic toxicity of the Substance. Furthermore, you have provided no experimental evidence to support that the methodology you used allowed to maximize the exposure to the test material. You indicate that toxic effects were observed but that exposure concentrations could not be quantified which questions the adequacy of the analytical method. Finally, the fact that measured exposure concentrations were variable and did not correlate to loading rates questions the adequacy of the test medium preparation method;
- the reporting of the study is not sufficient to conduct an independent assessment of its reliability. More specifically, considering the adsorptive properties of the Substance, in the absence of information on total dissolved organic carbon concentrations in the test solution, it is not possible to verify that the specifications of the OECD TG 211 in combination with the OECD GD 23 were met.

82 On this basis, the specifications of OECD TG 211 are not met and the information requirement is not fulfilled.

83 In your comments to the draft decision, you state that you consider the study (i) "*suffices the scientific and guideline requirements*". However, you do not provide specific information addressing the issues identified above. Therefore, the information provided in your comments does not change the assessment outcome.

#### *7.3. Study design*

84 OECD TG 211 specifies that, for difficult to test substances, 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" under request 2.

## 8. Long-term toxicity testing on fish

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

### 8.1. Information provided

86 You have provided:

- (i) a prolonged toxicity test on fish (2013), performed according to OECD TG 204 with the Substance.
- (ii) a statement to justify the omission of the study: *"According to REACH Annex IX Section 9.1 Long-term testing will only be proposed if the CSR indicates the need to investigate further effects on aquatic organisms. The substance is not classified for acute toxicity and is readily biodegradable. It is not classified as PBT or vPvB. Furthermore chronic NOEC values are available for Daphnia and algae which are the more sensitive species in acute studies. The CSR did not trigger any concern for long-term exposure therefore a study is scientifically unjustified"*.

### 8.2. Assessment of the information provided

#### 8.2.1. The OECD TG 204 is not a valid test guideline to meet this information requirement

87 To fulfil the information requirement, a study must be a long-term fish test. Guidance on IRs and CSA, Section R.7.8.4.1. specifies that only studies in which sensitive life-stages (juveniles, eggs and larvae) are exposed can be regarded as long-term fish tests.

88 Your registration dossier provides an OECD TG 204 study (i) in which only adults (based on reported fish size) were exposed to the test material.

89 This study does not provide information on the toxicity of the test material to all relevant sensitive life-stages (i.e. juveniles, eggs and larvae). OECD TG 204 only provides information on prolonged acute toxicity and, based on the above, it does not qualify as a long-term fish test. Therefore, this information is rejected.

90 In your comments to the draft decision, you disagree to perform the requested long-term toxicity test on fish, stating that *"in the prolonged toxicity to fish study (OECD TG204), adult zebra fish exposed to loading rates of 54 and 100 mg/L for 14 days, adverse effects were not observed"*.

91 ECHA reiterates that the submitted OECD TG 204 does not cover all relevant sensitive life stage and hence it does not qualify as a long-term fish study. The information provided in your comments does not change the assessment outcome.

92 Therefore, the information requirement is not fulfilled.

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

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

94 In your comments to the draft decision, you state that *"[t]he acute aquatic toxicity tests have been conducted on all 3 trophic levels (algae, daphnia and fish), the results indicate*

*that daphnia is the most sensitive species. Therefore, OECD TG210 study will not gain new hazard information, thereby avoid unnecessary animal testing”.*

95 ECHA reiterates that as explained in request 1, the Substance is poorly water soluble and hence you cannot rely on the availability of acute aquatic studies, and information on long-term toxicity on fish must be provided. The information provided in your comments does not change the assessment outcome.

96 Your adaptation is therefore rejected.

97 Therefore, the information requirement is not fulfilled.

### *8.3. Study design*

98 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.).

99 OECD TG 210 specifies that, for difficult to test substances, 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" under request 2.

## **9. Long-term toxicity on terrestrial invertebrates**

100 Short-term toxicity to invertebrates is an information requirement under Annex IX to REACH (Section 9.4.1). Long-term toxicity testing must be considered (Annex IX, Section 9.4., column 2) if the substance has a high potential to adsorb to soil or is very persistent.

### *9.1. Triggering of the information requirement*

101 Under Annex IX, Section 9.4., Column 2, for substances that have a high potential to adsorb to soil or that are very persistent, long-term toxicity testing must be considered instead of short-term. Guidance on IRs and CSA, Section R.7.11.5.3. clarifies that a substance is considered to be very persistent in soil if it has a half-life >180 days. In the absence of specific soil data, high persistence is assumed unless the substance is readily biodegradable. A substance is considered to be highly adsorptive if the log  $K_{ow}$  > 5 or it is ionisable.

102 As explained under request 3, you have not demonstrated that the Substance is readily biodegradable and therefore in the absence of data, high persistence is assumed.

103 Moreover, the Substance is considered highly adsorptive based on its log  $K_{ow}$  >6 and a log  $K_{oc}$  of >5 and it is ionisable.

104 Therefore, the Substance and its constituents have a high potential to adsorb to soil and the Substance is potentially very persistent and information on long-term toxicity on terrestrial invertebrates must be provided.

### *9.2. Information provided*

105 You have provided a short-term toxicity study to terrestrial invertebrates (2013, OECD TG 207) but no information on long-term toxicity to invertebrates for the Substance. Therefore, the information requirement is not fulfilled.

106 In addition, you have adapted this information requirement by using Column 2 of Annex IX, Section 9.4. To support the adaptation, you have provided following statement: *“The test substance is a material of limited and restricted use [...]. There will be no direct*

*release to the soil compartment from formulation or use. Furthermore, the substance is readily biodegradable and will not be released indirectly to soil via waste water. Therefore, no terrestrial studies will be performed as the criteria for adaptation of this endpoint have been fulfilled."*

### 9.3. Assessment of the information provided

#### 9.3.1. The provided adaptation does not meet the criteria of Annex IX, Section 9.4., Column 2

107 Under Annex IX, Section 9.4., Column 2, the study does not need to be conducted if direct and indirect exposure of the soil compartment is unlikely.

108 Guidance on IR and CSA, Section R.7.11.2.1., specifies that it is assumed that soil exposure will occur unless it can be shown that there is no sludge application to land from exposed STPs and that aerial deposition are negligible and the relevance of other exposure pathways such as irrigation and/or contact with contaminated waste is unlikely.

109 Under Section 3.5. of your technical dossier and/in the CSR, you report:

- widespread uses by professional workers and consumers of lubricants and greases in open system and you assigned ERC 8D for outdoor uses;
- widespread uses by professional workers and consumers of lubricants and greases in vehicles and machinery and you assigned ERC 9B for outdoor uses.

110 Based on the uses reported for the Substance, exposure of the soil compartment cannot be excluded. In particular, Table R.16-7 of ECHA Guidance R.16. specifies that the default worst-case release factors resulting from the conditions of use of ERC 8D and 9B is 20% and 5% respectively.

111 Therefore, your adaptation is rejected.

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

### 9.4. Study design and test specifications

113 To fulfil the information requirement, the test method(s) according to OECD TG 222, OECD TG 220, and OECD TG 232 are appropriate to cover the information requirement for long-term toxicity on terrestrial invertebrates (Guidance on IRs and CSA, Section R.7.11.3.1). You can choose any of these methods, but you must ensure that the Substance is within the applicability domain of the chosen test method.

## 10. Effects on soil micro-organisms

114 Effects on soil microorganisms is an information requirement under Annex IX, Section 9.4.2.

### 10.1. Information provided

115 You have adapted this information requirement by using Column 2 of Annex IX, Section 9.4. To support the adaptation, you have provided:

- (i) the same justification described in Section 9.2.
- (ii) the following statement: "*The LC50 (14-day) in Eisenia foetida (earthworm) is > 1000 mg/kg dry weight soil. In the absence of toxicity in the earthworm study [...], no additional terrestrial studies will be performed*".

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

#### *10.2.1. The provided adaptation does not meet the criteria of Annex IX, Section 9.4., Column 2*

116 Your adaptation is rejected based on the same reasons explained under Section 9.3.1.

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

117 A registrant may only adapt this information requirement based on the specific rules of Annex IX, Section 9.4., Column 2 or the general rules set out in Annex XI. It is noted that Column 2 of Annex IX, Section 9.4. does not allow omitting the need to submit information on effects on soil microorganism based on the lack of effects seen in a short-term toxicity study on terrestrial invertebrates.

118 Your justification to omit this information does not refer to any legal ground for adaptation under Annex XI to REACH.

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

120 Therefore, the information requirement is not fulfilled.

### *10.3. Study design and test specifications*

121 To fulfil the information requirement for the Substance the Soil Microorganisms: Nitrogen Transformation Test (EU C.21/OECD TG 216) is most appropriate for assessing effects on soil microorganisms for most non-agrochemicals (Guidance on IRs and CSA, Section R.7.11.3.1.).

## **11. Long-term toxicity on terrestrial plants**

122 Short-term toxicity to terrestrial plants is an information requirement under Annex IX to REACH (Section 9.4.3). Long-term toxicity testing must be considered (Annex IX, Section 9.4., column 2) if the substance has a high potential to adsorb to soil or is very persistent.

### *11.1. Triggering of the information requirement*

123 As explained in the request 9., the Substance and its constituents have a high potential to adsorb to soil and the Substance is potentially very persistent and information on long-term toxicity on plants must be provided.

### *11.2. Information provided*

124 You have adapted this information requirement by using Column 2 of Annex IX, Section 9.4. To support the adaptation, you have provided the same justification described in Section 10.1.

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

#### *11.3.1. The provided adaptation does not meet the criteria of Annex IX, Section 9.4., Column 2*

125 Your adaptation is rejected based on the same reasons as explained under Section 10.2. above.

126 Therefore, the information requirement is not fulfilled.

*11.4. Study design and test specifications*

- 127 The Terrestrial Plant Test (test method: OECD TG 208, with at least six species)/ ISO 22030 is appropriate to cover the information requirement for long-term toxicity on terrestrial plants. The OECD TG 208 considers the need to select the number of test species according to relevant regulatory requirements, and the need for a reasonably broad selection of species to account for interspecies sensitivity distribution. For long-term toxicity testing, ECHA considers six species as the minimum to achieve a reasonably broad selection. Testing must be conducted with species from different families, as a minimum with two monocotyledonous species and four dicotyledonous species, selected according to the criteria indicated in the OECD TG 208.



## 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 (2023).

**Guidance on intermediates**; ECHA (2010).

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 Bioaccumulation in aquatic species, preferably fish (Annex IX, Section 9.3.2.) and simulation testing (Annex IX, Section 9.2) are not addressed in this decision. This is because the result from the ready biodegradability study is needed to conclude whether the Substance or relevant constituent(s)/fraction(s) of the Substance is (are) P/vP and to decide whether a bioaccumulation study and simulation testing(s) are needed to conclude on the PBT/vPvB properties of the Substance. In such case, the results of the requested ready biodegradability study will also inform on the most relevant test material to conduct the bioaccumulation and simulation studies. These information requirement(s) may be addressed in a separate decision at a later stage.

This decision does not prevent ECHA from initiating further compliance checks at a later stage on the registrations present.

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

The compliance check was initiated on 22 February 2023.

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

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

ECHA took into account your comments and did not amend the request(s).

In your comments on the draft decision, you requested an extension of the deadline to provide information from 36 to 48 months from the date of adoption of the decision. You base your argument for the extension as 1) prenatal development test to be conducted in phase wise manner after 90-day repeated dose toxicity study and 2) lag time and delays in the laboratories. However, you did not provide any documentary evidence from a test laboratory. The given deadline allows sequential testing for PNDD and sub-chronic toxicity (90-days).

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

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;

| <b>Registrant Name</b> | <b>Registration number</b> | <b>Highest REACH Annex applicable to you</b> |
|------------------------|----------------------------|--|
| [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 (<https://echa.europa.eu/practical-guides>).

(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/group of constituents on the test results for the endpoint to be assessed. For example, if a constituent/group of constituents of the Substance is known to have an impact on (eco)toxicity, the selected Test Material must contain that constituent/group of constituents.

##### **(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 the careful identification and description of the characteristics of the Tests Materials in accordance with OECD GLP (ENV/MC/CHEM(98)16) and EU Test Methods Regulation (EU) 440/2008 (Note, Annex), namely all the constituents must be identified as far as possible as well as their concentration. Also any constituents that have harmonised classification and labelling according to the CLP Regulation must be identified and quantified using the appropriate analytical methods.

- The reported composition must also include other parameters relevant for the property to be tested, in this case, purity, composition (including carbon chain length distribution, degree of unsaturation, and information on branching of the constituents' structure).

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>).

## **2. General recommendations for conducting and reporting new tests**

### **2.1 Environmental testing for substances containing multiple constituents**

Your Substance contains multiple constituents and, as indicated in Guidance on IRs & CSA, Section R.11.4.2.2, you are advised to consider the following approaches for persistency, bioaccumulation and aquatic toxicity testing:

- the "known constituents approach" (by assessing specific constituents), or
- the "fraction/block approach", (performed on the basis of fractions/blocks of constituents), or
- the "whole substance approach", or
- various combinations of the approaches described above

Selection of the appropriate approach must take into account the possibility to characterise the Substance (i.e. knowledge of its constituents and/or fractions and any differences in their properties) and the possibility to isolate or synthesize its relevant constituents and/or fractions.

References to Guidance on REACH and other supporting documents can be found under Appendix 1.